MASARYK UNIVERSITY

Faculty of Medicine

PRACTICALS IN PHARMACOLOGY

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PREFACE

The textbook,"Practicals on Pharmacology", is a practical tool for pharmacology teaching at the Faculty of Medicine of Masaryk University in Brno. It is designed as a basis for individual study before practicals and for working with the text in practicals themselves. It includes chapters dedicated to general and specialized drug prescriptions, introduction to experimental pharmacology, and basic information for the practical use of computer software for the modelling of pharmacodynamical relations and pharmacokinetic analysis. The textbook is being published as the 2nd revised and completed edition (1st edition 2001) with modifications made in the section of prescriptions according to the terminology of the Czech Pharmacopoeia 2002 and valid legal rules. New chapters have been added (e.g. Introduction to phytopharmacology, and evaluation of pharmacokinetic data by the PK Solutions programme).

Apart from practical exercises, pharmacology teaching obviously consitss of lectures and seminars on general and specialized pharmacology, and the student is supposed to gather the knowledge for these from pharmacology textbooks, internet and other recommended sources; therefore, materials for more theoretically oriented seminars are not included in the contents of this textbook.

Naturally, the largest part of the textbook is dedicated to the introduction to general and special prescriptions. That is to say, on the contrary to other pharmacological fields, that the student does not have the opportunity to find this information in any such an integrated form as in this textbook. As the practical orientation and restricted contents of this textbook, more detailed information about modern ready-made pharmaceutical dosage forms manufactured by using special technologies could not be included; they represent the contents of lectures and seminars dedicated to innovative trends and new pharmaceutical technologies.

The part dedicated to general prescriptions includes overview of Latin terminology, overview of approved legal measures for drug handling, and reference to current Czech Pharmacopoeia and general rules for drug prescriptions. An important section is dedicated to the description and the characteristics of each of the pharmaceutical dosage forms of both ready-made preparations (RMP) and individually prepared preparations (IPP). This general section offers detailed instructions for RMP prescription and also an overview of the basic source materials, where one can find information about the actually registered medicines. However, the textbook does not´ contain any basic special prescription of a RMP, taking into account today's enormous expansion of drugs produced by different pharmaceutical companies on the market, and the extensive possibility to obtain the necessary information on RMP from an almost inexhaustible number of compendia and other materials, including the electronic database of AISLP (Automated information system of human, homeopathic and veterinary registered drugs for Czech and Slovak Republics), etc. It is neither possible nor necessary to deal with these in any more details in our preclinical field of studies.

In the chapters containing concrete cases of specialized prescriptions of individually prepared preparations (IPP in Czech, the collective of authors utilized the data obtained from the Brno region, especially from the hospital pharmacies with an extensive ambulant component, where the majority of individual prescriptions from diverse branches of medicine concentrate. It was a sort of surprise, even for us, to see how many classical and practically tested individually prepared prescriptions can still be found in these pharmacies nowadays, and how many of them are prepared daily. That is why we decided to include as many of these traditional prescriptions as possible, naturally after having modified them by strictly following the actual Czech Pharmacopoeia terminology for the denomination of active drugs, adjuvant substances and dosage forms of drugs. In this sense, this textbook could be an asset for the doctors willing to change their prescriptive habits, and, at the time of prescribing IPP, make use of the actual proper pharmacopoeic terminology.

The extensive text of the section dedicated to special prescriptions should not be understood as designated to be literally "memorized" in its full extent by the students for the exam. The text represents a broader selection of prescriptions in each chapter for the prescription practices, while while, at the same time, it offers examples of the application of the principles of effective pharmacotherapy with the prescription of IPP in those branches of medicine where individual drugs are still being used nowadays.

In the section dedicated to experimental pharmacology, the importance of a pharmacological experiment is explained in the context of modern trends and the level of evolution of pharmacology as a science field. It deals with laboratory animals and ethic principles of laboratory practice with live subjects and with the preparation of an experiment and elaboration of the experiment protocol. The students can use all this knowledge in their work with experimental animals in pharmacological practicals and in their own student research activities. In the last years, the experiments with animals in practicals underwent a radical restriction for time, ethic and economical reasons. Despite of the quickly growing number of videos, computer simulations of pharmacological processes and other didactic methods for pharmacology teaching, the authors consider the experiments as an important part of the teaching process.

The textbook also includes basic information and practical instructions for use of computer technology in pharmacological practicals, particularly instructions for the work with programmes for modelling of pharmacological experiments on animals (Microlab software), for solving of pharmacotherapeutical situations (programme "Studie") and for pharmacokinetic analysis using a PC (programmes MW Pharm, PK Solutions).

Chapters on drugs of plant origin, their terminology, their chemical constituents and an overview of basic indications of herbal drugs have been included to make the individual preparation for the practicals dedicated to phytopharmacology easier. The concrete possibilities of medicinal use of herbal drugs and preparations are cited in the chapters on special prescriptions. The nomenclature of pharmacopoeial medicinal drugs, plant preparations and mother plants used in the textbook strictly corresponds to the terminology of the current Czech Pharmacopoeia.

The authors thank to all who collaborated in the preparation of this textbook with their suggestions and comments, namely to RNDr. Jana Střítecká and the collective of the pharmacy of the St. Anne's Faculty Hospital in Brno, prof. MUDr. Alena Pospíšilová, CSc., Head of the Dermatovenerological Clinic of the Faculty Hospital in Brno, PharmDr. Miroslav Dostálek, Ph.D. and other willing collaborators from the Department of Pharmacology of the Faculty of Medicine, Masaryk University in Brno. Without their help, this study material could not fulfill the purpose of being an up-to-date and practical tool for pharmacology studies at the Faculty of Medicine of Masaryk University in Brno. Our special thanks go to prof. MUDr. Hana Kubešová, CSc., for a careful reviewing of the first edition and valuable suggestions that distinctively contributed to the professional and didactical level of this textbook.

1. INTRODUCTION TO GENERAL PRESCRIPTIONS

1.1. OVERVIEW OF LATIN TERMINOLOGY FOR DRUG PRESCRITION

For drug prescription of bulk medicines, so-called ready-made preparations (RMP), or individually prepared medicines (IPP), a special terminology is used. It results from Latin and partially Greek word stems. Therefore it is necessary to use the correct forms of denominiations of prescribed drugs according to the current Pharmacopoeia and the basis of Latin grammar, too.

For prescriptive purposes, the knowledge of selected nouns and adjectives and their nominative, genitive and accusative singular and nominative and accusative plural forms, is especially important. Only in some settled expressions, the singular and plural forms of ablative are used. Furthermore, cardinal numerals and some imperative and subjunctive verbal forms are used in prescriptions. Among the prescriptive formulations, some settled prepositional expressions can be found. Abbreviations are widely used in prescriptions which makes the knowledge of these essential.

SUBSTANTIVES

Ist declension – feminines

Example: gutta = drop

sg.:	**a**	pl.:	**-ae**
1.	gutt**a**	1.	gutt**ae**
2.	gutt**ae**	2.	–
4.	gutt**am**	4.	gutt**as**

ampulla	ampule(ampoule,vial)	lana	wool, cotton
aqua	water	litra	litre
capsula	capsule	massa	mass
cera	wax	mixtura	mixture
formula	prescription, formula	olla	jar
gelatina	gelatine	resina	resin
gutta	drop	scatula	box
herba	herb	tabuletta	tablet
lagena, lagoena	bottle	tinctura	tincture
pasta	paste	tuba	tube
planta	plant		

IInd declension – masculines

Example: sirupus = syrup

sg.:	**-us**	pl.:	**-i**
1.	sirup**us**	1.	sirup**i**
2.	sirup**i**	2.	–
4.	sirup**um**	4.	sirup**os**

bacillus (stillus)	stick	globu(lu)s	globe, ball
bolus	bolus	numerus	number
comp. bolus (f)	clay	succus	juice
bulbus	bulb	sirupus	syrup

II[nd] declension – neutres

Example: vitrum = vial (up to 100 ml)

sg.	-um	pl.:	-**a**
1.	vitr**um**	1.	vitr**a**
2.	vitr**i**	2.	–
4.	vitr**um**	4.	vitr**a**

Remember: All neutres have the same form in nominative and accusative both singular and plural!

acidum	acid	infusum	infusion
balneum	bath	linimentum	liniment
collyrium	eye lotion	liquidum	liquid
decoctum	decoction	oculentum	eye ointment
dotum	poison	oleum	oil
(comp. antidotum	antidote)	pericarpium	skin, pericarp
emplastrum	plaster	praeparatum	preparation
extractum	extract	remedium	drug, curative substance
folium	leaf	suppositorium	suppository
gossypium	cotton-wool	unguentum	ointment
granu(lu)m	grain, granule	vaselinum	jelly
guttatorium	dropper applicator	venenum	poison
		vitrum	vial

III[rd] declension – masculines, feminines, neutres

III[rd] declension – masculines

Example: pulvis = powder

sg.:	-**is**	pl.:	-**(er)es**
1.	pulv**is**	1.	pulver**es**
2.	pulver**is**	2.	–
4.	pulver**em**	4.	pulver**es**

adeps, -ipis	grease, lard	infans, -tis	child
cortex, -icis	cortex	liquor, -oris	liquid
cremor, -oris	cream	pulvis, -eris	powder
flos, -ris	flower	sal, salis	salt

III[rd] declension – feminina

Example: expeditio = treatment pack

sg.:	-**io** (-as, -ix)	pl.:	-**iones** (-es)
1.	expedit**io**	1.	expedit**iones**
2.	expedit**ionis**	2.	–
4.	expedit**ionem**	4.	expedit**iones**

compositio	composition	mucilago, -inis	mucus
diagnosis, -is	diagnosis	pars, -tis	part
dosis, -is	dose	pix, -cis	tar
emulsio	emulsion	radix, -icis	root
expeditio	drug package	solutio, -onis	solution
infusio	infusion (i.v.)	substitutio	substitution
inhalatio	inhalation	suspensio	suspension
iniectio	injection	unitas, -atis	unit

III[rd] declension – neutres
Example: gramma = gram

sg.:	-**a**	pl.	-**ata**
1.	gramm**a**	1.	gramm**ata**
2.	gramm**atis**	2.	–
4.	gramm**a**	4.	gramm**ata**

clysma, -tis	infusion (rect.)	miligramma	miligram
gargarisma	gargle	lac, lactis	milk
gramma	gram	semen, -inis	seed

Remember: Nouns of the III[rd] declension have the same form in nominative and accusative.

IV[th] declension – masculines, feminines
Example: spiritus – spirit (m)

sg.:	-**us**	pl.:	-**us**
1.	spirit**us**	1.	spirit**us**
2.	spirit**us**	2.	–
4.	spirit**um**	4.	spirit**us**

fructus (m)	fruit	spiritus (m) (also ethanolum, -i)	spirit
manus (f)	hand	usus (m)	need

V[th] declension – masculines, feminines
Example: dies (m) = day

sg.:	-**es**	pl.:	-**es**
1.	di**es**	1.	di**es**
2.	di**ei**	2.	–
4.	di**em**	4.	di**es**

dies, -ei (m)	day
species, -ei (f)	species
species, -erum (f plurale tantum)	tea mixture, species

ADJECTIVES

Adjectives of different nominative forms for every gender I[st] and II[nd] declension

(masculines, feminines, neutres)

sg.: -**us**, (-**er**), -**a**, -**um** pl. -**i**, -**ae**, -**a**

aegrotus	ill	maximus	maximal
alius	another, other	minimus	minimal
adspersorius	dusting	obductus	covered, coated
adultus	adult	ophthalmicus	ophthalmological
amplus	wide	proprius	proper
amylaceus	amylaceous	pulveratus	pulverized
compositus	composed	purificatus	purified
concentratus	concentrated	purus	pure
depuratus	purified	ruber	red
dilutus	diluted	siccus	dry
divisus	divided	singulus	simple
fluidus	liquid	spissus	dense, thick
fuscus	dark	subcutaneus	subcutaneous
gelatinosus	gelatinous	suillus	pork (suis = pig)
guttatus	dropping	varius	various
intravenosus	intravenous	vitreus	vitreous, glass

Adjectives of one form for masculine and feminine and another for neuter III[rd] declension

(masculines + feminines, neutres)

m. f. n.
sg.: -**is**, -**is**, -**e**

m. f. n.
pl.: -**es**, -**es**, -**ia**

aequalis	equal	officinalis	officinalis (included in Pharmacopoeia)
enteralis	intestinal	oralis	oral
fortis	strong	originalis	original
intradermalis	intradermal	parenteralis	parenteral
intramuscularis	intramuscular	rectalis	rectal
nasalis	nasal	tenuis	thin, tenuous
mollis	soft	vaginalis	vaginal

Adjectives of one form for all genders III[rd] declension

(masculines + feminines + neutres)

t m., f., n.
sg.: -**x**, -**ns**

m. f. n.
pl.: -**es**, -**es**, -**ia**

adiuvans	additional, complementary	enterosolvens	enterosolvent
corrigens	corrective	infans	infantine, child
constituens	constituting, generating	laxans	laxative
duplex	double	simplex	simple
emoliens, leniens	emollient	solvens	soluble

NUMERALS

The cardinal numerals are used in prescriptions to express the **doses** of curative and auxiliar substances. The doses are cited in Arabic numerals and in some cases they must be written in words in parentheses, e.g. drugs of abuse and psychotropic substances "...0.02 (miligrammata viginti)". The cardinal numerals are also used to express the **number** of units, drug packages, drops, etc. The quantity is expressed in Roman numerals and written in words and in parentheses - „Exp. orig. No. II (duas)". Cardinal numbers 1,2,3 and hundreds from 200 to 900 are declinable and it is necesarry to know the endings of their Latin forms of nominative and accusative for all genders.

			m.	*f.*	*n.*		
1	I	1. p.	unus	una	unum	(only sg.!)
		4. p.	unum	unam	unum	
2	II	1. p.	duo	duae	duo	(only pl.!)
		4. p.	duos	duas	duo	
3	III	1. p.	tres	tres	tria	(only pl.!)
		4. p.	tres	tres	tria	

4	IV	quattuor
5	V	quinque
6	VI	sex
7	VII	septem
8	VIII	octo
9	IX	novem
10	X	decem
11	XI	undecim
12	XII	duodecim
15	XV	quindecim
19	XIX	undeviginti
20	XX	viginti
25	XXV	viginti quinque (quinque et viginti)
28	XXVIII	duodetriginta (viginti octo)
30	XXX	triginta
40	XL	quadraginta
50	L	quinquaginta
60	LX	sexaginta
70	LXX	septuaginta
80	LXXX	octoginta
90	XC	nonaginta
99	XCIX, IC	nonaginta novem
100	C	centum
102	CII	centum duo
200	CC	ducenti, ducentae, ducenta
300	CCC	trecenti, -ae, -a
400	CD	quadringenti, -ae, -a
500	D	quingenti, -ae, -a
600	DC	sescenti, -ae, -a
700	DCC	septingenti, -ae, -a
800	DCCC	octingenti, -ae, -a
900	CM	nongenti, -ae, -a
1000	M	mille
1550	MDL	mille quingenti quinquaginta
2000	MM	duo milia
3000	MMM	tria milia

1 %	una pars centesima	1/2	pars dimidia
50 %	quinquaginta centesimae	1/3	pars tertia
0	nullum, zero	1/4	pars quarta

bis	twice
ter	three times
quater	four times

VERBS

The prescriptive language includes only a few imperatives and present passive subjunctives that are used in settled expressions indicating instructions for preparation or marking of the medicine before it is given to the patient. Normally, they are expressed by a settled abbreviation (e.g. „M. f. …, D. S.“).

Imperative

sg. 2. pers.	Recipe!	take!	Expedi!	deliver!
	Da!	give!	Misce!	mix!
	Adde!	add!	Signa!	mark!
	Cave!	beware, avoid!	Solve!	solve!
	Divide!	divide!	Sterilisa!	sterilize!

Present active subjunctive

sg. 3. pers.	Fiat	It is being done
pl. 3. pers.	Fiant	They are being done

Present passive subjunctive

sg. 3. pers.	Detur	It is being given
	Signetur	It is being marked
	Sterilisetur	It is being sterilized
	Repetatur	It is being repeated
pl. 3. pers.	Dentur	They are being given
	Signentur	They are being marked

ADVERBS

statim	immediately
guttatim	by drops
cito	quickly

PREPOSITIONS

With accusative:

ad	to, into	per	through, during, by
ante	before	secundum	according to, after
intra	inside, in		

With ablative:

cum	with	sine	without
e, ex	from, out of	sub	under
pro	for		

With accusative and ablative:

in	in, on (what), inside of, for (what)
sub	under

PRESRIPTIVE EXPRESSIONS AND ABBREVIATIONS

Ad usum medici	Ad us. med.	For doctor's use
Ad usum meum	Ad us. meum	For my use
Ad usum proprium	Ad us. propr.	For one's own use
Ad usum internum	Ad us. int.	For internal use
Ad usum externum	Ad us. ext.	For external use
Ad usum alium	Ad us. al.	For other use
Ad manus medici	Ad manus med.	To doctor's hands
Pro medico (Medico)	Pro med.	For a doctor
Pro ordinatione	Pro ord.	For use at the doctor's
Pro adulto		For an adult
Pro adultis	Pro adult.	For adults
Pro infante		For a child
Pro infantibus	Pro infant.	For children
Ad capsulas gelatinosas	Ad caps. gelat.	Into gelatine capsules
Ad vitrum guttatum	Ad vitr. gutt.	Into a dropper container
Ad lag(o)enam (amplam, – fuscam, pro infusione)	Ad lag. (ampl., – fusc., pro infus.)	Into a bottle (wide-mouthed, – dark, for infusion)
Sub signo veneni	Sub sign. ven. (S.s.ven.)	Marked as poison
Sine conservante	Sine conserv.	Without conservation additive
Sine antimicrobico	Sine antimicr.	Without antimicrobial additive
Suo nomine	Suo nom.	With its name (i.e.of the drug)
Cum formula (the whole formula)	C. form.	With a copy of the prescripiton
Ana (partes aequales)	aa	In equal portions
Quantum satis	q.s.	As many as necessary
Unitas internationalis	u.i., U.I.	International unit
Expeditio originalis	Exp. orig.	Original package
Tabuletta obducta	Tabul. (tabl.) obduct.	Coated tablet
Massa tabulettarum	Mass. tabul.	Tablet mass
Massa pro suppositoriis	Mass. pro supp.	Supossitory base, supp. mass
Dentur tales doses	D. t. d. (D. tal. dos.)	Give such doses
Divide in doses (aequales)	Div. in dos.	Divide into (equal) doses

Periculum in mora	–	Danger in delay
Bis in die	b.i.d.	Twice daily
Ter in die	t.i.d.	Three times a day
Omni die	o.d.	Once a day, every day
Numerus (numero, -are)	No.	Quantity, number

1.2. GENERAL RULES FOR DRUG PRESCRIPTION

1.2.1. Basic legislation standards

Legislation measures related to research, processing, preparation and production, distribution, expedition or sale and use of pharmaceuticals and medical preparations, i.e. medicament manipulation, refers to the valid Pharmaceuticals Act and from the related acts and regulations.

According to the current legislation, the terms of pharmaceuticals, medical preparation, substance defined as follows:

Pharmaceuticals are medical substances or their compounds or medical preparations that are determined for being administered to people or animals.

Medical preparation is any substance or a combination of substances determined for therapy or prevention of diseases in people or animals. Furthermore, a medical preparation is considered to be any substance or combination of substances that can be administered to people or animals with the purpose of determination of medical diagnosis or renewal, adjustment or influencing of their physiological functions.

Medical preparations are adjusted into a certain pharmaceutical form, packaged in convenient packages and duly marked (for administration to humans – "humane medical preparations" or for administration to animals – "veterinary medical preparations").

Medical preparations are, according to the law, also the disinfection and disinfestation preparations determined for a direct contact with the organism of a human being or animal, immunobiological preparations, transfusion preparations and blood derivatives, radiopharmaceuticals, homeopathic preparations, medicinal teas and herbal mixtures and therapeutic dietetics.

Ready-made preparation (RMP), i.e. bulk medicine, is any medical preparation introduced to the market in a final form under a special name and in a special package.

The term **Individually prepared preparation (IPP)** is not directly defined as a medical preparation made mostly at a pharmacy, or also at the transfusion service facility or at nuclear medicine station, according to the medical prescription for an individual patient.

Medical substance is any substance, regardless of its origin which can be

a) human – e.g. human blood, its components and preparations made from human blood,
b) animal, e.g. microorganisms, complete animals, parts of their organs, animal secreta, toxins, extracts or preparations made from blood,
c) herbal or chemical

These are substances that show pharmacological or immunological effects or have effect on metabolism; these can also be substances serving for prevention, therapy of diseases, diagnosing and influencing on physiological functions.

Over-The-Counter-Drugs (OTC) are humane pharmaceuticals, which according to the registration resolution can be sold without medical prescriptions.

Adjuvant substances are the substances, which are used in the dose without their own therapeutic effect. These substances

a) allow or facilitate the manufacture, preparation and storage of pharmaceutical preparations or their application,
b) influence positively the pharmacokinetic properties of the medical substances contained in pharmaceutical preparations.

Generally, term **drug** is understood to be the medical substance or preparation in a specific pharmaceutical dosage form ready for use, and administration to the patient.

Food supplements, foodstuff and fodders, cosmetic preparations, products for plant protection, laboratory diagnostics and disinfection and disinfectation preparations, which are not designed for a direct contact with the human or animal organism, are not considered as pharmaceuticals. The products mentioned must not be marked by a pharmaceutical indication.

1.2.2. Pharmacopoeia

Publications containing aggregated data about medicinal substances, healing preparations and helping compounds as well as information about their processing, preparation, control, storage, prescription and distribution are issued in the majority of world countries; these printed materials are published as documents of normative character and are usually called **Pharmacopoeia** (from Greek *pharmacon* = drug and *poieo* = prepare). Substances presented in pharmacopoeia were traditionally called **officinal** drugs and today they are **pharmacopoeial** substances. Other medicines, which are not mentioned in the Pharmacopoeia because they are less common or not involved into the list of medicines, are called **non-officinal** drugs. Obsolete medicinal preparations, i.e. those which were already deleted from the current Pharmacopoeia, are called **obsolete** drugs. However, even the obsolete drugs may be prescribed in justified cases; if they were earlier classified as pharmacopoeial preparations, they should be prepared in accordance with technological procedures given by earlier pharmacopoeias.

For the sake of unification of pharmacopoeial rules and standards existing in different countries, the World Health Organisation elaborated and international document Pharmacopoeia Internationalis. In Europe, the difficult task to publish a unified pharmacopoeia called **European Pharmacopoeia** (with an official abbreviation **Ph. Eur.**) was assumed by the European Council. The issuing of European Pharmacopoeias has started in **1964** when the European Council decided on the base of the Treaty No. 50 to elaborate a unified European Pharmacopoeia and publishing it in the English and French languages. The frst edition of European Pharmacopoeia was published in a series of volumes and supplements within the period of 1964–1977. A rapid development in the fields of development of medicinal preparations and of requirements of regulatory authorities of European countries as well as the

associated needs to revise the current regulations forced the corresponding bodies to prepare further reeditions and to publish further supplements.

The support of public health was declared to be a general objective of the European Pharmacopoeia; its main task is to provide common standards for health experts and other people dealing with the quality aspects of drugs as a base for their safe use, to facilitate a free movement and distribution of medicinal preparations within the EU countries and to assure the quality of medical preparations exported from EU into third countries.

1.2.3. Drugs of abuse and psychotropic substances

Rules and regulations for handling with drugs of abuse and psychotropic substances and with preparations containing compounds with dependence potential, and their precursors result from the valid legislation.

Prescription of narcotics and psychotropic substances. In wording of current Czech legislation, pharmaceuticals containing drugs of abuse and psychotropic substances should be prescribed on prescriptions and/or order forms with an oblique blue strip.

1.2.4. Rules for the prescription of medical preparations

The medical prescription is an official document compiled in accordance with certain fixed rules. By means of this medical prescription the physicians asks the pharmacists either to issue or to prepare a medical preparation in a certain pharmaceutical dosage form and in a given amount. Every issued preparation must have a legible instruction for use.

The pharmaceuticals may be prescribed only by the physicians providing either medical or veterinary care in the extent of their capabilities and also all physicians providing first aid within the scope of their first-aid activities.

In the Czech Republic, the medical prescription is written (in accordance with traditional principles) in Latin and only the part designated for the patient (i.e. *Signatura*) is written in Czech (or in other language understandable for the patient). The prescription must have all parts filled up/ and must be legible. No strikes through should be made in this document. If a correction is made, it should be signed by the physician following the abbreviation „corr.“ (*correxit* – corrected). The prescription should be written in a non-erasible manner (ballpoint pen, stamp, typewriter, PC etc.).

Ready-made preparations (RMP) (earlier *specialities*) are distributed into pharmacies by manufacturers (pharmaceutical companies) as final preparations ready to be issued by the pharmacy to patients without any further modifications. Nowadays, bulk medicines completely predominate in the total number of prescribed pharmaceuticals and there is a general increasing trend in their use. Mass production performed in accordance with principles of Good Manufacturing Practice (GMP) and on the base of obligatory methods assures a high quality and standard of these preparations on one hand and supplies with modern forms of medicines on the other hand because these are manufactured by means of advanced technologies that could not be used in pharmacies for individual production of drugs.

Individually prepared preparations (IPP) (earlier *magistraliter*) are prepared in the pharmacies on the base of individual medical prescriptions. The extent of preparations prescribed and prepared as IPP differs in dependence on individual subject areas; more frequently these prescriptions occur in branches using drugs for local application (e.g. ophthalmology, dermatology, ORL, dentistry). Individual preparation of these medicines at the moment of their actual need enables to avoid the application of stabilizers and antimicrobial additives/admixtures, which can cause sensitization and allergic reactions which are indispensable and non-avoidable in case of RMP with a longer period of expiration. The IPP form of drugs enables individualization of prescriptions as far as composition and pharmaceutical dosage form are concerned. Sometimes it can also show a positive psychological effect in a patient. However, there is also a certain risk resulting from the possibility of mistakes made when preparing medicines and/or from the occurrence of drug-drug incompatibilities of physical (e.g. non-miscibility of individual components) or chemical (e.g. chemical reactions between individual components) nature.

RECEIPT COMPOSITION

Inscriptio – the heading of the prescription, which contains columns for the code of health insurance company, registration number and series.

Personalia aegroti – patient's personal data (name, surname, birth number and domicile).

Invocatio – address, induced by the abbreviation *Rp.* (*recipe* – take). The abbreviation is preprinted in the left upper corner of the prescription part (*Ordinatio*). The physician ticks this abbreviation to verify that he/she checked it up both from the formal and factual points of view.

Ordinatio – the actual prescription of the healing preparation. Under the abbreviation *Rp*. it is at first mentioned of which the preparation is composed – ***Compositio*** (in a narrower sense of word also prescription - ***Praescriptio***,). In the case of RMP, this part involves the trade name of the preparation in the nominative with specification of the required pharmaceutical dosage form, dose and package of the prescribed medicine. In the case o IPP they involve a list of pharmacopoeial (officinal) names of prescribed substances in the genitive of singular and their dosages.

The following part of the prescription is called ***Subscriptio*** – instructions for the pharmacy indicating how many packages should be issued (in the case of RMP) or how the preparation should be made of the prescribed components (in the case of IPP).

The part ***Signatura*** contains instructions how the preparation should be used/taken by the patients.

Parts *Subscriptio* and *Signatura* will be described in detail in Chapter 1.2.5.

Date

Date of issue is an indispensable part of the prescription, because it determines the length of validity of the prescription.

Last but not least, the stamp of the health facility, the identification of the physician (usually contained in the stamp) **and the physician's personal signature** are the essentials of the prescription; as the prescription is not valid without them.

1.2.5. General principles of the prescription of ready-made preparations (bulk medicines)

Ready-made preparations (RMP) (earlier also called „specialities“) are medical preparations manufactured by the pharmaceutical companies to be issued by the pharmacy to patients without any further modifications**.** They are introduced into the marked under their trade names (see below).

Marking of RMP

Requirements concerning data which should be presented on BM/RMP packages (both on their outer and inner parts) and information presented on package leaflets are specified in the registration regulations of the State Institute for Drug Control (in Czech SÚKL).

RMP are manufactured in charges (charge = amount of product manufactured in one production cycle; homogeneity of all preparations manufactured within each cycle is a common feature of all manufactured preparations). The charge number must be given on both the external and the internal package of the preparation.

RMP are usable for a limited time interval after the date of their production and the length of this period is dependent on the stability of the preparation. The manufacturer is obliged to mention the usable life of the preparation on the outer and inner package (Example: “Best before 07/2007“). This usable life must be given above all on preparations, the efficiency of which is extremely time dependent (above all in case of antibiotics); the end of this usable life is usually mentioned on the package as the expiration date (abbreviated as Expir. or Exp.) and after it the preparations cannot be used without a special permission.

The outer package of the preparation must contain the following data: (1) name, i.e. registered trade mark or generic name and the name of manufacturer (if the preparation is made under a non-protected name); (2) composition of the preparation, i.e. Latin pharmacopoeial (officinal) names of effective agents with data about their doses and/or concentrations in each package; (3) names of auxilliary substances used; (4) form of the drug; (5) number of doses in the package and/or the size of the package; (6) fly sheet and or reference to the information presented in package leaflet; (7) date of expiration; (8) special warnings (e.g. „Keep out the reach of children“); (9) special storage conditions (e.g. „Store at temperatures below 25 °C, store in darkness “) and the instruction „Unused drugs should be returned to the pharmacy “; (10) name and address of the registration holder; (11) serial number of registration; (12) batch number.

The inner package (blister pack, vial etc.) must also present the most important data about the content, i.e. at least the name of the preparation, non-protected pharmacopoeial name of the effective agent, dosage and form of the drug, batch number and expiration date.

Rules of RMP prescribing

1. **The full name of the preparation in the first grammatical case** should be written in the first row of the part ***Praescriptio***; this name should be written in the form, which is written in publications about registered healing preparations, i.e. most frequently in the current Pharmindex Vademecum but also in e.g. Automatised Information System of Healing Preparations (in Czech abrr. AISLP, see below). **The abbreviation of the drug form** is an indispensable part of the name (this should be mentioned always); the **strength**, i.e. the

dosage (concentration) should be mentioned in case that the preparation is manufactured in several therapeutic doses and/or concentrations.

If the name of the healing preparation is identical with the non-protected (generic) name, then it is necessary to present also the name of the company, which introduced the preparation into the market; this is due to the fact that that products of several manufacturers with the same generic name and the same therapeutic dose may be available in the market (e.g. METHOTREXAT LACHEMA 10 por. tbl. nob., METHOTREXATE-TEVA 10 MG por. tbl. nob., etc.). Manufacturer's specification is required not only because of very often marked differences in the price of individual preparations but also with regard to possible differences in the method of production, which result from the use of different adjuvant and corrective substances (these may influence above all biological availability and tolerance of the preparation).

2. If the medicine is manufactured in various **therapeutic dosages** and/or **concentrations** and the physician does not specify its dose/concentration in the prescription, the pharmacy must not issue the preparation to the patient without the prior consultation with the physician (usually by phone). However, this dosage/concentration need not be sufficiently effective for the concrete patient under given conditions.

   The dose is mostly given in milligrams (and/or their integral multiples or fractions) and the weight unit is often omitted (e.g. PARALEN 500 sup., DIGOXIN 0.125 LÉČIVA por. tbl. nob.). Concentration is usually in percents (e.g. PROCAIN LÉČIVA 1% inj. sol.) or as the amount of the/a substance in a certain volume (e.g. SANDOSTATIN 0.5 MG/ML inj. sol.). The dose of the pharmaceutical/drug may be also given in international units (e.g. INSULATARD 100 IU/ML inj. sus.).

3. In the following row, it is necessary to specify the **required number of packages of the preparation**, i.e. in case of RMP divided into individual doses it is necessary to mention the number of pieces in the required strength (e.g. tbl 10x 1 mg, inj. 5x 1ml/1mg). In non-divided pharmaceutical dosage forms (ung., gtt., liq. etc.) it is obligatory to mention the specification of the package (e.g. ung. 1x 20 g, gtt. 1x 10 ml 10%, liq. 2x 500 ml).

4. In case of RMP, the ***Subscriptio*** part indicates how many original packages – *Expeditiones originales,* abbreviated as *Exp. orig.* (sometimes it is also possible to find data specifying the form of package: *Tuba originalis – Tub. orig., Lagena originalis – Lag. orig.* etc.) are required by the physician. The number of prescribed packages must correspond with the needs and must be selected in such a way that the patient with a chronic disease should visit the physician at least every three months. In the majority of preparations the size of 1 package corresponds with one curative course. In case of prescribing three or more packages, the exclamation mark (!) should be stated in the *Subscriptio* part following the number of packages.

   The number of prescribed packages is given in the subscription in the form of accusative of singular and/or plural, because the expression is related to the imperative *Recipe* = take (refers to accusative) in the part *Invocatio.*

   Expeditionem originalem numero unam *Exp. orig. No. I. (unam)*

Expeditiones originales numero duas *Exp. orig. No. II. (duas)*

The number of packages should be written in Latin (in words in parentheses).

