



# Drug delivery approaches.

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# Structure of the lecture

1. Classification of administration routes
2. Factors related to administration route selection
3. Characteristic of administration routes
4. Innovative administration routes



# Administration/effect of drug

## Local

- drug absorption is limited
- effect aimed on target

tissue/organ

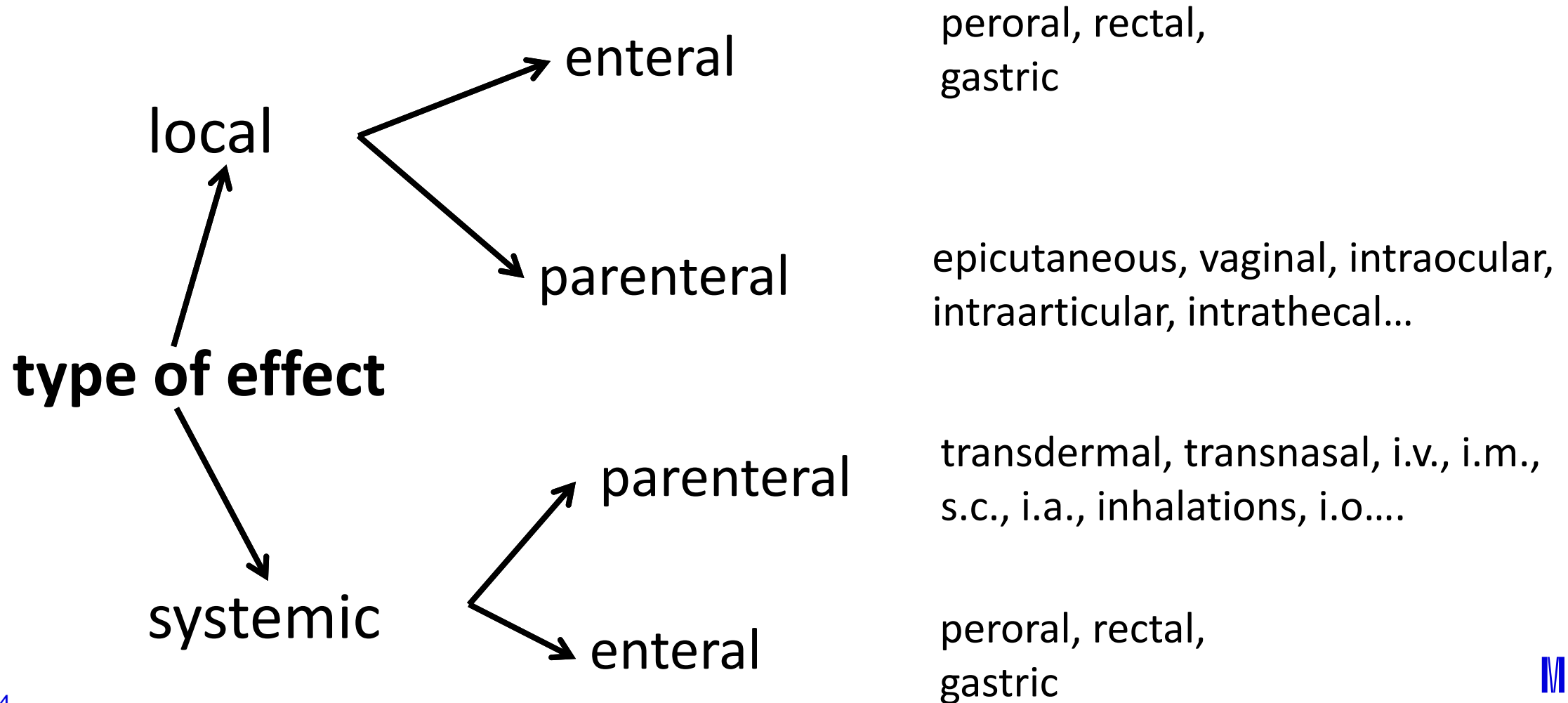
- low risk of AE
- effect depends upon final concentration

## Systemic

- drug is absorbed to systemic circulation
- possible influence on whole body
- higher risk of AE
- effect depends on dose, bioavailability and DDF



# Classification of administration routes



# Classification of administration routes



- with regard to the disruption of natural protective barriers

## Non-invasive

- vaginal, (intrauterine?)
- sublingval
- epicutaneous
- oral
- intranasal
- inhalational
- rectal
- ...

