MUNI
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MUCOADHESIVE SYSTEMS

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Theory of dosage forms

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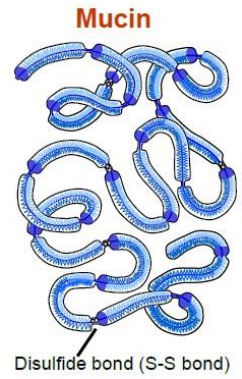
Adhesion - adhesive effect

Bioadhesion – formation of bonds between two biological surfaces or between a biological and a synthetic surface (which may be formed by interacation with cells or slime = mucus layer, respectively)

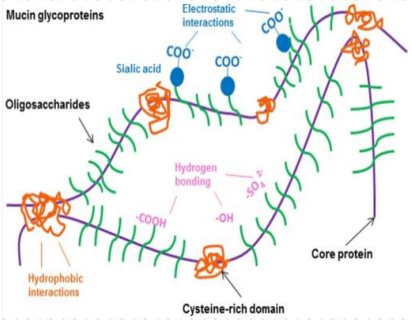
Mucoadhesion - adhesion to the mucus layer covering the mucosal epithelium (surface)

- *oral cavity, eyeball, nose, respiratory tract, GIT and vagina*

Mucus composition: mucin glycoproteins (0.5 - 5%), lipids, inorganic salts, nucleic acids, enzymes and water



Mucin and mucus layer



MUCIN - *peptide backbone* and *oligosaccharide side chains* of 2 to 19 units (galactose, fructose, N-acetylglucosamine, N-acetylgalactosamine and sialic acid) linked to the protein backbone through H-bonds.

- at neutral pH it is an anionic polyelectrolyte
- *lubricating* and *protective function*

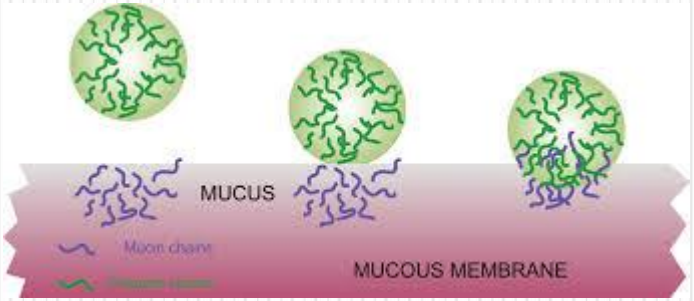
The average thickness of the mucous layer varies from 0.7 microns in the oral cavity to 50 - 450 microns in the stomach.

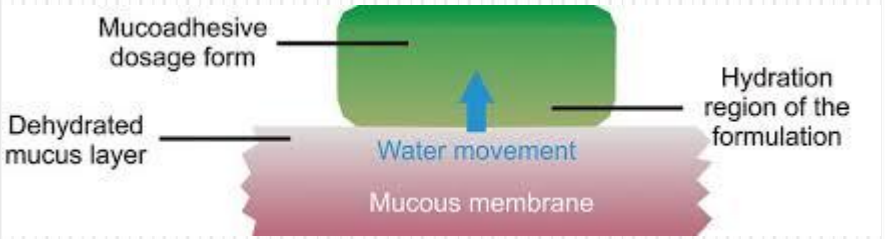
Mucus forms in the “goblet cells“, in the oral cavity also as a part of saliva.

Formation and influencing of the mucoadhesion

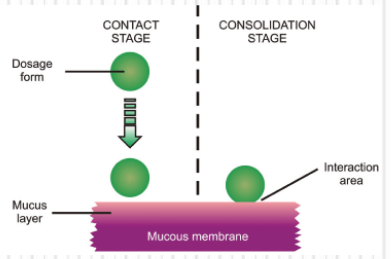
3 phases of medicinal product adhering to the mucosa:

- tight contact of WET! swelling polymer with tissue
- polymer throughput the mucus layer and interpenetration of polymer chains and mucin
- formation of weak physico-chemical bonds between interlocked chains





Mucoadhesion Formation and Influencing of the Process



The process of adhesion - 2 basic steps:

1) *contact phase* between mucosa and mucoadhesive dosage form
2) interconnection of mucoadhesive material and mucus (*consolidation*)

During the close contact between mucoadhesives and glycoproteins´ network of mucus, the polymer is wetted and swells. Interpenetration of mucoadhesive polymers chains and mucus leds to formation and stabilization of adhesive bonds by weak chemical interactions.

Mucoadhesion Formation and Influencing of the Process

Five mucoadhesion theories

Difusion - penetration and interlacing of polymer chains and mucus. The degree of penetration is dependent on the mobility and flexibility of the chains, the concentration gradient and the diffusion coefficient.

Electron - electron transfer between the mucoadhesive substance and mucus on the interface where is formed electric double layer. Adhesion occurs due to attractive forces.

Wetting - ability of the mucoadhesive to spread on the biological surface and to allow a close contact with the tissue.

Fractional - describes the energy required to separate the two adhering surfaces.

Adsorption - based on interactions of atoms and functional groups due to the physico-chemical properties in close contact with polymeric chains.

2 basic types of chemical bonds:

Strong primary bonds – covalent interactions are not desirable for the adhesive bonds

Weak secondary bonds – *van der Waals forces*, *ionic* and *hydrogen* bonds create during contact of mucoadhesives and mucus.

The adhesion strength - conditioned by the number of binding sites. Polymers with higher Mw and c of polar groups are more reactive, i.e. form stronger mucoadhesive bond.

Mucoadhesion Formation and Influencing of the Process

Mucoadhesion process is influenced by many factors which must be taken into consideration by development of a suitable mucoadhesive dosage form.

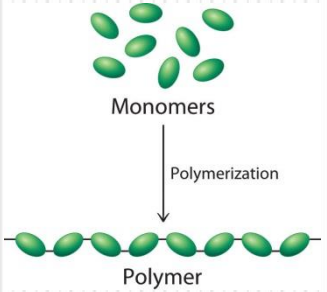
Factors of organism	-	turnover time of mucus molecules (47-270 min)
	-	mucosa movements (eating, drinking, speaking)
	-	mucosa disorders (infections, cancer, saliva)
Outer factors	-	contact time
	-	application force
	-	pH (influences adhesion, swelling)
Polymer properties	-	swelling
	-	rheological prop. (chain interpenetration)
	-	internal cohesion
	-	Mw
	-	degree of crosslinking
	-	the concentration of functional groups

Mucoadhesive polymers

Polymers of hydrophilic nature, swelling, with a large number of polar groups, having visco-elastic properties.