The part ***Signatura*** of the RMP prescription must contain also all necessary data, which inform patient about the proper use of the preparation respecting the optimum dosage scheme (in the legible form and without any abbreviations). Although the original packages contain always a leaflet, this does not need to correspond with individual requirements of the patient. Information for the patient is written in Czech following the abbreviation of the Latin expression *Detur, signetur (D. S.)* = to be given, to be marked.

If the drug should be delivered into the hands of the physician, it is written in the Signatura in Latin: *„Pro medico“, „Ad usum medici“*. The medicines for the own use of the physician can be labeled as *„Ad usum proprium“, „Ad usum meum“* or *„Pro me“*. Remember: RMP "signatura" should never contain the expression „Suo nomine“ or „Cum formula“ because RMP packages are equipped with all essential data already in the production plant.

5. The prescription of drugs of abuse and psychotropic substances in the RMP form follows the prescription rules presented in Chapter 1.2.3.

Examples of RMP prescriptions:

a) A common medical preparation – ibuprofen in a coated tablet is produced under its generic name, that is why the manufacturer is mentioned:

Rp.
Ibuprofen 400 Léčiva, por. tbl. flm.
por. tbl. flm.100 x 400 mg
Exp. orig. No. II (duas)
D. S. 1 tablet 3 times daily.

b) The drug of abuse – morphine hydrochloride trihydrate in coated sustained release tablets:

Rp.
Vendal retard 30 mg por. tbl. ret. (miligrammata triginta)
tbl. obd. 30 x 30 mg
Exp. orig. No. I (unam)
D. S. Pro medico.

Selected sources, according to which the RMP can be prescribed:

Pharmindex Vademecum – a brief version of Pharmindex Compendium, which contains basic information about RMP registered to the date of its publication. In the introduction, the vademecum contains a list of preparations arranged according to the so-called anatomic-therapeutic-chemical classification (ATC groups, red labelled section), the list of preparations arranged according to the pharmacopoeial (officinal) names of effective substances (blue labelled section) and also more detailed information about newly classified preparations (yellow labelled section). This is followed by the main text part itself, which contains articles arranged in alphabetical order according to trade names of preparations. The last part (in green labelled section) presents a directory of pharmaceutical companies, their representations and addresses of important for physicians and pharmacists.

Pharmindex Compendium – detailed articles (pharmacokinetic and pharmacodynamic properties, indications, contraindications, interactions etc.) about RMP registered to the date of the Compendium issue. The articles are arranged in alphabetical order according to trade names. There is also an electronic form of the Compendium on CD-ROM (Pharmindex CD) available.

Remedia Compendium – detailed articles dealing with pharmaceuticals in a survey way with the classification made according to indications.

Automatised Information System of Medical Preparations (in Czech abrr. AISLP), which is available both on CD-ROM and on the Internet. It provides information about human, veterinary and homeopatic medicines and also about means of health instrumentation and parapharmaceutics (e.g. foodstuff, vitamin and nutritional supplements, cosmetics, teas etc.), which are currently available in the Czech Republic and in Slovakia. This system is updated four times a year and contains data supplied by competent bodies. AISLP enables an interactive search of medical preparations according to a number of criteria (indication group, ATC classification, main active substance, trade name etc.). The database of preparations presents not only the registered name, pharmaceutical form, size of package, content of the main effective substance, manufacturer and country of origin but also current registrations, actual prices and limitations of sale. Further it contains also leaflets for patients, summary data about the preparation (SPC = **S**ummary of **P**roduct **C**haracteristics) and their digital photos.

1.2.6. General principles of the prescription of individually prepared preparations (IPP)

Compositio (Praescriptio)

In IPP prescriptions, the pharmaceuticals are presented according to their importance, i.e. from the therapeutically most important substances to the adjuvant substances. According to the efficiency and importance it is possible to distinguish:

- *remedium cardinale* – component showing the major therapeutic effect,
- *remedium adiuvans* – supplementary substance improving the effect of the major active component or attenuating its adverse effects,
- *remedium corrigens* – component modifying/ unpleasant taste and/or improving undesirable appearance and/or aroma of the preparation,
- *remedium constituens* or *vehiculum** – pharmaceutical excipient, indifferent auxilliary substance, in which the drug is solved and/or dispersed to give the preparation its final form and appearance (* = drug vehicle).

The prescribed medical preparation does not always need to contain all the above-mentioned components. Some drugs fulfil simultaneously the function of major and correcting component; vehicle need not be present for example in solid divided forms with doses higher than 100 mg. A simpler prescription is sometimes more advantageous both from the viewpoint of the therapeutic effect and of a lesser danger of formation of an incompatible mixture.

1. The name of each component (remedium) is written in a separate row starting with a cappital letter, in the Latin language and in the form defined in the valid Pharmacopoeia.

2. Names of drugs are mentioned in the genitive of singular (*Recipe Paracetamoli miligrammata quingenta*). Abbreviations are used in names of remedies only in those cases where they have an explicit meaning. Acceptable abbreviations of pharmaceuticals are presented in the Czech Pharmacopoeia.
3. Doses of individual components (both solid and liquid) are expressed in the prescription by Arab numerals in grams but the abbreviation "g" is not mentioned. Decimal point must not be left out even in the case that the whole number is mentioned (e.g. 2.0; 100.0). The content of drugs in injection and infusion solutions is given in grams but the amount of vehiculum in millilitres. If the drug is dosed in international units, it is necessary to write the abbreviation u.i. or U.I. (*Unitates Internationales*) following the dose written in Roman numerals.
4. If the dose of the liquid remedy is smaller than one gram, it can be expressed by means of drops in the prescription (instead of weight units). The number of drops is given in abbreviations *gtt.* (sg.) or *gtts.* (pl.); in relation to the phrase *„Recipe guttam, guttas"* this is the accusative. To avoid confusion with grams, the number of drops is given in Roman numerals and written in words in parentheses.

   The pharmacist is obliged to observe instructions issued by the physician. He/she must not issue more than the amount mentioned in the prescription; the only exception are indispensable indifferent auxilliary substances and additives. The pharmacist is obliged to check up doses prescribed by the physician. If the physician exceeds the maximum dose in the prescription without marking (see below), the pharmacist must not issue the preparation in such a dose without a previous consultation with the prescribing physician. If this is not possible, the pharmacist should correct the dose written in the prescription to the usual therapeutic dose, issues the preparation in this corrected dose and informs the physician about the performed correction. If the physician exceeds deliberately the maximum dose because of therapeutic reasons, he/she is obliged to write an exclamation mark (!) in the prescription and the dose should be written in Latin in parentheses.

5. The amount of vehiculum is written in the last row in the prescription. Frequently it is not expressed directly but only by means of a preposition *ad* written before the dose expressing the total amount of prescribed medicine. This means that the preposition *ad* can be in the prescription only once (in its last row).

   Example:

   Rp.

Paracetamoli	*0.1*
Lactosi	*0.4*

   or more frequently*:*

   Rp.

Paracetamoli	*0.1*
Lactosi	*ad 0.5*

6. It is also possible that in some prescriptions there are two or more pharmaceuticals in the same doses. In such a case it is not necessary to write the dose of each component but only for the last of these pharmaceuticals and write before it the abbreviation *aa* (*ana partes*

aequales – the same parts). The pharmacist then shall use this dose also for all compounds mentioned above (which are given without the dose).

Example:

Rp.

Natrii sulfatis
Magnesii oxidi *aa 50.0*

The pharmacist weight 50 g of each of these components so that the total amount will be 100 g.

- The expression *aa* can be also combined with the preposition *ad*; however, this is possible only in the last row and most frequently in the case of *vehiculum*:

Rp.

Natrii sulfatis
Magnesii oxidi *aa ad 100.0*

- The abbreviation aa may be used repeatedly in one prescription, e.g. when prescribing herbal tea mixtures:

Rp.

Chamomillae romanae floris
Menthae piperitae herbae *aa 50,0*
Foeniculi dulcis fructus
Anisi fructus *aa 10,0*

Subscriptio

In IPP prescription this part contains detailed instructions for the pharmacy how to prepare the preparation and how to issue it to the patient. Each drug form has a certain expression of subscription. Mostly the fixed Latin abbreviations are being used.

- Instructions for the pharmacist are given in a certain sequence. If the medicine has two or more components, the abbreviation *M. f. ...* is written in the first place; this means *Misce fiat* (sg.) or *Misce fiant* (pl.) – mix to make … The name of the requested drug form is written (again in the abbreviated form) behind this abbreviation.

Example:

Misce fiat pulvis	*M. f. pulv.*
Misce fiat solutio	*M. f. sol.*
Misce fiat unguentum	*M. f. ung.*
Misce fiant oculoguttae	*M. f. oculogutt.*

- If the healing preparation should be given to the patient divided into individual therapeutic doses then it is necessary to write the number of required doses in the following row. The number of doses (pills, suppositories) and/or original packages is expressed by means of the abbreviation *No.* (*numero*) and a Roman numeral, which is written in words in parentheses.

Example: *Dentur tales doses numero decem – D. t. d. No. X (decem)*

- In the following part of the subscription the physician may express in which package (capsule, vial etc.) the prepared drug should be issued (adjusted). The type of adjustation is often let to be decided by the pharmacist.

Examples of adjustation:

D. ad *vitrum guttatum*
D. ad lag(o)enam pro infusione
D. ad capsulam gelatinosam

- The subscription is finalised by other instruction for the pharmacist; these concern either further manipulation (e.g. *Sterilisetur!*) or addition of some applicator devices (e.g. *Adde bacillum!*).

Signatura

This is an important part of the prescription, which is written in Czech (and/or other language legible for the patient). It is marked with the abbreviation *D. S. – Detur (et) Signetur.*

- The Signatura must **exactly instruct** the patient which dose, in which intervals and how the preparation should be used. The pharmacist copies this instruction on the label of the healing preparation. It is not allowed to mention only general expressions (e.g. „Externally " or „According to the advice" on ther label. If the preparation should be used not orally, the physician must write in the *signatura* „Talcum powder ", „Eye drops " etc., to prevent its accidental peroral use. Thereafter the recommended dosage should follow. Labels of IPP preparations determined for internal use are white, for other routes of administration they are red.
- If a drug is **prescribed for the physician´s use**, the *signatura* is written in Latin *Ad usum medici, Pro medico* and/or a similar expression. Preparations determined for the use in the consulting room are labelled *Pro ordinatione.*

If the medical preparation is made in a pharmacy, it is always necessary to ask the pharmacist to state the content. The claimfor this marking is expressed either by words *S. suo nomine* (in case of simple prescriptions, when the composition of the medical preparation may be expressed by its name and dose and/or concentration) or by *S. cum formula* (in case of preparations containing two or more pharmacologically active substances; the pharmacist then writes the list of all components with corresponding doses on the label). This is never used in case of RMP.

- In case of medical preparations belonging into the category *Venena* (e.g. strong alkaloids in eye drops) it is suitable to mention/include the expression *Sub signo veneni!* in the signatura. The pharmacist then affixes the so-called **poison labelling** on the package, i.e. a label with the inscription „POISON ", which warns a patient that the preparation is only for external use and must not be taken orally. This marking is not performed automatically, the pharmacist affixes the poison label on request of the physician.

1.3. PHARMACEUTICAL DOSAGE FORMS

Pharmaceutical dosage form is the final presentation in which the drug is given to a patient. A correctly selected pharmaceutical dosage form predetermines the action of effective compounds in the organism and up to a high extent, the bioavailability of the drug and the velocity of the onset of its effect. The intensity and sometimes even the character of the pharmacological effect of a drug depend from it.

Generally, the pharmaceutical dosage forms are divided according to their consistence as follows

- solid,
- semi-solid (jelly-like or easily melting, soft),
- liquid,
- gaseous.

Determined pharmaceutical dosage forms are destinated **for internal use** (*Ad usum internum*, e.g. *Peroralia, Parenteralia*) or **other use** (*Ad usum alium*, e.g. *Ocularia, Nasalia, Unguenta*). They may contain only one therapeutic substance (e.g. *Pulveres simplices*) or more effective components (e.g. *Pulveres compositi, Species*) in combination with adjuvant agents or without them. The pharmaceutical dosage forms are either **specific in their shape**, usually administrated to the patient divided in separate therapeutic doses, or **non-specific in their shape**, where the patient, during the topical or other application, follows the instructions stated in the prescription part *Signatura*.

Table 3. **Overview and nomenclature of pharmaceutical dosage forms according to the Czech Pharmacopoeia 2005**

Division based on the routes of administration

Peroral preparations	Peroralia
Oromucosal preparations	Oromucosalia
Preparations for dental use	Stomatologica
Cutaneous and transdermal preparations	Dermatologica et transdermalia
Eye preparations	Ocularia
Ear preparations	Auricularia
Nasal preparations	Nasalia
Rectal preparations	Rectalia
Vaginal preparations	Vaginalia
Parenteral preparations	Parenteralia
Preparations for inhalation	Inhalanda
Uretral and intravesical preparations	Urethralia et intravesicalia
Implants	Implantata

Division based on consistence:

SOLID PHARMACEUTICAL DOSAGE FORMS
Praeparata solida

Specific in shape (single-dose)

Tablets	Tabulettae (Compressi)
Uncoated tablets	Tabulettae non obductae
Coated (obducts)	Tabulettae obductae (Obductettae)
Film-coated tablets	Tabulettae filmo obductae
Gastro-resistant tablets	Tabulettae enterosolventes
Sublingual tablets	Tabulettae sublinguales
Buccal tablets	Tabulettae buccales
Muco-adhesive buccal tablets	Tabulettae buccales mucoadhesivae
Effervescent tablets	Tabulettae effervescentes
Tablets disperged in the mouth	Tabulettae pro orodispersione
Chewable tablets	Tabulettae manducabiles
Tablets for preparation of peroral solution	Tabulettae pro solutione perorali

Prolonged-release tablets	Tabulettae cum liberatione prolongata
Modified-release tablets (retarded release)	Tabulettae cum liberatione modificata (Retardettae)
Capsules	Capsulae
Hard capsules	Capsullae durae
Soft capsules	Capsulae molles
Gelatine capsules	Capsulae gelatinosae
Starch capsules/Cachets	Capsulae amylaceae
Gastro-resistant capsules (hard, soft)	Capsulae enterosolventes (durae, molles)
Prolonged-release capsules	Capsulae cum liberatione prolongata
Modified-release capsules	Capsulae cum liberatione modificata

<u>Non-specific in shape</u> (multidose)

Dusting powders (topical powders)	Pulveres adspersorii
Peroral powders	Pulveres perorales
Effervescent powders	Pulveres effervescentes
Grained powders (granules)	Granula (Pulveres granulati)
Coated grained powders	Granula obducta
Gastro-resistant granules	Granula enterosolventia
Grained powders with prolonged release	Granula cum liberatione prolongata
Controlled release grained powders	Granula cum liberatione modificata
Herbal teas (curative teas; tea mixtures)	Species

Other solid forms: Lozenges (pastilles)
Microforms (microcapsules, microspheres, liposomes, pellets), etc.

SEMI-SOLID PHARMACEUTICAL DOSAGE FORMS
Praeparata semisolida

<u>Specific in shape</u> (single-dose)

Suppositories (rectal, vaginal)	Suppositoria (rectalia, vaginalia)
Pessaries (vaginal balls)	Globuli vaginales

<u>Non-specific in shape</u>

Ointments (unguents)	Unguenta
Cutaneous ointments	Unguenta cutanea
Eye ointments	Unguenta ophthalmica (Ocularia semisolida)
Nasal ointments	Unguenta nasalia
Ear ointments	Unguenta auricularia
Creams	Cremores(cutanei,ophthalmici,nasales, auriculares)
Pastes	Pastae
[Liniments	Linimenta – unofficial]
Therapeutic plasters (Patches)	Emplastra medicinalia
Transdermal patches	Emplastra transcutanea

LIQUID PHARMACEUTICAL DOSAGE FORMS
Praeparata liquida

Liquids	Liquida
Peroral liquids	Liquida peroralia

Peroral drops	Guttae perorales
Peroral solutions	Solutiones perorales
[Aromatic waters	Aquae aromaticae – unofficial]
[Infusions, decoctions	Infusa, Decocta – unofficial]
Tinctures	Tincturae
Liquids for other use	Liquida ad usum alium
Eye drops	Oculoguttae
Ocular waters	Aquae ophthalmicae
Ear drops	Otoguttae
Nasal drops	Rhinoguttae
Nebuliser solutions	Solutiones ad nebulisationem
Liquid powders	Pulveres adspersorii liquidi
Parenteral liquids	Liquida parenteralia
Injections	Iniectiones
Injection solutions	Solutiones iniectabiles
Infusions	Infusiones
Infusion solutions	Solutiones pro infusione
Powders for solutions for infusion	Pulveres pro solutione infundibili

GASEOUS PHARMACEUTICAL DOSAGE FORMS
Praeparata gaseosa

Medicinal gases	Gasa medicata
Gases for inhalation	Gasa ad inhalationem
Aerodispersions	Aerodispersiones
Medicinal foams	Spumae medicatae
Preparations for inhalation	Inhalanda

1.3.1. Solid pharmaceutical dosage forms

Pulveres perorales (non divisi)

Peroral powders for internal use (undivided)

These are preparations, non-specific in shape, composed of loose particles with diverse grade of desintegration. They contain one or more effective compounds, mostly without an admixture of indifferent adjuvant compounds. They are administrated either in their loose form with the help of measurers or domestic measuring devices like a teaspoon (3-5 g), spoon (10-15 g), knifetip (0.5 – 1 g) or dissolved in water or other suitable drink.

This form is used only for prescription of very slightly effective drugs, whose dosing can be done by the patient without any considerable danger (salinic laxatives, antacids, activated carbon, etc.).

In the prescription, we state the total ammount of drug for the whole cure (dosis curativa), in the *signatura*, there will be the indication of a single dose and number of daily doses.

An example of a prescription of salinic laxatives in the IPP:

Rp.

Natrii sulfatis
Magnesii sulfatis heptahydrici aa ad 200,0
M. f. pulv.
D. S. One table-spoon into a glass of lukewarm water. Drink on empty stomach.

Pulveres adspersorii

(Pulveres ad usum dermicum)
Dusting powders, topical powders, cutaneous powders)

These are powders milled as fine as possible destinated for local actuation on the skin, not so often on mucosas or injured or surgically uncovered hypodermic tissues. They are mostly prescribed in dermatology for the antiseptic and antiprurigineous effect, for drying, cooling, degreasing. They also offer a mere mechanical protection of the skin against external influences and UV radiation. Powders permeable, they do not obstruct perspiration and normally do not have a negative influence on physiologic functions of the skin. Sometimes, they can substitue for a light bandage or an ointment.

The powders contain one or more effective substances in a suitable concentration: boric acid – **Acidum boricum**, salicylic acid – **Acidum salicylicum**, racemic menthol – **Mentholum racemicum**, bismuth subcarbonate – **Bismuthi subcarbonas**, ichthamole – **Ichthammolum**, naphthol – **Naphtholum** (non-officinal) and others. Indifferent covering powders do not contain any effective substance, only the powder basis.

As the powder basis is most frequently used a mixture of same parts of zinc oxid **– Zinci oxidum** and talc – **Talcum**. The zinc oxid ensures a long-lasting stability of the powder and inactivity towards present effective compounds. Furthermore, it performs antiseptic actions. The talcum is a powdered and hydratated magnesium silicate of greasy touch and ensures a good adherence to the skin. Moreover, there can be magnesium oxid - **Magnesii oxidum** and calcium carbonate – **Calcii carbonas** used in the basis, in RMP, there is also advantageously used bentonite– **Bentonitum**. As to organic basis, there can be used wheat-search – **Tritici amylum** and rice-search – **Oryzae amylum** in the powders. The phytoid searches are very fine and adherent. Nevertheless, especially on steamy places, they tend to burgeon quickly, form lumps and represent a fertile soil for microorganisms. That's why, the anorganic basis are generally given preference in powders for a prolonged use.

Cosmetic powders, called talcum powders, apart from the common bases (e.g. talc) contain other skin-softening compounds, pigments, aromatic additives, etc.

A prescription of a powder includes in the *Compositio* a specification of effective compounds and components of the bases, being the amount of effective compounds counted to correspond to the correct concentration in percents of the prescribed powder. To express the necessary amount of the powder bases, the abbreviations „ … *aa ad* …", i. e. „ … by equal portions into …" are used.

The total amount of a powder depends from the size of the treated area and duration of the cure. Normally 30-50-100 grammes are prescribed.

The subscription of a powder includes the order: *„Misce fiat pulvis adspersorius“* – for short *„M. f. pulv. adspers.“*.

The powders are adjusted into pots or powdering boxes – *„D. ad scatulam adspersoriam“* with a red label stating for external use.

An example of a prescription of adstringent powder with 5% of tannin as IPP:

Rp.
Tannini *2,5*
Zinci oxidi
Talci *aa ad 50,0*
M. f. pulv. adspers.
D. S. Powder. Cover the afflicted place several times a day.

Pulveres perorales divisi

Divided peroral powders

These are solid single-dose preparations destined for peroral use. They contain one or more effective compounds mixed with a suitable adjuvant or without it. This form si used to prescribe very effective (Venena) and effective (Separanda) compounds, in which case it is inadmissible to let the patient detract the separate doses from the total amount. When these are prepared individually, the pharmacy prepares and delivers the powder to the patient divided into separate therapeutic doses.

Divided powders as IPP are prepared within the range of weight of 0.1-0.5 (max. 1.0) g, the optimal weight of a powder is 0.3–0.4 g. Should the weight of the drug in 1 powder be less than 0.1 g, it is completed with an indifferent vehicle (rem. constituens) up to the optimal weight. In the process of weighing an amount of effective substance lesser than 0.05 g, to reduce the inaccuracy of weighing, so-called trituration may be used, which means mixing the effective substance with milk sugar in the proportion of 1 : 9, or 1 : 99, 1 : 999, respectively.

As vehicle, lactose – **Lactosum** (milk sugar, formerly Saccharum lactis) is mostly used. It has only a slightly sweet taste and dissolves slowly in water. It is not hygroscopic, on the contrary to the previously used vehicle: sucrose – **Saccharosum** (extracted from sugar cane or sugar beet) which has a high intensive sweet taste and dissolves easily in water.

Separate powders are normally delivered in hard gelatine capsules – presentation *“Ad capsulas gelatinosas“*, even in the case when the physician does not state the requiered coating in the prescription (see also the paragraph Capsulae). Only exceptionally, the powders are delivered in paper sacks “*Ad chartas“* or “*Ad chartas paraffinatas“* – e.g. with hygroscopic and volatile compounds. These are meant for the preparation of a drug solution by the patient by himself, dissolving the dose in a glass of water, etc.

Prepared powders are delivered in small plastic jars with preimpressed white labels provided with instructions for use.

There are two possible ways of divided powder prescription:

Dispensed form: In the prescription, we state the dose of each component per one powder. In the subscription, we state the number of doses the pharmacist has to prepare according to the order: *“Dentur tales doses numero…“*, in abbreviation “*D. t. d. No. …“* or “*D. tal. dos. No. …“*.

Divided form: in the prescription, we state the dose of every component necessary to prepare the total quantity for all prescribed doses, that is to say we have to multiply the separate doses of all components by the number of total doses. The order to divide into a certain number of doses in the subscription is as follows: "*Divide in doses numero ...",* in abbreviation "*Div. in dos. No. ...".*

Note: for a physician, it is more advantageous to use the dispensed form of prescription, as there exists less possibility of error in the calculation of the doses.

Example of procedure of prescribing divided powders in **dispensed form:**

We are going to prescribe 10 powders with spasmolytic papaverine (papaverine hydrochloride) – *Papaverini hydrochloridum*, where one therapeutic dose is 0.05 g. As the weight of the drug is lower than the admissible weight of the powder, we'll complete with lactose up to the weight of 0.4 g.

Rp.
Papaverini hydrochloridi 0,05
Lactosi ad 0,4

The subscription will contain the order: "Mix until a powder is created" – "*Misce fiat pulvis",* in abbreviation *"M. f. pulv.".* In the next line, we state how many doses should be delivered: *"D. t. d. No. X (decem)".* The powders will be delivered in gelatine capsules according to the order: "*Ad capsulas gelatinosas",* in abbreviation "*Ad caps. gelat.".*

The whole prescription will be as follows:

Rp.
Papaverini hydrochloridi 0,05
Lactosi ad 0,4
M. f. pulv.
D. t. d. No. X (decem)
Ad caps. gelat.
**S. For pain 1–2 capsules, maximum 6 pieces per day.*

The same prescription in divided **form:**

Rp.
Papaverini hydrochloridi 0,50
Lactosi ad 4,0
M. f. pulv.
Div. in dos. No. X (decem)
Ad caps. gelat.
**D.S. For pain 1–2 capsules, maximum 6 pieces per day.*

* Note: Within a prescription in dispensed form, if the order for delivery "D. ..." is already stated in the subscription, it is not necessary to repeat it in the prescription *signatura*. That's why in the first prescription, there is only "S.". In the prescription in divided form, the order for delivery is not stated, that is why it says "D.S.".

Pulveres granulati

Grained powders (granules)

Grained or granulated powders are loose materials composed of particles, nonhomogeneous in form and size that include therapeutic compounds and adjuvants. They may serve as an intermediate product in the manufacturing of tablets (so-called granulate) or they are

destined for peroral use within bulk drugs (RMP) (laxatives, antacids, X-Ray diagnosics). They are distributed in bags for separate use or as undivided powders for use by spoons.

Species

Herbal teas, (tea mixtures)

The preparation of teas from tea mixtures is the easiest form of therapeutic use of effective compounds contained in plants. The tea mixtures are mixtures of drugs, i.e. dry plant parts normally desintegrated into prescribed size of particles.

Tea mixtures are over-the-counter drugs and usually they are paid for by the patient. Normally, they are prescribed as bulk drugs (RMP), in specialized pharmacies, the preparation of individually composed tea mixtures is possible.

The easiest way to prepare teas from soft parts of plants (leaves, flowers, tops) is pouring over one spoon of prehumified drug (about 3-5 g) one cup (cca 250 ml) of boiling water. Teas made from hard plant parts (cortex, roots, rhizomes) are normally prepared by boiling one full teaspoon (about 3-6 g) in a cup of water. Seeds containing oils (e.g. *Anisi fructus, Foeniculi dulcis fructus*) are only infused, boiling would damage the effective substances. More details about teas – chapter 4.2.

Example of a prescription of expectorant tea mixture divided in its components:

Rp.
Thymi herbae
Althaeae radicis
Plantaginis folii *aa ad 150,0*
M. f. species
D. S. Tea mixture. Infuse 1table-spoon in a cup of boiling water,
Leach out for 10 –15 min. A cup of hot tea 3–4 times a day.

Tabulettae

Tablets

The most widely used pharmaceutical dosage form is tablets. They are solid pressed preparations, normally in the form of a flat cylinder, disc or lentil, frequently with a division groove. They are prepared by pressing the semiproduct, so-called granulate. They are prepared as bulk drugs (RMP), in some pharmacies fitted with tabletting equipment, they can be prepared according to an individual prescription.

As to their contents, tablets belong to multicomponent preparations. They are composed of one or more effective compounds and adjuvants forming a so-called tablet base. Normally, the tablet base has a complex composition, ensuring the qualities requiered for an optimal bioavailibility of drugs, as may be desintegrability*, resistance to acid pH and others (fillings, dry or humid binders, looseners, slippery and anti-adhesive compounds, components modifying the release of the drugs, colouring compounds, flavour correctors).

* As adjuvants that substantially improve the tablet qualities (increase of solubility of drugs and their desintegrability, covering of unpleasant smell or taste, diminishing of risk of interactions among the tablet components), the cyclic polysacharids, so-called cyclodextrines are used in modern pharmaceutics.

Tablets are normally designed for peroral use (Tabulettae perorales). After its swallowing, the drug absorbs from the digestive system and acts systemically *Tabulettae orales* – oral tablets , especially *Tabulettae sublinguales* – sublingual tablets (linguets), are not swallowed but located under the tongue and absorbed through the sublingual venous plexus. Their advantage is a very quick onset of the effect and a good dose controlabillity (the absorption ends by taking the tablet out of the mouth). Similarly, oromucosal tablets – *Tabulettae oromucosales*, chewable tablets – *Tabulettae manducabiles* and bucal tablets – *Tabulettae buccales* liberate effective compounds already in the oral cavity. Oromucosal tablets are normally destined for local action on the oral mucosa and bucal tablets for a slow absorption of compounds from the oral cavity. Among modern forms that allow gradual release and absorption of drugs, there belong also so- called bioadhesive tablets. Effervescent tablets - *Tabulettae effervescentes* contain hydrogene bicarbonate and lemon or tartaric acids as sparkling base, and serve for preparation of a sparkling solution for peroral use. The advantage of effervescent tablets is the faster onset of the drug effect compared to classical tablets.

Tablets may serve for other purposes. Vaginal tablets – *Tabulettae vaginales* are destined for insertion into the vagina, *Tabulettae pro solutione* or *Tabulettae pro dispersione* serve for preparation of liquid forms for external use, e.g. for desinfection, compressions, wash-outs. Tabulettae implantabiles are implanted into the subcutis and the drug (e.g. hormone) is being absorbed from it gradually, sometimes during several months. *Tabulettae pro iniectione* serve for preparation of solutions for injections or infusions when they are needed. A special group is formed by diagnostic tablets and test tablets for laboratory diagnostic purposes.

The prescription of tablets as IPP can be done either in divided or dispensed form, just as in the case of divided powders or suppositories. In the prescription, we state the names of effective compounds with their doses, the composition of adjuvants and their amount is usually left to be determined by the pharmacist: *„Massae tabulettarum quantum satis“*, in abbreviation *„Mass. tabul. q.s.“*. In the case of dispensed form, the instruction: *„... ut fiat tabuletta*“ follows. In the case of divided form the instruction is as follows *„... ut fiant tabulettae No. ...“*, in abbreviation *„... ut f. tabul. No. ...“*.

Example of prescription of tablets with dihydric quinidine sulfate in dispensed form:

Rp.

Quinidini sulfatis dihydrici 0,2
Mass. tabul. q.s. ut f. tabul.
D. t. d. No. XXX (triginta)
S. Every 6 hours 1 tablet.

The same prescription in divided form:

Rp.

Quinidini sulfatis dihydrici 6,0
Mass. tabul. q.s. ut f. tabul. No. XXX (triginta)
D. S. Every 6 hours 1 tablet.

Tabulettae obductae

Coated tablets, obducts

These are preparations similar to tablets in their appearance and form. However, their core is coated by one or more layers. Tablets coated in one layer, normally made of polymere forming a thin film, are called coated tablets. Multilayer coatings are made of mixture of different adjuvant compounds, including flavour, smell and colour correctors. They usually form a glossy coloured surface. These tablets are called drageed tablets (dragée) and are very popular with the patients. Gastro-resistant tablets represent a special type whose coating preserves the effective compounds from the acid enviroment of the stomach.

Tablets with prolonged or modified release - Tabulettae cum liberatione prolongata seu modificata are prepared using suitable adjuvants or special technologies with the aim of achieving the desirable velocity effective compounds release. The modified-release is usually achieved using a gastro-resistant (enterosolvent) or other, frequently multilayer, coating, installing the substance into a methacrylate skeleton, and so on. All the types of coated tablets belong among bulk drugs (RMP).

Capsulae

Capsules

Capsules represent a modern and practical form of making both, RMP and IPP. These are single-dose preparations of different shapes and sizes for peroral administration. They contain therapeutic compounds together with adjuvants or without them. They are installed into an edible hard or soft coating, normally based on gelatine. Release of the contents of the capsules and its subsequent absorption is produced after breaking down of the coating by the digestive juices. Capsules are manufactured in different volumes, their volume is designated by numeral symbols (e.g. #0 – 0.68 ml, #4 – 0.21 ml).

The content of the solid capsules is normally loose. As to the soft capsules, it is possible to introduce even liquid or highly viscous therapeutic preparations of hydrophobic (oleophilic) character, emulsion of water/oil type, etc. Capsules are kept in a dry place at temperatures of 15–25 °C.

Gastro-resistant (enterosolvent) capsules – *Capsulae enterosolventes*, represent a special type resistant to the acid environment of the stomach. This is ensured either by using an enterosolvent coating of formaldehyde and gelatine or by filling the current capsules with particles of drug with enterosolvent coating. In a similar way, the capsules with prolonged or modified-release are prepared – Capsulae cum liberatione prolongata seu modificata.

Implantata

Implants

These are sterile solid preparations with size and form suitable for parenteral implantation that enable protracted, i.e. long term release of active substances, e.g. hormones. They are delivered separately in sterile containers.

Microforms
(microcapsules, liposomes, pellets)

These are modern bulk pharmaceutical dosage forms composed of miniature particles, more often used as forms with modified-release or controlled distribution. **Microcapsules** are miniature equivalents to *Capsulae*, the individual particles have a core containing the drug coated with a polymer layer. **Liposomes** are miniature vesicles containing drug, normally formed of phospholipids. They are normally administered intravenously and are captured by monocyte-macrophage system. Afterwards, they can be targetedly distributed into immunologically active organs, tumor tissue, etc. **Pellets** are microparticles with high homogeneity of its contents, that include only the drug and at the very most one adjuvant. They are filled into gelatine capsules, similarly to microcapsules. In this way, multiple pharmaceutical dosage forms are created with exactly controlled release of effective compounds. They will be treated in more detail in lectures and seminars.

