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Drug delivery approaches.

Ondřej Zendulka

1 Dpt. of Pharmacology, Faculty of Medicine, MU

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

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Administration/effect of drug

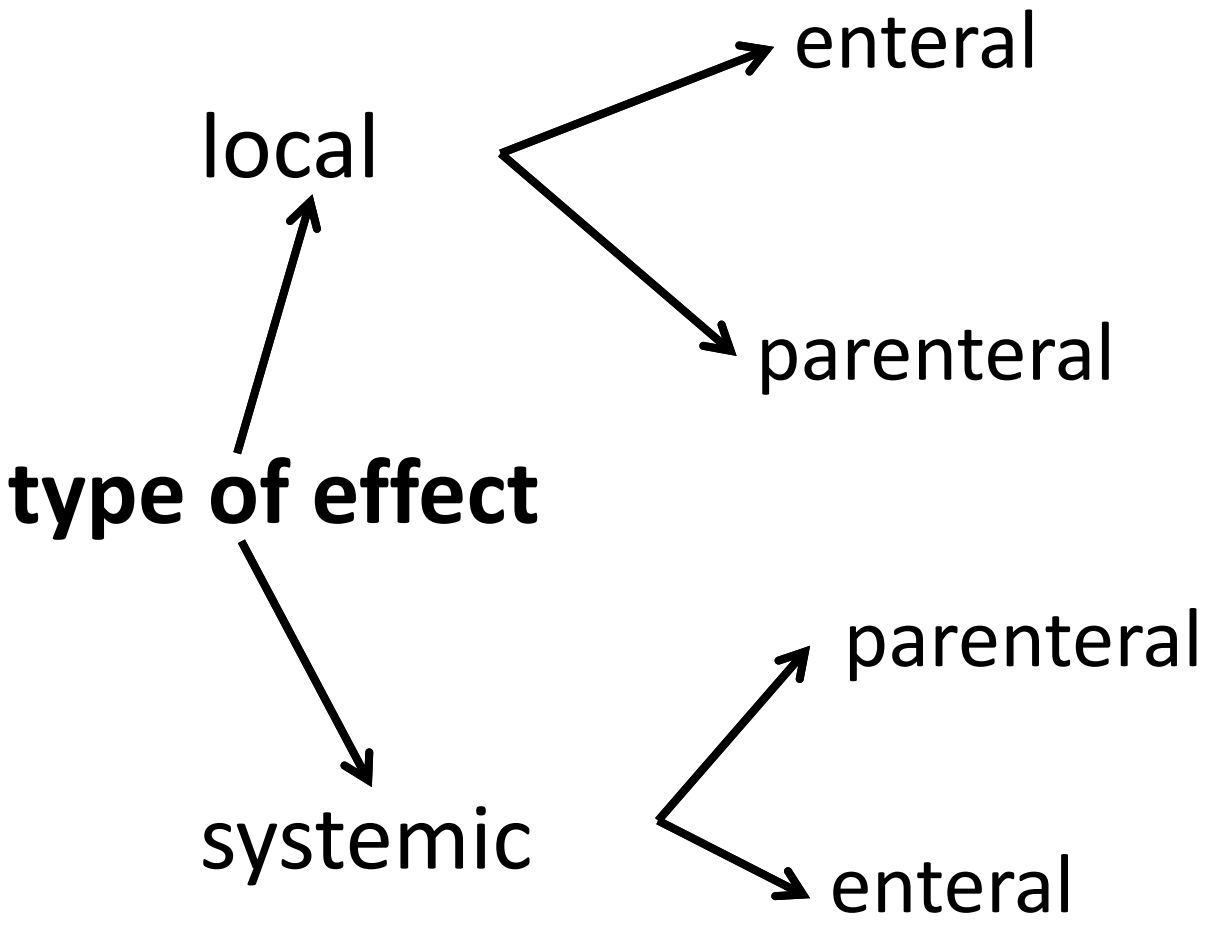
Local

- 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



peroral, rectal,
gastric

epicutaneous, vaginal, intraocular,
intraarticular, intrathecal…

transdermal, transnasal, i.v., i.m.,
s.c., i.a., inhalations, i.o.…

peroral, rectal,
gastric

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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
- intraartrerial
- intraoseal
- intramuscular
- subcutaneous
- intradermal
- implants
- …

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Classification of administration routes

- with respect to administration schedule

Intermitent 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
- subcatous/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 differentialy with respect to diagnosis
- local administration prefered
- acute situations – fast onset of effect required

Benefit:risk ratio

- the more severe, the „more risky“ administration

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Comorbidities

- can block distinct administration routes
- can influence drugs efficacy

Comedication

- risk of drug-drug interactions

Administration routes - local effect

- intraurethral, intravesical, intracavernal
- dental, gingival
- endotracheopulmonal

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Administration routes - local effect

- intraaural
- intraamniotic
- intracoronar, intraarterial

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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