- Hydrophilicity, swelling
- The presence of groups forming H-bonds (-OH, -COOH, $-CONH_2$, $-SO_3H$, -SH)
- Non-toxicity, non-irritation, suitable pH
- The ability to adhere to the mucosa rapidly
- Sufficient mechanical resistance
- Do not support secondary infections (dental caries)

Mucoadhesive polymers



Division according the origin / charge:

Synthetic: derivatives of polyacrylic acid (polycarbophil, carbomer), polyvinylpyrrolidone, polyethylene oxide

Semi-synthetic: cellulose derivatives (oxycellulose, sodium carboxy methylcellulose, hydroxypropyl methylcellulose,…), chitosan

Natural: gelatin, pectin, hyaluronic acid, sodium alginate, xanthan gum

kationic (chitosan), *anionic* (polyacrylates, CMC), *neutral* (PVP, HPMC)

Mucoadhesive polymers

Technological division:

Hydrogels forming polymers: crosslinked structure - prevents rapid dissolving, and helps them to retain water

Polyacrylates - ability to inhibit proteolytic enzymes, the disadvantage is acidic surface reaction (pH≈3,5)

carbomers and *polycarbophils* - have the same base in acrylic acid; differ in crosslinking

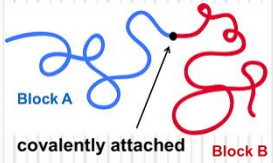
Chitosan – cationic, possibility of substituting by ingredients with SH-groups *ethylene vinyl alcohol, polyethylene oxide, polyvinyl alcohol, sodium alginate, guar gum, karaya gum, xanthan gum, etc.*

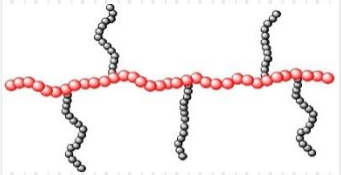
Mucoadhesive polymers

Technological division:

Co-polymers: combination of advantageous properties of components

blocked co-polymers x *grafted* polymers

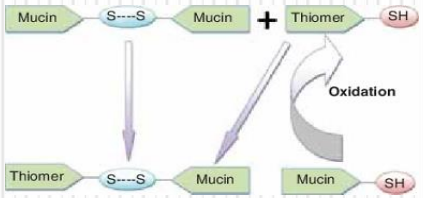




Polyacrylates (Eudragit), chitosan-cysteine, chitosan-4-thiobutylamide conjugates and *conjugates of chitosan-thioglycolic acid*

Mucoadhesive polymers

Technological division:



Thiomers: created by fixation of compounds with thiol groups to mucoadhesive polymers (classified also as copolymers)

SH groups bind to glycoproteins of mucus layer and create inter- and intra-molecular bonds inside them = strong adhesive properties.

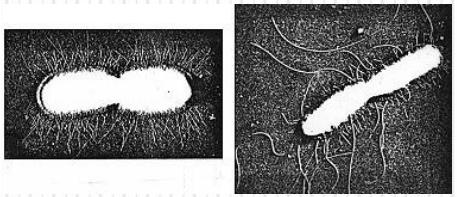
Inhibition of enzymes from the group of Zn-dependent proteases (bind Zn+)

Cationic thiomers - particularly chitosan derivatives (e.g. chitosan-N-acetylcysteine, chitosan-cysteine, chitosan-thioglycolic acid)

Anionic thiomers (e.g. carboxymethyl-cysteine, cysteine-alginate)

Mucoadhesive polymers

Technological division:

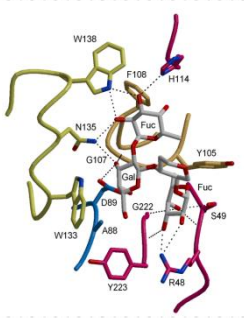


Mussel adhesive protein: the "blue mussels„ - *Mytilus edulis*

The adhesive bonds of marine organisms are based on two processes: secretion of adhesive biopolymer to the substrate, followed by formation of cohesive bonds between the further polymer layer which is deposited on the surface of the first layer.

Bacterial mucoadhesives: pathogenic bacteria have surface structures capable of binding to mucus and cellular receptors. This feature is supported by the ability to induce endo- and transcytosis in target cells, which makes them suitable carriers for targeted drug delivery across GIT mucosa.

Mucoadhesive polymers



Technological division:

Lectins: mucoadhesives of 2nd generation - substances with the ability to bind specifically to epithelial cells (mediated by a receptor-ligand system)

Substances that recognize oligosaccharide sequence on the surface of target cells and specifically bind to them - cytoadhesion (without prior binding to a mucus layer).
Beans phytohemagglutinin (Phaseolus vulgaris)
Lectin from the juice of ripe tomatoes (Lycopersicon esculentum)
Lectin of wheatgerm (WGA) and *nettle* (UDA)

By current methods of genetic engineering can be lectins specifically changed at the molecular level, and used to prepare new bioadhesive drug carriers.

Mucoadhesive polymers

Summary:

Hydrogel-forming polymers	• *Cellulose Derivatives* *Polyacrylates* *Xanthan Gum* *Guar Galactomannan* *Sodium Alginate* *Chitosan*
Co-polymers	• *Blocked and grafted polymers*
Thiolated polymers	• *Chitosan-N-acetylcysteine* *Chitosan-cysteine* *Chitosan-thioglycolic acid* *Carboxymethyl-cysteine* *Alginate-cysteine*
Polymers of other structure	• *Mussel Adhesive Protein* *Lectins* *Silicones* *Bacterial Mucoadhesive*

Mucoadhesive formulations and their use

Most often intended for the application in the GI or respiratory tract.

Liquid: emulsions, suspensions (Nystan™)
Semisolid: pastes, gels (Corsodyl®), ointments
Solid: tablets (Suscard®, Loramyc®), films

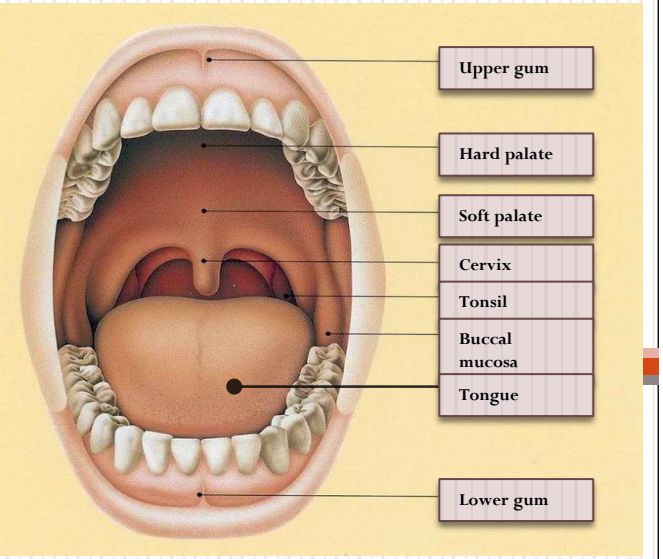
Local therapy:

antibiotics, antimycotics, anaesthetics, antiseptics,...

Systemic therapy:

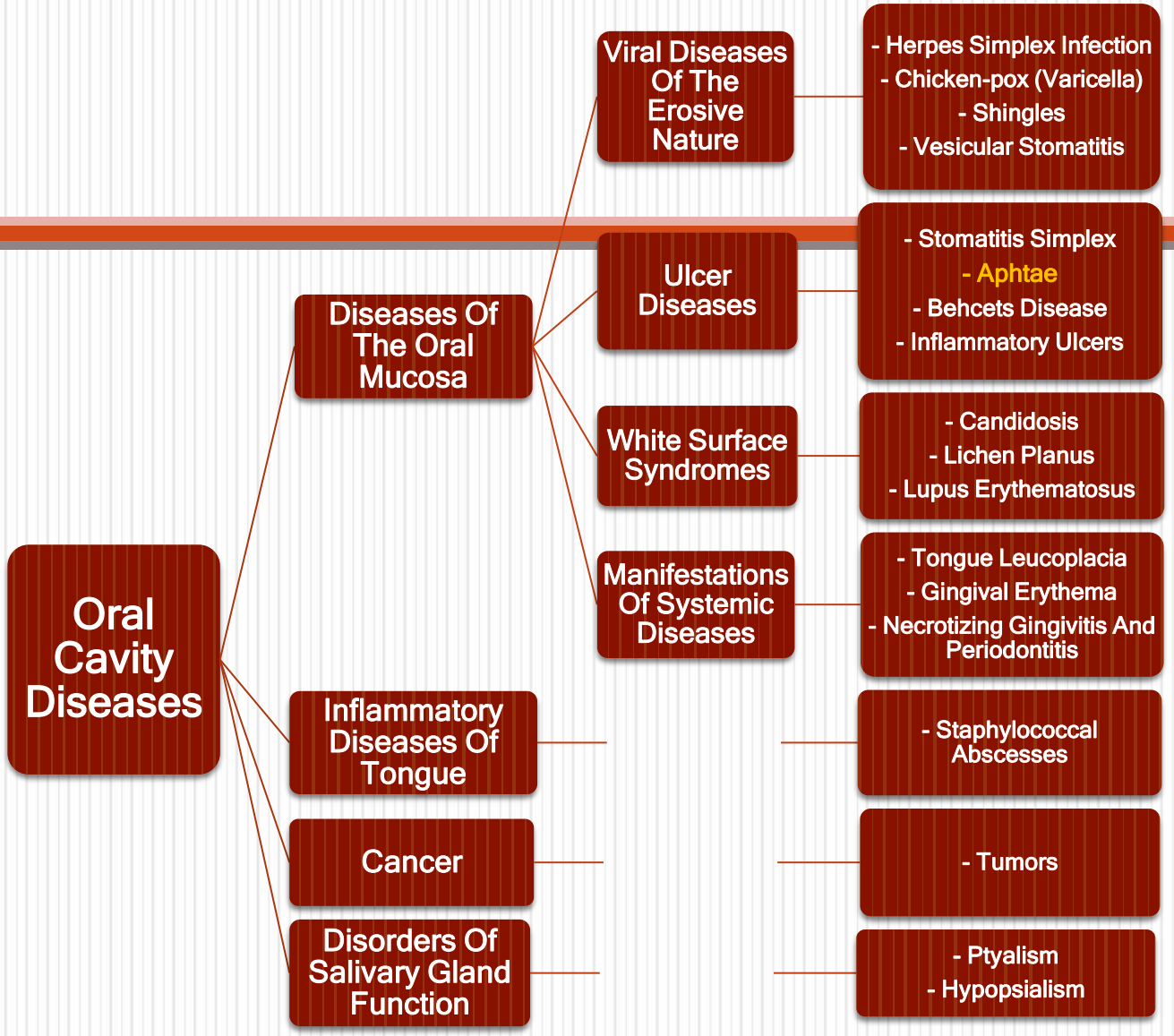
hormones (peptide origin), vasodilators, bronchodilators, analgetics,...

Oral cavity

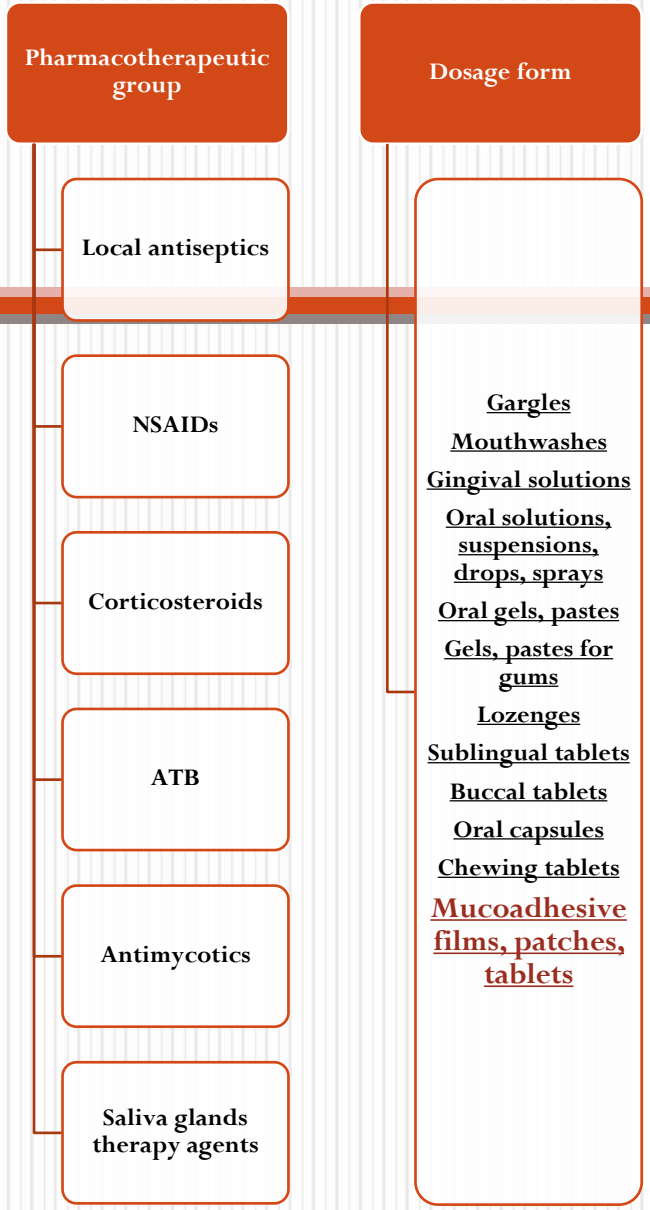


- due to its connection with food intake, breathing and speaking processes permanently exposed to external influences
- oral cavity illness = manifestation of the imbalance between aggressive and protective factors in the body
- diseases of the oral cavity often the first symptoms of serious illness
- oral health reduces the incidence of many pathological conditions (cardiovascular disorders, respiratory infections, diabetes etc.)

Oral cavity - diseases



Oral cavity - therapy



Oral cavity as the application site

Oral cavity and its mucosa (especially buccal) forms a convenient area for applying dosage forms with both local as well as systemic effect.

Oral application advantages:

- sufficient surface area and rich blood supply
- accessibility
- good permeability of non-keratinized areas of the oral mucosa
- circumventing the liver first pass effect
- good patient acceptance - increased the therapy compliance and effectiveness
- easy and rapid removal of the drug (if necessary)
- oral mucosa has the ability of fast regeneration
- can be used also for uncooperative patients
- presence of saliva provides a sufficient amount of aqueous medium for the dissolution of the API
- low enzymatic activity and non-aggressive environment
- the possibility of using **mucoadhesion** phenomenon

Oral cavity as the application site

Disadvantages and limitations:

- small absorption area compared to the intestine (100-200 cm^2)
- strong barrier properties of keratinized areas of the oral mucosa
- mucus layer capable of drug binding
- continuous saliva secretion, leading to dilution of the API
- saliva swallowing may lead to loss of dissolved or suspended drugs and its unwanted getting into the lower parts of the GIT
- aggressive influence of drinking, food intake, chewing and speaking
- potential pathological condition of the oral cavity

Oral dosage forms

Oral preparations *(Oromucosalia)*

- solid, semisolid or liquid preparations containing one or more APIs, intended for administration into the oral cavity and/or oropharynx to achieve local or systemic effect.

According to Ph. Eur. oral preparations can be divided into two basic categories:

- Dosage forms with *mucoadhesive* properties
- Formulations, where mucoadhesive properties are not required (*orodispersible*)

Mucoadhesive dosage forms

Modern therapeutic systems, which ensure prolonged resistance of the drug on the mucosa.

Liquid MDF (mouthwashes, sprays, gargles) - solutions, emulsions or suspensions of drug in an aqueous solvent with the addition of mucoadhesive polymer. Their limit is a short residence time at the application site.