1.3.2. Semi-solid pharmaceutical dosage forms

These are preparations meant for external application (skin, mucosas) or insertion into body orifices (rectum, vagina). The released therapeutic compounds can act locally (topically) or systematically (after their absorption from the site of administration). At normal temperature, the preparations have semi-solid consistence and can be plastically deformed, and at the body temperature, they turn soft or they melt. They can be specific in form (Suppositoria – suppositories, Globuli – pessaries) or non-specific in form (Unguenta – ointments (unguents)), Cremores – creams, Pastae – pastes, Linimenta – liniments, Emplastra – plasters, Collemplastra – sticky plasters, Collodia – collodions, Sapones medicati – medicinal soaps).

Suppositoria
Suppositories

Suppositories are single-dose preparations of cylinder or cone form, 2-4 cm long, pointed on one side, destined for insertion into the rectum *(Suppositoria, Suppositoria rectalia)* or for a local action into the vagina *(Suppositoria vaginalia)*. At normal temperature, they are solid and at the body temperature, they melt or dissolve. They are prepared with 2-3 g of weight for adults (pro adultis) and 1 g for children (pro infantibus). The suppositories must be firm, compact enough with intact and smooth surface.

They contain one or more curative compounds as desintegrated as possible dissolved or disperged in the suppository base. **Cacao oleum** – cocoa oil and **Adeps neutralis –** neutral fat is most frequently used as oleophilic (hydrophobic) suppository base. As hydrophilic base, gel-forming mixtures can be used, such as **Gelatinae glycerogelatum** – glycerinated gelatine (Massa glycerogelatinosa), i.e. solution of gelatine in glycerol with admixture of water. Macrogoles are often used in individually prepared suppositories. The suppository base may contain other adjuvants, e.g. antimicrobial agents, antioxidants, slippery compounds and compounds that increase viscosity, e.g. Cera alba. (Note: On the contrary, the viscosity of the base may be diminished by e.g. paracetamol).

The mixture of drugs and suppository base is called suppository mass. Suppositories are prepared by melting, i.e. pouring the suppository mass into a suitable mold (suppository mold) and subsequent cooling or by cold pressing.

The prepared suppositories are wrapped in celophane or in plastic or in metal-coated films. They must be kept in a dry place at temperatures under 20 °C. For easier application, the best place is a refrigerator.

Suppositories as IPP are prescribed, similarly to divided pills, in dispensed or divided form. For minor possibility of a mistake while converting the doses, even in this case, the dispensed form is recommendable. The base is selected by the physician, according to the characteristics of the drug.

Dispensed form: the doses of drugs for preparation of one suppository and the denomination of suppository base are stated in the prescription, but not its amount. The amount of the base is selected by the apothecary himself according to the instruction (*q.s.*, as much as needed), e.g. *„Cacao olei quantum satis ut fiat suppositorium"*, in abbreviation *„Cacao ol. q.s. (ut) f. supp."* or *„Massae glycerogelatinosae quantum satis ut fiat suppositorium"*, in abbreviation *„Mass. glycerogelat. q.s. ut f. supp."* for a hydrophilic base. If we leave the selection of the base to the apothecary, we can use a general order: *„Massae pro suppositoriis quantum satis..."*, in abbreviation „*Mass. pro supp. q.s. ..."*.

In the case of suppositories for children, moreover, the order *„... fiat suppositorium pro infantibus"*, in abbreviation *„... f. supp. pro inf(ant)."* is stated.

The subscription includes information about the demanded number of suppositories, e.g.: *„Dentur tales doses No. X (decem)*", in abbreviation *„D. t . d. No. X (decem)"*.

Divided form: the separate doses of drugs are multiplied by the demanded number of suppositories. For the suppository base, only its nature is stated, not the amount *(q.s.)*. Therefore, we state the number of suppositories directly in the instruction *„Cacao olei q.s. ut fiant suppositoria No. X (decem)"*, in abbreviation *„Cacao ol. q.s. ut f. supp. No X (decem)"*, which can not be used in the dispensed form because the doses prescribed for one suppository would be divided into 10 suppositories and the patient would result underdosed.

The prescription *signatura* must contain exact instructions for use, including where to insert the suppository.

Example of prescription of suppositories with spasmolytic effect – dispensed form:

Rp.

Atropini sulfatis monohydrici	*0,0005*
Papaverini hydrochloridi	*0,05*
Cacao olei q.s. ut f. supp.	
D. t. d. No. XV (quindecim)	
S. Insert 1 suppository into rectum, maximum 3 per day.	

The same prescripiton – divided form:

Rp.

Atropini sulfatis monohydrici 0,0075
Papaverini hydrochloridi 0,75
Cacao olei q.s. ut f. supp. No. XV (quindecim)
D. S. Insert 1 suppository into rectum, maximum 3 per day.

Globuli vaginales

Pessaries, vaginal balls

These are preparations of spherical, egg-shaped, or suppository-like form, generally with 4 g weight that resemble, as to their consistence and suppository base, rectal suppositories. They are prepared by pressing or by pouring into a mold. In children's gynecology (*virgo intacta*), vaginal suppositories with form of rectal suppositories are used instead of balls.

Drugs contained in vaginal balls and other vaginal preparations perform mainly anti-inflammatory, antiseptic or spermicide action. Special vaginal forms used for resorptive action (vaginal rings, inserts, vaginal sponge) contain mostly steroid hormones and serve for hormonal contraception.

The prescription of individually prepared vaginal balls is similar to suppositories, glycerinated gelatine or cocoa oil is usually used as a base.

Example of prescription of individually prepared vaginal balls with sodium tetraborate decahydrate (Borax) – dispensed form:

Rp.

Natrii tetraboratis decahydrici 0,6
Massae glycerogelatinosae q.s. ut f. glob. vag.
D. t. d. No. XX (viginti)
S. Insert 1 pessary into the vagina nightly.

Unguenta

Unguents, ointments

Unguents are topical, semi-solid preparations, non-specific in shape, destined for application on skin or mucosas for their local action on body surface or penetration of drugs through the skin. They can also have a softening or protective action. At normal temperature, they have a semi-solid consistence, at a body temperature, they turn soft and smeary.

Unguents must be non-irritating, stable enough, homogeneous, and smeary and they should not have much influence on skin physiological processes (warm expenditure, perspiration, etc). They are more likely used for chronic processes and the drugs that they contain, penetrate the skin slowly, but to deeper layers. The quality of effect is determined by the concentration of drug, selected unguent base (pharmaceutical excipient**)**, use of adjuvants, blood supply of the site of application, size of absorption area, contents of water in the cornified layer, by the application site itself, etc.

Unguents contain effective substances in necessary concentration mixed into unguent base (ointment-base). Should the ointment be composed only of unguent bases without any effective drug, we refer to it as so-called <u>indifferent unguent/ointment</u>.

According to the unguent base, we divide the unguents into:

- Hydrophobic (oleophilic, lipophilic) unguents that do not mix with water or tissue liquid. Unguents prepared from hydrophobic bases do not penetrate deep, and they act more superficially. They are compatible with the majority of drugs. Bases used for preparation of hydrophobic unguents, may be of natural origin: white vaseline – **Vaselinum album**; yellow vaseline – **Vaselinum flavum**; pork lard – **Adeps suillus**; white bee wax – **Cera alba**; liquid paraffin – **Paraffinum liquidum**.
- Hydrophilic (oleophobic, lipophobic) unguents, that mix with water and penetrate more deeply and are suitable for application into hairy skin. It is well combinable with drugs of acid or alcalic nature. Their base is normally composed of a mixture of liquid and solid macrogoles (polyethylene glycols) – **Macrogolum®.**
- Emulsifying unguents that can form emulsion of water-in-oil type (w/o) or oil-in-water (o/w). In dermatology and cosmetics, emulsions of a type w/o are very often used. Their base are hydrophobic unguents and there are emulsifiers of a type w/o present, e.g sheep's wool grease – **Adeps lanae**, sheep's wool grease alcohols – **Alcoholes adipis lanae**, cetylalcohol – **Alcohol cetylicus**, monoglycerides, fatty alcohols, etc. We refer to so-called emulsifying oil-unguents. Their advantages are good smeariness, easy penetration of drug into deeper levels of skin, non-irritation, capacity of accepting and binding of water and tissue liquid. Among oil-unguents, there belong commercially produced composed ointment-base – **Synderman®**, **Cutilan®, Neoaquasorb® or Pontin®**. Within the group of emulsifying unguents of the o/w type, there is commercially produced a composed ointment-base which is essentially amphiphilic that behaves like hydrophilic — **Ambiderman®**.

In dermatology, there is also used a range of officinal ointment-base or unguents, e.g. simple unguent – **Unguentum simplex**; boric acid unguent 10% – **Acidi borici unguentum 10%**; ichthamol unguent – **Ichthammoli unguentum**; zinc unguent – **Zinci oxidi unguentum**, etc., where the physician does not need to describe all the components in the prescription, stating only the preparation under its pharmacopoeial denomination.

Prescription of individually prepared unguents:

In the prescription, we state the denominations of effective drugs and ointment-base in genitive singular. Their amount is stated in grams so that the preparation with desired concentration is created. The subscription includes the order *„Misce fiat unguentum"– „M. f. ung."*. In the prescription *signatura*, we state the denomination of the pharmaceutical dosage form – "Unguent" and instructions for use. Prepared unguents are delivered in jars provided with red label, for other uses, stating the denomination or composition of the unguent and instructions for use.

Usually prescribed amounts of unguents:

Eye, nasal, ear ointment	10–20 g
Facial, hand ointment	20–30 g

Distal extremities (limbs) ointment	80–100 g
Unguent for larger body areas	150–200 g

Example of prescription of 100 g of unguent with epithelising effect:

The drug is 2% boric acid and the base is white vaseline. The patient will apply the unguent 2 times a day on the affected areas.

Rp.

Acidi borici 2,0
Vaselini albi ad 100,0
M. f. ung.
D. S. Unguent. Apply twice daily in a thin layer on the affected areas.

Unguenta ophthalmica (**Ocularia semisolida**)

Eye ointments

They represent finely elaborated unguents prepared from drug and sterilized non-irritating ointment-base destined for application into the conjunctival sac. Special vehiculum for the preparation of an eye ointment is officinal **Unguentum ophthalmicum simplex** – simple eye ointment, which is sterile emulsifying base containing 8 parts of white vaseline, 1 part of sheep wool wax and 1 part of liquid paraffin.

For prescription of an eye ointment, we proceed in the same way as in the case of other unguents. In the part *Subscriptio*, we state the expression *„Misce fiat unguentum ophthalmicum" – „M. f. ung. ophth."*. Should it be obvious from the prescription of the special base that the unguent is destined for its application into the eye, it si possible to state only *„Misce fiat unguentum" – „M. f. ung."*. The period uf usability does not exceed 7 days. Eye ointments are delivered in tubes or suitable jars, in the case of delivery in jar, it is necessary to ask for a stick *(Adde bacillum!)* as application device.

Example of a prescription of ophthalmic unguent containing 2% pilocarpine hydrochloride – parasymphatomimetic suitable for treatment of glaucoma:

Rp.

Pilocarpini hydrochloridi 0,2
Unguenti ophthalmici simplicis ad 10,0
M. f. ung.
D. ad ollam
Adde bacillum!
S. Eye ointment. Apply into both eyes nightly.

Cremores

Creams

They are emulsion or suspension-emulsion preparations containing at least 15% of water. They are used for their softening, hydratating or cooling actions, but also for their anti-inflammatory and anti-mycotic effects. According to the characteristics of the cream base, oleocreams and hydrocreams are prepared. Creams have more tenuous consistence than unguents, they are more smearable and have more physiological effect comparing to unguents. Greasy creams contain vegetable oils, dry creams contain more water. Examples of officinal

creams: **Cremor refrigerans** – cooling cream, **Alcoholum adipis lanae cremor** – cream with alcohols from sheep wool fats. Creams are normally prescribed as bulk medicines (RMP).

Pastae

Pastes

Pastes are emulsion or suspension-emulsion preparations with harder consistence than unguents and, apart from the drug and paste base, they contain 25–50 % of powdered solid compounds (zinc oxide, wheat starch, etc.) Pastes do not turn substantially soft at body temperature and they act superficially only. Thanks to their porosity, they do not prevent perspiration. They are applied in thicker layer and normally are bepowdered with a suitable indifferent talc. Some types of pastes may be prescribed as officinal preparations. Examples: **Zinci oxidi pasta** – zinc paste, **Zinci oxidi pasta mollis** – soft zinc paste.

Example of prescription of a 5% coal-tar paste in an officinal zinc paste.

Rp.

Lithanthracis picis	*2,5*
Zinci oxidi pastae	*ad 50,0*

M. f. pasta
D. S. Paste. Once a day apply in higher layer.

Linimenta

Liniments

They are semi-solid, tenuous or jelly-like preparations destined for application on the skin, to be rubbed into the skin, eventually for a massage. More often, they contain derivants (i.e. compounds that increase the blood perfusion of the skin under the area of application and therefore accelerate the healing of chronic inflammation processes in articulations or muscles) as therapeutic components and antirheumatics and antiinflamatory agents. A common component of liniments for patients with articulation rheumatism and patients confined to bed for a long term use to be camphor, for its derivative action, and menthol for its cooling action, on the contrary. Liniments may be prescribed as IPP or RMP, also officinal preparations are available, e.g. Pain-Expeller sol.

Emplastra transcutanea

Transdermal plasters (patches)

These modern pharmaceutical dosage forms, exclusively prescribed as RMP, are flexible sticky preparations for application on the skin containing one or more drugs. The therapeutic compounds released from the transdermal plaster, after passing the skin barrier, penetrate into the systemic blood or lymphatic circulation and cause a systemic effect. This type of pharmaceutical dosage form is denominated as transdermal therapeutic system (TTS). After the application, the contained effective substance is fluently released in predetermined amount and during predetermined time, being its plasmatic levels during the time of release from the plaster practically equal. Among the advantages of this pharmaceutical dosage form is first of all the easy application by simple placing on the skin (better compliance), the capacity of creating a prolonged and constant concentration in plasma especially of those drugs that have a shorter biological half-time. There is also the possibility to avoid the metabolic degradation of the

effective substance in the organism during its first pass through the liver (*"first-pass"* effect). Another advantage is the possibility to interrupt in any moment the drug afflux into the organism simple withdrawing of the preparation from the skin or the possibility of decreasing the dose and frequency of administration of the drug, reducing in this way the appearance of adverse effects.

The TTS, that found their utilization in practice, form two basic subgroups: a) TTS composed of polymer matrix, b) TTS, where the release of the drug is controlled by a membrane. In matrix systems, the effective drug under the covering plaster is dispersed in polymer matrix that can have adhesive properties as well. Should this not be like this, it is necessary to add another layer, an adhesive one. A more sophisticated type of this system is composed of reticularly organized polyacrylate polymer where the effective drug is dispersed. The membrane controlled systems are composed of the covering layer under which the resorvoir with solution of effective drug is located. In between the effective drug and the skin, there is a special micropore membrane that allows slow and prolonged release of the drug towards the skin (in some cases, it can be even gel, etc). This system adheres to the skin thanks to a silicon adhesive layer.

The transdermal plasters are a modern pharmaceutical dosage form especially advantageous with some drugs (hormones, analgesics, antiemetics, etc.). Examples: estradiol (estradiolum) in preparation of Climara plaster and Estraderm TTS 25 (50, 100) plaster; fentanyl in preparation of Durogesic 25 μg/h (50, 75, 100 μh/h) plaster; nicotine – Nicorette 5 mg/16 hours (10, 15 mg/16 hours) plaster.

1.3.3. Liquid pharmaceutical dosage forms

Liquida

Solutions

Solutions are liquid preparations destined for internal or other application. They can have the characteristics of true solutions (ion or molecular dispersions) or non-true solutions (colloidal dispersions) of drugs in a suitable solvent.

True solutions may be applied in peroral, injection or external route of administration according to the characteristics of the drug. Total dissolution of the drug ensures the total homogeneity of the preparation. True solutions must be clear or almost clear, non-turbid, without traces of non-dissolved drug or sediments.

Non-true solutions, that is to say colloid dispersions of fine particles, must be permanently homogeneous. Colloid solutions are formed for example by sulphur (Sulfuris colloidalis et technetii [^{99m}Tc] solutio iniectabilis) used as radiopharmacon, also by siliceous acid, starches, proteins.

As solvents for the preparation of true and non-true solutions, the following compounds are used: **Aqua purificata** – purified water, **Aqua pro iniectione** – injection water, **Aqua conservans** – conservative water (water with methylparaben and propylparaben), **Ethanolum 60%** – ethanol 60% (syn. Spiritus dilutus, spirit 60%), **Ethanolum 85%** – ethanol 85% (syn. Spiritus concentratus, spirit 85%), **Ethanolum 96%** – ethanol 96% (syn. Ethanolum 96 per centum, spirit 96%). Suitable vehicles for lipophilic compounds are oils, e.g.. **Helianthi oleum raffinatum** – purified sunflower oil, **Olivae oleum raffinatum** – purified olive oil, **Arachidis**

oleum – peanut oil. In liquid preparations for the skin and mucosas, there is normally glycerole 85% –**Glycerolum 85%**.

Solutions belong among the most favourite pharmaceutical dosage forms, especially due to the possibility of their application in diverse ways and for their generally high bioavailability.

Note: : The current Pharmacopoeia denominates all liquid pharmaceutical dosage forms as **liquida** (abbr. *liq*.), in the subscription is then stated "*M. f. liq.*". It is a broader term (in general liquids) which comprises both true and non-true solutions, suspensions or emulsions. The prescribed liquid preparations are often true solutions. Therefore, it is not a mistake to use in the subscription, when prescribing them as IPP, the expression **solutio** (*„M. f. solutio"*). When prescribing suspensions or emulsions, it is possible to specify the given pharmaceutical dosage form (e.g. liquid topical powder – suspensio – *„M. f. susp."*) in the subscription instead of stating the expression *„M. f. liq."*

Liquida peroralia

Peroral liquids

These are liquid preparations that can be administered to the patient in the form of drops (Guttae) or with the help of spoons or tea-spoons. The most suitable form is selected according to the solubility of the drug, the admissible concentration of the drug that does not irritate the mucosas of the digestive apparatus, according to the taste characteristics of the drug and taking into account which form is the best one for the patient. Aromatic waters (Aquae aromaticae) are administered by spoons and tinctures (Tincturae) in drops. Peroral solutions are often used for children due to their easy application and better possibility of individual dosing comparing to tablets or capsules.

Solutions for peroral use are divided into separate doses by the patient according to the instruction in the prescription *signatura*. When prescribing a solution, we do not divide it into separate individual doses. In the prescription, we state the total amount of drugs and solvent. The calculation of the total amount of each component results from the form of dosing (drops, spoon), the daily doses and the number of days of use.

To determinate correctly the amount of solvent (vehicle) necessary for the preparation of a solution for peroral use, it is essential to know the approximate relations between the weight units and applied volumes:

1 g = 1 ml of aqueous solution	= 20 drops
1 g of oil solution	= 40–50 drops
1 g of ethanol solution	= 50–60 drops
1 spoon/ table-spoon	= 15 g of aqueous solution
1 dessert (children's) spoon	= 10 g of aqueous solution
1 teaspoon	= 5 g of aqueous solution

Process of prescription of peroral liquids administered in form of drops

Drops (Guttae) fulfill the requirement of accurate dosing normally given by the contents of strongly effective drug dissolved in small amount of solvent. When prescribing, we normally prescribe the separate therapeutic dose of the drug into 20 drops (1g of aqueous solution, about 0.3 g of spirit solution), or into 5-10-15 drops (0.25–0.5–0.75 g of aqueous solution). The total

quantity of prescribed drops is normally oscillates between 10-25 g. Drops are delivered in a dropper container *(Ad vitrum guttatum).*

We will explain the process of drops prescription with the following example:

We want to prescribe an aqueous solution of atropine sulfate monohydrate – *Atropini sulfas monohydricus,* used peroraly with spasmolytic indication. Separate therapeutic dose of atropine will be 0.0005 g (i.e. 0.5 mg). Purified water – *Aqua purificata,* will be used as vehicle. The patient will use the preparation by 20 drops 3 times a day during 10 days.

We will start with the following consideration:

- First of all, we will establish the total amount of solution:

The patient will use the solution by 20 drops, i.e. 1 g of aqueous solution 3 times a day, i.e. 3 g a day. The calculated amount of solution for 1 day will be multiplicated by the number of days of its use

3 g x 10 = 30 g of solution

- We have established the total amount of prepared solution and now we need to assess the necessary dose of atropine sulfate: 0.0005 g of drug must be contained in 20 drops, i.e. in 1 g of solution, therefore, in 30 g of solution there must be 30 doses, i.e. 30 x 0.0005 = 0.015 g of atropine sulfate.

The prescription will be as follows:

Rp.

Atropini sulfatis monohydrici 0,015
Aquae purificatae ad 30,0
M. f. liq.
D. ad vitr. gutt.
S. 20 drops 3 times a day .

Note: When prescribing a preparation containing more drugs with different therapeutic doses, obviously we have to make the same calculation for each drug.

Process of prescription of solutions administered by spoons

Especially in pediatrics, the solutions administered by spoons are more frequently prescribed individual liquid preparations comparing to drops. We can prescribe in this way the same drugs as in the case of drops and moreover, difficultly soluble drugs or drugs that must be diluted so that they do not irritate the mucosa of the digestive system. However, it is necessary to take into account that dosing by spoons is less accurate than by drops. When prescribing solutions administered by spoons, we proceed in a similar way as when prescribing drops for peroral use with the difference that the therapeutic dose of the drug will not be contained in 1 g of solution (20 drops) but in 5 g (tea spoon) or 12 g (table spoon). Thus, the total quantity of prescribed solution will be higher, normally 50-100 g for solutions by tea spoons and 150-250 g for solutions dosed by table spoon.

The unpleasant flavour of the solution may be modified by adding a **corrigent**. Syrups are generally used, normally 15-20 g of syrup into 100 g of final solution (15-20% concentration), for children under 10 years and in therapeutic syrups even more (up to 30-50%). Syrups are

concentrated solutions of sugars in water or in fruit juice or herbal drug leachings, frequently aromatized and coloured. For a simple correction of flavour, **Sirupus simplex** – simple syrup or **Aurantii sirupus (according to the Czech Pharmacopoeia)** – orange syrup is used. Some of the syrups show a slight curative effect, e.g. antitussive and expectorant **Althaeae sirupus –** althaea syrup or **Thymi sirupus compositus (according to the Czech Pharmacopoeia) –** composed thyme syrup**.**

The finished preparation is delivered to the patient in narrow-nech bottles, so-called vials. It is necessary to state the form of adjustment in the subscription only in the case when we claim a special type of vial, e.g. dark vial *(Ad lagenam fuscam).*

Example of prescription:

As a drug against cough with expectorant and bronchodilating effect, we want to prescribe a solution with two effective compounds: ephedrine hydrochloride - *Ephedrini hydrochloridum*, whose single therapeutic dose is 0.025 g and natrium iodide – *Natrii iodidum* with a dose of 0.5 g. The patient will use 1 table spoon 2 times a day during 5 days. We will modify the flavour by adding simple syrup – *Sirupus simplex*. The vehicle used will be *Aqua purificata*.

The prescription is as follows:

Rp.

Ephedrini hydrochloridi	*0,25*
Natrii iodidi	*5,0*
Sirupi simplicis	*30,0*
Aquae purificatae	*ad 150,0*

M. f. liq.
D. S. 2 times a day 1 tablespoon.

Aquae aromaticae

Aromatic waters

Aromatic waters are prepared as saturated aqueous solutions of volatile compounds, normally essential oils from aromatic plants with characteristic smell and flavour (e.g. from fennel or anise fruits, peppermint herb, etc.). Especially for children, officinal **Aqua carminativa** – carminative water and **Aqua carminativa rubra** – red carminative water are used as preparation against flatulence.

Example of a prescription of red carminative water with carminative effect:

Rp.

Aquae carminativae rubrae	*200,0*

D. S. Red carminative water.
3 times a day 1 tablespoon after meal.

Infusa, decocta

Infusions, decoctions

These are traditional, nowadays only exceptionally prescribed liquid preparations for peroral use by tablespoons or teaspoons, prepared by leaching desintegrated herbal drugs in water. The convenient type of extraction method is selected according to the characteristics of

each drug – according to the hardness of the drug and character of effective compounds. Infusions differ from decoctions by the manner of leaching.

Infusum – infusion are usually prepared by pouring boiling water over the drug prehumified in water with normal temperature and leaving it in boiling bath for 5 minutes. Afterwards, it is leached in a covered pot for 45 minutes. After filtering, it is completed up to the prescribed quantity. As infusions, also so-called macerations, i.e. leachings in cold water (at normal temperature), are prescribed.

Decoctum – decoction is prepared by pouring boiling water over the prehumified drug, leaving it in boiling bath for 30 minutes. Then, the decoction is filtered and completed up to the prescribed quantity.

Due to their low stability and other inconvenient characteristics, nowadays we hardly find infusion or decoction prescriptions and in general, the pharmacies do not prepare them. They are substituted by curative teas that are prepared by the patient himself/herself according to the instructions, either as infusion or as decoction, at the time of need.

Tincturae

Tinctures

These are concentrated spirit leachings of drugs or spirit solutions of extracts destined for peroral use. The way of preparations and final concentration of each tincture is given by the Pharmacopoeia, the physician does not have to know it and state it in the prescription. They are dosed by drops, the therapeutic dose is normally contained in 10-20 drops (1 g of spirit solution = 60 drops!). The total quantity prescribed is usually 10-20 g of tincture. The most frequently prescribed officinal tinctures are **Tinctura amara** – bitter tincture (for appetite increase) and **Valerianae tinctura –** valerian tincture (for falling asleep easier).

Example of prescription of valerian tincture serving for general calming down of the patient:

Rp.

Valerianae tincturae 20,0
Ad vitr. gutt.
D. S. 2 times a day 20 drops.

Among traditional prescriptions, there also appear so-called aromatic alcohols. These are less concentrated ethanol solutions of oils for internal and external use (e.g. **Anisi spiritus compositus**, **Camphorae spiritus**).

Liquida ad usum alium

Liquids for other use

True and non-true solution for compresses, for spreading on skin and musosas or for washings, eventually for instillation into the ear or nose, belong to this group.

Solutions for compresses and spreading

These are liquid preparations most frequently used in dermatology. We will deal their prescription in more detail in the chapter on dermatological prescriptions (chapter 2.4.). In their

prescriptions, we state the quantity of drug and solvent always in "g", so that a solution with desired concentration is formed. We use the expression in "g", even in the case of mixture of two or more liquid compounds. The prescribed quantity of solution depends from the size of treated area, way and frequency of application, supposed period of treatment and stability of the effective drug in the solution.

Example of prescription of 2% salicylic spirit for desinfection, cooling and drying of the skin:

Rp.

Acidi salicylici *2,0*
Ethanoli 60% *ad 100,0*
M. f. liq.
D. S. Salicylic spirit. Spread 4–5 times a day on affected area.

Otoguttae

Ear drops

As auricular drops, solutions, suspensions or emulsions are used, applicated into the external acoustic duct by drops or for a washing-out. Similar rules as for other solutions for other use are valid for auricular drops. They may be stabilized by antimicrobial admixtures (selection of the pharmacist) or isotonized. Usually, they are prepared in the quantity of 20 g. They are administered in drops; the dropper applicator must have a rounded edge. In the prescripton, we state the claim of delivery of the dropper applicator *(Adde guttatorium!)*. In the prescription, it is necessary to state possible requierement of sterility using the order *„Sterilisetur! “*. In the prescription "signatura" of IPP, we state “Ear drops” and instruction for use.

Rhinoguttae

Nasal drops

These are liquid preparations destined for nose dropping, for nose washing-out or for spraying. Normally, they are destined for local effect on nasal mucosa, however, the nasal application may be used as an alternative way for systemic treatment (nasal vaccines, calcitonine, oxytocine, etc.)

For an individual prescription and preparation of nasal drops, similar rules to auricular drops are valid. The solution is adapted to isotonic concentration with the serous fluid (this demand does not have to be indicated in the *Subscriptio*) and actual acidity of 6.7–7.6. This demand must be stated by the physician in the subscription using the order “ *M. f. solutio isotonica isoacida“*. It is also necessary to indicate the demand of sterility in the prescription. The prescribed quantity of nasal drops is usually 10-20 g. The prescription *signatura* includes the order “Nasal drops” and instruction for use. For hygienical reasons, dropper applicator is not used any more; nasal drops are delivered in dropper containers.

Example of prescription of nasal drops – so-called "borephedrine":

Rp.

Ephedrini hydrochloridi	*0,2*
Acidi borici	*0,6*
Aquae purificatae	*ad 20,0*

M. f. sol. isoac.
D. ad vitrum guttatum!
D. S. Nasal drops. 1–2 drops into each nostril, maximally 4 times a day.

Oculoguttae – eye drops
Aquae ophthalmicae – eye lotions
(formerly frequently used the group denomination: Collyria)

These are sterile liquid preparations destined for application into the eye. Eye drops - ***Oculoguttae (Guttae ophthalmicae)*** are destined for dropping into the conjunctival sac, eye lotions ***Aquae ophthalmicae*** are destined for washing-out the eyes. They can be prescribed as IPP as officinal preparations, e.g. **Natrii tetraboratis oculoguttae –** borax eye drops or zinc sulfate eye drops. Nowadays however, RMP predominate significantly within the prescriptions of eye drops and lotions.

Eye preparations must be always prepared in aseptic conditions according to the principals stated in the Pharmacopoeia. As vehicle for aqueous solutions, **Aqua pro iniectione** – water for injection solution is added. We practically do not find any longer oil bases. The eye reacts very sensitively to the different osmotic pressure and acidity of the administered solution in comparison with tears. That is why the hypotonic aqueous solutions are automatically modified to isotonic, not being necessary to state the request in the prescription. Nevertheless, the demand of acidity adjustment must be indicated in the prescription stating *„M. f. sol. isoacida"*. The modification of pH is reached by adding suitable buffers. Should it be necessary that the preparation is sterile, in the prescription, there must be always stated the order *„Sterilisetur!"*. However, the pharmacist always adds an antimicrobial admixture (e.g. thiomersal). He does it always except for the case when the physician indicates *„Sine antimicrobico"* in the prescription or for the case of single-dose packaging of eye preparation. Eye solutions may also defer as to their viscosity (the increment of viscosity is usually given by an admixture of polymeres) or superficial tension.

Both, eye drops and eye lotions are prepared in a pharmacy and their period of expiration is normally limited to 1-2 weeks. The pharmacy states this date on the label.

We prescribe eye drops in the amount of 10 g, ophthalmic waters of maximum of 200 g. From the prescription, it must be absolutely clear for the pharmacist that he is dealing with a preparation for administration into the eye. Therefore, we state in the subscription one of the expressions *„M. f. oculoguttae"* or *„M. f. aqua ophthalmica"*.

In case of highly effective alcaloids, as atropine, pilocarpine, physostigmine, etc., the physician may state the order of denominating as posions – *„Sub signo veneni"* in the prescription *signatura*, so that the patient and his/her family members are warned against its accidental consumption and intoxication.

Example of prescription of eye drops with 1% homatropine hydrobromide as mydriatic:

Rp.

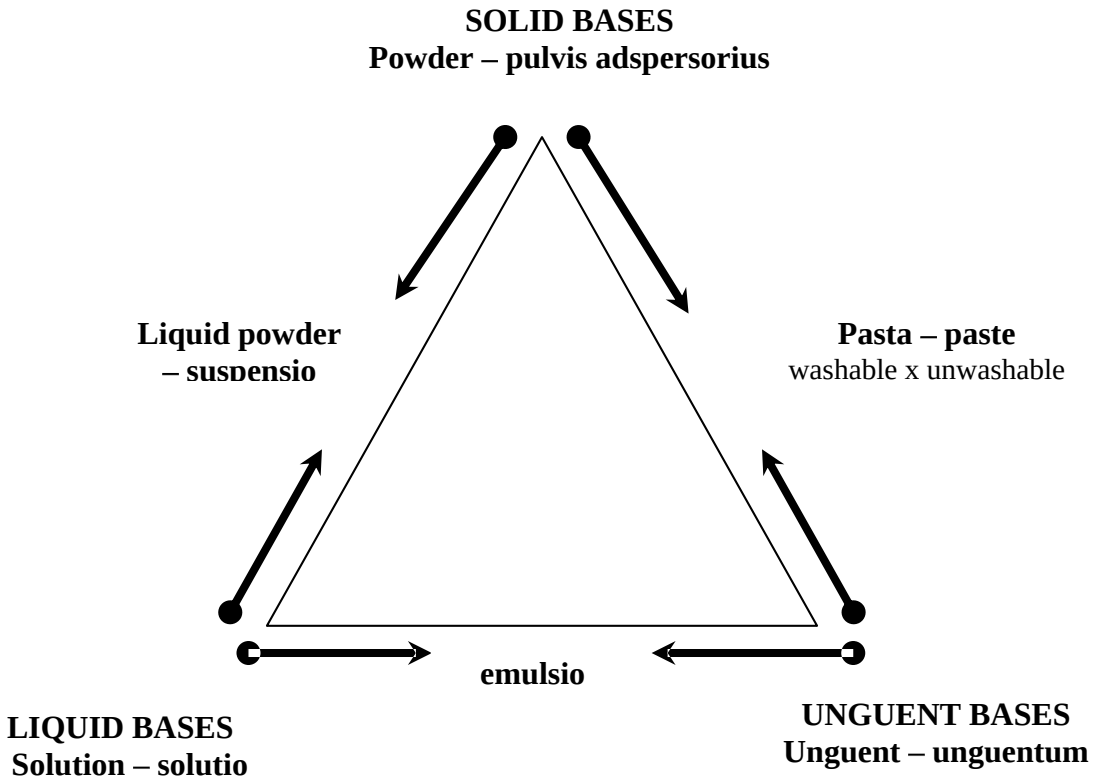
Homatropini hydrobromidi 0,1
Aquae purificatae sterilisatae ad 10,0
M. f. oculoguttae
Ad vitr. gutt.
D. S. Eye drops. 1–2 drops into both eyes.
Sub signo veneni!