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Intrathecal/intracerebral/intracerebroventricular administration

- to the subarachnoideal space

/brain/ brain ventricles

Intraarticular administration

- analgesics/antiphlogistics
- hyaluronic acid
- for local effect

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Administration routes for local and systemic effect

- vaginal, intrauterinne
- dermal/transdermal
- intranasal/transnasal
- inhalational
- rectal
- oral/transbucal, sublingual
- peroral

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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 unconciousness
- variable drug absorption

Oral/sublingual/buccal administration

- fast onset of systemic effect
- oinly for small and lipiphilic molecules
- sprays, tablets, dispergable films
- analgesics – fentanyl, buprenorfin
- hypnotics – zolpidem
- vasodilators – nitroglycerine
- antiemetics – ondansetrone
- homeopatics, alergens, cannabis….

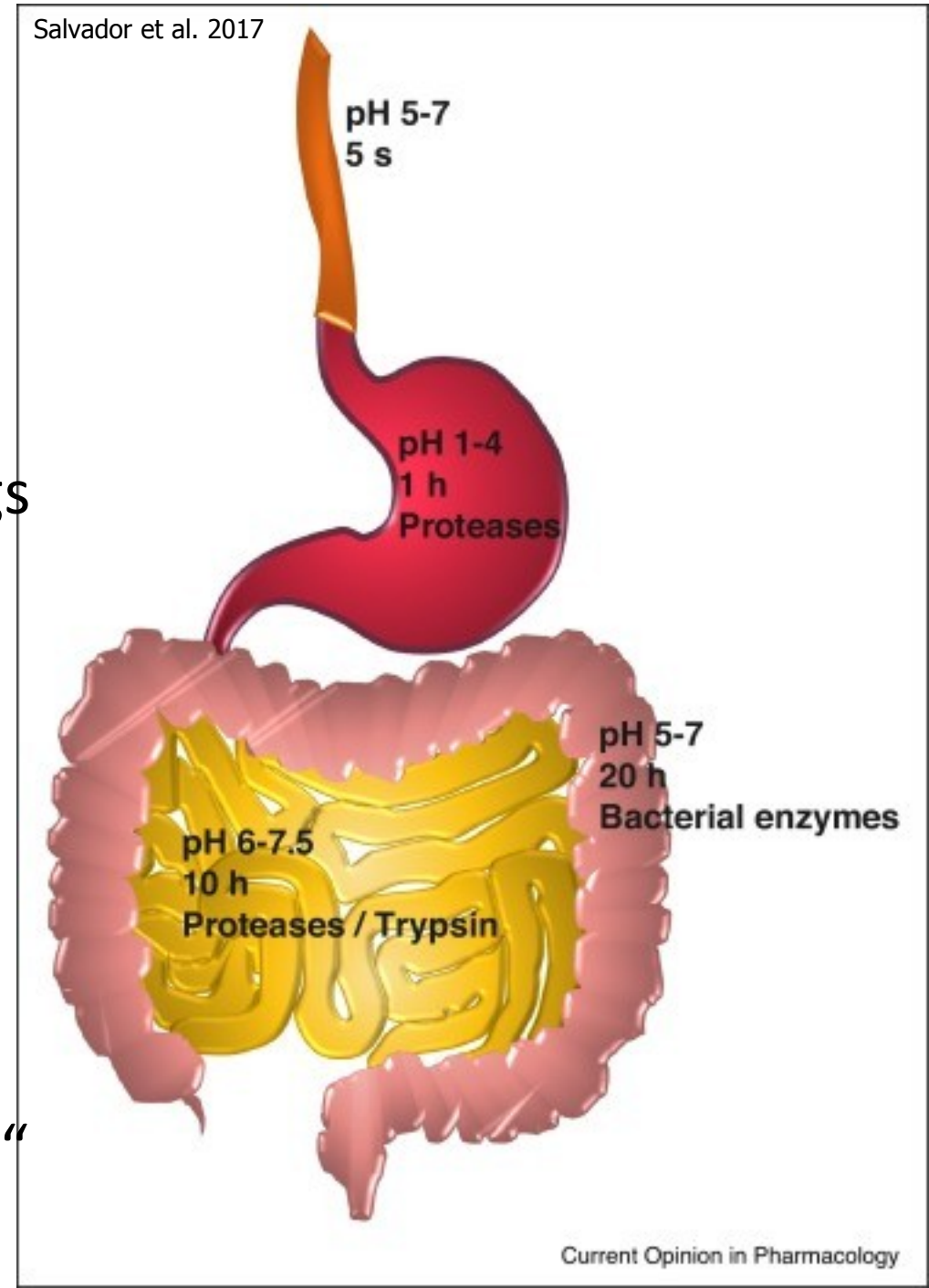
Peroral administration

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“



Administration routes for mainly systemic effect

- intravenous/intraosseous
- intramuscular
- subcutaneous injections and implants

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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 posssibilities 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