Semisolid MDF (gels, pastes) – easily applied, the dose is not exact (not for strongly active API).

Solid MDF (tablets, lozenges, **films**) - best stability and resistance on the mucous membrane, may cause discomfort during speaking or eating.

Mucoadhesive dosage forms

Overview

Mucoadhesive dosage forms		
Solid	Semisolid	Liquid
tablets films lozenges wafers and lyophilizates powders micro- and nano-particles	ointments gels creams pastes	solutions liquid aerosols medicated paints

Mucoadhesive preparations and their use

Tradename	Mucoadhesive polymer	Manufacturer	Dosage form
Buccastem	PVP, xanthan gum, carubine	Rickitt, Benckiser	Tablets
Suscard	HPMC	Forest	Tablets
Gaviscon liquid	natrium-alginate	Rickitt, Benckiser	Oral solution
Orabase	pectin, gealatin	ConvaTech	Oral pasta
Corsodyl gel	HPMC	Glaxosmithkline	Oral gel
Corlan pellets	gum arabic	Celltech	Pelets
Fentanyl Oralet	CP 934, NaCMC	Lexicomp	Lozenges
Miconaczole Lauriad	modified starch, CP 934	Bioalliance	Tablets
EmezineTM	CP 934, PVP K-30	BDSI's	Tablets
Strain SR	CP 974, HPMC K4M	Ardana	Tablets
Zilactin	HPC	Zila	Buccal films
Luborant	NaCMC	Antigen	Artificial saliva
Saliveze	NaCMC	Wyvern	Artificial saliva
Tibozole	PC, CP 934-P	Tibotec	Tablets
Aphtach	HPC, PAA	Tejin Ltd	Tablets
Buccastem buccal	xanthan gum	Reckitt	Tablets

Mucoadhesive preparations and their use

Mucoadhesive films

Mucoadhesive oral tablets

+ Local and systemic therapy
+ Non-invasive route of administration
+ Good bioavailability of the active substance
+ Convenient method of administration, allowing the patient to eat and drink
+ Dosing accuracy
+ Appropriate method of drug administration for patients with swallowing difficulties
+ Easy interruption of the drug supply e.g. when side effects occur
+ Mechanized and automated production technology
+ Minimum moisture content to ensure DF stability
+ The possibility of producing DF with controlled release

- Ingredients may cause local irritation
- Limited dose of drug that can be applied in this way
- Damage of the mucosal epithelium may affect the absorption of API

Mucoadhesive films

- most researched mucoadhesive dosage formulations
- mucoadhesive films resemble classical patch which, however, adhere to the mucosa using the mucoadhesion process

Breakyl® (fentanyl) indicated for the treatment of breakthrough pain in adults with cancer who are already receiving maintenance opioid therapy

Mucoadhesive films

- most often used - **buccal** films
- mono-layered or multi-layered strips, in which are as excipients used mucoadhesive polymers
- in terms of residence time on the buccal mucosa can be divided into *permanent* and *dispersible*

Permanent buccal films (syn. buccal patches) containing insoluble outer layer, and at the end of the application interval must be removed.

Dispersible mucoadhesive buccal films are subject to a gradual erosion or dissolution and disintegrate in the oral cavity in time.

Mucoadhesive films - advantages

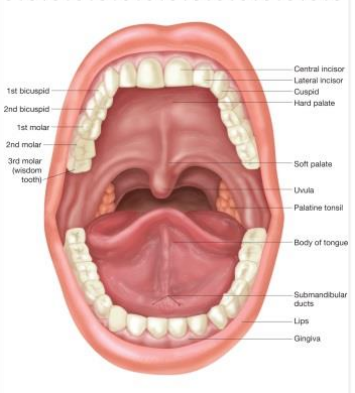
- Flexibility, easy and painless application ⟶ compliance
- Prolongation of time remaining on the mucous membrane
- Easy removal if needed
- Ensure accurate dosage
- Improved bioavailability
- Covering the lesion surface

⟶ extending the active pharmacotherapy, reducing the need for repeated applications and reduce financial demands of treatment

Mucoadhesive films - characterization

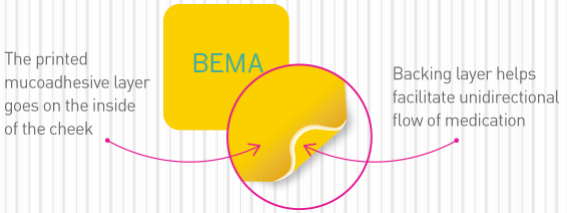
- may consist of several layers, on which depends the direction of API release
- could be used for *local* and also *systemic* application – depends on dosage form design
- DF of the buccal mucoadhesive films nature can have different structures in addition to a method of dispersion of the drug inside them
- based on these factors is defined the direction and the speed of API release
- we can distinguish monolayer, multilayer, matrix or reservoir type of MOFs

Mucoadhesive films



DF typically composed of several layers:

- mucoadhesive
- backing
- middle layer – control drug release rate



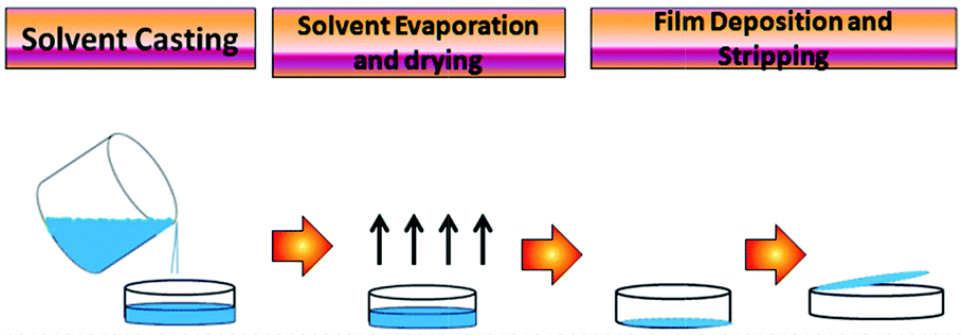
Preparation:

- solvent casting method
- method of impregnation
- extrusion, printing, electrospinning

Mucoadhesive films - preparation

Solvent casting method

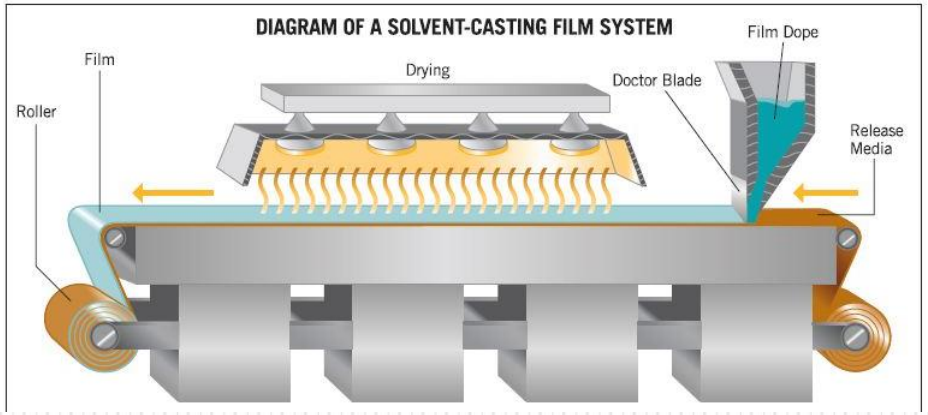
- most widespread technology for producing of MAF for its simplicity and ease of process instrumentation
- problem may be to ensure good rheological properties of the dispersion, homogeneity and the absence of air bubbles - the uniformity of the film
- time-consuming process and sometimes used solvents are a burden for the environment