Pulveres adspersorii liquidi

Liquid powders

Liquid powders are semiliquid suspensions destined for application on the skin for their cooling, antiitching, drying and antiseptic effects. They contain very finely desintegrated drugs in prescribed concentration and other components forming the suspension base. The base is composed of solid and liquid phases, representing the liquid phase bigger proportion in the total quantity of liquid powder, normally 60-70 %.

The solid base is more frequently formed of two equal parts of zinc oxide – **Zinci oxidum**, with adstringent a slightly anti-inflammatory effects, and talc **– Talcum** which adheres well to the skin and increases the evaporation of liquid components of the base.



The liquid base is composed of several parts: **Glycerolum 85%** – glycerol 85% is almost always present as it keeps the solid particles in suspension, moistens the skin and elevates its

wettability, ensuring the adhesion of the liquid powder. Another usual component is **Aqua purificata** – purified water and **Ethanolum 60% -** diluted alcohol, normally forming 1/10 of the content. Thanks to evaporation, alcohol has cooling and consequently anti-itching effect, nevertheless it is not an indispensable part of a liquid powder. Instead of aqueous, colloid solutions may be used as vehiculum, as may be **Bentoniti magma** – bentonite magma (5% aqueous suspension of bentonite) or **Silica colloidalis anhydrica** – colloid waterless tetrachloride oxide, used in 3–5% concentration. These colloid bases ensure the stability and homogeneity of the liquid powder through their thixotropic properties, i.e. reversible conversion into gel at longer standstill and passing back to solution if shaked. The prescription of liquid powders may simplified using officinal base containing same parts of zinc oxide, talc, glycerole and bentonite – **Zinci oxidi suspensio** (zinc oxide suspension), instead of writing out all solid and liquid phases of the indifferent base.

When prescribing, we state the order *"Misce fiat suspensio"* in the subscription, in abbreviation *"M. f. susp."*. Liquid powders are normally delivered to the patient in plastic jars, it is not necessary to assign the packadging. Apart from the denomination of the pharmaceutical dosage form and instructions for use, there usually is the order "Shake well before use!".

Example of prescription of an indifferent liquid powder:

Rp.

Zinci oxidi	
Talci	*aa 15,0*
Ethanoli 60%	*10,0*
Glyceroli 85%	*15,0*
Aquae purificatae	*ad 100,0*

M. f. susp.
D. S. Liquid powder. Daub over the affected area every 2 hours.
Shake well before use!

Iniectiones

Injections (syn. Iniectabilia)

These are sterile solutions, emulsions or suspensions destined for parenteral injecting by means of a syringe. In the case of drugs that are not stable in a solution, the ampoules or vials contain only sterile dry substance in powder, tablet or lyofilized form and the injection solution is prepared by adding a solvent in sterile conditions at the time of need just before its application. All drugs, adjuvants and solvents used must comply with the requirements of the Pharmacopoeia.

As *vehiculum* for injection aqueous solutions, exclusively **Aqua pro iniectione** – water for injections may be used, which is depyrogenized sterile and purified water. Oil injection solutions are prepared from sterile sunflower or olive oils. Bulk injection preparations contain sometimes for technological reasons other adjuvants and solvents, as ethanol, glycerol, polypropyleneglycol, etc.

Hypotonic aqueous injection solutions are modified to solutions isotonic to human blood during their preparation. This is normally done by adding sodium chloride or other suitable substance that must not react chemically with any component of the injection solution or alternate its action.

Similarly, the existing acidity of aqueous solution is modified with the help of suitable buffers to isoacidic solutions to human blood or serum, if possible to pH 7.2–7.4.

To ensure the chemical and physical stability of injection solutions, it is allowed to add stabilizers, e.g. antioxidants and chelateformers.

Injection preparations must be free of all forms of microorganisms, that is why they are sterilized in one of many procedures prescribed by the Pharmacopoeia. Sterilization is carried out immediately after closing the filled ampoules or vials. Most often, hot air, re-boiling or high pressure steam sterilizations are used. Drug solutions that do not accept hot sterilization are sterilized e.g. by action of gases and vapours with germicide effects, bacterial filtration, action of ionizing or ultraviolet radiation. In the case of therapeutic preparations that can not be sterilized in any common way, so-called aseptic preparation in special aseptic boxes is performed.

Should it not be possible to sterilize the preparation in any way or in the case of injection preparations intended for use by parts (multidose), antimicrobial admixtures are added, e.g. phenole, benzylalcohol, phenylmercuric salt, etc. Nevertheless for example, these adjuvants must not be added into solutions for peridural and intrathecal application and into intravenous infusions administered in larger volumes.

Injection preparations are filled into sterile ampoules (contents 1-30 ml), injection vials, so-called peniciline vials (content 20–50 ml) or into infusion bottles (contents more than 100 ml). Colourless glass is used for their manufacturing. The contents of injection liquid inside them is about 1/10 higher comparing to the prescribed volume, having in mind its loss while drawing into a syringe.

In monodose injection preparations, the drug dose in the real volume of injection liquid in the ampoule or vial must not pass the maximum individual dose for an adult established by the Pharmacopoeia.

Injection prescription

Injection preparations, in their absolute majority, are prescribed as bulk therapeutic preparations. Only exceptionally, one can meet their individual preparation in higher standard hospitals where the pharmacies have a special equipment and aseptic box. However, it is necessary to handle individually prepared injection prescription for the need of prescription of some injections that are not prepared as bulk drugs, e.g. some less usual concentrations of local anaesthetics or other special solutions.

When prescribing injections in the form of IPP, we state the doses of drugs in grams, just like with other drugs, the quantity of solvent, though, in volume units, therefore in mililitres. During the preparation, the whole prescribed volume of vehicle is added to the weighed dose of drug that is why we do not indicate the preposition *"ad"* in front of the number indicating volume. It is not necessary to state the abbreviation "ml" for the vehicle volume. The composition of vehicle is given, i.e. also by the manner of how will the injection be administered (i.v., i.m., s.c).

It is possible to prescribe injections in dispensed or divided form. For lesser possibility of mistake in the calculation of drug quantity, we give preference to the dispensed form.

For dispensed form of prescription, we proceed in the familiar way. We state the amount of drug and the dose of vehicle for one injection and we indicate how many doses should be prepared and delivered in the subscription. The subscription includes the order for solution preparation, mostly isotonic and isoacidic – "*M. f. solutio isotonica isoacida"*. Moreover, it is necessary to state the type of required container – "*Ad ampullas", "Ad vitrum pro iniectione"*. For sterilization, we indicate the order "*Sterilisetur!"*.

The prescription *signatura* for individually prepared injections always contains the expression "*Suo nomine"* or "*Cum formula"* to indicate the content, as the injections are destined for application by physician and not by the patient himself/herself. That is why the prescription *signatura* also includes the order *"Ad usum medici"* or similar. Normally there are no detailed instructions for use.

Example of injections containing caffeine with sodium benzoate *(Coffeinum et natrii benzoas)* in dose of 0.25 g:

Rp.

Coffeini et natrii benzoatis	*0,25*
Aquae pro iniect.	*2,0*

M. f. sol. isoton. isoac.
D. t. d. No. V. (quinque) ad amp.
Sterilisetur!
S. Suo nomine. Ad usum medici.

Infusiones

Infusions (syn. Infundibilia, Infusiones intravenosae)

These are sterile solutions with ion, molecular or colloid dispersion characteristics administered into the organism in bigger volumes through intravenous drop infusion.

Injection water **– Aqua pro iniectione** is used for their preparation. In no case, oil solutions or macrodispersions, as suspensions or emulsions, may be used for an infusion. Within bulk drugs manufacturing, with the help of special technologies, it is possible to prepare infusions containing very finely disperged emulsion of oil/water type, e.g. in solutions for parenteral nutrition.

Similar strict requirements established by the Pharmacopoeia for the praparation of injection solutions are valid for infusion solutions. Solutions for infusion may be hypertonic, however never highly hypotonic. Solutions may be slightly alcalic or acid, possible demand of isoacidity must be stated in the prescription. Sterility is achieved in the same ways as described for injection preparations. Due to a bigger volume administered, antimicrobial admixture must not be used.

Infusion solutions are prescribed as **IPP** in total volume of 100–400 (–1000) ml, only exceptionally higher (e.g. solutions for intermitent peritoneal dialysis). Amount of drug is expressed in grams into certain volume of solvent so that a solution with requiered concentration is created (preposition *"ad"* is not stated in this case). The composition may also be expressed in substance volume in mol/l, which is common e.g. for solutions intended for qualitative and quantitative modification of internal environment (see chapt. 2.9).

They are delivered in infusion bottles under the direction of the physician in the subscription "*Ad lagenam(s) pro infusione"*, in abbreviation "*Ad lag. pro infus."*. In the

prescription part *Signatura*, there will be stated the order for marking the contents on the container – "*Suo nomine"* or "*Cum formula"* and delivery for physician´s use.

Some commonly used infusion solutions may be prescribed as officinal preparations with standard composition. More detailed information about the composition of infusion preparations can be found in the chapter 2.9. Infusiones.

Example of prescription of 5 bottles with 400 ml of glucose infusion solution in 5% isotonic concentration.

Rp.

Glucosi	*20,0*
Aquae pro iniect.	*ad 400,0*

M. f. sol.
D. t. d. No. V (quinque)
Ad lag. pro infus.
Sterilisetur!
S. Cum formula. Ad usum medici.

Praeparata ad irrigationem

Preparations for washing-out

These are sterile aqueous big-volume preparations prescribed exclusively as bulk drugs destined for washing-out of body cavities, open lesions and surfaces, e.g. during surgical interventions. They are prepared by dissolving of one or more drugs, electrolytes or osmotically active compounds in water which complies with the requirements of the article *Aqua pro iniectione* or contain only water (water for washing-out). Solutions for washing-out are normally isotonic to blood, they are delivered in single-dose containers and are destined for single use.

1.3.4. Gaseous pharmaceutical dosage forms

The whole group consists of bulk preparation delivered in special pressure containers.

Gasa medicata

Medicinal gases

They are used for special therapeutic and diagnostic purposes, for example nitrous oxide – Nitrogenii oxidum (N_2O) for general anaesthesia, carbon dioxide – Carbonei dioxidum (CO_2), oxygene – Oxygenum (O_2), nitrogene – Nitrogenum (N_2), compressed mixture of 95% oxygene and 5% carbon dioxide – "Carbogen", compressed air – Aer medicinalis. They are stored under pressure in steel containers marked in colours and description. Their characteristics must comply with the current Pharmacopoeia.

Aerodispersiones

Aerodispersions

These are molecular, colloid and macroscopical dispersed systems of gaseous, liquid or solid drugs in gas, most often in air. Aerodispersible preparations are manufactured as potential aerodispersions, which means preparations whose proper aerodispersion is created at the moment of their application.

Molecular and colloid aerodispersions (aerosols) are inhaled directly from the evironment into which they evaporate or they are administered with the help of a suitable instrument into the nasopharynx, eventually as far as the lungs where they produce local or systemic effect.

Molecular aerodispersions are formed by vapours of volatile liquid drugs, solutions or mixtures of volatile liquid and solid drugs in air and they originate at normal temperature (by high tension of vapours) or after heating up. The size of disperged particles is lesser than 0.5 μm.

Colloid aerodispersions are formed by dispersion of non-volatile compounds or solutions in air or other gas. The size of disperged particles is lesser than 0.5–5 μm.

Macrodispersible aerodispersions (sprays – nebulae) contain bigger, even macroscopic, particles of liquid or solid drugs in air. The size of disperged particles is bigger than 5 μm , that is why they sediment more quickly. They are not destined for inhalation. They are used for application of therapeutic compounds on skin, mucosas, subcutaneous tissues, into body cavities or even for desinfection of air, etc. They are delivered in pressure containers with a suitable applicator or in containers with a mechanical nebulizer. It is the case of for example *Praeparata liquida nasalia pro aerodispersione* – liquid nasal sprays, i.e. solutions, emulsions or suspensions destined for injecting into the nasal cavity, or *Pulveres adspersorii pro aerodispersione* – nebulizing powders, *Praeparata auricularia pro aerodispersione* – ear sprays. As an example of a preparation in spray *(Praeparationes pro macrodispersione)*, we can cite bulk preparations Septonex spray, Miacalcic Nasal spr. nas.

Spumae medicatae – healing foams

(synonyms: Musci medicati, foams with drugs)

These are macrodispersions with a big volume of gas (normally air) disperged in a liquid. The liquid phase contains curative compounds, superficially active substance enabling foaming and other adjuvants. According to their structure, they may be classed into hydrodispersible or oildispersible systems. The healing foam is formed after releasing the liquid phase from the pressure container provided with a valve and foam dispenser *(Praeparata pharmaceutica in vasis cum pressu* – Therapeutic preparations in pressure container).

They are destined for local treatment of pathologically altered skin, mucosa and exposed tissues. They adhere well on skin, do not irritate and they penetrate well into skin wrinkles and lashes. They are convenient for hairy and intertrigineous skin surfaces, they are also used as rectalia or vaginalia.

Example: PANTHENOL drm. spr. sus. (dexpanthenol spray)

Inhalanda

Inhalation preparations

Inhalation preparations are liquid or solid preparations destined for administration in the form of vapours, aerosols or very fine powders. For inhalations, only preparations with maximum size of dispersible particles of 10 μm may be used so that the substantial part enters into the inferior airways. Should the size be bigger, the particles adhere to the trachea and bronchial mucosa, do not penetrate as far as alveoli and cause additional irritation of airways. The size of aerosol particles depends from the apparatus used for the creation of aerodispersions and for their application.

They contain one or more therapeutic compounds dissolved or disperged in a suitable vehicle. Apart from that, inhalation preparations contain propelents (i.e. low-boiling point gases or liquids fluidized or compressed by pressure), solvents, antimicrobial admixtures in appropriate concentration, solubilizators or stabilizators. Adjuvants must not have adverse influence on the function of mucosas or cilias in the airways.

Inhalation preparations are delivered in multi- or single-dose containers. They are administered according to the type of preparation either with a nebulizer, dosing pressure inhalator or inhalator for dry powder.

Dosed pressure preparations for inhalation *(Inhalanda in vasis cum pressu doses emittentia)* are solutions, suspensions or emulsions delivered in special containers (pressure containers) provided with a dosing valve. They are kept under pressure with the help of suitable propulsive mixtures of fluidized propelents that can be solvent at the same time. Fluidized gases are for example halogenated hydrocarbons (especially fluorderivatives and hydrocarbons with low molecular weight (e.g. propane and butane). Compressed gases are for example carbone dioxide, nitrogen and nitrogen oxide. Suitable solvents and solubilizators may be added. The number of doses in the container is marked on the packing.

1.4. DRUG DOSING IN CHILDREN

Drug doses in suckling infants and children under 15 years of age can not be mechanically derived from doses for adults by mere translation in according to the child´s age with regard to physiological divergence in pharmacokinetics and reactivity to drugs in each age stage. Apart from age, also weight, body surface, individual susceptibility, health state and other abnormalities are important factors for calculation of drug doses in children.

The most reliable information on children doses is normally offered by the manufacturers in the enclosed instructions on bulk drugs. Should the pertinent information be missing in these instructions, estimation of a dose may be made with the help of one of the below stated methods. Doses of many drugs are not a simple linear function of body weight and age. In majority of drugs, it has been demostrated that younger the child, narrower the correlation of a child dose to the body surface area. That is why the body surface area is more appropiate and exact value to which a children dose should be related.

For calculation of a dose based on body surface area, we can use this formula:

$$\text{Approximate children dose} = \frac{\text{child's body surface area in m}^2}{1.73} \times \text{adult dose}$$

Child's body surface area in m^2 is determined either using nomograms (from child's body height and weight) or this empirical formula

$$\text{Child's body surface area in m}^2 = \frac{7 \times \text{age (years)} + 45}{100}$$

Obtained values correspond approximately to the data of Czech Pharmacopoeia.

Children doses calculated according to these formulas or stated in the Pharmacopoeia are decisive when prescribing and delivering drugs. Should the physician exceed them deliberately, he must indicate this fact in the prescription adding an exclamation mark (!) and stating the corresponding dose in letters similarly to the case of exceeding the maximum doses in adults. If the exceeding of a children dose is not indicated as required, the pharmacist will ask the physician to complete the prescription. Should the physician be unavailable, the pharmacist carries out the correction of the dose to a therapeutical one, confirming the modification with his signature and informing the doctor afterwards.

1.5. INSTRUCTIONS FOR PRACTICAL PREPARATION OF PHARMACEUTICAL DOSAGE FORMS

Solid pharmaceutical dosage forms preparation:

Divided powders for oral use

Prepare 5 gelatine capsules with paracetamol and caffeine according to the following instruction:

Rp.

Paracetamoli	*0,1*
Coffeini	*0,05*
Lactosi	*ad 0,3*

M. f. pulv.
D. t. d. No. V (quinque) ad caps. gelat.
S. When fever take 1 capsule, drink it down.

We calculate and weigh the drugs for the whole number of divided powders, mix thoroughly all the components in a china grinding mortar. We divide it in estimated 5 equal parts onto hard cards, performing a check weighing of at least two of them. The difference from the weight of 0.3 g must not exceed 10%. We fill the gelatine capsules with separate powders with the help of special equipment in the following way:

Capsule opening: We insert closed but still not locked capsules into the orifices of the panel No. 1 and, using a slight pressure, we introduce them to the level of inferior panels. Attention – the fixing screw No. 4 must be loose!

After settling the capsules we put the plexiglass lid on and fix it with the latch. We start tightening the screw so that the inferior parts of the capsules are fixed by a slight pressure. After that, we open the capsules elevating the panel No.1 with fixed lids.

Capsule filling and closing: We loosen the screw No. 4 and introduce with pressure the inferior parts of the capsules to the level of the panel No. 2. We retighten the screw. With a glass hopper and stick, we introduce separate doses of pills into the capsules. When filled, we totally loosen the screw No. 4, put on the panel No. 1 back again. We "close" the capsules with a uniform slight pressure of the base (inferior) panel against the panel No. 1.

We put the prepared capsules into a folder and provide the box with a prescription signature, preparation date and signature.

Preparation of semi-solid pharmaceutical dosage forms:

Rectal suppositories for children

Prepare 10 antipyretic suppositories for children with paracetamol according to the following instruction:

Rp.

Paracetamoli 0,1
Cacao olei q.s. ut f. supp. pro infant.
D. t. d. No. X (decem)
S. 3 times a day, insert 1 suppository into the rectum.

We calculate and weigh the total amount of paracetamol for 10 suppositories and desintegrate thoroughly in a china mortar. Afterwards, we weigh cocoa oil in a quantity necessary for the preparation of ten 1g suppositories into a stainless mortar and melt it under an infra-lamp. We do not overheat the melting as an overheated mass is difficult to solidify. In the meantime, we clean the suppository form with cotton-cellulose dipped in paraffin oil. We put paracetamol into the melting and while mixing continually we pour gradually the prepared suppository mass into the orifices so that 10 equal suppositories are made. We may accelerate the solidification of the suppositories introducing the form with the prepared supossitories into a refrigerator.

When the suppositories are solid enough, we remove them from the unscrewed form, eventually wrapping them with a cellophane film, and locate them into a jar provided with a white label with the prescription *signatura*.

Unguentum acidi borici

Prepare 50 g of unguent containing 10% of boric acid according to the following instruction:

Rp.

Acidi borici 5,0
Vaselini albi ad 50,0
M. f. ung.
D. S. Boric ointment. Spread on affected area 3 times a day.

We weigh the necessary amounts of both components, using a weighing foil for vaseline weighing. We melt the vaseline in a stainless mortar under an infra/lamp. After the base is melt, we gradually add into the melting boric acid, mixing continuously. We cool the mixture down to the room temperature, mixing continuously. We install the prepared unguent into a jar provided with a red label with prescription "signatura".

Unguentum leniens

Prepare a softening unguent according to the following instruction:

Rp.

Cerae albae	
Cetacei	*aa 5,0*
Helianthi olei	*35,0*
Ricini olei virginalis	*7,0*
Aquae purificatae	*10,0*
Citri etherolei	*gtts. III (tres)*

M. f. ung.
D. S. Hand-softening unguent.

We melt the first two components in a stainless mortar under an infra-lamp. In beakers, we weigh the prescribed quantities of oils and they are added to the melting. The melting is kept warm under the infra-lamp until the total melting of the mixture. We leave the pot with the melting totally solidify without mixing in a cold water bath. In the meantime, we warm a measured quantity of water in a beaker up to about 45 °C. Afterwards, the solidified mass is spread with the help of a spatula until it turns foam-like and white (consistence of thick whipped cream). Mixing continuously, we add warm water part by part. Finally, we admix 3 drops of aromatic oil. The finished unguent is separated into jars and marked with prescription *signatura* on a red label.

Pasta zinci oxidi

Prepare 50 g of zinc paste according to the following instruction:

Rp.

Zinci oxidi	
Tritici amyli	*aa 12,5*
Vaselini flavi	*ad 50,0*

M. f. pasta
Da ad ollam!
D. S. Zinc paste. Apply 2 times a day and bepowder.

We mix thoroughly the weighed amounts of zinc oxide and wheat-search in a melamine mortar. We weigh the yellow vaseline on a weighing foil and melt it in a metal pot under an infra-lamp. We add the solid components to the melted vaseline and we mix in a water bath until completely cooled. We put the finished preparation into a jar and provide it with a prescription *signatura* on a red label for external use.

Liquid pharmaceutical dosage forms preparation:

Jarisch solution

Prepare 100 g solution for compresses containing 2% of boric acid and 4% of glycerole according to the following instruction:

Rp.

Acidi borici	*2,0*
Glyceroli 85%	*4,0*
Aquae purificatae	*ad 100,0*

M. f. sol.
D. S. Jarisch solution.
For warm compresses two times a day.

Purified water is warmed in a beaker up to about 50 °C. We weigh the boric acid and melt it in warm water, after cooling down to the room temperature, glycerole is admixed. We filter the solution into a clear-glass vial, close with a stopper and provide with texture. The vial is marked with the prescription *signatura* on a red label.

Liquid powder

Prepare 50 g of liquid powder containing 0.5% of racemic menthol according to the following prescription.

Rp.

Mentholi racemici	*0,25*
Zinci oxidi	
Talci	*aa 7,5*
Glyceroli 85 %	*10,0*
Silicae colloidalis anhydricae 3%	*ad 50,0*

M. f. susp.
D. S. Liquid powder. Every 2 hour spread on the affected area.
Shake well before use!

We weigh the prescribed amount or racemic menthol and desintegrate it thoroughly in a mortar. In beakers, we weigh the necessary amount of glycerole and suspension of colloid waterless silicon dioxide ("Aerosil"). We add it gradually to the powder components, mixing continuously. We introduce the finished preparation into a jar providing it with a red label with the prescription *signatura*.

2. INTRODUCTION TO THE SPECIAL PRESCRIPTIONS OF INDIVIDUALLY PREPARED PREPARATIONS

The following text represents the introduction to the prescription of the IPP (individually prepared preparation) in three medical areas in which, beside the mass production, also the products made in a pharmacy on the basis of individual prescriptions are included. A special prescription will be treated in full within the scope of the relevant clinical subjects.

The brief notes to the individual chapters are to help an easier grasping of the significance of the individual medical substances and their combinations in the prescriptions. The common single therapeutic doses (DTS, *dosis therapeutica singula*) of the basic pharmaceuticals that appear in the prescriptions are stated. The doses are principally given in grams and their portions, this is why the „g" unit is not stated.

2.1. DRUGS IN CNS DISEASES

2.1.1. Hypnotics and sedatives

The prescription of hypnotics and sedatives today is almost exclusively represented by the RMP prescriptions. Only the herbal preparations with hypnosedative effects are sometimes prescribed in the IPP form. They are used in the form of species/tea or drops.

Herbal drugs and officinal preparations:

- **Valerianae radix – Valerian root; Valerianae tinctura – Valerian tincture** (*Valeriana officinalis* **–** Common Valerian)
- **Melissae folium – Balm leaf; Melissae herba – Balm herb** (*Melissa officinalis* – Lemon Balm)
- **Lupuli flos – hop flower** (*Humulus lupulus* – Hop)
- **Crataegi folium cum flore – hawthorn leaf with flower** (*Crataegus monogyna, laevigata* etc. – Common Hawthorn, Midland Hawthorn etc.)
- **Millefolii herba – milfoil herb** (*Achillea millefolium* **–** Milfoil or Yarrow)
- **Hyperici herba – tutsan toppings** (*Hypericum perforatum* **–** St. John's Wort)

Example of a tea mixture with sedative effects:

Rp.
Hyperici herbae
Melissae folii
Millefolii herbae
Valerianae radicis *aa 25,0*
M. f. species
D. S. 1 tablespoon of the mixture per teacup.
A cup of warm tea in the morning and in the evening.

Prescription of Valerian tincture:

Rp.
Valerianae tincturae *25,0*
Ad vitrum guttatum!
D. S. 20 drops 3 times per day

2.1.2. Psychostimulants

In the IPP form, only **caffeine** is prescribed, which helps excess fatigue, improves psychic activity and acts as a weak central analeptic (stimulates heart activity, blood circulation and breathing).

Coffeinum	orally	DTS	**0.05–0.25**
Caffeine	s.c. (subcutaneously), carefully i.v. (intravenously)	DTS	**0.05–0.1**

Note: Caffeine is only slightly soluble in water and therefore it can be prescribed in solid dosage forms. In liquid preparations, a bivalent caffeine salt *Coffeinum et Natrii benzoas* – caffeine with sodium benzoate is usually used, which is easily soluble in water.

Prescription of caffeine in gelatine capsules:

Rp.
Coffeini *0,1*
Lactosi *ad 0,5*
M. f. pulv.
D. t. d. No. X (decem) ad caps. gelat.
S. 1 capsule when tired, maximum 3 per day.

2.1.3. Analgesics

Opioid analgesics

This group's basic substance is **morphine** used as a strong and effective analgesic-anodyne. Most often it is prescribed in the injection form of RMP, but sometimes it is convenient to prescribe it in the form of an IPP (peroral preparations, rectal suppositories), especially for chronic pains of tumorous origin/in cancer etc. However, due to the high percentage of pre-system elimination (so-called "first pass effect"), the oral morphine therapy is sufficiently efficient only in dosages exceeding the common therapeutic doses recommended by Czech Pharmacopoeia and served in maximum 4–5 hour intervals (if it is not a RMP with sustained release).

It is a narcotic substance – while prescribing it, all the requirements of the valid legislation related to the prescription of narcotics and psychotropic substances must be met.

Morphini hydrochloridum trihydricum	i. v., i. m., s. c.	DTS	**0.005–0.02**
Morphine-hydrochloride trihydrate	orally	DTS	**0.01–0.02**
			(! and more)
	rectally	DTS	**0.015–0.03**

Morphine in syrup prescription:

Rp.
Morphini hydrochloridi trihydrici 0,6! (miligrammata sescenta)
Sirupi simplicis 20,0
Aquae purificatae ad 100,0
M. f. sol.
Ad lagenam fuscam
D. S. 1 teaspoon every 4 hours.

Prescription of morphine in suppositories:

Rp.
Morphini hydrochloridi trihydrici 0,03 (miligrammata triginta)
Massae pro supp. q. s. ut f. supp.
D. t. d. No. XX (viginti)
S. Insert 1 suppository before going to sleep

Analgesics – antipyretics

Substances from this group are prescribed for their analgesic effect mainly for ~~the~~ somatic and neuralgic pains –arthralgia, myalgia, inflammation pains, headache and toothache (they practically do not affect the visceral pain) and furthermore for the antipyretic effect – they reduce a pathologically increased temperature.

Aniline derivatives:

Paracetamolum	*p. o.*	DTS	**0.5–1.0**
paracetamol (acetaminophen)	*p. rect.*	DTS	**0.5**

At present, it is one of the most used and best accepted analgetics and antipyretics. It has not anti-inflammatory effects. It is the basic part of most analgetic and antipyretic

mixtures made as ready-made or individual preparations. It is only slightly soluble in water, Therefore it is prescribed only in solid (and semi-solid) pharmaceutical dosage forms.

Another aniline derivative with similar effects is the precursor of paracetamol **propacetamol**, prescribed only as a RMP.

Derivatives of the salicylic acid:

Acidum acetylsalicylicum	analgesic-antipyretic:	*p. o., rect.* DTS **0.5–1.0**
Acetyl salicylic acid	antirheumatic:	*p. o* DTS **1.0**; pro die **4.0–6.0**
	antiaggregans:	*p. o* DTS **0.06–0.1** (once per day)

Formerly a widely used analgesic and antipyretic; nowadays, its main indication is the antiaggregative, anti-inflammatory and antirheumatic therapy. The reason of its limited use is mainly the irritation of stomach mucous membrane with the risk of haemorrhage in the GIT, increased propensity to haemorrhage, hypoprotrombinemia, kidney disorders, frequent allergies, neurotoxicity, risk of the Rey syndrome in children. It is barely soluble in water and this is why it is not prescribed in liquid pharmaceutical dosage forms.

Natrii salicylas *p. o., i. v.* DTS **1.0–2.0**
sodium salicylate
Weak analgesic-antipyretic, rather an anti-inflammatory used mainly in the antirheumatic indication. Due to its easy solubility in water, it is prescribed in solutions for oral use.

Pyrazolone derivatives:

Substances of this group have strong antiflogistic, analgetic and antipyretic effects. Due to serious side effects (haematopoiesis disorders even to agranulocytosis, gastroduodenal ulcers, CNS irritation, interstitial nephritis, in aminophenazone even potential carcinogenity after oral administration) they are used as analgesics-antipyretics less often and only temporarily. More often we meet them in RMP with indications of antirheumatics and anti-gout drugs.

The main representatives of the group are: metamizole sodium salt **– Metamizolum natricum**, propyphenazone **– Propyphenazonum**, aminophenazone **– Aminophenazonum,** phenazone – **Phenazonum**. They are usually administered orally or in the form of suppositories, DTS **0,3–0,5**.

In IPP prescriptions we meet them only seldom, they are part of several ready made preparations analgetic-antipyretic mixtures (e.g. Algifen).

Other substances, adjuvants:

The effect of the basic substances from the analgetic-antipyretic group tends to be often potentiated in analgesic mixtures by an addition of a weaker opioid analgesic - codeine, as well as substances from other drug groups (psychostimulants, anxiolytics, neuroleptics etc.),

which have a weak or practically no analgesic effect alone, but in combination with the basic analgesics-antipyretics they intensify or potentiate their effects.

Codeini phosphas hemihydricus-codeine-phosphate hemihydrate *p.o*. DTS **0.015–0.03**
Coffeinum – caffeine *p.o*. DTS **0.05–0.25**
Diazepamum – diazepam *p.o*. DTS **0.002–0.005**
Ergotamini tartras – ergotamine--tartrate *p.o., rect.* DTS **0.001–0.003**
Guaifenesinum – guaifenesin *p. o*. DTS **0.1–0.2**
Chlorpromazini hydrochloridum – chlorpromazine-hydrochloride *p. o., rect.* DTS **0.025–0.1**
Levomepromazini hydrochloridum – levomepromazine-hydrochloride *p. o.* DTS **0.025–0.05**

Practical notes on the prescription of analgetic-antipyretic compounds:

1. Combinations of the basic analgesics-antipyretics from the above mentioned chemical groups are not rational – they have an identical mechanism of action (inhibition of COX), on the other hand they increase the risk of adverse drug reactions. The analgesic-antipyretic prescription should contain one basic active ingredient (preferably paracetamol) complemented with an adjuvant drug, e.g. codeine, caffeine etc.
2. Due to increased haematopoiesis disorder risk, we avoid combinations of derivatives of pyrazolone with phenothiazine neuroleptics (chlorpromazine, levomepromazine).
3. Formerly common usage of barbiturates as part of analgesic IPP and RMP compounds is irrational and obsolete; barbiturates do not increase the analgetic effect of the basic analgesics, they even decrease the effect of the salicylates, and may increase the paracetamol toxicity. As strong inductors of microsomal enzymes they accelerate their own metabolism as well as that of other drugs. Last but not least, they belong to the substances with an increased risk of drug addiction.