## Invasive

- intravenous
- intraarterial
- intraosseal
- intramuscular
- subcutaneous
- intradermal
- implants
- ...

# Classification of administration routes



- with respect to administration schedule

## Intermittent use

- repeated use
- plasma level fluctuation
- all administration routes
- local and systemic use

## Continuous use

- constant speed of drug administration = constant plasma level of drug
- intravenous
- intramuscular
- subcutaneous/implants
- intravaginal/intrauterine
- intrathecal
- transdermal



# Physical-chemical properties of drug

- lipophilicity/hydrophilicity, solubility
- chemical structure/size of molecule
- pH/pKa
- availability of pharmaceutical form



# Therapeutic indication + severity of disease

- the same drug administered differentially with respect to diagnosis
- local administration preferred
- acute situations – fast onset of effect required

## Benefit:risk ratio

- the more severe, the „more risky“ administration





# Comorbidities

- can block distinct administration routes
- can influence drugs efficacy

# Comedication

- risk of drug-drug interactions

# Administration routes - local effect



- intraurethral, intravesical, intracavernosal
- dental, gingival
- endotracheopulmonary

# Administration routes - local effect



- intraaural
- intraamniotic
- intracoronar, intraarterial



## Ocular/conjunctival administration

- usually eye drops and ointments
- local effect
- risk of systemic AE
- specific quality requirements - sterility

## Intraocular administration

- intravitreal implants and injections in macular degeneration



# Intrathecal/intracerebral/intracerebroventricular administration

- to the subarachnoideal space

/brain/ brain ventricles

# Intraarticular administration



- analgesics/antiphlogistics
- hyaluronic acid
- for local effect

# Administration routes for local and systemic effect



- vaginal, intrauterine
- dermal/transdermal
- intranasal/transnasal
- inhalational
- rectal
- oral/transbuccal, sublingual
- peroral



# Vaginal, endocervical, intrauterinal

- 1. local effect
- minimum of AE
- specific adjuvants ↓ pH
- antibiotics, antimycotics, antiparasitics

## 2. systemic effect

- vaginal rings intrauterine devices
- controlled drug release
- contraceptives



# Epicutaneous/transdermal administration



## Local effect

- ointments, creams, solutions, patches
- minimal AE
- dermatology

## Systemic effect

- transdermal administration
- mainly patches
- continuous release
- local+systemic AE
- high compliance
- easy discontinuation



# Intranasal/transnasal administration

- drops, sprays, ointments
- local effect - antiseptics, ATB
  - antihistamines, decongestants
  - antiphlogistics
- systemic effect - analgesics, antivirotics
  - hormones (ADH, gonadotropin, insulin)



# Inhalation

- gases, aerosols
- systemic effect – general anesthetics
- local effect – antiasthmatics
- fast onset of effect
- minimal presystemic elimination
- administration from spray cans or other instruments (turbohaler, dischaler, nebuliser)

# Rectal administration



- suppositories, capsules, tablets, foams, tampones
- alternative for peroral administration in case of nausea/vomitting or unconsciousness
- variable drug absorption



# Oral/sublingual/buccal administration

- fast onset of systemic effect
- only for small and lipophilic molecules
- sprays, tablets, dispergable films
- analgesics – fentanyl, buprenorfin
- hypnotics – zolpidem
- vasodilators – nitroglycerine
- antiemetics – ondansetron
- homeopatics, allergens, cannabis....