Mucoadhesive films - preparation

Solvent casting method

- dispersion preparation
- transfer of its predetermined volume into the casting mold
- drying = solvent evaporation
- cutting the film into the desired shape and packing



Mucoadhesive films - preparation

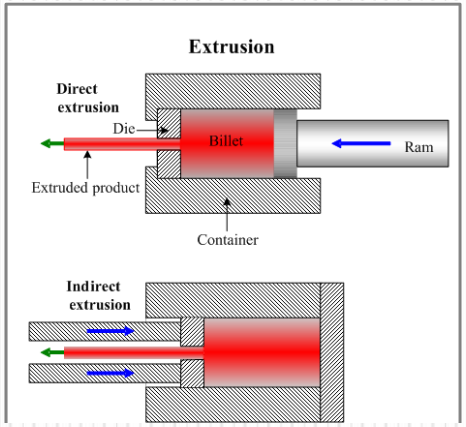
Extrusion

- can proceed either at high (hot melt extrusion) or lower temperatures (cold extrusion)
- highly variable instrumentation
- „hot melt extrusion“ is often used for manufacturing of MAF
  - \+ no need to use any solvents
  - \+ processing time is shorter, the process is effective, the films are more stable
  - \- financial demands through specialized equipment
  - \- not suitable for thermo-labile substances

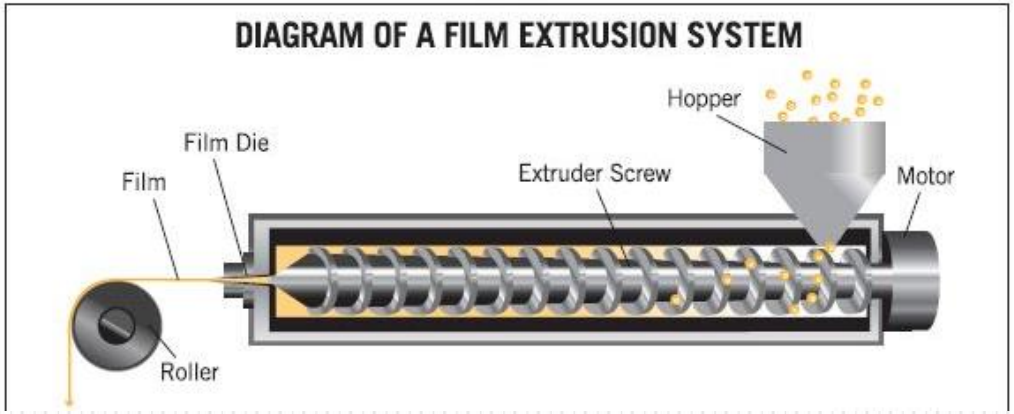
Mucoadhesive films - preparation

Extrusion

- insertion of active substances and excipients into the extruder
- melting and homogenization using pressure and elevated temperature
- extruding the melted material through a shaping orifice
- cooling the resulting extrudate



Ram extrusion



Screw extrusion

Mucoadhesive films - preparation

Extrusion

- used **polymeric substances** and **plasticizers**

Polymers: *polyvinyl pyrollidone, PEG (macrogols), cellulose ethers, polyacrylates, polyoxy ethylene, polylactic a polyglycolic acid, modified starches, sugars, sugar alcohols* and *waxes*

The decisive factor for these materials is its ability to be melted, miscibility with the API, its stability, etc.

Plasticizers: *triacetin, citric acid esters* or *macrogols*

- decrease the melting point

Mucoadhesive films - preparation

Printing of API onto non-medicated films

- 2D and 3D (multilayer)

The advantage of the method is to **individualize** the amount of the drug (dose) for a specific patient since under this technology it is possible to create a film with a wide range of API content and thus the possibility to create individualized formulation tailored to the patient.

The future perspective is that it will be possible to use this method directly by pharmacist immediately before dispensing medicine, simply by applying API onto the carrier film.

Mucoadhesive films - evaluation

- testing of MAF is not uniform
- there is used number of pharmacopoeial methods for evaluation of similar dosage forms (transdermal patches)
- there is a problem of comparing the results of different scientific studies
- necessary is testing on volunteers and patients, because some properties such as taste of the preparation, mucosal irritation, salivation, residence time, etc. can not be simulated in laboratory conditions

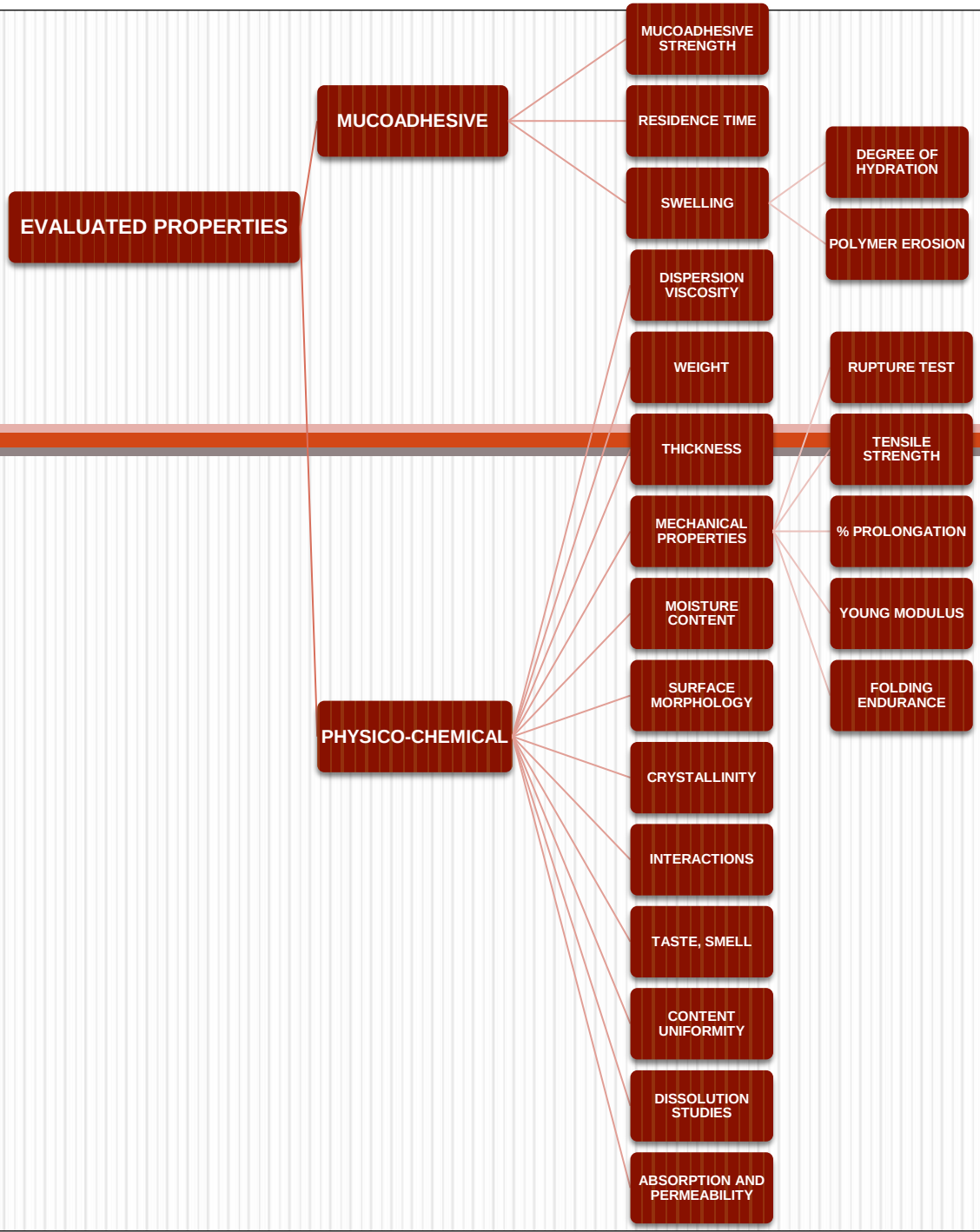
Mucoadhesive films - evaluation

Evaluation of MAF:

1) mucoadhesive properties (mucoadhesive strength, swelling, residence time on mucosa surface, etc.)