Examples of analgetic compounds prescription in the form of IPP:

Prescription of an analgesic compound on the basis of paracetamol in suppositories:

Rp.
Paracetamoli *0,5*
Propyphenazoni *0,25*
Coffeini *0,05*
Cacao olei q. s. ut f. supp.
D. t. d. No. XV (quindecim)
S. When in pain,-insert 1 suppository into rectum.

Prescription of an analgetic compound on the basis of Acetyl salicylic acid in capsules:

Rp.
Acidi acetylsalicylici *0,4*
Codeini phosphatis hemihydrici *0,02*
Coffeini *0,08*
M. f. pulvis
D. t. d. No. XX (viginti) ad caps. gelat.
S. When in pain, take 1 capsule, maximum 4-times per day.

Prescription of an analgesic compound for the therapy of an acute migraineous fit:

Rp.

Ergotamini tartratis	*0,002*
Paracetamoli	*0,3*
Coffeini	*0,1*
Codeini phosphatis hemihydrici	*0,01*

M. f. pulv.
D. t. d. No. XX (viginti) ad caps. gelat.
S. When in pain, take 1 pill, maximum 3 times per day.

Prescription of suppositories for the therapy of an acute migraineous fit:

Rp.

Ergotamini tartratis	*0,002*
Aminophenazoni	*0,3*
Coffeini	*0,1*
Diazepami	*0,005*

Massae pro supp. q. s. ut f. supp.
D. t. d. No. XX (viginti)
S. When in pain, insert1 suppository into rectum, maximum 3-times per day.

2.2. DRUGS FOR RESPIRATORY SYSTEM DISEASES

2.2.1. Antitussives

Antitussives alleviate cough either via a general attenuation of the relevant centre (**central antitussives**), or hinders reflectoric induction of cough on the periphery by covering the mucous membranes of the upper respiratory tract with a protective layer, which also acts as a suppressant on the mucosal nerve terminations (**mucilagines**). The central antitussives have rather limited indications in the common therapy, because they impede the purification of the bronchial mucous membranes and favour mucus retention. Therefore they are indicated only for the dry non-productive cough, e.g. the dry phase of bronchitis and pleuritis, and furthermore during an instrumental examination of air passages. They are not convenient for the acute bronchitis with increased bronchial secretion.

To relieve from irritating cough disturbing the sleep, there may well be applied the mucilaginous drugs (e.g. Ribwort Plantain – *Plantago lanceolata*, Mullein – *Verbascum phlamoides*, Marsh Mallow – *Althaea officinalis* – see chapter Expectorants), which have a calming and protective effects on the mucous membranes and therefore decrease the irritation to cough. It is not convenient to combine the central antitussives with expectorant substances, because the resulting effect may be evencontradictory. However, their combination with mucilaginous drugs is favourable.

Central antitussives

These are substances derived from the group of opioid analgesics, in which the selective inhibition of the cough centre is strongly predominant, and on the contrary, significantly inhibited is the analgetic effect as well as other opiate effects. In the IPP form, the most commonly prescribed drug is codeine. However, it has a limited use, mainly because the cough inhibition is associated with the disadvantageous decrease of bronchial recrement, depression of the breathing centre, release of histamine, and therefore with a susceptibility to bronchoconstriction.

It is better to use the non-codeine antitussives (butamirate, dropropizine etc.), which are spared from such undesirable effects. They are prescribed only as RMP.

Codeini phosphas hemihydricus *p.o.* DTS **0.015–0.03**
Codeine-phosphate hemihydrate

It is prescribed in oral solid and liquid pharmaceutical dosage forms. It is easily soluble in water.

Prescription of codeine in capsules (divided form):

Rp.
Codeini phosphatis hemihydrici 0,3
Lactosi ad 3,0
M. f. pulv.
Div. in dos. No. X (decem)
Ad capsulas gelatinosas!
D. S. In case of necessity 1 capsule, maximum 4 times per day.

Prescription of codeine with liquid Ribwort Plantain extract in drops:

Rp.
Codeini phosphatis hemihydrici 0,5
Plantaginis extracti fluidi 5,0
Aquae purificatae ad 20,0
M. f. sol.
Ad vitrum gutattum!
D. S. 20 drops 3 times per day.

2.2.2. Expectorants

Expectorants are drugs that facilitate the expulsion of accumulated bronchial secreta. They are administered when it is necessary to clear the mucous membrane and renew its function. In acute bronchitis, they are administered from the 3rd or 4th day when the mucus secretion phase begins to prevail over the original dry bronchitis phase. An important condition of the effective expectoration is a sufficient liquid supply.

Expectorants are divided into secretolytics, secretomotorics and mucolytics. **Secretolytics** increase the formation of tenuousmucus diluting the viscous secret. **Secretomotorics** accelerate the transport of secreta in bronchi and consequently their removal from the air passages. **Mucolytics** decrease the visco-elasticity of the bronchial secret, liquefying the clinging secreta through the change of its physical any chemical properties, most frequently through the fragmentation of fibrous molecules of sputum.

In expectorant compounds, there often appear also the substances with adjuvant effects, such as bronchodilators ($beta_2$ sympathomimetics), substances increasing the contractive capacity of diaphragm (partial effect of theophylline) and the so-called bronchial hypertonics, i.e. substances increasing the expiratory vigour (pilocarpine, partly ipeca preparations).

Secretolytics

These are substances of both herbal and synthetic origin that increase the secretion of tenuous serous or mucoserous secreta through a direct or indirect stimulation of bronchial glands. Most often there are represented the substances acting through a reflexive vagus mechanism stimulating afferent parasympathetic fibres in the gastric mucous membrane leading to the vomiting centre. From there, impulses are led through n. vagi toward bronchial glands which increase secretion. However, serous secretion increases simultaneously also in the salivary and lachrymal glands, and in the nasal mucosa, which may cause subjective troubles. While overdosed, nausea or even emetic effects occur, from which the "nauseous" expectorants name is derived. These are the reflexive effects of saponins, guaifenesin, preparations from ipecacuanha, and partly also salinic expectorants (potassium iodide, ammonium chloride etc.)

After being absorbed from the gastrointestinal tract, substances with a direct secretolytic effect are partially excreted through the lungs and they stimulate the bronchial glands to increased secretion. This is the stimulatory effect mainly of the essential oils and partly also the salinic expectorants (the excretion of ammonium and iodide ions by the bronchial mucous membrane after oral administration). The osmotic effect, the reduction of the surface tension of mucus etc. also have their share in the secretolytic effect of some vegetal substances.

Guaifenesinum –Guaifenesin p. o. DTS **0.2–0.3**

Synthetic substance from the anxiolytic group has a slight secretolytic effect. It is used in composite IPP and RMP preparations.

Saponins

Substances lowering the surface tension of the bronchial mucous membrane. Out of the officinal herbal drugs, there belong e.g.:

- **Primulae radix –** Primrose root (*Primula veris* or *P. elatior* – Cowslip, Oxlip),
- **Ononidis radix** – Restharrow root (*Ononis spinosa* – Spiny Restharrow).

Into herbal infusions for home preparation, also non-officinal drugs with saponin can be recommended: **herb of Hyssop** (*Hyssopus officinalis*); **root of Elecampane** (*Inula hellenium*) that has also a peripherally antitussive effect; **rhizome of Pimpernel** (*Pimpinella saxifraga*).

Herbal secretolytics acting mostly through a stimulatory mechanism:

- **Thymi herba** – Thyme herb; **Thymi extractum fluidum** – Thyme liquid extract (*Thymus vulgaris* – Common Thyme, Garden Thyme,
- **Anisi fructus** – Aniseed fruit; **Anisi spiritus compositus** – Aniseed spirit compound (*Pimpinella anisum* – Aniseed).

Salinic expectorants

This is a long-known group of substances causing an increased formation of tenuous secreta and reduction of mucus viscosity. They act through several mechanisms, out of which

the most significant one is the reflexive vagous one and direct stimulation of secretion of bronchial glands. They mostly release viscous secreta also from the lower air passages and smaller branches of the bronchial stem. They are prescribed only into solutionsfor oral use, the unpleasant taste is improved by syrups.

Kalii iodidum – potassium iodide, the most effective substance from the group. Due to the possible adverse drug reactions it is administered only for short terms. **DTS 0.3–0.5**

Natrii iodidum – sodium iodide has similar, but weaker effects than those of potassium iodide. It is prescribed mainly in the paediatric practice. **DTS 0.3–0.5** (up to 10 years of age 0.2)

Ammonii chloridum – ammonium chloride increases expectoration mainly through the reflexive mechanism of stomach mucosa irritation. Its effect is weaker than that of potassium iodide. It is a standard component of the classic expectorant compound „Mixtura solvens".

DTS 0.3–0.6

Ammonii bromidum – ammonium bromide, due to its unpleasant flavour, the least prescribed substance from this group. **DTS 0.3–0.5**

- A formerly popular drug prescribed in IPP form (syrup of ipecac) with a strong secretolytic effect used to be also the **Ipecacuanhae radix –** Ipeca root (*Cephaëlis ipecacuanha* – Ipecacuanha) belonging among the so-called nauseous expectorants (the active component alkaloid emetine). The ipeca root and the liquid ipecacuanha extract prepared from it – **Ipecacuanhae extractum fluidum normatum** and the ipecacuanha tincture – **Ipecacuanhae tinctura normata** belonged to the officinal pharmaceuticals.

Secretomotorics

These are substances accelerating the purification of the mucous membrane of the air passages of the accumulated secreta. The main action mechanism is the acceleration of the movement of ciliary epithelium in the large and medium bronchi; the substances acting through this mechanism are called 'ciliomimetics'. The movement of cilia is increased by salinic expectorants, $beta_2$ sympathomimetics and a number of vegetal substances. On the contrary, the inhibition of the cilia movements is caused by peppermint extracts (menthol), whose addition into expectorant mixtures in larger quantities usually lacks an effect.

Vegetal expectorants usually have a very complex influence on the air passages; beside the acceleration of the mucus transport, they act secretolytically, and also slightly as bronchodilators, antiseptics, they promote blood circulation in lung tissues, and through the content of mucilaginous substances they alleviate the irritation to cough.

Drugs with a predominantly secretomotoric effect:

- **Althaeae radix** – Marshmallow root; **Althaeae folium** – Marshmallow leaf; **Althaeae sirupus** – Marshmallow syrup (*Althaea officinalis* – Marsh Mallow),
- **Plantaginis folium** – Ribwort leaf; **Plantaginis extractum fluidum** – liquid extract of Ribwort;
  Plantaginis sirupus – Ribwort Plantain syrup (*Plantago lanceolata* – Ribwort Plantain),
- **Farfarae folium** – Coltsfoot leaf (*Tussilago farfara* – Coltsfoot).

Drugs with high contents of mucous substances (mucilaginous drugs – used also as the so-called peripheral antitussives):

- **Liquiritiae radix** – Liquorice root; **Liquiritiae extractum fluidum ethanolicum normatum** – ethanolic liquid extract of Liquorice (*Glycyrrhiza glabra* – Liquorice),
- **Verbasci flos** – Mulleins flower (*Verbascum phlamoides et densiforme* – Orange Mullein and Great Mullein).

As the main active substances in the IPP prescriptions there appear salinic expectorants with well proven efficacy. Other efficient substances are prescribed as adjuvants and there are different views of their therapeutic value. In acute viral respiratory inflammations, the expectorants in solutions for oral use can be combined with antipyretics and anti-inflammatory agents.

Prescription of expectorant mixture with potassium iodide and Plantain syrup:

Rp.

Kalii iodidi	*4,0*
Plantaginis sirupi	*30,0*
Aquae purificatae	*ad 150,0*

M. f. sol.
D. S. 1 spoon 4 times per day.

„Mixtura solvens“ with a strong expectorant effect:

Rp.

Ammonii chloridi	*4,0*
Liquiritiae extracti sicci	*6,0*
Aquae purificatae	*ad 100,0*

M. f. sol.
D. S. 1 spoon in hot tea or milk 3–4 times per day.

Prescription of expectorant-antitussive mixture with codeine and potassium iodide:

Rp.

Codeini phosphatis hemihydrici	*0,2*
Kalii iodidi	*3,0*
Anisi spiritus compositi	*10,0*
Aquae purificatae	*ad 100,0*

M. f. sol.
D. S. 1 teaspoon 3 times per day.

Prescription of aniseed mixture for children with Marshmallow syrup, benzoate and sodium salicylate:

Rp.

Anisi spiritus compositi	*2,0*
Natrii benzoatis	
Natrii salicylatis	*aa 1,0*
Althaeae sirupi	*30,0*
Aquae purificatae	*ad 100,0*

M. f. sol.
D. S. 1 teaspoon 4 times per day.

2.2.3. Antiasthmatics

Antiasthmatics sometimes still prescribed as IPP are pharmaceutical preparations designed for a maintainance state without the asthmatic fit. In the fit period, effective bronchodilatory and anti-inflammatory drugs are applied in the form industrially manufactured aerodispersions RMP – see Inhalanda 1.3.4.

Seldom prescribed individual preparations used orally between the fits contain bronchodilators acting through different mechanisms, furthermore adjuvant drugs from the expectorant, sedative and anxiolytic groups, in case of necessity also then antipyretics or antihistaminics.

Substances producing bronchodilatation

Beta-sympathomimetics: usually ephedrine-hydrochloride – **Ephedrini hydrochloridum**, DTS **0,02**.

Methylxantines: usually, aminophylline is prescribed – **Aminophyllinum**, DTS **0.25–0.5**. It is well soluble in water, suitable for both solid and liquid pharmaceutical dosage forms.

Bronchoconstriction blocking substances

Anticholinergics: pure atropine or other pure alkaloids are not used for bronchodilatation purposes due to undesirable drying the mucosa out, increasing of sputum viscosity and other unfavourable effects.

- In theory, a dispensatory extract from a dry standardised belladonna leaf can be prescribed as IPP**– Belladonnae folii extractum siccum normatum** – DTS **0.06** (**Belladonnae folium** – belladonna leaf, *Atropa belladonna* – belladonna lily); in practice, we do not encounter such an approach any more.

Antihistaminics: only in type of asthma with a documented histamine component, for example promethazine-hydrochloride – **Promethazini hydrochloridum**, **DTS 0.01–0.025** – can be used in IPP prescriptions.

Expectorants: **Kalii iodidum**, **DTS 0.3–0.5**; **Natrii iodidum**, **DTS 0.3–0.5**.

Sedatives, anxiolytics: **Diazepamum**, **DTS 0.002–0.005**; **Phenobarbitalum natricum –** phenobarbital sodium salt, **Phenobarbitalum –** phenobarbital; **DTS 0.02–0.05**.

Expectorant and anxiolytic:

Guaifenesinum, **DTS 0.15–0.3**.

Prescription of antiasthmatic preparation between attacks ~~fits~~ in a solution with aminophylline, phenobarbital sodium salt and expectorant additives:

Rp.

Aminophyllini	
Kalii iodidi	*aa 3,0*
Phenobarbitali natrici	*0,3*
Althaeae sirupi	*30,0*
Aquae purificatae	*ad 150,0*

M. f. sol.

D. S. 1 spoon 3 times per day.

Prescription of antiasthmatics with bronchodilatory components in capsules (suitable for the allergics):

Rp.

Ephedrini hydrochloridi	*0,025*
Aminophyllini	*0,25*

M. f. pulv.
D. t. d. No. XX (viginti) ad caps.
S. In case of problems, 1 capsule, maximum 3 times per day.

Prescription of antiasthmatics with bronchodilatory and antiallergic components in solution:

Rp.

Aminophyllini	*5,0*
Kalii iodidi	*10,0*
Ephedrini hydrochloridi	*0,5*
Anisi spiritus compositi	*6,0*
Aquae purificatae	*ad 250,0*

M. f. sol.
D. S. 1 spoon maximum 3 times per day.

2.3. DRUGS FOR DIGESTIVE SYSTEM DISEASES

2.3.1. Amara, stomachics

These are herbal medicines with characteristic of bitter taste. After ingestion in the form of drops, they arouse reflexive increase of gastric secretion; they promote appetite and improve digestion. They are used only in short-term treatment; during a long-term usage they gradually lose effect. The effect can rather be expected in younger patients with preserved secretory capacities of the gastric mucosa than in persons with atrophic changes in GIT associated with achlorhydria.

Herbal drugs contain either pure bitter principles (amara pura, stomachica) or they contain also other digestive substances that increase the blood circulation in the gastric mucosa and promote also the formation of bile (cholekinetic effect). The latter group includes amara aromatica – aromatic bitter principles (e.g. wormwood topping), amara acria – sharply irritant bitter principles (e.g. cinnamic essence), amara adstringentia – adstringent bitter principles (e.g. condurango bark), amara mucilaginosa – mucoid bitter principles (coltsfoot leaf, liquorice root).

Amara pura – pure bitter principles:

- **Gentianae radix** – gentian root (*Gentiana lutea* – Great Yellow Gentian)
- **Centaurii herba** – centaury herb (*Centaurium erythraea* – Common Centaury)
- **Cinchonae cortex –** Peruvian bark (*Cinchona pubescens* – Bark tree)

Amara aromatica – aromatic bitter principles:

- **Absinthii herba –** wormwood herb (*Artemisia absinthium* – Absinthe Wormwood)
- **Millefolii herba –** yarrow herb (*Achillea millefolium* – Common Yarrow)

- **Aurantii dulce pericarpium** – sweet orange pericarp (*Citrus aurantium* – Bitter Orange)

Officinal **Tinctura amara** – bitter tincture contains bitter principles from the yellow gentian root, topping of common wormwood, sweet orange pericarp, leaf of marsh trefoil (Trifolii fibrini folium) and cinnamic essence (Cinnamomi etheroleum).

Prescription of the bitter tincture:

Rp.
Tincturae amarae *20,0*
D. S. 20 drops half an hour before meal.

2.3.2. Acidificants

Hypoacidity with dyspeptic problems is partly adapted by the administering of **Acidum hydrochloricum 10%** – hydrochloric acid 10%. It is not a true substitution (the amount of the acid added is too small), but in the acid environment the peptic activity of pepsin and gastric motility increases.

Rp.
Acidi hydrochlorici 10% *50,0*
D. S. 10–20 drops in a glass of water, to be drunk with a straw during the meal.

2.3.3. Antacids

Substances from this group achieve to lower acidity of the gastric contents, mostly by the neutralization of HCl, the increased pH in the stomach then leads to the inactivation of pepsin. Some substances (RMP containing the aluminium compounds) also balance the bile acids or act as cytoprotectives. They are administered during problems or as prevention between meals and before bedtime.

In therapy, the so-called non-systematic antacids are preferred (magnesium aluminate – **Magnesii aluminas**, aluminium phosphate – **Aluminii phosphas hydricus**, light magnesium oxide – **Magnesii oxidum leve**, calcium hydrogen phosphate – **Calcii hydrogenophosphas** and other complex compounds. These antacids are poorly resorbable and act for a longer time. They are prescribed mostly as RMP (e.g. MAALOX por. tbl. mnd., por. sus.).

The so-called systemic antacids are absorbed into the circulation and may cause general adverse effects caused mainly by release of carbonic acid (e.g. metabolic alkalosis after a long-term administration of sodium bicarbonate), this is why they are administered only in single or short-term treatment to manage acute problems. The substances belonging among these resorbable – system antacids, calcium carbonate – **Calcii carbonas** and sodium bicarbonate – **Natrii hydrogenocarbonas,** are sometimes prescribed as IPP. Better properties are typical of magnesium hydroxide – **Magnesii hydroxidum** ("milk of magnesia"), which has a fast and longer-lasting effect, it is resorbed from the GIT only in a small extent and acts also as a light purgative. In the indication group of antacids, also the so-called "covering mixtures" can be added that are used for the inhibition of acidic secretion and protection of stomach mucosa (mucoprotection) to alleviate peptic ulcer problems.

Prescription of antacid mixture in divided powders:

Rp.
Magnesii oxidi levis
Natrii hydrogenocarbonatis aa 0,5
M. f. pulv.
D. t. d. No. XX (viginti)
Ad chartas!
S. While experiencing problems, 1 powder in 1 dl of water. At maximum 6 times per day.

Prescription of mucoprotective so-called "covering" mixture for hyperacidity and peptic ulcer:

Rp.
Codeini phosphatis hemihydrici 0,015
Calcii carbonatis
Calcii hydrogenophosphatis aa 0,4
M. f. pulv.
D. t. d. No. XXX (triginta) ad caps. gelat.
S. 1 capsule 3 times per day.

2.3.4. Spasmolytics

A group of substances from several pharmacological groups, used to relieve from painful spasms of digestive tract's smooth muscles, biliary and urinary tract. The spasmolytic effect is reached either through the blockade of parasympathetic receptors (parasympatholytics or cholinolytics, also called **"neurotropic" spasmolytics**) or through a direct effect on the smooth muscle cell, e.g. by increasing the intracellular concentration of cAMP by blocking phosphodiesterasis (the so-called. **"musculotropic" spasmolytics** of the papaverine type).

A positive effect on hypertony and hyperkinesis in the digestive tract area, especially in irritant colon, is brought by substances acting through other mechanisms, e.g. trimebutin (antagonist of enkephaline receptors) or pinaverine (blocker of Ca^{2+} channels in the smooth muscles of digestive tract), prescribed only as RMP.

In the IPP, the combination of several effects is used frequently, mainly in neurotropic and musculotropic spasmolytics. To reinforce the analgesic effect in the renal and biliary colic, but also in spastic migraine and dysmenorrhoea, analgesics are added into spasmolytic mixtures (paracetamol, propyphenazone, codeine). The preparations are then called spasmoanalgesics.

Parasympatholytics (neurotropic spasmolytics):

Atropini sulfas monohydricus – atropine sulfate monohydrate p. o. **DTS 0.0005–0.001**

Belladonnae folii extractum siccum normatum p. o., rect. **DTS**
– dry standardized extract from belladonna leaf **0.03**

Scopolamini hydrobromidum trihydricum
– scopolamine hydrobromide trihydrate p. o. **DTS 0.0003**

Musculotropic spasmolytic:

Papaverini hydrochloridum – papaverine hydrochloride p. o., rect. **DTS 0.05–0.1**

Prescription of spasmolytic mixture in capsules:

Rp.

Atropini sulfatis monohydrici 0,0005
Papaverini hydrochloridi 0,05
Lactosi ad 0,4
M. f. pulv.
D .t .d. No. XV (quindecim) ad caps. gelat.
S. When experiencing problems, 1 capsule, 2 times per day at the most.

Prescription of spasmoanalgesic in capsules:

Rp.

Paracetamoli 0,5
Codeini phosphatis hemihydrici 0,015
Papaverini hydrochloridi 0,05
M. f. pulv.
D. t. d. No. XX (viginti) ad caps. gelat.
S. When in pain, 1 capsule, 4 times per day at the most.

Prescription of spasmoanalgesic in suppositories:

Rp.

Codeini phosphatis hemihydrici 0,02
Papaverini hydrochloridi 0,06
Atropini sulfatis monohydrici 0,0003
Cacao olei q.s. ut f. supp.
D. t. d. No. XX (viginti)
S. When in pain, insert 1 suppository into rectum, 3 times per day at the most.

2.3.5. Carminatives, deflatulents

Substances releasing painful tensions in the enterocoele and facilitating the exit of intestinal gases include mainly silicons (e.g. simethicone), which are not absorbed from the GIT and cause an increase of surface tension of liquids in the lumen of digestive tract. They are prescribed exclusively in the form of RMP (e.g.: ESPUMISAN por. cps. mol, LEFAX por. sus.).

Similar effects are carried by essential herbal drugs, which positively affect impairments involving excessive formation of gases in colon (meteorism, flatulency). Most of them have slight spasmolytic (antispasmodic) and local anaesthetic effects.

Examples of carminative drugs:

- **Anisi fructus –** anise fruit, **Anisi etheroleum** – Anise essential oil (*Pimpinella anisum* – Pimpernel Anise),
- **Carvi fructus –** Cumin fruit, **Carvi etheroleum –** Cumin essential oil (*Carum carvi* – Caraway, Persian cumin),
- **Foeniculi dulcis fructus –** Sweet Fennel fruit, **Foeniculi etheroleum –** Fennel essential oil (*Foeniculum vulgare* – Fennel),
- **Chamomillae romanae flos** – flower of Roman Chamomile (*Chamaemelum nobile* – Roman Chamomile),
- **Menthae piperitae herba** – herb of Peppermint, **Menthae piperitae folium** – peppermint leaf, **Menthae piperitae etheroleum** – Peppermint essential oil (*Mentha piperita* – Peppermint),

- **Caryophylli flos –** Clove flower, **Caryophylli etheroleum** – essential oil of Clove (*Eugenia caryophyllus* – Clove*).*

Aqueous solution of the above essences with ethanol ingredient, tinted and flavoured with simple sirup is called **Aqua carminativa rubra – Red flatus water:**

Rp.
Aquae carminativae rubrae 150,0
D. S. 3 times per day 1 tablespoonful after the meal.

2.3.6. Cholagogs

The function of gall-bladder and efferent bile ducts are favourably influenced by substances boosting bile formation – choleretics – and accelerating the emptying of gall-bladder – cholekinetics. Clinically more significant group are choleretics including firstly the synthetic substances prescribed as RMP (hymecromon, fenipentol and choleic acid – e.g. RMP Isochol, Febichol), as well as the officinal herbal drugs with cholagogue effects:

- **Agrimoniae herba – sicklewort tops** (*Agrimonia eupatoria* – Common Agrimony, Sicklewort),

Taraxaci radix cum herba – Dandelion root with herb (*Taraxacum officinale* – Common Dandelion),

- **Boldo folium –** Boldo leaf (*Peumus boldus* – Boldo),
- **Frangulae cortex –**Buckthorn bark (*Rhamnus frangula* – Alder Buckthron),
- **Marrubii herba** – Horehound herb (*Marrubium vulgare* – Common Horehound), a j. They are used in the form of tea mixtures.

2.3.7. Laxatives

Medicaments facilitating the expulsion of excreta through various mechanisms. Volume laxatives (e.g. methyl cellulose, some herbal drugs) increase the volume of stool and accelerate intestinal peristalsis, for optimum effect, sufficient intake of liquids is necessary, at least 2 litres per day. Osmotic laxatives (salinic laxatives, i.e. non-absorbable sodium and magnesium salts, glycerol 85%) bind water in the intestinal lumen and consequently stimulate the mucosa to higher secretion of water and electrolytes. **Softening agents** include mineral oils (**Paraffinum liquidum** – liquid paraffin), swelling agents (Agar-agar, Linseed – **Lini semen**), in water they form colloid solutions increasing the intestinal content, and **Glyceroli suppositoria** – glycerol suppositories. These are hydrophylic suppositories containing sodium carbonate decahydrate, stearid acid, glycerol 85% (84–87 % of total content) and purified water. Nowadays, they are prescribed only as RMP – SUPPOSITORIA GLYCERINI LÉČIVA rct. sup.

Contact laxatives belong to the strongest laxatives, acting through direct irritation of colon mucosa, and it is not possible to administer them in long term due to risk of intestinal motility disorders. Synthetic contact laxatives are derivatives of the formerly used phenolphthalein (e.g. bisacodyl), prescribed only as RMP. Herbal contact laxatives are contained in the following drugs, from which a tea mixture or extract are prepared:

- **Sennae folium –** Senna leaf, **Sennae angustifoliae fructus** or **Sennae acutifoliae fructus** – fruit of Alexandrian Senna (*Cassia senna angustifolia* or *acutifolia*),
- **Rhei radix** – Rhubarb root (*Rheum palmatum* or *Rheum officinale* – Chinese Rhubarb),

- **Rhamni purshianae cortex** – Purshian Buckthorn bark (*Rhamnus purshianus* or also *Frangula purshiana*),
- **Ricini oleum virginale –** Virgin Castor oil or **Ricini oleum hydrogenatum** – hydrogenated Castor oil, i.e. powdered or coagulated virgin Castor oil (*Ricinus communis* – Castor Oil Plant) rates among the so-called drastic laxatives and is administered by teaspoons.

Salinic laxatives: In the IPP form, mainly salinic laxatives are prescribed **Natrii sulfas –** sodium sulfate (Glauber salt) and **Magnesii sulfas heptahydricus –** magnesium sulfate heptahydrate (bitter salt); a weak laxative effect is attributed also to **Magnesii oxidum leve** – light magnesium oxide. They are prescribed in the form of non-divided powder – then they are administered principally in a glass of lukewarm water (effect in 3–5 hours), magnesium sulfate heptahydrate also in the form of 20–25% aqueous solution.

Prescription of 20% solution of magnesium sulfate heptahydrate – "bitter salt":

Rp.
Magnesii sulfatis heptahydrici 20,0
Aquae purificatae ad 100,0
M. f. sol.
D. S. 1–2 tablespoonfuls in the morning on empty stomach, wash down well with water.

Prescription of fluid paraffin:

Rp.
Paraffini liquidi 100,0
D. S. 1–2 times a day 1 table spoonful.

Prescription of officinal glycerol suppositories:

Rp.
Glyceroli suppositorii 2,35
D. t. d. No. V (quinque)
S. In the morning insert 1 suppository into the rectum.

2.3.8. Antidiarrhoics

The therapy of diarrhoea always requires a good knowledge of the cause. The substances slowing down the intestinal passage and putting off defecation have only an auxiliary significance in the therapy of diarrhoea and they are indicated in cases of otherwise unmanageable diarrhoeas (opioids, e.g. **Codeini dihydrogenophosphas**, **Ethylmorphini hydrochloridum**), is strong hypermotility and spasticity of the intestinal tract (neurotropic and musculotropic spasmolytics), in excessive secretion of water and electrolytes through the intestine mucosa (adstringents, e.g. tannin). They are never administered in cases of alimentary intoxications and diarrhoeas of infectious origin. Also in the course of cure by these preparations, it is necessary to take heed of a sufficient intake of liquids and electrolytes. Antidiarrhoics are prescribed predominantly in the form of RMP.

Intestinal adsorbents

In toxoinfectious diarrhoeas and alimentary intoxications, the first choice drug is **Carbo activatus** – activated carbon (also known as adsorbent or medicinal carbon or animal charcoal). It is an inert substance with large surface and therefore a high adsorbent capacity. It has a slight

constipation effect, which can be treated with salinic laxatives. It is prescribed in the form of RMP (e.g. CARBOSORB por. plv. sol.) or as IPP – in non-divided powder form. It is administered in the dosage of 2–3 g several times a day, preferably in aqueous suspension.

Prescription of activated carbon with sodium sulfate as non-divided powder:

Rp.
Carbonis activati *40,0*
Natrii sulfatis *ad 50,0*
M. f. pulv.
D. S. Every 3–4 hours 2 teaspoonfuls in a glass of lukewarm water.

2.4. DERMATOLOGICS

In dermatological indications, the pharmaceutical dosage forms used are liquid, solid and semi-solid, the general characteristics of which was described in detail above in chapter 1.3. The following chapter represents the basic dermatological IPP, which will be taught in full within field of study Dermatology.

SOLUTIONS

The form of drugs often used is the aqueous, alcoholic (ethanolic) or alcohol-aqueous solution, often made with an addition of glycerol. They are designated for spreading, compresses or baths.

Aqueous solutions are applied in the form of airy compresses (in an open form, without tying) in acute drippy and pustular (pemphoid) processes, to segregate crusts or to purify fistulas and ulcerations. The evaporation of the fluid base has a cooling effect; adstringent ingredients diminish the oozing and help to renew the barrier function of the skin. Fomenting compresses are applied on inflammatory and bounded oedematous symptoms.

The solutions prescribed for antiseptic, antibacterial and anti-inflammatory effect often contain **Acidum boricum** – boric acid in 2–3% solution ("boric water"; however, its antimicrobial effect is disputable, because *in vitro* it does not sufficiently inhibit the growth of microbes), or in the so-called Jarisch´s solution – **Solutio Jarisch**, also **Kalii permanganas** – potassium permanganate (popular name "potash“) used in pink-coloured solution.

- A popular compress agent is also the home-made infusion (infusum) of **Chamomillae romanae floris** – Chamomile flower (*Chamaemelum nobile* – Roman Chamomile), but the number of chamomile-allergic patients increases.

As adstringent agents inhibiting exudation of drippy surfaces, the following substances are prescribed: **Tanninum** – tannin 1–3 %, **Argenti nitras** – silver nitrate 0.5–1 %. The officinal **Aluminii acetotartratis solutio** – solution of acetate and tartrate of aluminium, known as the Burrow's solution, has a strong adstringent effect. It is usually diluted for usage in 1:10 ratio.

The prescription of the Jarisch´s solution containing 2 % of the boric acid and 4 % of glycerol in aqueous basis without an antimicrobial admixture:

Rp.
Acidi borici *20,0*
Glyceroli 85% *40,0*
Aquae purificatae *ad 1000,0*
M. f. sol.
Sine antimicrobico!
D. S. For preparation of warm compresses.