# Peroral administration

## 1. for local effect

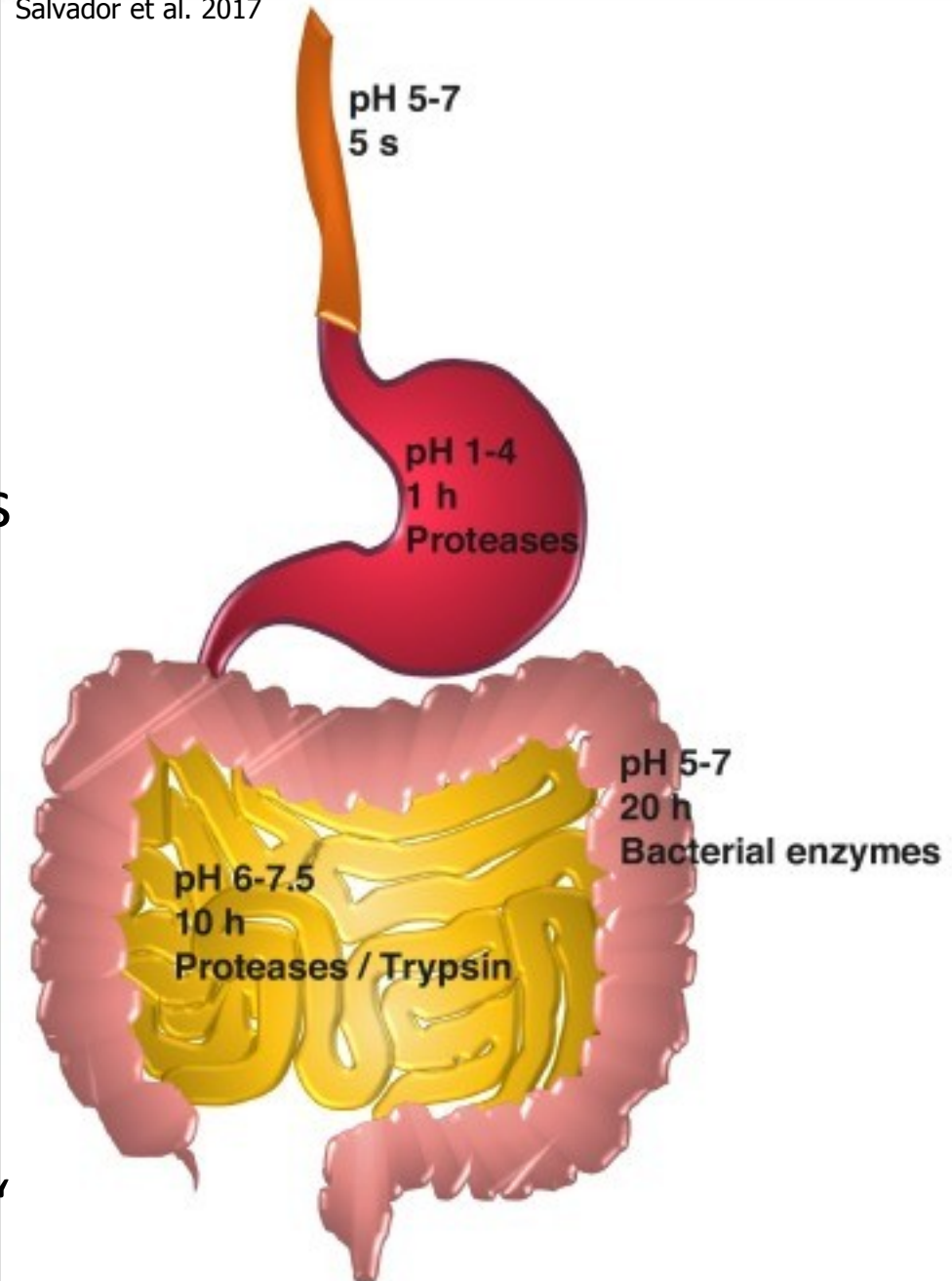


- minimal AE
- risk of interaction with coadministered drugs
- antacids, laxatives, antibiotics

## 2. for systemic effect

- drug absorbed from different parts of GIT
  - can be influenced by DDF
- „slow“ effect onset
- the effect depends on patients „compliance“

Salvador et al. 2017



Current Opinion in Pharmacology

# Administration routes for mainly systemic effect



- intravenous/intraosseous
- intramuscular
- subcutaneous injections and implants

# Injections



## **intravenous, (intraarterial)**

- injection/infusion
- 100% bioavailability, „immediate“ effect
- true solutions + emulsions

## **intramuscular**

- max. volume 5 ml
- to *m. glu. maximus*
- absorption: solution > emulsion > suspension

## **subcutaneous**

- to 2 ml
- variable absorption with regard to adipose tissue



# Injections



## **intradermal**

- minimal volume
- diagnostic purposes

## **intraosseal**

- alternative to i.v.
  - injection/infusion
- 
- Eg. Atropine onset of the effect
  - i.v. 30-90 s; s.c. 15-30 min; i.m. 30-45 min

# Implants



- degradable/nondegradable
- usually s.c. or intraocular
- systemic/local effect
- continuous/pulsatile release = continuous/repeated drug administration
- increased patient's compliance
- complicated discontinuation



# Innovations in drug administration

- new possibilities of administration routes are probably depleted => modification of DDF
- the goals are:
  1. increase of drug safety/decrease of drug toxicity
  2. increase the efficacy of administered dose
  3. increase the patient's compliance



# More about innovations in drug administrations:

- Current Opinion in Pharmacology, Vol. 36, 2017