2) testing of physico-mechanical properties (dispersion viscosity, content uniformity, weight, thickness, mechanical durability, surface pH, surface morphology, organoleptic properties, moisture content, stability, interactions between polymers and drugs, drug release rate, absorption and permeability of drug through mucosa, etc.)

Summary


EVALUATED PROPERTIES
MUCOADHESIVE
MUCOADHESIVE STRENGTH
RESIDENCE TIME
SWELLING
DEGREE OF HYDRATION
POLYMER EROSION
PHYSICO-CHEMICAL
DISPERSION VISCOSITY
WEIGHT
THICKNESS
MECHANICAL PROPERTIES
RUPTURE TEST
TENSILE STRENGTH
% PROLONGATION
YOUNG MODULUS
FOLDING ENDURANCE
MOISTURE CONTENT
SURFACE MORPHOLOGY
CRYSTALLINITY
INTERACTIONS
TASTE, SMELL
CONTENT UNIFORMITY
DISSOLUTION STUDIES
ABSORPTION AND PERMEABILITY

Mucoadhesive films - research

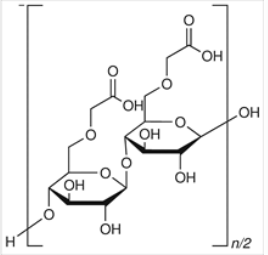
- oral mucosal diseases meet the majority of population
- caused by its continuous exposure to external influences
- lesions in OC are painful, they reduce the quality of patient life
- in pharmacotherapy of mucosal defects are mouthwashes, gels and pastes with relatively short residence time
- covering lesions by MA films - more effective pharmacotherapy (separation of lesion, prolonged effect)

Buccal films as dressing of lesions

Formulation, development, preparation and evaluation of flexible mucoadhesive films for the local treatment of defects of the oral mucosa.

Basic MA polymer: **carmellose**

(Blanose 7LF-PH, Ashland Aqualon, USA)



Preparation method: solvent casting

Evaluation: optical analysis
texture analysis (Texture Analyzer CT3, Brookfield, USA)
- mechanical durability against pressure and tearing
surface pH, swelling
in vitro residence time
in vivo evaluation

Optimization of film composition

Plasticizer

- **glycerol (PEG,** PG, triethylcitrate, dibutylsebacate)

Addition of MA polymers

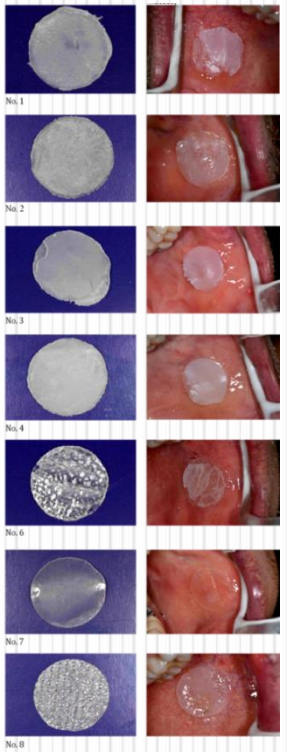
- **polyethylene oxide** (Polyox™ WSR 301)
- HPMC K100LV and HPMC E4M

Incorporation of HCMC as the non-woven textile from Hcel HT

- method of impregnation

Backing layer

hydrophilic – 5% EC x hydrophobic – bone was (vaselina alba + cera alba)



Composition and evaluation of films suitable for *in vivo* tests

	NaCMC[a]	Glycerol[a]	PEO[a]	textile	backing layer
sample 1	2 %	2 %	-	no	hydrophobic[b]
sample 2	2 %	2 %	-	yes	hydrophobic[b]
sample 3	2 %	2 %	0,5 %	no	hydrophobic[b]
sample 4	2 %	2 %	0,5 %	yes	hydrophobic[b]
sample 5	2 %	2 %	-	no	EC
sample 6	2 %	2 %	-	yes	EC
sample 7	2/4 %	2/3 %	0,5 %	no	EC
sample 8	2 %	2 %	0,5 %	yes	EC

[a] in casting dispersion
[b] blend of white beeswax and white petrolatum in ratio 55:45

18 + 9 mL casting solution (48 + 48 h drying)
4,5 mL backing layer

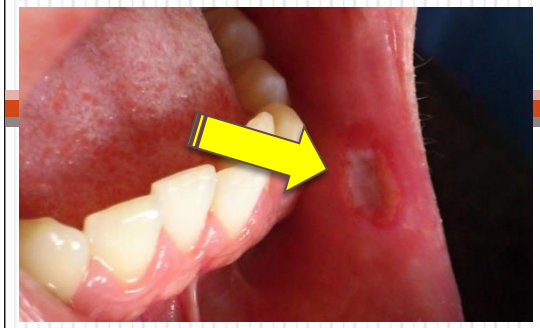
In vitro residence time	h:min
sample 1	6:15
sample 2	4:49
sample 3	> 8:00
sample 4	6:48
sample 5	4:57
sample 6	1:07
sample 7	> 8:00
sample 8	2:20

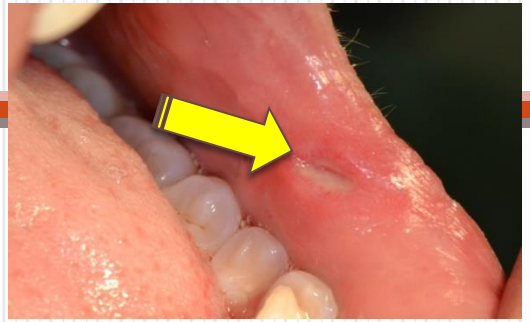
	Composition of backing layer	*2% NaCMC 2% glycerol*		*2% NaCMC 2% glycerol +textile*	
		no co-polymer	*+ Polyox 0,5%*	*no co-polymer*	*+ Polyox 0,5%*
	Sample nr.	*1+5*	*3+7*	*2+6*	*4+8*
	Thickness (μm)	327.25	293.09	302.97	300.27
Tensile testing	**Tensile strength (N)**	9.04	11.79	7.65	6.63
	Work done (mJ)	117.68	132.57	26.21	21.81
	Deformation (mm)	20.17	18.69	3.94	3.61
Penetration testing	**Penetration force (N)**	6.26	6.90	4.42	3.65
	Work done (mJ)	12.09	12.23	4.81	4.30
	Deformation (mm)	4.41	4.27	2.43	2.61
	Surface pH	6.61	7.17	5.11	5.18