Note: The Jarisch solution prescribed in the form of an officinal preparation (Solutio Jarisch) contains an antimicrobial additive, usually 0.1% methylparaben, which however is not desirable for sensitive skin.

Prescription of potassium permanganate („potash“) for home preparation of solution for compresses or baths:

Rp.
Kalii permanganatis *10,0*
D. S. A few grains in warm water to prepare a light pink solution for compresses (bath).

Prescription of 3% aqueous solution of tannin for compresses:

Rp.
Tannini *15,0*
Aquae purificatae *ad 500,0*
M. f. sol.
Ad lagenam fuscam
D. S. For compresses. Expired on the day 3!

Prescription of 1% aqueous solution of silver nitrate for compresses, e.g. for the treatment of varicose ulcers:

Rp.
Argenti nitratis *10,0*
Aquae purificatae *ad 1000,0*
M. f. sol.
Ad lagenam fuscam
D. S. For compresses.

Prescription of aluminium acetate and tartrate solution (Burrow´s solution):

Rp.
Aluminii acetotartratis solutionis *500,0*
D. S. Dissolve 1 part in 9 parts of water. For compresses.

To disinfect small wounds and surface scratches, or to disinfect mucous membranes, a 3% diluted solution of hydrogen peroxide – **Hydrogenii peroxidum 3%** is used:

Rp.
Hydrogenii peroxidi 3% *100,0*
Ad vitrum fuscum
D. S. For disinfection of small wounds.

Alcoholic solutions are prescribed mainly for their antiseptic effect, but they also cause cooling, desiccation and defatting of skin. Alcohol and glycerol contained in the liquid basis also increase the solubility of some components hard to dissolve in water, mainly organic dyes, iodine or salicylic acid.

Salicylic acid – **Acidum salicylicum** is hard to dissolve in water, easy to dissolve in alcohol. It has an antiseptic effect in 1–5% concentration and is the basic component of the so-called "salicylic spirit".

Iodine – **Iodum** disposes of reliable antiseptic effect. In IPP, it is used in several forms. The so-called "iodine tincture" is an ethanolic solution of iodine containing 6.5 % of free iodine and 2.5 % of potassium iodide of 95% ethanol – **Iodi solutio ethanolica**.

Out of the iodine preparations, there is also the officinal aqueous solution of iodine, the so-called Lugol's solution containing 1 % of free iodine and 2.5 % of potassium iodide – **Iodi solutio aquosa**, glycerol solution of iodine ("Iodine-glycerine") – **Iodi solutio glycerolica** designated for mucosa spreading, and an aqueous solution of iodoxamer – **Iodoxameri solutio aquosa**.

For inflammatory and infectious diseases, a complex of iodine and povidone – **Povidonum iodinatum**, is used as an antiseptic of the oral cavity and pharynx, prescribed most often in the RMP form of Jodisol and Jox preparations in solution and spray.

The antiseptic effect of the so-called "gentian-violet", with dispensatory description methylrosanilinium-chloride **– Methylrosanilinii chloridum**, is used in the officinal as well as individually prepared alcohol-aqueous and aqueous 0.5–2% solutions. According the Pharmacopoeia, the officinal are **Methylrosanilinii chloridi solutio 0.5%** (aqueous solution) and **Methylrosanilinii chloridi solutio 2%** (alcohol-aqueous solution). Alcoholic solution of methylrosanilinium-chloride is also prescribed in a mixture with glycerol 85% due to its antiseptic effect on the mucosa of the oral cavity – see chapter 2.5.

Prescription of 2% alcoholic solution of salicylic acid – "salicylic spirit":

Rp.
Acidi salicylici *2,0*
Ethanoli 60% *ad 100,0*
M. f. sol.
D. S. For spreading.

Prescription of alcoholic solution of iodine for disinfection:

Rp.
Iodi solutionis ethanolicae *20,0*
D. S. For treatment of areas around wounds.

Prescription of 1% alcohol-aqueous solution of methylrosanilinium chloride ("gentian-violet"):

Rp.
Methylrosanilinii chloridi *1,0*
Ethanoli 60% *10,0*
Aquae purificatae *ad 100,0*
M. f. sol.
D. S. For spreading on skin.

DUSTING POWDERS

Particles of these powders increase the skin's surface and cause its cooling and calming. Dusting powders are indicated in acute skin inflammations without symptoms of oozing, in itching affections, and on wet souring where they decrease attrition of clinging surfaces and support evaporation.

The active components of the dusting powders may have antiseptic, anti-inflammatory, adstringent or cooling effects (see liquid powders). Indifferent powders contain only the powder bases without active substances, they are used for powdering-out of pastes for drying and mechanic protection of the skin.

Prescription of indifferent dusting powder:

Rp.
Zinci oxidi
Talci *aa ad 100,0*
M. f. pulv. adspers.
D. S. Dusting powder.

Prescription of dusting powder with 5% ichthamol:

Rp.
Ichthammoli *2,5*
Zinci oxidi
Talci *aa ad 50,0*
M. f. pulv. adspers.
D. S. Dusting powder.

LIQUID POWDERS

Liquid powders have a cooling, covering and calming effect, especially on itching skin affections and strongly irritant skin surfaces. The antipruritic effect is reached by means of drowning the itching feeling in a feeling of a different quality, usually through an intensive cooling of the skin. The cooling feeling caused by the mere evaporation of water from the base can be accentuated by adding 60% ethanol – **Ethanolum 60% (**formerly Spiritus dilutus), forming usually 10–20 % of the total volume. The cooling feeling is increased also by the admixture of racemic menthol – **Mentholum racemicum** 0.5–1.0%. Other used curing components are: ichthamol – **Ichthammolum** 3.0–5.0% (mixture of ammonia salts os sulfonic acids acquired from tar containing organically bound sulfidic sulphur), coal-tar – **Lithanthracis pix** 3.0–5.0%, naphtol – **Naphtholum** (formerly Beta-naphtholum) 0.5–1.0%. **Acidum salicylicum** 2–5% (incompatible with zinc oxide; there is a possibility of precipitation of zinc salicylate and degradation of the mixture).

Indifferent adjuvant substances used in the liquid powders are stated in the general part – chapter 1.3.3.

Prescription of antipruritic liquid powder with 0.5 % of menthol:

Rp.

Mentholi racemici	*0,5*
Zinci oxidi	
Talci	*aa 15,0*
Bentoniti	*3,0*
Ethanoli 60%	*10,0*
Glyceroli 85%	
Aquae purificatae	*aa ad 100,0*

M. f. susp.
D. S. Liquid powder. Shake well before use.

PASTES

Pastes are used for the therapy of subacute and chronic skin diseases, such as eczemas, fungal diseases etc. There are used eiher water-washable pastes (e.g. RMP with Aquasorb) or non-washable ones (base of Vaselinum album or Vaselinum flavum, Adeps suillus, Synderman). After daubing on the skin they are usually bepowdered with indifferent dusting powder.

The officinal zinc paste – **Zinci oxidi pasta** containing zinc oxide, wheat starch and yellow vaseline in ratio 1 : 1 : 2 can be prescribed as indifferent washable paste, or the officinal zinc paste containing 50 % of ZnO – **Zinci oxidi pasta 50%**. Officinal are also the zinc paste with 2% salicylic acid – **Zinci oxidi pasta salicylata** and soft zinc paste – **Zinci oxidi pasta mollis**, consisting of 30% zinc oxide in the base made from lanalcol ointment and sunflower oil.

The "zinc oil" is prescribed as IPP – it is a mixture of equal portions of zinc oxide and sunflower oil, used for its cooling and drying effects in the cure of irritant dermatoses. For the treatment of oozy surfaces it can be combined with Jarisch´s or Burrow's solutions.

Beside the **Acidum salicylicum** 2–10%, the active components of pastes are often also **Lithanthracis pix** 3-5-10% (e.g. in the "Pix paste"), **Ichthammolum** 3-5%, **Cloroxinum** 5%.

Among the soft pastes with anti-inflammatory, calming and adstringent functions, there belongs **Magnesii hydroxidum colloidale** – colloidal magnesium hydroxide, which is available as RMP Polysan pst. It is commonly prescribed in a mixture together with an equal portion of sunflower oil (produced also in RMP Polysan cum oleo helianthi). It is applied on 1st grade burns, solar dermatitis, intertrigo etc.

Prescription of indifferent non-washable paste with a base containing lard and Synderman:

Rp.

Zinci oxidi	
Talci	*aa 15,0*
Adipis suilli	
Syndermani	*aa ad 100,0*

M. f. pasta
D. S. Paste. Apply in a thin layer and powder it.

Prescription of indifferent washable paste with a base containing Aquasorb:

Rp.
Zinci oxidi
Talci *aa 7,5*
Aquasorbi *ad 100,0*
M. f. pasta
D. S. Paste. Apply in a thin layer and bepowder it.

Prescription of non-washable paste with 5 % of coal-tar – "Pix paste":

Rp.
Lithanthracis picis *5,0*
Acidi salicylici *2,0*
Zinci oxidi
Talci *aa 15,0*
Syndermani *ad 100,0*
M. f. pasta
D. S. Paste. Apply in a thin layer and bepowder it.

OINTMENTS (UNGUENTS)

They are designated to treat chronic both inflammatory and non-inflammatory skin processes; on the contrary, they worsen acute and subacute inflammations. Ointments significantly decrease water evaporation and heat removal from the skin surface. Active agents from ointments penetrate slowly, but deep in the cutis layers.

Active substances in unguents are usually **Acidum salicylicum** acting in the concentration of 2 – 5% as antiseptic, antiseborrhoeic and keratoplastic, but in the 10–20% concentration as significantly keratolytic; **Acidum boricum** acting as mild disinfection in 5–10% concentration, and accelerating the epithelization of wounds; **Lithanthracis pix** 3–5–10% for chronic eczemas. Examples of oleo-ointments used often in dermatology (the way of use will be treated within the field of dermatology):

Prescription of officinal boric ointment 10% containing the boric acid and white vaseline:

Rp.
Acidi borici unguenti 10% *100,0*
D. S. Ointment.

Prescription of the so-called borargent ointment with 1 % of silver nitrate:

Rp.
Argenti nitratis *1,0*
Aquae purificatae *1,0*
Acidi borici unguenti 3% *ad 100,0*
M. f. ung.
D. S. Ointment.

Prescription of ointment with 2 % salicylic acid and lard:

Rp.
Acidi salicylici
Ricini olei virginalis *aa 2,0*
Adipis suilli *ad 100,0*
M. f. ung.
D. S. Ointment for hairy parts of the head.

Prescription of Andrew's ointment to treat child dermatitis, intertrigo etc.:

Rp.

Acidi salicylici *1,0*
Lavandulae etherolei Syndermani *2,0*
Vaselini albi *aa ad 100,0*
M. f. ung.
D. S. Andrew's ointment.

Camphoric ointment for treatment of varicose ulcers:

Rp.

Camphorae racemicae *5,0*
Acidi borici unguenti 3% *ad 100,0*
M. f . ung.
D. S. Camphoric ointment for varicose ulcers.

Pharmacopoeia allows the prescription of other officinal composite ointments and creams as well as high-quality bases for ointments and creams. The officinal 10% salicylic ointment – **Acidi salicylici unguentum** (10% of salicylic acid in yellow vaseline) is used for a single removal of corneous cutis layer (keratolytic effect). As officinal oleo-ointments, for instance, the ichthamol ointment – **Ichthammoli unguentum** and the composite ointment with fish oil – **Jecoris aselli unguentum compositum** are often used. Among the officinal oleo-creams, excellent characteristics are provided e.g. by the cooling cream – **Cremor refrigerans**.

2.5. PRESCRIPTION OF IPP IN OTORHINOLARYNGOLOGY

OTOLOGICS (AURICULARIA)

As IPP are prescribed drugs for the therapy of surface affections of the external auditory canal, for restriction of cerumen recrement and softening and removal of cerumen.

The softening of cerumen is done chiefly by instillation of 3% hydrogen peroxide – **Hydrogenii peroxidum 3%** heated to body temperature, and furthermore by various oils, e.g. by liquid paraffin – **Paraffinum liquidum**, or a solution consisting of the same proportion of glycerol 85% and ethanol 96%. To restrict the cerumen secretion a 3% solution of boric acid in ethanol 85 % (formerly Spiritus concentratus) is used.

Solution for softening of a cerumen plug:

Rp.

Glyceroli 85%
Ethanoli 96% *aa ad 10,0*
M. f. sol.
Ad vitrum guttatum.
D. S. Ear drops.

Solution for restricting the formation of cerumen:

Rp.
Acidi borici *0,6*
Ethanoli 85% *ad 20,0*
M. f. sol.
Ad vitrum guttatum.
D. S. Ear drops. Instil once in 3–5 days.

Otorhinolaryngology as well as stomatology sometimes use the so-called **Bonain's anaesthetic solution** (as a preparation for paracentesis, it is introduced onto the eardrum on a small tampon for 5–10 minutes). Phenol – Phenolum gently cauterises the corneous layer on the eardrum and facilitates an easier penetration of the local anaesthetic (cocaine – opiate!) into the depth.

Rp.

Cocaini hydrochloridi *2,0 (grammata duo)*
Phenoli
Mentholi racemici *aa 2,0*
Epinephrini tartratis sol. 1:1000 gtts. XV (quindecim)
M. f. sol.
D. S. Solutio Bonain.
Ad usum medici.

In lighter inflammatory affections of the external auditory canal the ear drops of the following composition are used:

Rp.

Acidi borici *1,5*
Acidi salicylici *0,25*
Ethanoli 96 % *15,0*
Aquae purificatae *ad 50,0*
M. f. sol.
Ad vitrum guttatum.
D. S. Ear Drops. Instil 3 times per day.

RHINOLOGICS (NASALIA)

To treat diseases of the nose and lateral nasal sinuses, sometimes also in olfactory dysfunctions, nasal drops are used. They contain antiseptics, anti-inflammatory agents, substances for decongestion of the nasal mucosa, for restriction of secretion and softening of dried secreta, aromatic admixtures for release of breathing passages in cases of head-cold.

To decongest the nasal mucosa, the nasal drops containing ephedrine-hydrochloride – **Ephedrini hydrochloridum** at the concentration of 0.5–1.0% are mostly used. In IPP prescriptions sometimes also naphazoline-nitrate 0.05–0.1% – **Naphazolini nitras** is contained.

For antiseptic effects, **Acidum boricum** 3% or sodium tetraborate – **Natrii tetraboras** 2% are prescribed, furthermore also carbethopendecinium-bromide **– Carbethopendecinii bromidum** 0.02–0.05% and a complex compound of silver proteinate with diacetyltannin, i.e. diacetyltannin albuminate of silver – **Argenti diacetyltannas albuminatus** 4–6%. Sterile purified water – Aqua purificata sterilisata is mostly used as the vehicle in nasal drops prescriptions. To increase viscosity of the solution, polymers are added, e.g. Carmellosum natricum – sodium carmelosa (the sodium salt of carboxymethylcellulose).

A convenient combination of antiseptically and vasoconstrictivelly acting drops are the officinal nasal drops with boric acid (3 %) and ephedrine-hydrochloride (1 %) in purified water – **Acidi borici rhinoguttae cum ephedrino**.

Prescription of nasal drops with adstringent and antiseptic effect:

Rp.

Argenti diacetyltannatis albuminati 1,0
Carmellosi natrici 0,4
Aquae purificatae sterilisatae ad 20,0
M. f. sol.
Ad vitrum guttatum.
D. S. Nasal drops. Instil 3 times per day.

Prescription of the so-called "blue nasal drops" with antiseptic and vasoconstrictive effect (blue colour is caused by the antiseptic methylthionine chloride hydrate):

Rp.

Carbethopendecinii bromidi 0,01
Ephedrini hydrochloridi 0,2
Methylcellulosi 0,4
Natrii chloridi 0,174
Foeniculi etherolei gtt No. I
Methylthioninii chloridi hydrici sol. 1% q.s.
Aquae purificatae sterilisatae ad 20,0
M. f. sol.
D. S. Blue nasal drops. Instil 3 times per day.

Prescription of nasal drops with Menthol and Eucalyptus essential oil:

Rp.

Mentholi racemici 0,1
Eucalypti etherolei 0,2
Helianthi olei ad 20,0
M.f. sol.
D. S. Nasal drops.

OROPHARYNGOLOGICS

Drugs used for local therapy of inflammatory, mycotic and other diseases of the oral cavity and pharynx are applied in the pharmaceutical dosage forms of solutions for spreading, spraying, gargling or rinsing. Adstringents, antiseptics, anti-inflammatory agents and mucolytics are most often contained in the preparations.

Herbal tinctures with adstringent effect are prescribed as adstringents, such as.:

- **Ratanhiae tinctura** – Rhatany tincture (*Krameria triandra* – Peruvian Rhatany, drug *Ratanhiae radix* – Rhatany root),
- **Gallarum tinctura –** Oak Gall tincture (*Quercus infectoria* – oak; *Galla* – Oak Gall, dried oak spangle forming on the oak buds after being punctured to host eggs of insect *Cynips tinctoria),*
- **Myrrhae tinctura –** Myrrhic tincture.

Infusions made from Salvia and Tormentil are also often used:

- **Salviae herba** – Sage herb or **Salviae officinalis folium** – Sage leaf and also **Salviae tinctura** – Sage tincture (*Salvia officinalis* – Common Sage),
- **Tormentillae tinctura** – Tormentil tincture and infusion from **Tormentillae rhizoma** – Tormentil rhizome (*Potentilla erecta* – Tormentil; infusion from the rhizome is used also internally as a strong antidiarrhoic).

Anti-inflammatory effect is used in the infusion made from the blossom of Roman chamomile – **Chamomillae romanae flos**, often in combination with **Salviae officinalis folium**. To make use of the active ingredients in chamomile, a standardized liquid extract from the chamomile flowers is used in various indications still more often rather than an infusion from the drug.

For antiseptic effects and cure of aphthae in the oral cavity, aqueous or alcohol-aqueous solutions of organic dyes are prescribed for both children and adults, such as the officinal solutions of gentian-violet (methylrosanilinium-chloride) **– Methylrosanilinii chloridi solutio 0,5% seu 2%** or the solution of methylene blue (methylthioninium-chloride hydrate) – **Methylthioninii chloridum hydricum 1–2%** (see also chapter 2.4.), usually with glycerol 85% (10 % of volume).

The disinfecting effect of **Hydrogenii peroxidum 3%** – solution of hydrogen peroxide 3 % and **Formaldehydi solutio 35%** – solution of formaldehyde 35% is used, e.g. in the so-called "Kutvirt gargling water". Antiseptic and deodorant effects are shown by **Natrii benzoas** – sodium benzoate, **Natrii perboras** – sodium perborate and **Natrii tetraboras** – sodium tetraborate.

Viscous and sticky mucous secretion is favourably affected by the mucolytic **Natrii chloridum** – sodium chloride, **Natrii hydrogenocarbonas** – sodium bicarbonate as well as the aforementioned sodium benzoate – **Natrii benzoas**.

- To relieve swallowing difficulties in pharyngitis, **Lini semen** – Linseed (*Linum usitatissimum* – Common Flax) and other mucilaginosa have proven beneficial.

A convenient component of preparation for the spreading of oral mucosa is **Glycerolum 85%** – glycerol 85%.

Prescription of the mixture of tinctures with adstringent effect:

Rp.
Ratanhiae tincturae
Gallarum tincturae
Myrrhae tincturae *aa ad 30,0*
M. f. sol.
D. S. For oral cavity treatment.

Prescription of the so-called "Borax-glycerol" for oral cavity mucosa spreading in case of candidosis:

Rp.
Natrii tetraboratis decahydrici *5,0*
Glyceroli 85% *ad 50,0*
M. f . sol.
D .S. Apply on the affected sites several times a day.

Prescription of gargling water according to Kutvirt – "gargarisma Kutvirt“ (2 portions of racemic menthol, 5 portions of rhatany tincture, 10 portions of formaldehyde 35% solution, ethanol 85%):

Rp.

Mentholi racemici	*1,0*
Ratanhiae tincturae	*2,5*
Formaldehydi solutionis	*5,0*
Ethanoli 85%	*ad 50,0*

M. f. sol.
D. S. Kutvirt's gargle.
20 drops in a glass of lukewarm water to gargle.

Prescription of a salty gargle (Salia aromatisata pro gargarismate, „4 Na“) in undivided powder:

Rp.

Natrii benzoatis	
Natrii chloridi	
Natrii perboratis	
Natrii hydrogenocarbonatis	*aa 25,0*
Menthae piperitae etherolei	*0,5*

M. f. pulv.
D. S. On the tip of a knife, to be dissolved in a glass of lukewarm water for gargling.

2.6. PRESCRIPTION OF IPP IN SURGERY

Recipes of IPP in surgery tend to be rather rare and include mainly disinfectants, antiseptics, drugs accelerating wound-healing and contused injuries, and liniments for immobile and long-lying patients.

For superficial disinfection of smaller injuries, disinfection of wound surroundings and operation area, beside the bulk preparations containing carbetopendecinium-bromide, benzethonium-chloride, benzododecine-bromide, the prescribed iodine compounds stated in chapter 2.4 or organic dyes may use the IPP.

For disinfective and tectorial effects in superficial wounds and smaller surgical interventions, the preparation **"Solutio Novikov"** is traditionally used. Beside the adstringent and anti-inflammatory tannin and ricine (castor) oil, it contains the non-officinal components Viride brillans (brillant green) and Collodium elasticum (Elastic collodion), which are available in pharmacies often as IPP:

Rp.

Viridis brillantis	*2,0*
Ethanoli 85%	*2,0*
Tannini	*5,0*
Collodii elastici	*ad 200,0*

M. D. S. Solutio Novikov.
Ad usum medici.

In septic inflammations in arthral surgery and dentistry, the so-called **Chlumsky solution** is used, containing phenol and racemic camphor in ethanol basis:

Rp.

Phenoli	*30,0*
Camphorae racemicae	*60,0*
Ethanoli 96%	*ad 100,0*

M. f. sol.
D. S. Chlumsky solution.
Ad usum medici.

For short-term therapies of contusive injuries and to speed up the healing process, it is possible to use the **Vishnevsky balm** (there are several variants). Its main component is the Peruvian balm – **Balsamum peruvianum** 20%, which is a balm obtained from the Myroxylon (*Myroxylon balsamum*) bark; it is well-soluble in virgin ricine (castor) oil **– Ricini oleum virginale**, which is therefore prescribed as a vehicle. The Peruvian balm easily sensibilizes the skin, therefore it is not used in a long run or repeatedly. Another component of the prescription is the non-officinal bismuth tribromphenolate – **Bismuthum tribromphenolas**, called "Xeroform".

Prescription of the Vishnevsky balm:

Rp.

Balsami peruviani	*20,0*
Bismuthi tribromphenolatis	*5,0*
Ricini olei virginalis	*ad 100,0*

M. f. susp.
D. S. Balm Vishnevsky.
Shake well before use!

Example of liniment for long-lying patients:

Rp.

Camphorae racemicae	
Mentholi racemici	
Polysorbati 80	*aa 10,0*
Ethanoli 96%	*100,0*
Aquae purificatae	*ad 1000,0*

M. f. sol.
D. S. Liniment, apply several times a day.

2.7. LOCAL ANAESTHETICS

Local anaesthetics produce local anaesthesia by means of reversible blockade of impulse transmission through sensitive neurons. Anaesthesia is done for the most part by RMP of local anaesthetics in convenient concentration with a vasoconstrictive vehicle or without it. Individual preparation of local anaesthetics comes into consideration in substances that are not available as bulk drugs (e.g. **cocaine**, **tetracaine**) or in concentrations of the RMP. Another reason for prescribing them in the form of IPP may be the sensibility of the patient to the content of preservatives (e.g. methylparaben, propylparaben, chlorhexidine), which are always present in commercially produced anaesthetic solutions.

Individual local anaesthetics

Clinically, amide type substances (**trimecaine**, **lidocaine**, **articaine**, **bupivacaine** etc.) are used more often these days, less often it is so with anaesthetics of ester nature (**cocaine**, **procaine**, **tetracaine**, **benzocaine**). The individual anaesthetics have a varying effect intensity, we divide them into the weak (**procaine**, **benzocaine**), medium (**trimecaine**, **lidocaine**, **mepivacaine**, **prilocaine**) and strong (**tetracaine**, **bupivacaine**, **ropivacaine**, **articaine**) groups. They are divided also according to the duration of action (e.g. procaine has a short action; trimecaine, lidocaine, articaine have action of medium length; tetracaine, bupivacaine, ropivacaine have a long action). Local anaesthetics are made in hydrochloride salts.

Substances usable for individual preparation of local anaesthetics solutions:

Trimecaini hydrochloridum – trimecaine-hydrochloride (original Czech substance – RMP Mesocain) is a basic amide anaesthetic with medium action and universal usage for various kinds of anaesthesia. Usable concentrations: anaesthesia of mucosa 4 %, cornea 1-2 %, infiltration 0.5–1 %, field block 1–2 %. It is used also for prevention and therapy of ventricle arrhythmias (1% solution without epinephrine). It is very similar to lidocaine-hydrochloride, **Lidocaini hydrochloridum**.

Procaini hydrochloridum – procaine-hydrochloride. Classic local anaesthetic, less used these days. As an ester derivative of *p*-aminobenzoic acid, it often causes allergies. It is suitable for injection anaesthesia and vagosympathetic blocks, not for surface anaesthesia, because it has not sufficient penetration into deeper skin and mucosa layers. Usable concentrations: infiltration anaesthesia 0.5–1 %, field block 1–2 %, spinal anaesthesia 4–5 %, vagosympathetic Vishnevsky block 0.25 %.

Tetracaini hydrochloridum – tetracaine-hydrochloride. It is a rather toxic ester derivative of *p*-aminobenzoic acid, designated only for the surface anaesthesia of mucous membranes in 1% (max. 2%) concentration.

Cinchocaini hydrochloridum – cinchocaine-hydrochloride (also dibucaine-hydrochloride). Highly efficient, but also very toxic derivative of amide-type chinoline with strong and long-term effect, used for surface anaesthesia only.

Cocaini hydrochloridum – cocaine-hydrochloride. Natural alkaloid with strong and short anaesthetic effect on mucous membranes. Due to its high toxicity and addiction risk (narcotic substance!) it is not available as the RMP. Usable concentrations: cornea anaesthesia 2–5 %, mucous membranes anaesthesia 5–10 % (max. 1 ml).

Other local anaesthetics are only prescribed as RMP.

Vasoconstrictive admixtures

Vasoconstrictive substances with $alfa_1$-sympathomimetic effect are often added to local anaesthetic solutions. Local vasoconstriction has several purposes: it prolongs and intensifies the effect of anaesthetics, limits haemorrhage from the operational field and at the same time diminishes the acute toxicity of anaesthetics by limiting their absorption from the site of application into system circulation. Vasoconstrictive substances are either already contained in commercial preparations or they are added to anaesthetic solutions under aseptic conditions right before use.

The most often used admixture is **Epinephrini tartras** – **epinephrine tartrate** (adrenaline) in the concentration of 1 : 100 000 to 1 : 200 000. In practice, the commercial 0.1% aqueous solution of epinephrine-hydrochloride (1 : 1000) is usually used for these purposes, in the Czech republic it is RMP ADRENALIN LÉČIVA inj. sol., 1 ampoule = 1 mg in 1 ml. For practical reasons, in IPP prescription the dosage of this epinephrine solution for the individual types of local anaesthesia is determined in number of drops per 10 ml of anaesthetic:

Eye and mucosa anaesthesia	10 drops per 10 ml
infiltration anaesthesia	1 drop per 10 ml
field blocking	5 drops per 10 ml

Note: admixture of epinephrine can be dangerous in areas supplied by terminal arteries (fingers, penis, auricle) – risk of ischaemic gangrene!

Beside epinephrine, it is also possible to use **Phenylephrini hydrochloridum** – phenylephrine-hydrochloride or **Naphazolini hydrochloridum** – naphasoline-hydrochloride for vasoconstriction. In dentistry, a synthetic vasopressin derivative deprived of an antidiuretic effect, e.g. ornipressin, can be used as a vasoconstrictive agent. In any of the vasoconstrictive admixtures, the maximum dosage given in the Pharmacopoeia must not be exceeded.

LOCAL ANAESTHESIA TECHNIQUES

Topical – surface anaesthesia

This is anaesthesia of mucous membranes of the nose, mouth, throat, eye cornea, lower air passages, oesophagus or genitals via the direct administration of anaesthetics in miscellaneous pharmaceutical dosage forms (solution, gel, ointment) onto the site of action. It is impossible to use procaine for this.

Surface anaesthesia of eye cornea

It is done by repeated instillation of anaesthetics solution (about 3 times 1 drop in intervals of 30–60 seconds) into the conjunctival sac. In IPP prescription, it is possible to use 1–2% solution of trimecaine-hydrochloride, or 2–5% solution of cocaine-hydrochloride. Due to small content of the applied anaesthetics, vasoconstrictive admixture is not usually added.

Example of 2% trimecaine-hydrochloride solution prescription in the form of IPP:

Rp.

Trimecaini hydrochloridi	*0,2*
Aquae pro iniectione	*ad 10,0*

M. f. oculoguttae
Ad vitrum guttatum!
D. S. Cum formula. Ad usum medici.

Surface anaesthesia of nasal and rhinopharynx mucosa

It is done by rubbing with a swab or brush dipped in an anaesthetics solution or by means of a sprayer, where there is, however, a danger of system toxicity in case of the solution running down the pharynx. In IPP prescription, there appears 4% solution of trimecaine-hydrochloride, rarely also 5–10% solution of cocaine-hydrochloride or 1% solution of tetracaine-hydrochloride.

A vasoconstrictive admixture is always necessary, most often it is epinephrine-tartrate (Epinephrini tartras 1 : 1000) in proportion of 10 drops per 10 ml.

Example of prescription of 4% trimecaine-hydrochloride solution with epinephrine-tartrate in form of IPP:

Rp.

Trimecaini hydrochloridi 0,4
Aquae pro iniectione ad 10,0
Epinephrini tartratis 1 : 1000 gtts. No. X (decem)
M. f. sol. sterilis
D. t. d. No. X (decem) ad ampullas
S. Cum formula. Ad usum medici.

Eutectic mixture of local anaesthetics (EMLA)

For small dermato-surgical interventions and painless venipuncture in children, it is possible to use 5% mixture of lidocaine and 5% prilocaine in ointment basis (they form an eutectic mixture, i.e. a mixture the melting point of which is lower than the melting point of its components). The substances penetrate well into the skin, anaesthetize the cutis to the depth of approx. 15 mm. The condition of a sufficient effect is the coverage of the ointment with an occlusal plaster bandage and a sufficient action length: 1–4 hours.

Infiltration anaesthesia

Anaesthetics are usually injected in the subcutaneously, intradermally or intramusculary (e.g. sport accidents, lacerated wounds, before suture in obstetrics etc.). Sterile isotonic anaesthetic solutions are used, e.g. 0.5–1% trimecaine-hydrochloride (less often 0.5–1% procaine-hydrochloride) with vasoconstrictive admixture (epinephrine-tartrate 1 : 1000 in proportion of 1 drop per 10 ml). It is necessary to respect the disproportionately increasing toxicity of anaesthetics when using higher concentrations.

Trimecaine and procaine can be prescribed as a RMP either with commercial names (Mesocain 1% and 2% inj.) produced in various volume packagings (80–500 ml). The commercial preparations do not contain the vasoconstrictive admixture, epinephrine-tartrate in the relevant concentration is added usually before application (applied also for field blocking).

Example of prescription of 0. 5% procaine-hydrochloride solution with epinephrine-tartrate in the form of IPP:

Rp.

Procaini hydrochloridi 0,4
Aquae pro iniectione ad 80,0
Epinephrini tartratis 1:1000 gtts. No.VIII (octo)
M. f. sol.
D. t. d. No. XX (viginti)
Ad vitrum pro iniectione
S. Cum formula. Pro ordinatione.

Note.: A special form of infiltration anaesthesia is **regional intravenous anaesthesia**, when the anaesthetic is applied into previously depleted (emptied of blood) venous system of a limb ligated with a tourniquet.

Field blocking anaesthesia (block of nerve trunks)

- **Peripheral nerve blocks:** To block the individual nerves, a small amount of anaesthetics is injected into the vicinity of peripheral nerve or the nerve trunk in approximately double concentration than that in infiltration anaesthesia. The effect is fast and the duration is long. On the contrary, while **blocking the nervous bundles** (plexus brachialis, lumbosacralis), a large amount of anaesthetics in lower concentration is applied into the immediate proximity of the nerve trunks. The onset of the effect is slower.

For peripheral blockade, **1%–2% trimecaine-hydrochloride** or **procaine-hydrochloride solutions** can be used. It is necessary to adhere strictly to the admissible volume of the applied solution with regards to the intoxication risk, the volume should never exceed 10–20 ml. It is always necessary to add the vasoconstrictive admixture, epinephrine-tartrate 1 : 1000 is usually used, in the proportion of 5 drops per 10 ml of solution.

Form of prescription is similar to the infiltration anaesthesia.

In the following example, the prescription is given of **procaine-hydrochloride in 2% concentration with epinephrine-tartrate field blocking anaesthesia (peripheral block) in the form of IPP** (in this concentration is not produced as a RMP):

Rp.