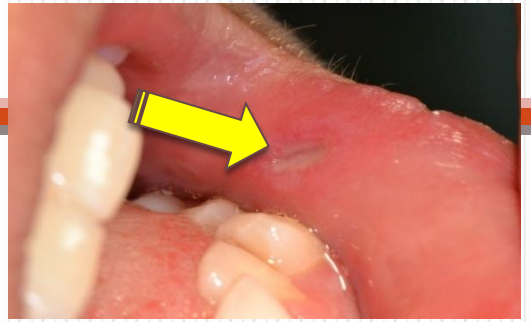
- about 35 patients – pain perception improvement, faster healing

Composition and evaluation of films suitable for *in vivo* tests

Control group

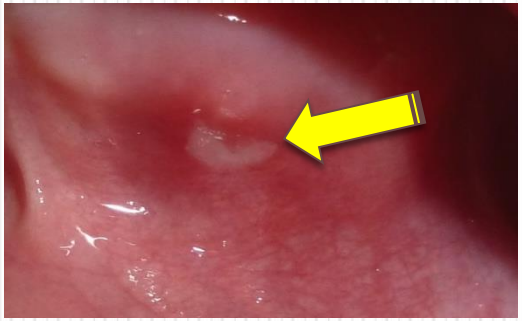


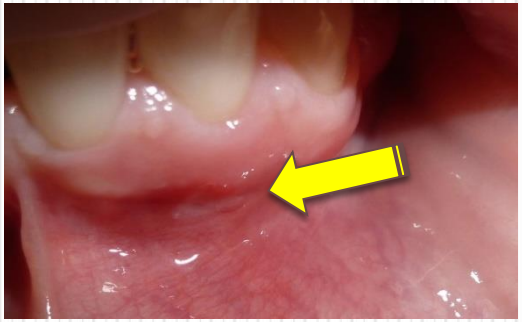


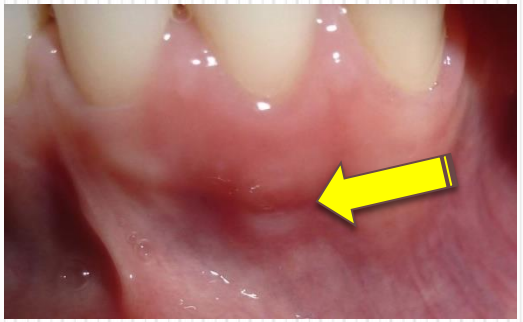


Day 1 ***Day 3*** ***Day 5***

Experimental group with applied MA film



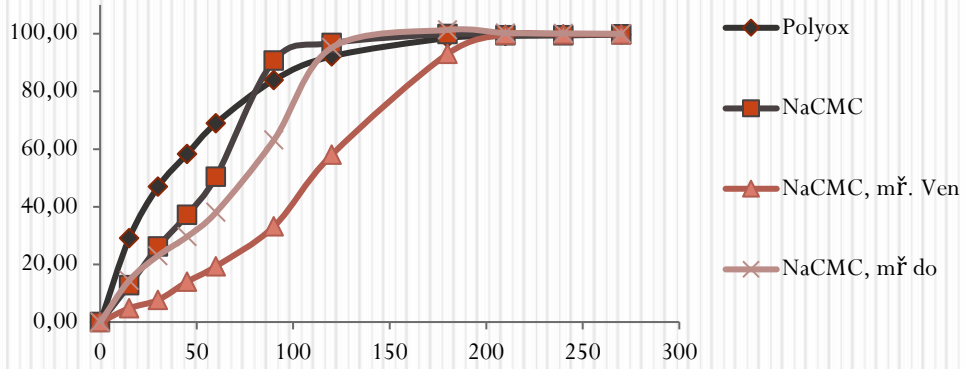




Films containing antimycotic agent

Formulations containing NaCMC adhere longer, but need longer contact times to attach. Films consisting of Polyox adhere quickly, but the residence time is shorter.

Composition	Residence time in vitro (min)
2% Polyox, 3% Glycerol	22,4 ± 4,3
4% NaCMC, 3% Glycerol	43,6 ± 4,3
2% Polyox, 3% Glycerol, non-woven textile with SD 0,4	-
4% NaCMC, 3% Glycerol, non-woven textile with SD 0,4 (externally)	**73,5 ± 7,3**
4% NaCMC, 3% Glycerol, non-woven textile with SD 0,4 (internally)	59,8 ± 5,2



Films containing antimycotic agent

Efforts to extend the period of residence and optimize the dissolution profile (CPX, nystatin) - tests on rabbits

Composition:

- 4% NaCMC, 3% Glycerol and Polyox

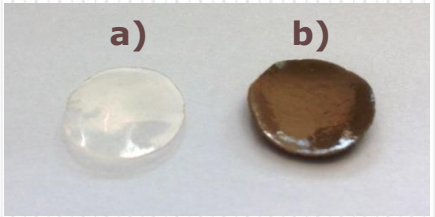
+ **Hcel HT with DS = 0,4000, 35 gsm**

+ Montanglycol wax, Eudragit NM 30 D
(inside and also as backing layer)

MA films with nanocomposite clay material

Treatment of oral cavity infections

- the current market lacks the appropriate dosage form for local long-acting treatment
- effort to avoid systemic treatment
- solution may be mucoadhesive films containing antimicrobial nanocomposite



MUCOADHESIVE FILMS
a) without nanocomposite
b) with vermiculite/chlorhexidin

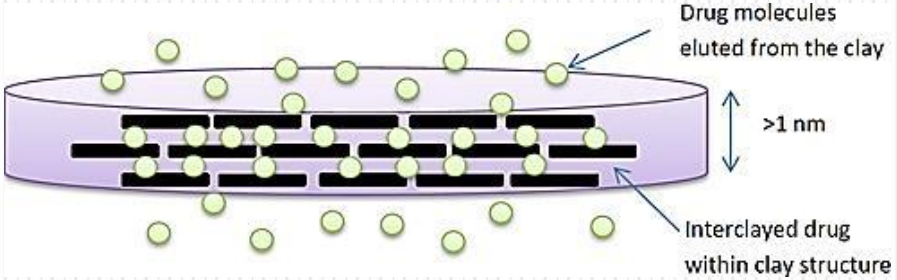
antibacterial nanocomposite

- anorganic carrier modified by antimycotic or antibacterial substance
- by binding the drug to a suitable carrier can be provided

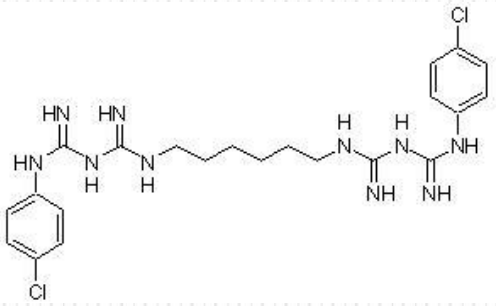
⇒ transport to the specific site of the body

⇒ controlled release

⇒ minimization of side effects



MA films with nanocomposite clay material



API with antimicrobial effect

CHLORHEXIDIN DIACETATE/DIGLUCONATE

- bivalent surface active biguanidine
- inflamation treatment, desinfection of the oral cavity
- acts against many G- and G+ bacteria, yeasts, lipophilic viruses, etc.