Procaini hydrochloridi 0,2
Aquae pro iniectione ad 10,0
Epinephrini tartratis 1:1000 gtts. No. V (quinque)
M. f. sol.
D. t. d. No. XX (viginti) ad ampullas
Sterilisetur!
S. Cum formula.
Ad usum medici.

- **Central nervous blocks** (high field blocking) are carried out by means of solutions with a similar concentration of anaesthetics as the peripheral blocks. The onset of action is slower and lasts for a medium to very long period of time, in consonance with the substance used. It can be the **paravertebral anaesthesia** (administration of anaesthetics to the outlets of spinal nerve roots from the spinal channel) or the **epidural anaesthesia** (administration of anaesthetics into the epidural space in the caudal or thoracic section in the spinal channel). In the epidural anaesthesia, vasoconstrictive admixture is not added as it does not influence the anaesthetics absorption rate.

- In **subarachnoidal (spinal) anaesthesia** the trunks of spinal nerves are blocked by application of several ml of local anaesthetics at a higher concentration into the subarachnoidal space. The solutions need not to be isotonic, by using hypo- or hyperbaric solution and positioning of the patient it is possible to reach anaesthesia in the necessary area (high, medium, low or sellar anaesthesia). Vasoconstrictive admixture is not added. The absorption of anaesthetics is very slow, the duration of the effect is short, medium or long, depending on the choice of the substance used.

2.8. PRESCRIPTION OF IPP IN OPHTHALMOLOGY

Ocularia – eye preparations

In ophthalmology, mainly drug forms for surface application in conjunctival sac (eye drops– **Oculoguttae**, eye waters (lotions) – **Aquae ophthalmicae**, eye ointments – **Unguenta ophthalmica**) are used to reach the highest possible concentration of the medical substance at the site of action. Specific application ways are also used, such as subconjunctival injected application in cases when the local therapy is not sufficiently effective (e.g. for antiinfection drugs, mydriatics, corticosteroids), sometimes even intraocular injections. Ocularia contain substances with antiseptic, anti-inflammatory, antimicrobial or antiviral, adstringent, mydriatic or miotic effect, they also serve as optical diagnostics, or for protection of conjunctiva from desiccation and for eye humectation.

In acute catarrhal conjunctivitis drops and ointments with antiseptic and antiflogistic effect are applied, in chronic conjunctivitis and blepharoconjunctivitis adstringents are used. Both of these drug groups are often combined in preparations with vasoconstrictive (anemisin) substances – epinephrine-tartrate 0.1% or ephedrine-hydrochloride 0.5–1%; however, epinephrine can not be combined with silver salts due to epinephrine's fast decomposition (chemical incompatibility).

Antiseptics

Antiseptics used in ophthalmology act through various mechanisms bacteriostatically to bactericidally. They are used in conjunctivitis therapy, for eye tranquillisation after removal of foreign particles, for irrigation after searing with acids or lyes and the next step after the previous thorough irrigation with water, for compresses in inflammatory illnesses of eyelids (blepharitis, hordeolum), in conditions after extraction of corneal corpuscles. In ointment form they are suitable for traumatic injuries to eyelids.

In RMP, quarternary ammoniac salts are used most often as ophthalmic antiseptics, e.g. **Carbethopendecinii bromidum –** carbethopendecine-bromide (RMP: OPHTHALMO-SEPTONEX gtt. ophth., ung. ophth.) or **Benzododecinii bromidum** – benzododecine-bromide component of RMP: - OPHTHAL liq. ophth).

In IPP prescription, complex organic silver compound appears often: silver diacetyl-tannin albuminate – **Argenti diacetyltannas albuminatus,** „targesin“ in 2% eye drops or silver nitrate – **Argenti nitras** in 0.25–0.5% aqueous solution.

Prescription of 0.5% eye drops with silver nitrate:

Rp.

Argenti nitratis	*0,05*
Aquae pro iniectione	*ad 10,0*

M. f. oculoguttae
Ad vitrum guttatum!
D. S. Eye drops. 3 times a day 1–2 drops into each eye.

Very light or disputable antiseptic effect in usable concentrations is assigned to **Acidum boricum –** boric acid, often used separately as well as in combined preparations. Officinal preparations **Acidi borici aqua ophthalmica** – eye water with boric acid (the so-called ophthalmic "boric water") or **Acidi borici oculoguttae** – eye drops with boric acid are sterile

isotonic 1.65–1.75% solutions of boric acid (H_3BO_3) with thiomersal as antimicrobial ingredient.

Prescription of officinal eye water with boric acid for eye irrigation:

Rp.
Acidi borici aquae ophthalmicae 150,0
D. S. For eye rinsing.

Officinal borax eye drops with boric acid – **Natrii tetraboratis oculoguttae cum acido borico** (solution of 0.25% sodium tetraborate in ophthalmic boric water with antimicrobial ingredient thiomersal), also called boric eye drops, have antiseptic as well as adstringent effects.

Adstringents

The basic agent of the group is **Zinci sulfas** – zinc sulfate, which has slight adstringent and (according to some authors, disputable) antiseptic effect. It is zinc salt well soluble in water, used in 0.1–0.25% concentration (Attention: do not interchange with zinc oxide – Zinci oxidum, which is not soluble in water and is used in dusting powders). The zinc eye drops can be broken down as IPP or officinal eye drops with zinc sulfate can be prescribed: "zinc eye drops" – **Zinci sulfatis oculoguttae**, containing beside 0.25% zinc sulfate also 1.62 % boric acid and 0.03 % sodium tetraborate with antimicrobial agent thiomersal.

Prescription of IPP zinc eye drops with vasoconstrictive admixture epinephrine-tartrate:

Rp.
Zinci sulfatis 0,025
Aquae pro iniectione ad 10,0
Epinephrini tartratis 1 : 1000 gtts. No. X (decem)
M. f. oculoguttae. Ad vitrum guttatum!
D. S. Every 3 hours instil into both eyes.

Mydriatics and cycloplegics

Substances dilating the pupil and at the same time inducing temporary cycloplegia, i.e. paralysis of the ciliary muscle with disqualification of accommodation, used in examination of the eyeground (**diagnostic mydriatics**). Mydriatics and cycloplegics can also serve for the cure of intraophthalmic inflammations (**therapeutic mydriatics**). The suppression of accommodation is favourable also in cases of iridocyclitis where accommodation causes pain.

Therapeutic mydriatics act long and are used in iridocyclitis therapy for long-term dilation of the pupil to prevent adhesions of the iris with the lens (posterior synechia) and for calming of sore iris; they are often combined with phenylephrine in 10 % solution (in children and cardiacs 2.5 %). A representative of the IPP prescribed therapeutic mydriatics is atropine-sulfate monohydrate **– Atropini sulfas monohydricus** used in eye drops with 0.5–1% **c**oncentration, the effect lasts for 3–7 days. The scopolamine-hydrobromide trihydrate – **Scopolamini hydrobromidum trihydricum** in 0.1–0.25% solution acts for a shorter time (effect about 24 hours). Both these substances, atropine and scopolamine, can be used also in eye ointments in equal concentrations.

Diagnostic mydriatic homatropine-hydrobromide – **Homatropini hydrobromidum** in 1% concentration serves only to simplify the examination of the eyeground, it acts briefly (several hours) and more weakly.

Prescription of eye drops with 1% homatropine-hydrobromide:

Rp.
Homatropini hydrobromidi 0,1
Aquae purificatae sterilisatae ad 10,0
M. f. oculoguttae
Ad vitr. gutt.
D. S. Eye drops. 1–2 drops into both eyes.
*Sub signo veneni!**

Miotics (Antiglaucomatics)

These are substances used earlier to cure glaucoma of the open angle, diminishing the intraocular pressure by narrowing the pupil and thus improving the outflow of the intraocular fluid through the trabecular tissue. These are substances from the parasympathomimetic group, the most common of which in IPP prescription is pilocarpine, less often it is physostigmine. Pilocarpine-hydrochloride – **Pilocarpini hydrochloridum** is prescribed in drops 1–3% (officinal **Pilocarpini hydrochloridi oculoguttae** are 1% or 2%), the offset of the effect is usually within 15 minutes and only lasts for 3–4 hours; pilocarpine in the form of ophthal gel is applied usually for night, the effect then lasts for up to 24 hours after application. Physostigmine-salicylate – **Physostigmini salicylas** is prescribed in 0.1–0.25% eye ointment rather than in solutions. In IPP it can be combined with pilocarpine.

Prescription of eye drops with miotic effect (pilocarpine-hydrochloride 3%, physostigmine-salicylate 0.25%):

Rp.
Pilocarpini hydrochloridi 0,6
Physostigmini salicylatis 0,05
Aquae purificatae sterilisatae ad 20,0
M. f. oculoguttae
Ad vitr. gutt.
D. S. Eye drops. 2 drops 3 times a day into the right eye.
*Sub signo veneni!**

Prescription of eye ointment with miotic effect (physostigmine-salicylate 0.2 %):

Rp.
Physostigmini salicylatis 0,02
Unguenti ophthalmici simplicis ad 10,0
M.f. oculentum
Adde bacillum!
D.S. Eye ointment. Apply nightly into the right conjuctival sac.
Sub signo veneni!

* Note: It is advisable to equip the solutions of very efficient substances, used here as mydriatics and miotics, with a "Poison Label" with direction "*Sub signo veneni!*", because those are generally very efficient substances (Venena) in high concentration, and in accidental use intoxication might occur. The designation of preparation with a “Poison Label” is not a duty of pharmacy. Transient evidences

of slight intoxication can sometimes be caused by atropine in 1% concentration even after local application into eye, especially in small children and elderly.

Pharmaceuticals used for lack of tears

The lack of tears or some of their component (aqueous, mucous or lipidic) can be cured only with big difficulties. Tears can be substituted with an aqueous solution of minerals (e.g. **Ringer's solution**), which however must be applied in very short intervals. Therefore, substances increasing viscosity are added into preparations designated for a therapy of conditions with lack of tears: e.g. hypromellose **– Hypromellosum**. To protect the conjunctiva from drying out and to humidify the eye, there is e.g. the officinal **Oculoguttae viscosae isotonicae** – viscous isotonic eye drops containing 0.5 % hypromellose, 0.9 % of sodium chloride with antimicrobial ingredient of carbethopendecinium-bromide, so-called "artificial tears").

Pharmaceuticals used in ophthalmology for diagnostic purposes

Fluorescein natrium salt **– Fluoresceinum natricum** 0.5–2% and **Bengal red** (**Roseum bengalense natricum** 2%, non-offic.) are used for diagnostic procedures, e.g. while examining a disturbed cornea with damaged epithelium. Fluorescein is used also in aplanatic tonometry. Bengal red is suitable for affection of conjunctiva epithelium. Both substances are prescribed only in the IPP eye drops.

Adjuvant pharmaceuticals in ophthalmology

For cornea damages of different etiology, adjuvants are used to support metabolic and resorption processes in the eye. Resorption process in the eye (resorption of exsudate, small haemorrhage etc.) is accelerated for example by isotonic solutions of inorganic iodine salts (e.g. the officinal **Kalii iodidi oculoguttae**). The effect mechanism is allegedly incumbent on the release of histamine, which causes vasodilatation. Even bigger anabolic effect on the cornea cells is elicited by androgenes or synthetic anabolics. Their general disadvantage is the insolubility in water, which is why salts of their esters are used which, after being applied in the lower eyelid space, they are metabolised into the active ingredient itself (e.g. Nandroloni natrii sulfas).

2.9. INFUSIONS

Infusiones (Synonyms: Infusiones intravenosae, intravenous infusions)

Infusion solutions are used to treat water and electrolyte disturbancies, electrolyte balance and osmotic conditions in acute impairments of alimentation state of a specific patient. The following text contains the introductory information to the problem; the practical usage of these solutions will be treated within the scope of the individual clinical specialisations.

To treat the impairments of internal environment and nutritive state, a wide scale of Czech and foreign-made preparations that cover the necessities of infusion treatment is available. Selected pharmacies in the Czech Republic can prepare infusion solutions of IPP according to the individual necessities of health care workplaces.

Adjustment of impairments of aqueous and electrolytic management and acid base equilibrium

In principle, two types of solutions are used, which can be isoionic, hypoionic or hyperionic:

a) balancing solutions for global adjustment of electrolyte loss – with their composition they approximate the extracellular liquid (ECL)

b) corrective solutions for covering of qualitatively specific electrolyte losses.

Isoionic solutions:

Distribution of full electrolytes should be neutral, i.e. it should not influence electrolyte balance. They include in particular:

Electrolytic full solution (EL 1/1). With its composition, it is closest to the ECL, HCO_3^- is replaced by lactate. It contains Na^+, K^+, Ca^{2+} and Mg^{2+} in the quantity corresponding to the physiological concentration. It is instrumental to replacement of iso-osmotic fluid losses.

Initial full solution (I 1/1). Cations are replaced with Na^+, anions out of 2/3 with chlorides and out of 1/3 with lactate. Therefore it does not contain K^+. Its indication is the initial adjustment of the ECL volume in an unknown function of kidneys.

Correction of misbalance of individual electrolytes:

Saline – "Physiological" solution (F 1/1) – the denomination is historical, its composition does not correspond with the ECL composition; it contains one third more chlorides and has low pH. It is commonly used as a carrier of other pharmaceuticals, it is not appropriate for adjustment of hypovolemia.

Single-molar solution of KCl „M“ (contains 1 mmol K^+ and 1 mmol Cl^- in 1 ml), i.e. 7.45% solution of KCl.

Single-molar solution of $NaHCO_3$ „M“ (contains 1 mmol Na^+ and 1 mmol HCO_3^-), i.e. 8.4% solution of $NaHCO_3$ – serves to adjust coverage of basis' deficiency.

Composite solutions:

Among the most commonly used solutions belong the composite solutions of electrolytes, glucose, lactates or acetates for adjustment of electrolyte balance that are prescribed under abbreviations or denominations by their authors' names. The list of the available solutions can be found e.g. in the Remedia Compendium periodical unlike in the Czech Pharmacopoeia does not contain them. They are prescribed usually upon a call slip as bulk drugs (RMP) – name of the preparation in nominative and the required volume, number of infusion bottles (glass) or plastic bags (PVC, PP) in subscription. Commonly prescribed solutions are the following:

Darrowi infusio – Darrow's solution for infusion: slightly hypertonic, contains high concentration of potassium (35.8 mmol/l), furthermore sodium chloride and sodium lactate.

Hartmani infusio – Hartman's solution: slightly hypotonic, contains sodium chloride, potassium chloride, calcium chloride, magnesium chloride and sodium lactate.

Ringeri infusio – Ringer's solution: isotonic, contains sodium chloride, potassium chloride and calcium chloride.

Other composite solutions: **Ringeri infusio cum natrii lactate** – Ringer's solution with sodium lactate (Ringer-lactate); **EL 1/1** – electrolytic full solution; **Natrii chloridi infusio** – infusion solution of sodium chloride.

A rather frequent way of individual preparation of infusion solutions at individual health care workplaces is the so-called **modular way**, when the infusion preparations are composed according to the specific necessities of the patient. They consist of several basic solutions (e.g. "six-molar" $NaHCO_3$, 5% glucose, "saline" etc.) and usually single-molar concentrates of NaCl, KCl, $NaHCO_3$, arginine-hydrochloride and others.

Infusion solutions for blood pH adjustments

Alkalising solutions are used for correction of the metabolic acidosis. Most commonly used are **Natrii hydrogenocarbonas** – sodium bicarbonate 4.2–8.4–13% or the so-called trometamol – **Trometamolum** (THAM 1/1) in combination with NaCl and KCl. Also alkalising concentrates are available.

Acidificating solutions: **Ammonii chloridum** – ammonium chloride, **Arginini hydrochloridum** – arginine hydrochloride, contain chlorides in abundance to correct metabolic alkalosis. Also acidificating concentrates are available.

Osmotherapeutics

These are osmotically effective solutions that, after intravenous administration, cause rise of osmotic pressure of plasma. There comes water transfer from intracellular to extracellular space and instigation of intensive osmotic diuresis – the so-called forced diuresis. These substances are excreted by glomeruli, but practically they are not resorbed in tubules, with which they carry water. They are indicated in therapeutically resistant oedemas and ascites, in renal insufficiency, which is not connected with ECL deficiency and does not respond to furosemide, in certain intoxications with substances excreted by kidneys (barbiturates, benzodiazepines, non-steroid anti-inflammatory agents and others.), in increase of intraocular and intracranial pressure and in eclampsia. The condition of osmotic diuresis is a sufficient supply of fluids.

Most commonly, **10% or 20% solution of mannitol** – **Mannitolum** (osmotic efficiency is 550 or 1100 mosm/kg) is used. Other hyperosmotic solutions: **40% glucose solution** – **Glucosum** and **40% urea solution** – **Ureum** are less used as osmotherapeutics.

Carrier solutions

Isotonic solutions of electrolytes or glucose are used also as the so-called carrier solutions for I.V. application of pharmaceuticals. Drugs that require long-term maintenance of constant therapeutic level and also substances that cannot be administered in another way are infused, such as pharmaceuticals with too short half-life in another routes of administration (e.g. antiarrhythmics, oxytocin etc.) or those in which we want to ensure a quick effect, continuous supply and a long-term maintenance of the therapeutic level (antibiotics in serious, life-threatening infections, norepinephrine in states of shock etc.).

Pharmaceuticals are usually added before applications into the carrier solution. It is possible to combine more pharmaceuticals, if they are mutually compatible together and with the solution. Some substances can only be mixed in the infusion set (e.g. by means of the Y-

connective etc.). However, when administering more drugs at a time in one solution, there is a high risk of incompatibilities, therefore the physician must always have thorough knowledge of the suitable and unsuitable combinations, and in case of uncertainty always consult with the pharmacist.

Means of parenteral nutrition

These infusion solutions are designated for a full nutritive securing of the patient, therefore it must contain: water, energetic supply, i.e. saccharides or lipids, amino acids, minerals, trace elements and vitamins. In patients where it is impossible to administer bigger volumes of water (cardial decompensation, oliguria, anuria etc.), concentrated nutrient solutions are used with avail. Their application, however, is possible through central venous catheter.

In long-term full parenteral nutrition, it is necessary to administer also the **lipid emulsions (LE)**. LE cover the need of essential fatty acids, they are resources of phosphor, and they prevent the development of hepatic steatosis. The chief fat source in lipid emulsions is soybean oil (Soiae oleum), less often it is cotton seed oil (Gossypii oleum).

With their composition and element size, the lipid emulsions should be close to the natural transport form of lipids from the digestive tract, i.e. chylomicrons. One gram of fat has energetic content of approximately 37.6 kJ. Dosing of lipid emulsions in the adults is 1–1.5 g of fat per 1 kg of weight per day. Maximum 30–40 % of the energetic necessity can be covered by means of LE.

Amino acid solutions are divided into nutrition solutions (amino acids for synthesis of corporal proteins, possibly ensuring of energetic needs) and specialised solutions, which beside the nutritive functions, fulfil also the specific metabolic function in certain metabolic impairments (liver or kidney failure). Recently, there appear specialised amino acid solutions with a high representation of branched-chain amino acids and ketoanalogs of amino acids, which are used for their anabolic properties (traumas, burn injuries etc.).

Saccharides are the most accessible energetic source for parenteral nutrition. In parenteral nutrition, solutions with various concentrations of monosaccharides (glucose, xylitol etc.) are used. The solutions are prepared in 5–40 % concentrations; also 50% or 60% glucose solutions are used rarely. Whenever possible, we prefer glucose, at the same time complemented by insulin in dosage of 1 unit per 3–4 grams of glucose. In cachectic patients, the insulin dosage is decreased.

Infusion solutions containing glucose:

Glucosi infusio 5–10–20–40% – infusion solution of glucose (5% infusion is approximately isotonic);

Glucosi infusio cum natrii chlorido – infusion solution of glucose and sodium chloride (iso-osmolar);

Glucosi infusio cum electrolytis – infusion solution of glucose and electrolytes (iso-osmolar);

Glucosi infusio cum natrii lactate cum electrolytis – infusion solution of glucose, sodium lactate and electrolytes (iso-osmolar).

Other solutions with sacharide content: **Glyceroli infusio cum glucoso** – infusion solution of glycerol and glucose, **Xylitoli infusio** – infusion solution of xylitol.

Note.: Sorbitoli infusio – infusion solution of sorbitol and Fructosi infusio – infusion solution of fructose are practically not in use any more due to the possibility of congenial intolerance with fatal after-effects.

Example of prescription of 10% glucose in infusion RMP:

Rp.
Infusio glucosi 100 g/l MVM G 10 inf. col.
inf. sol. 1x 250 ml (glass)
Lag. orig. No. X (decem)
D. S. Pro medico.

Alcohol solutions over 5 % and some other high-concentration solutions irritate the peripheral vein strongly and it is only possible to administer them in central catheter. Nowadays, the only indication of the I.V. alcohol infusion is the intoxication with methanol and ethylene glycol.

Concentrated solutions for injections or infusions

Concentrata pro solutione infundibili ─ concentrates for preparation of infusion solution are diluted with a prescribed volume of prescribed liquid before administration. After dilution they meet the requirements set out for injections or infusions.

Calcium, magnesium and phosphor concentrates are also used.

Coverage of plasma and circulating blood losses

Colloid solutions of substances with relatively high molecular weight are used, the colloid osmotic pressure of which equals or supersedes the oncotic pressure of plasma. Iso-oncotic solutions serve for a primary volume replacement, this is why they are often used as first aid. Their molecules carry water and keep it in circulation. Hyperoncotic solutions quickly increase intravasal oncotic pressure and lead to streaming of the fluid from intracellular and extracellular fluids to capillaries. They are administered in various forms of shock and in serious dehydratations. Forms used in the first place are: **Gelatina** – gelatine (Haemaccel infusion 3.5%), **Hydroxyethylamylum –** hydroxyethyl amyl (HAES-Steril 6%, 10%), **Dextranum –** dextran 6% (watch out for frequent allergies, even anaphylaxis!), less often it is **Albuminum humanum** – human albumin 5% or 20%.

2.10. LIGAMENTA

Dressing materials

Dressing materials are fibrous, woven or unwoven products from natural or synthetic materials, designated for coverage of wounds and body defects, to fixation or mechanic protection of surfaces or stypsis. They are prescribed in the form of bulk drugs (type or company brand, specification of their width and length, size, or possible requirement of sterility etc.) to special medical material orders or call slip, not on common prescription forms.

Fibres – Lanae

Filamentous hairs from seeds of the *Gossypium* genus, cellulose or viscose fibres. According to Czech Pharmacopoeia they include: **Lana gossypii depurata** – cleaned dressing cotton wadding; **Lana mixta depurata** – cleaned dressing wadding (mixture); **Cellulosum ligni** – cellulose wadding; **Lana cellulosi regenerati** – viscose wadding.

Tissues (woven fabrics) – Telae

Woven products from cotton or mixture of cotton and viscose rayon staple. They are used either as mouth-screens, scarves or as hydrophilic gauze with loose edges.

Bandages – Fasciae

These are bands of fabrics with firm or loose edges, from cotton or mixture of cotton and viscose clip, usually with hydrophilic properties with the width of 10–200 mm. Narrow bandages (width 10–40 mm) are called tamponade bandages. In cases of injuries elastic bandages of varying elasticity are used for fixation**.** The usage of gauze compressions made in the dimensions of 50x 50 mm to 150x 150 mm is also frequent. Fixation bandages can be finally secured with elastic meshwork – "PRUBAN".

Impregnated bandaging materials – Ligamenta impraegnata

An important group of bandage materials consists of impregnated open-meshed fabrics ("greasy gauzes") made under **SANAVEL** brand name and used for special purposes (burns, defects after irradiation, wound and decubitus healing etc.). They are prepared for instance with FRAMYKOIN drm. plv. ads., chlorophyll pigment, white vaseline (white petrolatum), Peru balsam essential oil and others.

3. INTRODUCTION TO EXPERIMENTAL (PRECLINICAL) PHARMACOLOGY

3.1. SIGNIFICANCE OF PHARMACOLOGICAL PRECLINICAL EXPERIMENT

Pharmacology, biomedical field dealing with studies of interaction of chemical compounds and live organism, since long time ago does not investigate only what effects have compounds applied into the organism or on its surface, but above all how – through what pharmacological mechanism – are they able to cause those effects. In today's experimental pharmacology, the aim is not only to investigate the effects of compounds potentially planned to be administered to humans (such as drugs, diagnostics or compounds that enter into contact with the organism from the environment, e.g. with food or in other ways) but often also to study exogenous administration of chemically well defined compounds natural to the body. In this second case, the results of pharmacological experiments can reveal physiological processes, their role and course up to its molecular level and their mutual interconnection in the live organism unknown until now. On the basis of these findings, even the search for suitable (e.g. therapeutic) exogenous interventions into the functions of the organism may be quicker and more successful.

3.1.1. Experimental animals

Since the times of Ancient Greece, animals have been used for above stated biomedicinal investigation purposes. Comparative physiology, molecular biology, genetics, psychology, pharmacology and other study fields have gradually and unequivocally confirmed a number of interspecies congenialities within the human and animal physiological mechanisms. That is why even nowadays, animal kingdom, limited to so-called laboratory animal species, is still the source of experimental live organism, live isolated organs, tissue cultures or their fractions.

According to the "European Convention" (www.uku.fi/laitokset/vkek/Sopismus/convention.html) signed on 18. 3. 1986, these are the laboratory animal species: laboratory mouse – *Mus musculus*, laboratory rat – *Rattus norvegicus*, guinea pig – *Cavia porcellus*, gold hamster – *Mesocricetus auratus*, rabbit – *Oryctolagus cuniculus*, domestic dog – *Canis familiaris*, domestic cat – *Felis catus*, common guail – *Coturnix coturnix*. Experimentally mostly used – from 85 to 90 % - are mice and rats. For a more efficient use of laboratory animals, genetically defined strains are bred, e.g.:

- outbred strain – every individual in the population is one and only, the populations are easily and cheaply accesible;
- inbred strain – all the individuals come from one couple and from brothers and sisters mating. The genetical uniformity diminishes the variability of experimental results, improves their generalization and estimation of an experimental error;
- mutant strain – serves as a biomodel (e.g. hypertension, obesity, diabetes mellitus), nowadays, it is possible to obtain such strains through genetic manipulation called "knock-out" (certain gene removal)
- transgenic strain – is obtained by targeted insertion of certain gene into the genome, which, similarly to mutant strain, means that it is possible to study its concrete biological role.

The "European Convention" allows the use of experiments on animals for biomedical investigation, security control of chemical compounds and products (drugs, cosmetic preparations, cleaning products, pesticides, industrial chemicals, and others) and educational purposes that are significant for man, but also for animals and plants. They were established as follows:

a) avoidance or prevention of disease, ill-health or other abnormality, or their effects, in man, vertebrate or invertebrate animals or plants, including the production and the quality, efficacy and safety testing of drugs, substances or products;
b) diagnosis or treatment of disease, ill-health or other abnormality, or their effects, in man, vertebrate or invertebrate animals or plants;
c) detection, assessment, regulation or modification of physiological conditions in man, vertebrate and invertebrate animals or plants;
d) protection of the environment;
e) scientific research;
f) education and training;
g) forensic inquiries

In the Czech Republic, the laboratory animals breading and use is overruled by the Ordinance 311 of the Ministry of Agriculture dated from December 4, 1997 to the Article 29 of

the Law of the Czech National Council No. 246/1992 of the Codex about protection of animals against maltreatment, in the version of the Law No. 162/1993 of the Codex which is in concordance to the above stated European Convention and principles of ICLAS (International Council for Laboratory Animal Science), established in the year 1979, and of course of the czech association CLASA (Czech Laboratory Animal Science Association) which is a member of the european society FELASA (Federation of European Laboratory Animal Science Associations).

3.1.2. Ethics of use of experimental animals

Together with the progress of biomedical sciences, the use of animals for experimental purposes has been gradually growing and at the same time also fears about the justificability of these proceedings. Organized fight for animal welfare and protection has been probably initiated by the philosopher Jeremy Bentham in the year 1789 by the declaration: "The question is not, Can they *reason*?, nor Can they *talk*? but, Can they *suffer*?" In the 19th century, " Society for Prevention of Cruelty to Animals" were founded in Great Britain and in the USA. In Great Britain, first laws "against cruelty" were passed. The fundamental significance for current principles of experimental use of animals had the publication by British researchers W. M. S. Russel and R. L. Burch "The Principles of Humane Experimental Technique" published in the year 1959 (the whole text can be found on the web site http://altweb.jhsph.edu/). In the book, the principles of so-called "Three R's" (Replacement, Reduction, Refinement) were formulated. Nowadays, they are requiered by laws of many countries, including Czech Republic. (One can get detailed and maintained information on the web site http://www.nal.usda.gov/awic/, which is presented by the centre "Animal Welfare Information Center, U.S.A.".)

The principle of "**Replacement**" is normally interpreted as search for so-called alternative methods instead of proper experiments on animals. Nevertheless, today the question is still not a total exclusion of animals from experiments ("Absolute Replacement"), but also a substitution of experiments on a whole animal using only their tissues or cells ("Relative Replacement"). In case of impossibility of exclusion of the experiment on a whole animal due to the character of the investigated biological problem, sophisticated statistics procedures are opted for, that allow a significant reduction ("**Reduction**") of animals used keeping the validity of obtained results. In all experiments on animals, it is lawfully obligatory for the people to choose from all the available procedures those that minimize general suffering of the animal and suppress or eliminate pain ("**Refinement**").

An abundantly used example of cumputer modelling (virtual reality) for educational purposes where there exist enough input data (see e.g. programme „Microlabs for Pharmacologist" by the Dutch author Dr. Henk van Wildenburg - chapter 3.2.1; information on other possibilities is continuously provided on the web site http://www.eurca.org administrated by the centre of Edinburgh and Utrecht Universities EURCA = European Resource Centre for Alternatives in higher education). Another very successful example of the principle of "Replacement" is the development of barrier system of collagen matrix that serves as "synthetic skin" (Corrositex) for compound corrosive effects testing when the liquid detection system changes its colour when the compound crosses the barrier. Apart from opting for a statistical

evalutation suitable for small samples, it is possible to respect the principle of "Reduction" obtaning as many experimental results as possible from a minimized number of animals thanks to a consequent and well planned experimental study (e.g. if one researcher needs an animal's brain for his task, other organs or tissues of the same animal can be simultaneously used for other experimental studies).

The development of non-invasive diagnosis methods and laboratory analytical methods working with a minimal amount of biological material enables more and more the fulfillment of the principle of "Refinement", which goes together with a perfect and universal care for laboratory animals resulting from all the contemporary knowledge of their nutrition, hygienical, ethological (study of animal behaviour) needs. One part of the principle of "Refinement" is of course the correct manipulation of laboratory animals and *lege artis* application manners (see video "Work with laboratory animals" projected within pharmacology teaching at the Faculty of Medicine of MU)

The contribution of science based on investigations carried out with the help of live organisms in search of new diagnostical, therapeutical and preventive methods for prolonging the duration and the quality of life (see competent contemporary overviews on the web site http://www.fbresearch.org/education) is eloquent and explicit. The scientific knowledge is, and probably will be for a long time, based in experiment, in the case of biomedicine also in experiments on animals, as no cells growing outside of an integrated macroorganism nor any computer programmes are not able to substitute them for the time being. Consequently, the only rational solution for achievement of more progresses in biomedicine is to fulfill as strictly as possible all the set ethical aspects, so that the internal value of the animals used for experimental purposes is fully recognized and so that the people treat them with all moral obligations. The contrarious influence on animals used for experiments should always be compensated by a general benefit of obtained results.

3.1.3. Preparation of experiment, experiment project, experiment protocol

For the legal possibility to carry out experiments on animals, it is indispensable to obtain so -called "**accreditation**" of laboratory animal care according to the conditions established by the Law. The conditions deal with laboratory animal housing and care for them, and also with the requisites of professional personnel qualification.

The experiment **project** (preclinical studies) is presented to a professional commission for its authorization before it is started audit must contain following data: name of the person in charge, title of the study, target characteristics and expected benefits, description of the work method, reasoning of species selection, number of animals and explication of why it is not possible to choose alternative methods, way of marking and, if it is the case, mitigation of pain and other suffering of animals, stating the health risks for other animals or employees, housing of the animals during the experiment and way of treating them after the experiment is finished.

On every realized experiment on animals, a protocol must be taken down containing data about origin, tenancy, manipulation and experimental interventions (if it is the case, postoperative care after surgical intervention) and obtained results. One part of the protocol is a declaration of complying with the authorized project. After the finalization of the experiment, it is obligatory to supply statistical information on species, number and purpose of the used

animals to the correponding state commission that informs in an accorded way the Secretary General of the European Council.

3.2. USE OF COMPUTER TECHNOLOGY FOR PHARMACOLOGY TEACHING

3.2.1. Use of PCs for experiment simulation

MICROLAB –PC programmes by Dr. Hughes

This programme (collection of subprogrammes) was created by the author with the support of the European project EC COMETT (European Community programme on cooperation between universities and industry regarding training in the field of technology) and the pharmaceutical company SOLVAY DUPHAR, B. V. This provides a number of computerized pharmacological animal experiments (*in vivo* and *in vitro*) and pharmacotheraputic sitation of human medicine.

The programme MICROLAB is used in the practical part of peripheral and central nervous system teaching. Student observes a demonstration of some symptoms (e.g. ataxy, catalepsy, opistotonus, hypertony, hypotony, etc.) after the application of selected types of drugs (e.g. amphetamine, ether, cocaine, morphine, picrotoxine, strychnine, etc.). The programme offers an animated overview of every behaviour element of a laboratory mouse and samples of sequences of this behaviour, including the interactive possibility of training of behavioural elements registration by the observer. Observation and registration of each behavioural element serves for new psychoactive drugs effects study where the behavioural changes of laboratory animals after the application of these drugs represent the changes performed in the CNS.

3.2.2. Solutions of pharmacotherapeutical situations with PCs

„How do You decide?“

This didactic programme elaborated at the Faculty of Medicine of the University in Hradec Králové facilitates the training of individual solving of some therapeutic situations from concrete clinical practice. In the programme, there are model situations with a beforehand defined patient history and checkup results. The student’s task is to answer correctly a system of questions related to the given situation. There are always several varieties of answers. After choosing the answer, the PC evaluates the answer and writes if it was correct or not and why. One can proceed to the next question only after answering correctly the previous one. Detailed instructions for work with the programme STUDIE can be found in the beginning of the programme and it is necessary to become familiar with it.

The tasks from therapeutical situation include, among others, the following areas: oral anticoagulants, therapeutical monitoring of theophylline levels, adverse effects of gentamycine, cardiotonic digitalis intoxication, myocardial infarction treatment and its complications, antihypertensives and their adverse effects, antiarrhytmics, children acute lymphoblastic leukemia treatment, etc.

Four model studies of therapeutic situations with solving instructions can also be found in the addendum to the statewide textbook on pharmacology: "Základní a aplikovaná farmakologie – Basic and Applied Pharmacology" (ed.: D. Lincová, H. Farghali, Prague 2007).

3.2.3. Use of PCs for simulation of pharmacokinetic processes

Pharmacokinetic modelling with the help of the programme MW PHARM

The programme MW PHARM (Pharmacokinetic Analysis in Clinical Pharmacy) was created at the University of Groningen, Holland, by the collective directed by prof. Dr. D. K. F. Meier, as a user's programme for purposes of clinical pharmacokinetics. It is mainly used for plasmatic level course prediction after a single or repeated administration of a drug according to a selected optimalized dosage regimen without the necessity of direct control of the drug concentration in patient's blood samples. The programme also helps to solve possible pharmacokinetic problems and modification of dosing within clinical practice.

The programme is also useful for student's understending of basic pharmacokinetic actions and principles of so-called compartment kinetics, as it facilitates the simulation of concentration curve course of the selected drug and the calculation of pharmacokinetic parameters in relation to the route of administration and drug dose based on the selected compartment model. The programme is multilingual (not in Czech). The language is preselected from the MENU, English version is most often used and we recommend it to the students for their work with the programme.

Basically, the programme includes two parts: a) subprogramme for use in clinical pharmacokinetics (Main Menu points 1–7) and b) subprogramme KINFIT which allows a performance of a complete pharmacokinetic analysis of any drug with the help of a 1-, 2- or 3-compartment model after intravascular or extravascular administration. The separate programme KINBES serves for biological availability studies (Bioavailability Studies), it is not used for practical exercises.

For students' work with the programme MW PHARM within practicals, there are detailed instructions at hand.

Pharmacokinetic analysis with the help of the programme PK Solutions 2.0

The programme PK Solutions was created by the company Summit Research Services, Montrose, USA. It is a user's interactive programme that offers the possibility of complete non-compartment analysis of concentration curves after intravascular of extravascular administration of a drug. It does neither requiere programming knowledge nor deeper knowledge of exponential equation solving. The programme is fully automatized and runs under MS Excel™.

The programme is destined for teaching and investigation needs in the field of pharmacokinetics. It offers simple and fast method of concentration data evaluation ("curve stripping", "curve fitting") and calculation of more than 75 pharmacokinetic parameters including graphical presentation. It facilitates level course prediction after repeated drug administration on the basis of pharmacokinetic behaviour evaluation after a single dose administration. The comprehensible manual includes a complete explication of pharmacokinetic

actions and an overview of used exponential equations. For students'work with the programme within practicals, there are detailed instructions available.

More detailed information about the programme: http://www.SummitPK.com .

4. INTRODUCTION TO PHYTOPHARMACOLOGY

(Phyto = plant, herb)

Therapy using active constituents of medicinal plants is as old as the whole mankind. Still nowadays, it has an important position among pharmacotherapeutic approaches. Substances of herbal origin represent the therapeutical component of many RMP. The increasing interest of the public for the "green medicine", often due to certain disillusion caused by insufficiently effective synthetic drug treatments which often go along with unpleasant and many times even dangerous adverse effects, is having an inevitable projection into the medical practice. Especially the physicians in the first-line contact with the patients are more and more pressed on to answer questions related to the significance and efficacy of herbal preparations and their mixtures sold over the counter or home-made. They should also be able to make use of natural medicaments in convenient rational cases, as complementary and sometimes even basic treatment, whether as RMP with herbal base or IPP.

Another important task of the physicians and pharmacists is to rectify widely transmitted misleading information and warn the patients of uncritical confidence in extra-scientific literature data. To be able to comply with it, the physicians themselves should have a pertinent theoretical knowledge of herbal drugs, their desired and adverse effects, possibilities of therapeutic and prevention use of herbal parts, extracts or their combinations.

4.1. TERMINOLOGY, PARTS OF PLANTS

Natural medicaments – chemically isolated separate substances or their mixtures of biological origin, i.e. vegetable or animal, including their products used in treatments, prevention or diagnostics, or to influence human, eventually animal, physiological functions.

Herbal Drugs (preserved by drying) – whole plants (exceptionally animals, e.g. Spanish flies – *Cantharides*) or their parts, eventually their products (wheat starch – *Tritici amylum*, honey – *Mel***,** essential oil – *Etherolea*).

Ballast substances –constituents in plants without a specific pharmacological effect.

Parts of plants:

Herba – herb; is picked up with dry weather closely before the flowering period or during its beginning (exceptionally in full bloom) when the contents of effective substances are the highest.

Folium – leaf; leaves are picked up closely before flowering period or in the beginning of full vegetation.

Flos – flower; is picked up shortly after flowering. An exception is the Asteracae species (e.g. marigold flower – *Calendulae flos* and Roman chamomile flower – *Chamomillae romanae flos*) that are picked up before flowering as they continue spreading out after being picked up.

Fructus – fruit or its parts; they are usually picked up when completely ripe and when their contents of essential oils are sufficiently high as they are the principal effective components.

Radix – root; the most convenient time to pick it up is normally the end of vegetation period, i.e. autumn, exceptionally spring.

Cortex – skin, bark; is picked up in spring months, in the case of flowering woody species shortly before blooming when the flow of sap is at its maximum.

Succus – juice obtained by pressing of fresh herbs or their parts is the most regardful and possibly one of the most effective forms of herbal effective substances.

Other parts of plants: ***Bulbus –*** bulb; ***Glandula*** – gland; ***Lignum –*** wood; ***Pericarpium –*** pericarp ; ***Rhizoma –*** rhizome; ***Tuber –***tuber; ***Semen –*** seed; ***Stigma*** – stigma, ***Stipes*** – peduncle, sprout; ***Strobilus*** – strobile; ***Summitas –*** top.

4.2. HERBAL PREPARATIONS, DRUG DOSAGE FORMS

4.2.1. Species

Medicinal teas, herbal tea mixtures

Species are mixtures of herbal drugs disintegrated to a defined size of particles. They are delivered to the patient in loose state or in infusion bags and they are destined for home preparation of teas. Teas are aqueous leaches of herbal drugs or their mixtures. Their home preparation can be basically done in three ways: **Maceratio** – maceration, **Infusum** – infusion a **Decoctum** – decoction. The type of leach is determined by the effective substances, i.e. chemistry and also morphology of the herbal drugs. From soft parts of plants, i.e. flowers, leaves and herb, usually infusions are prepared. From hard parts of plants, i.e. roots, rhizomes, skin, hard fruits, decoctions are prepared. Drugs containing essential oils, even in the case of hard parts (seeds), must not be boiled, as the effective substances would get deteriorated by the ebullition. If it is not prescribed in a different way, generally the dose is 1-2 teaspoons of soft drugs for 200 ml, or 1 tablespoon for 250 ml of tea (1 l water = 1 cup).

- Macerate – leach at cold temperature: is convenient for application of mucilaginous drugs, as linseed, for extraction of mucilages, starch, essential oils and thermically instable substances (mistletoe) from herbal drugs (mistletoe).

  The preparation includes pouring cold water over the herbal drug and followed by leaching at room temperature (15–20 °C) for a specified time period (sometimes 30 minutes, other times 6-12 hours, (mostly over the night). Before use, the cold leach is strained. Usually it is warmed up a little and drunk lukewarm.

- Infusion: is prepared from drugs that are well leachable, e.g. leaves, herbs and flowers. An important part of the preparation is soaking the herbal drug in warm water so that its furled particles opened and swelled up. Afterwards, the herbal drug is emptied into a warmed up container (never a metal one!), prescribed amount of boiling water is poured over it and it is left for 15-30 minutes under a cover, stirring occasionally. After having been filtered, the infusion is drunk warm. Always one single dose

is prepared, it should not be prepared in advance (it should be optimally drunk within 12 hours after its preparation).

- Decoction – leach at high temperature: it is used for mixtures where the prevalent portions are hard parts of plants (roots, rhizomes, seeds, wood, etc.). During the preparation, water is poured over the drug in a china, glass or stainless pot, and it is it is left to boil gently. If possible, it is boiled in a water bath in a covered pot for 10-15 minutes since the beginning of ebullition. Hard wood and some root drugs are to be boiled for up to 30 minutes. Afterwards, the decoction is left still under the cover for about 10 minutes. It is filtered after cooling down, if necessary, it is completed up to its original volume.

  A decoction should not be stored, it is necessary to drink it on the same day of its preparation. By re-boiling, it turns valueless.

- Combined leaches: Some tea mixtures contain drugs that require different type of leach preparation, and then it is necessary to combine preparation forms. Infusion with decoction is prepared by making a decoction, removing it from the heat and adding the drug destined for preparation of the infusion. The pot is covered and after 15-20 minutes strained. Macerate-decoction is prepared by macerating the species in half of the prescribed volume of water, the leach is then decanted and the species is boiled in the remaining water. Afterwards, both leaches are poured together. Macerate-infusion is a very advantageous way of using herbal substances, applicable for the majority of tea mixtures. It is a leach at cold temperature combined with steaming. The drug is leached over the night in half of the volume of water, the leach is strained in the morning. The rest of the water at boiling temperature is poured into the leach, it is let to leach and strained again. Then, both leaches are poured together.

- Classical herbal tea is prepared by pouring cold water (about 3 l) over the herbal drug in the evening. It is left to leach under cover until the next morning. Afterwards, it is boiled for several seconds and left covered for some minutes. The tea is strained and one cup is drunk on empty stomach and the rest is drunk by sipping (from a thermal bottle) during the day.

The majority of teas are **served** on empty stomach and with no sugar. An exception represents so-called pectoral teas, which are often drunk after the meal and it is convenient to sweeten them with honey and drink as hot as possible. Diuretic teas are generally served between the meals usually in bigger volumes.

Common **daily dose** is a cup of tea 2-3 times a day, or 0.5-0.75 litres of tea drunk by sips during the day. Diuretic teas are served at minimum dose of 1 litre per day, nevertheless not more than 3 litres. Application of two bolus doses of 1 litre each and sipping the rest during the day is convenient. The stated doses are for adults, doses for children and in elderly must be proportionally diminished.

The composition of tea mixtures for treatment of certain pathological states and their symptoms has been settled down over the years. Today, a lot of well-proved herbal medicinal teas are prepared as RMP. The most important manufacturer of tea mixtures in the Czech Republic is Leros (http://www.leros.cz), producing mixtures under commercial denominations (DIABETAN por.spc., FYTOKLIMAN PLANTA por.spc.dos., PULMORAN por.spc., etc.) or under Latin denominations specifying the indications (SPECIES UROLOGICAE PLANTA, SPECIES CHOLAGOGAE PLANTA, SPECIES PECTORALES PLANTA); in the Slovak Republic, it is Slovakofarma, a.s. (http://www.slofa.sk).

Making an individual composition of tea mixtures, similarly to other herbal preparations, must be based not only on empiric experience but, above all, on good knowledge of contentual composition and pharmacological effects of prescribed herbal drugs and their combinations. The

most convenient way is to choose a tea mixture with one main component. No mixture should contain more than three basic components (it is not convenient that a tea mixture is destined "for gallbladder, kidneys, nerves and also against diarrhoea" at a time. It is very important to explain the patient to adhere strictly to the instructions for tea preparation (macerate – infusion – decoction, their combinations), as the therapeutic effect can be not only decreased but also totally extinguished by an improper preparation.

4.2.2. Other herbal preparations

Tincturae – tinctures

Tinctures (sometimes also called essences) are favourite and easily dosed pharmaceutical dosage forms. They are alcohol-aqueous or alcohol-ether extracts with standard concentration of effective substances stated in Pharmacopoeia. Normally they are drug leaches in 60% (40–70%) ethanol. They are prescribed in the quantity of 10-20 g and are dosed by drops (see chapter 1.3.3.). Example: *Valerianae tinctura*.

Extracta – extracts

Extracts are concentrated extracts of drugs obtained in different ways, most often by isolation with the help of ethanol and water, when a complete leaching (extracting) of effective substances is produced. Extracts can be liquid (*Extracta fluida*), thick (*Extracta spissa*) and dry (*Extracta sicca*). They normally represent a part of composite preparations for internal use. Example: *Liquiritiae extractum fluidum ethanolicum normatum.*

Aquae aromaticae – aromatic waters, **Spiritus aromatici** – aromatic spirits

True solutions originated by dissolving essential oils of characteristic aroma and flavours in water or ethanol. They have moderate therapeutic effects according to the character of the drugs used. They also serve as corrigents in liquid oral preparations. Examples: *Aqua carminativa, Anisi spiritus compositus.*

Sirupi medicati – medicinal syrups

Concentrated aqueous sugar solutions with an admixture of herbal drugs or solutions of saccharides in herbal drug leaches. They are used as flavour corrigents with moderate therapeutic effects. Example: *Althaeae sirupus.*

Dispersiones – dispersions

They are obtained by dispersing aqueous or alcohol extracts from drugs. They represent a modern pharmaceutical dosage form of dry extract, they have the advantage of exact dosing and simple conservation. That is why it is probable that they will be used even more in the future.

Among herbal preparations, one can also include **wines** and **medicinal vinegars**, used preferably as supportive dietetic preparations.

Among external pharmaceutical dosage forms, we can find herbal preparations as **herbal ointments** (marigold ointment), **herbal compresses** (comfrey, horse-chestnut) and **herbal plasters.**

4.3. HERBAL CONSTITUENTS, CHEMICAL COMPOSITION

Effective substances are contained in different parts of a plant. Within the same species, their contents may vary depending from the influence of factors as vegetation period, geographic position, way of drying, storage conditions, etc. Characteristic effect of a plant may be caused by one chemical substance, more often, though, by a group of substances or even a whole complex of constituents. For officinal drugs included in the Pharmacopoeia, the contentual composition of effective substances is exactly established and obligatory analytic procedures for contents determination are elaborated.

The effective substances from plants for medicinal use are basically obtained in three ways: 1. leaching for preparation of teas, tinctures and extracts; 2. obtaining of defined fractions, e.g. essential oils, tanning agents, etc.; 3. isolating of individual chemical compounds in pure state. Some chemically defined substances of plant origin are prepared synthetically, e.g. vitamin C, caffeine, papaverine, ephedrine.

Alkaloids

Nitrogen compounds of basic character that can be found in a number of plants. Their physiological significance is important as many of them belong among highly effective drugs and they are often even virulent poisons. Nitrogen is usually bound in heterocycle. According to the character of the heterocycle, alkaloids are divided into pyridine – nicotine (tobacco); piperidine – cocaine (poison hemlock); tropane – atropine, scopolamine, hyoscyamine (belladonna, datura, henbane); chinoline – quinine, quinidine (cinchona); isochinoline – opium alkaloids and papaverine (poppy), emetine (ipeca), tubocurarine (curare); indole – strychnine (strychnos); reserpine (rauwolfia); ergotamine (claviceps); „vinca“-alkaloids (periwinkle); physostigmine (calabar bean); imidazole – pilokarpine; steroid – solanine (aubergine), protoveratrine (hellebore); diterpenoid – aconitine (monkshood); pyrrolizidine – symphytine (comfrey, coltsfoot, dusty miller, butterbur).

Alkaloid amines

Alkaloids with nitrogen in lateral chain, usually highly effective and toxic. An example is ephedrine (ephedra); colchicine (meadow-saffron); taxanes) – taxine, taxole (yew-tree); mescaline, psilocybine (“magic mushroom”).

Glycosides

Group of substances of sugar character derived from glucose and other sugars. Nevertheless, on the contrary, glycosides do not have reduction properties. They crystalize easily, the crystals are soluble in water and their solutions are not sweet, but bitter. Their molecule is composed of glycone (sugar group) and genin (aglycone group). The composition of aglycone (genine) defines the chemical effect of the whole complex and consequently also the varied effects of glycosides. Some vegetal substances with glycoside bonds have still not been thoroughly investigated (dead-nettle, hawthorn).

According to the structure of aglycone, glycosides are divided to cyanogenic – splitting up hydrocyanic acid (bitter almonds, stonefruit seeds); steroid – mostly virulently poisonous (foxglove, adonis, lily-of-the-valley); anthraquinone – laxative emodines (aloe, buckthorn, rhubarb, senna); thioglycosides – (mustard, rape); flavonoids – a very ample group, e.g. rutin

(rue), silybine (milk thistle) etc.; phenole – urinary antiseptics, e.g. salicin (willow), arbutine (dogberry); aldehydic – vanillin; lactone – coumarin (snail-clover), psoralens, cantharidine (Spanish flies).

A special position among the glycosides belongs to **saponins**. They are compounds with a complicated chemical structure, widely represented in the vegetal realm. They belong to the glycoside group thanks to the content of sugar component in the molecule. They diminish surface tension. In their presence, little soluble substances emulsify to fine particles that can absorb more easily. Saponins are used as expectorants (Primrose, Mullein, Soapwort) or venotonics – aescine (Horse Chestnut). Diuretic and anthelmintic effects are also cited. Their presence in the bloodstream produces hemolysis (Herb Paris).

Stomachics (Amara)

Nitrogen-less substances of bitter taste, normally non-toxic, used for improvement of digestion and appetite. Chemically, they have diverse characters (glycosides, lactones, terpenes and others). Stomachics influencing GIT are divided to *Amara pura* – pure stomachics, *Amara aromatica* – aromatic stomachics that include also essential oils, and *Amara acria* – irritating stomachics. More in detail see chapt. 2.3.1.

Flavonoids

Phenolic substances are very common in plants and have beneficial effects and qualities similar to vitamins. They have a favourable effect on vessels, they normalize the capillary permeability, increasing their solidity. They support vitamin C effects, act also as choleretics and spasmolytics. They are contained for example in rue, hawthorn, lime-tree flowers and other plants.

Phytoncides

Substances contained in tissues of higher plants that participate in the resistance of higher plants to diseases, especially those provoked by bacteria or some fungi. These "vegetable antibiotics" act against bacteria, some viruses, fungi and parasites even in humans. The most noted are the bactericidal effects of phytoncides from Onion, Garlic, Horse-radish, Lemon-tree and St. John´s wort.

Terpenoids

Derivatives of unsaturated isoprene hydrocarbon, volatile and non-volatile, some very toxic. They are compounds of essential oils (ethereal, volatile oils), e.g. Peppermint, Lemon or Rose essential oils.

Among more important terpenoid compounds belong valepotriates– cyclopentene monoterpenes with hypnosedative effects from valerian (Valeriana), azulenes (Chamomile, Yarrow), monoterpenes and sesquiterpenes as menthol, geraniole, citronellol; bitter oils (Sagebrush, Marigold); poisonous terpenes with irritating effects on skin and mucosas including GIT (Juniper, Daphne, Spurges, Heathers).

Essential oils

Mixtures of aromatic substances with volatile character that can be found in different parts of plants. Essential oils are practically insoluble in water, they can be dissolved in ethanol and other organic solvents. Therapeutically, they are used as antiseptics, expectorants, diuretics, anti-inflammatory drugs, derivants, aroma and flavour corrigents/ of tea mixtures (Sweet Basil, Wild Thyme, Lemon Balm, Calamint, Marjoram, etc.).

Tannins

Derivatives of aromatic hydroxy-acids of bitter and acrid taste with adstringent and antidiarrhoic effects. The most important are tannins (Oak cortex, Willow, Goose-Grass, Easter-Ledges). They are very common in the vegetal realm, they are almost ubiquitar. Their therapeutic significance lies mainly in their adstringent effect, i.e. capacity to react with protein structures on mucosa and connective tissues surfaces and reinforce membranes. That is how tannins impede the penetration of bacterias and viruses; they have anti-inflammatory and slightly anaesthetic effects. They restrain sweating and exudation. Recently, their radioprotective effects are being investigated.

Glucoquinines – they depress plasmatic level of glucose and have anti-diabetic effects (blueberry leaf, green beans).

Lectines are toxic proteins – toxoalbumins (Mistletoe, Locust, oil tree, green beans).

Saccharides

Sugars – carbohydrates are direct products of photosynthesis. In plants, they exist as a source of energy in the form of monosaccharides that can inter-condense into two and up to seven saccharide units, forming di- up to oligosaccharides. By condensation into higher number of units, storage substances - polysaccharides are formed. They can appear also as structure components of cell walls and form in this way the skeleton of plant bodies. Sugars are also components of glycoside molecules and participate in the formation of mucus and tannins.

The most known natural source of sugars is honey – **Mel**, containing among others about 70–80 % of glucose, but also dog-rose fruit – **Cynosbati fructus** with about 30 % content of sugars.

Among carbohydrates, there belong also substances of no sweet taste that do not dissolve in water, e.g. cellulose (on the contrary, some substances with sweet taste insoluble in water do not belong among carbohydrates – e.g. glycerole and mannitol).

Among polysaccharides belong starches, cellulose, inulin, gum resins, gums and mucilages.

Amyla – starches differ substantially from sugars due to their character. In pharmacy, the most used starches are rice, wheat, corn and potato ones. They form a component of talcum powder, facilitating skin drying thanks to their water-binding capacity. They also bind secreta, sebum, etc. They diminish irritability of the skin and improve the slipperiness of the powders. For their swelling capacity, they are also used as adjuvants for the manufacturing of tablets, hydrophile (i.e. non-greasy) ointment and paste bases, internally they are used as demulcents and dietetics. Starch capsules and starch bandages are prepared from them.

Cellulosum – cellulose, composed of glucose subunits (polyglucane, about 14 000 units with atypical bindings) form the structural material of plants. It is used as bandage material obtained from cotton and wood fibres (cotton wool for bandages).

Inulin – another storage polysaccharide composed of fructose units. It is contained in representatives of the Campanulales and Asterales orders (e.g. root parts of Elecampane and Chicory). It is used for diagnostic purposes, as nutrition for diabetics and for fructose isolation.

Gum resins, gums and mucilages are either a natural part of plant bodies or are formed as consequence of external intervention and they flow out of injured places similarly to resin from needle leaf trees. Chemically they are close to cellulose and starch, as their basis is formed by sugars, especially arabinose and galactose.

Gum resins are special composed polysaccharides formed in many plants after injury. Pharmaceutically, gum arabic – *Gummi arabicum* is used, serving as emulsifier of binding for some drug dosage forms.

Mucilages are vegetal polysaccharides that swell heavily in water. They are formed in plants from storage substances or from structural polysaccharides. They are viscous or jellylike masses that do not dissolve in water but together with warm water they form viscous colloidal systems. Colloidal solutions of mucilages have protective effect on mucosas of the GIT and respiratory system. That is why they are therapeutically used as covering protective applications (rose-mallow, golden-rod, liquorice, linseed, comfrey root, marshmallow root).

The most known mucilage from seaweed is Agar-agar, used as moderate laxative. It appears as a component of hydrophilic ointment bases, it is a stabilizer of some two-phase drug preparations, and in microbiology it serves for culture media. Another typical representative of vegetal mucilages is tragant – dried exudation of trees of the *Astragalus* species that grow on the Balkan peninsula.

Waxes

Chemical substances similar to fats, but they are more stabile and resistant to high temperatures. Pharmacy uses almost exclusively animal waxes, most famous from these are beeswax – *Cera alba* and sheep wool wax – *Cera lanae*. Waxes are a component of ointment bases with protective and emulgating action.

Glycerophosphatides

They are affined to fats, they participate in their transport within the organism and they form a component of the membrane cell system. Pharmaceutically, the most important are lecithins which can be found in plants (soya beans) and also in animals (egg yolk). Lecithin is an excellent emulsifier. It is recommended as support treatment for atherosclerosis and nerve dysfunctions, nevertheless its effectivity is being disputed.

Vitamins

In the vegetal realm, there are a lot of plants and their products rich in different vitamins, e.g. dog-rose fruits contain a big quantity of **vitamin C**, **vitamin A** is formed in the organism from carotene from carrots, a rich source of **vitamins of group B** are ale yeasts and flower pollen, **vitamin P** – rutin can be found in rue, buckwheat, etc.

From vitamins, substances called **vitagenes** are earmarked. They can have structural significance and they are a source of energy (e.g. so-called **vitamin F** formed by higher unsaturated fat acids).

Coumarines

Lactons of coumarin acid (cis-o-hydroxycinnamic). It acts as sedative, spasmolytic and antithrombotic. In bigger doses, they can provoke hemorrhage and they are hepatotoxic (Woodruff, Common Melilot)

Greases and oils

Pharmacologically they are indifferent, they have healing action in preparations for burns. They are very rarely used separately, nevertheless they are an important component of oleophilic ointments and they are used as solvents of lipohilic drugs. As sources of oils, the following plants are used: linseeds, sunflower, olives, soya, peanuts, cacao-tree, ricinus, etc.

Organic acids

They equilibrate internal cell pressure and regulate cell membrane permeability of plants. Therapeutically, they act rather disparately, they often have laxative effect. They are contained in fleshy fruits (apples, pears) but also in other parts of plants (Sorrel, Nettle). Examples: citric acid, wine acid, oxalic acid, etc.

Steroids

Chemical group of substances of varied composition with important pharmacological effects, characteristic structure formed of carbon skeleton with four fused rings. Typical representatives of plant steroids (phytosterols) are phytoestrogens (e.g. in Hops), cardio-active glycosides (e.g. in Foxglove) and some other steroidal saponins.

4.4. DIVISION OF HERBAL PREPARATIONS ACCORDING TO THEIR USE

Herbal drug preparations have a wide range of use in therapy, prevention and after-treatment of diseases. According to their prevalent effect, this is their classical division into basic groups: diaphoretic drugs (**diaphoretics**), drugs with effect on heart (**cardiacs**), drugs with effect on nerves (**nervines**), drugs used for arteriosclerosis (**antisclerotics**), blood pressure diminishing drugs (**hypotensives**), drugs enabling expectoration (**expectorants**), drugs with effects on stomach functions (**stomachics**), drugs against flatulence (**carminatives**), drugs against diarrhoea (**antidiarrhoics**), cholegenic drugs (**cholagogs**), laxative drugs (**laxatives**), drugs against intestinal parasites (**anthelmintics**), drugs used as support preparations for diabetes (**adjuvant antidiabetics**), diuretic drugs (**diuretics**), drugs used for women's diseases (**gynecologics**), drugs that support milk secretion (**lactagoges**), drugs that suppress sexual instinct (**anafrodisiacs**), externally used drugs (**external drugs**).

More detailed information on specific possibilities of use of each of the pharmacopeoeic drugs and herbal preparations for modification of pathological states can be found in the corresponding chapters on special prescription in this textbook, concretely:

2.1.1. Hypnotics and sedatives
2.2.1. Antitussives
2.2.2. Expectorants
2.3.1. Amara, Stomachics
2.3.3. Antacids
2.3.4. Spasmolytics

2.3.5. Carminatives, deflatulents
2.3.6. Cholagogs
2.3.7. Laxatives
2.4. Dermatologics
2.5. Oropharyngologics

Conclusion

Rational use of therapeutic plants is a convenient and desirable component of complex pharmacotherapy. Herbal preparations may represent a suitable subsidiary and complementary therapy for many diseases, they can even neutralize adverse effects of chemical medicaments (antirheumatics, cytostatics, etc.).The phytotherapy is having success especially in chronic diseases with a functional component, e.g metabolic diseases or even short-term diseases like diarrhoea, cold, nausea, etc. The major field for medicinal herbs use is prevention and after-treatment of diseases of diverse origins.

Herbal therapy has normally a harmonic effect, as it includes specifically efficient components and also substances that support unspecifically the defence capacity of the organism. Plants and products made of them are valuable sources of vitamins, fibre, mineral salts and enzymes. Herbal drugs can be conveniently combined with chemical ones. They can act as adjuvants, which enable to lower the dosing, they can also reduce the appearance of chemical drugs' adverse effects when administered on a long-term basis.

Nevertheless, it is necessary to remember that herbal preparations are not always totally harmless, they can provoke adverse effects, including hypersensitive reactions. Some of them can interact significantly and even dangerously with chemical drugs due to the enzyme induction (St. John´s Wort) or inhibition (grapefruit juice). All these are reasons for the future physicians to know the basic principles and possibilities of rational use of herbal drugs in complex therapeutic procedures and disease prevention.

Appendix 1.

OVERVIEW OF PHARMACOPOEIAL DENOMINATIONS OF DRUGS USED IN PRESCRIPTIONS

Latin pharmacopoeial (officinal) names

Acidum acetylsalicylicum
Acidum boricum
Acidi borici unguentum 3%, 10%
Acidum hydrochloricum 10%
Acidum salicylicum
Adeps suillus
Althaeae radix
Althaeae sirupus
Aluminii acetotartratis solutio
Aminophenazonum
Aminophyllinum
Ammonii chloridum
Anisi fructus
Anisi spiritus compositus
Argenti diacetyltannas albuminatus
Argenti nitras
Aqua carminativa rubra
Aqua pro iniectione
Aqua purificata
Atropini sulfas monohydricus
Balsamum peruvianum
Bentonitum
Bismuthi tribromphenolas*
Cacao oleum
Calcii carbonas
Calcii hydrogenophosphas
Camphora racemica
Carbethopendecinii bromidum
Carbo activatus
Carmellosum natricum
Cera alba
Cetaceum*
Chamomillae romanae flos
Citri etheroleum
Cocaini hydrochloridum
Codeini phosphas hemihydricus
Coffeini et natrii benzoas
Coffeinum
Collodium elasticum*
Diazepamum
Ephedrini hydrochloridum
Epinephrini tartras
Ergotamini tartras

Ethanolum 60%, 85%, 96%
Eucalypti etheroleum
Foeniculi dulcis fructus
Foeniculi etheroleum
Formaldehydi solutio 35%
Gallarum tinctura
Glucosum
Glyceroli suppositorium
Glycerolum 85%
Helianthi oleum
Homatropini hydrobromidum
Hydrogenii peroxidum 3%
Hyperici herba
Ichthammolum
Iodi solutio ethanolica
Kalii iodidum
Kalii permanganas
Lactosum
Lavandulae etheroleum
Lini semen
Lipogenolum P.P.*
Liquiritiae extractum siccum*
Lithanthracis pix
Magnesii oxidum (leve)
Magnesii sulfas heptahydricus
Melissae folium
Menthae piperitae etheroleum
Menthae piperitae herba
Mentholum racemicum
Methylcellulosum
Methylrosanilinii chloridum
Methylthioninii chloridum hydricum
Millefolii herba
Morphini hydrochloridum trihydricum
Myrrhae tinctura
Natrii benzoas
Natrii chloridum
Natrii hydrogenocarbonas
Natrii iodidum
Natrii perboras
Natrii salicylas
Natrii sulfas
Natrii tetraboras decahydricus
Papaverini hydrochloridum
Paracetamolum
Paraffinum liquidum
Phenobarbitalum natricum
Phenolum
Physostigmini salicylas
Pilocarpini hydrochloridum

Plantaginis extractum fluidum
Plantaginis folium
Plantaginis sirupus
Polysorbatum 80
Procaini hydrochloridum
Propyphenazonum
Ratanhiae tinctura
Ricini oleum virginale
Silica colloidalis anhydrica
Sirupus simplex
Quinidini sulfas dihydricus
Talcum
Tanninum
Thymi herba
Tinctura amara
Trimecaini hydrochloridum
Tritici amylum
Unguentum ophthalmicum simplex
Valerianae radix
Valerianae tinctura
Vaselinum album
Vaselinum flavum
Viride brillans*
Zinci oxidi pasta
Zinci oxidum
Zinci sulfas

** Preparations marked with a star are not officinal according to the Czech Pharmacopoeia 2005..*

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Practicals in Pharmacology

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