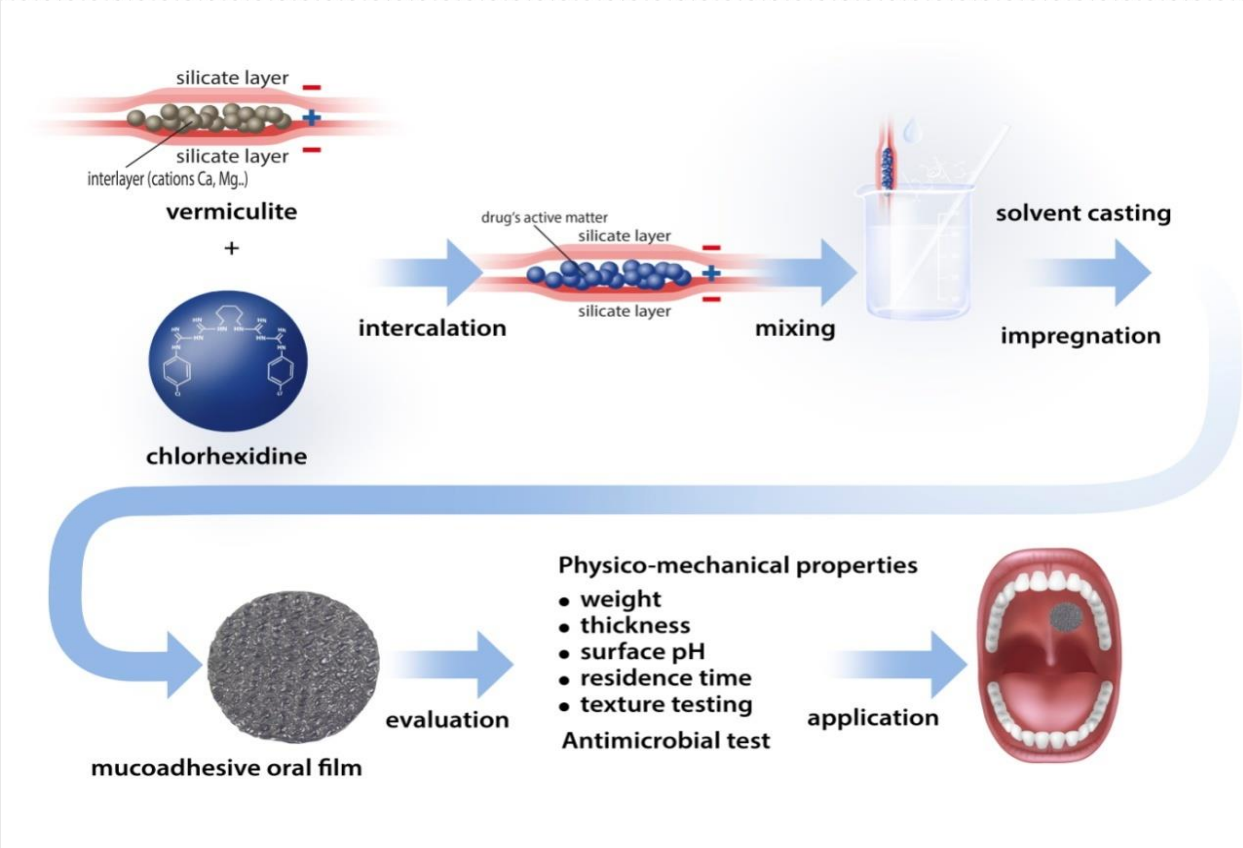
prepared samples

- two API concentrations - 10 and 20 mg of diacetate (CHDAC) or digluconate (CHDG)

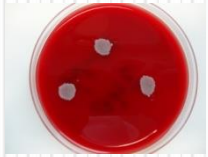
two preparation methods:

solvent casting (smooth samples) x impregnation of non-woven textile (H-Cel HT, marked M)

MA films with nanocomposite clay material



MA films with nanocomposite clay material



Antimicrobial tests

strain	sample	Exposure time										
		30	60	90	120	180	240	300	24	48	72	96
S. aureus	10CHDAC	NM	NM	NM	NM	NM	NM	NM	55	0	0	0
	10CHDAC-M	NM	0	0	0	0	0	0	0	0	0	0
	20CHDAC	NM	NM	NM	NM	NM	NM	NM	0	0	0	0
	20CHDAC-M	NM	0	0	0	0	0	0	0	0	0	0
	10CHDG	NM	NM	NM	NM	NM	NM	NM	NM	0	0	0
	10CHDG-M	0	0	0	0	0	0	0	0	0	0	0
	20CHDG	NM	NM	NM	NM	NM	NM	0	0	0	0	0
	20CHDG-M	NM	7	0	0	0	0	0	0	0	0	0
C. albicans	10CHDAC	NM	NM	NM	NM	14	11	10	11	0	0	0
	10CHDAC-M	NM	NM	NM	NM	4	3	0	0	0	0	0
	20CHDAC	NM	NM	NM	NM	NM	NM	26	29	0	0	0
	20CHDAC-M	3	1	0	6	3	2	5	0	0	0	0
	10CHDG	NM	NM	NM	NM	NM	NM	NM	NM	23	0	0
	10CHDG-M	NM	NM	NM	NM	NM	NM	NM	NM	10	0	0
	20CHDG	NM	NM	NM	NM	NM	NM	NM	100	0	0	0
	20CHDG-M	NM	NM	NM	NM	NM	NM	15	13	8	0	0

NM = not countable (more than 300 CFU)

MA films with nanocomposite clay material

10CHDAC-M and 20CHDAC-M – most effective (STAU and CAAL)

10CHDG-M and 20CHDG-M – most effective against STAU

10CHDAC and 10CHDG – less effective against STAU

20,10CHDG and 10CHDG-M – less effective against CAAL

Against STAU were samples with Hcel HT always more effective!
Against CAAL was only 20CHDAC-M better than without Hcel HT!

API	Mucoadhesive polymer
Antiseptics	
chlorhexidin-digluconate	Chitosan
chlorhexidin-diacetate	Ethylcellulose
cetylpyridinium-chloride	Polyvinyl alcohol, hyetellose or chitosan
Antihistamines	
chlorfeneramin-maleate	Polyethylen oxide
Analgetics	
buprenorfine	Carbopol 934, polyiso butylene, polyiso propene
Anti-anginal agents	
isosorbid-dinitrate	hypromellose, ftalate of hypromellose
Anaesthetics	
lidokain	Hyprollose
Antimycotics	
mikonazol-nitrate	carmellose, chitosan, polyvinyl alcohol, hyetellose, hypromellose
Calcium channel blockers	
nifedipine	alginates, methyl cellulose, polyvinyl pyrolidone, PEG
Beta-blockers	
metoprolol-tartrate	Eudragit® NE 40D with hypromellose, carmellose or carbopol
Antivirotics	
acyklovir	Copolymer of acrylic acid and PEG
Antibiotics	
tetracykline	Colagen
Hormones	
melatonine	Carbopol 934-P, poly isobutylene
oxytocin	Carbopol 974-P
testosterone	polycarbofil, Eudragit® S-100
kalcitonine	polycarbofil, Eudragit® S-100
protireline	hyetellose, hyprollose, polyvinyl pyrolidone, polyvinyl alcohol
triamcinolone-acetonide	carbopol, poloxamer, hypromellose
Insuline a antidiabetics	
insuline	gelatin, Carbopol 934-P
glibenclamide	chitosan, polyvinyl pyrolidone
Antiastmatics	
terbutaline	Carbopol 934 and 971, hypromellose, hyetellose, carmellose
Antioxidants	
ipriflavone	PLGA, chitosan

Thanks for your attention.