

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

Classification of administration routes

Pharmacological differences

pharmacodynamic

- difference in the character of the effect of drug
 - ethanol, iodine (topically/systemic)

pharmacological

- difference in the site of action (local vs. systemic)
 - H₁ antihistamines in nasal drops and tablets
- differences in onset/duration of effect, toxicity
 - fentanyl i.v. vs transdermal, vancomycin per os vs. i.v.

Administration/effect of drug

Local

- drug absorption is limited
- effect aimed on target

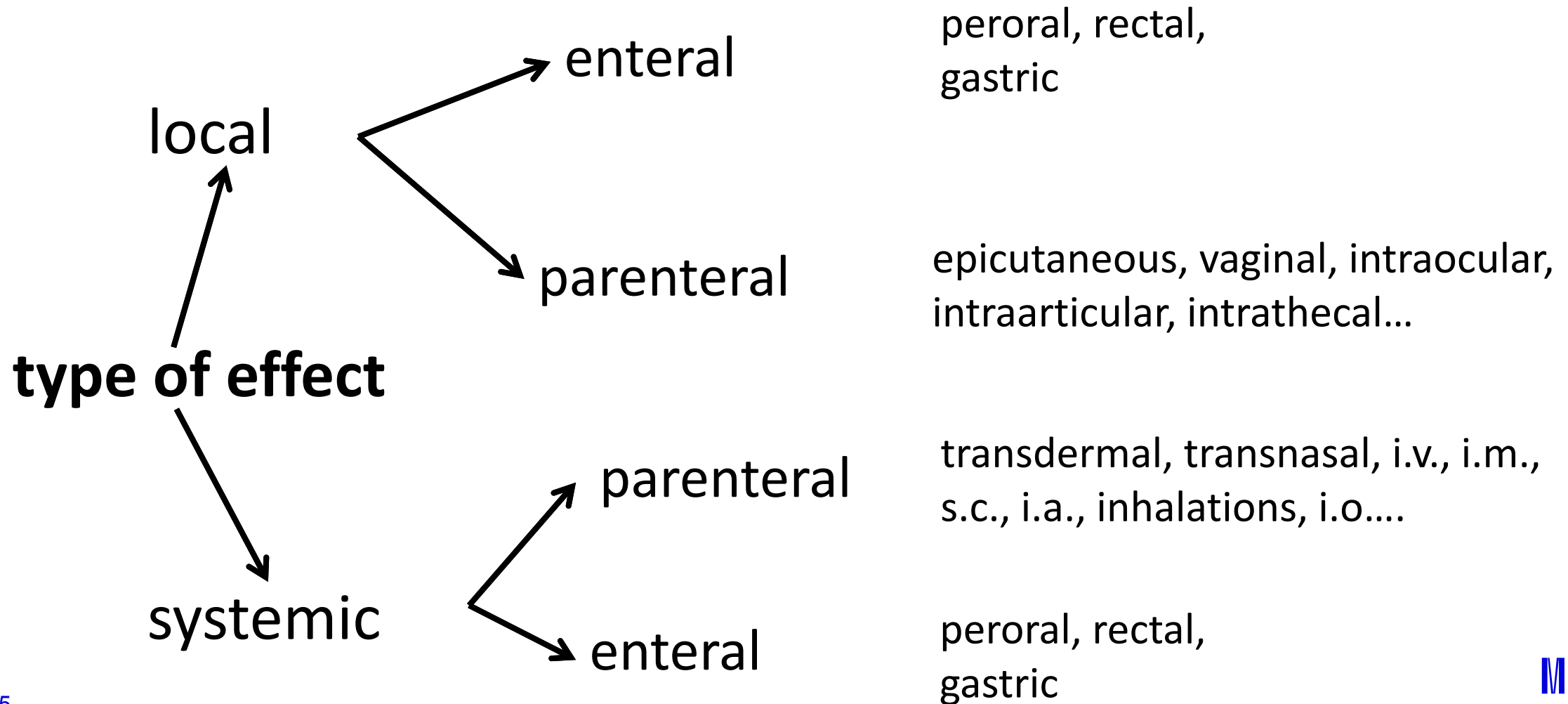
tissue/organ

- 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
- endotracheopulmonal

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

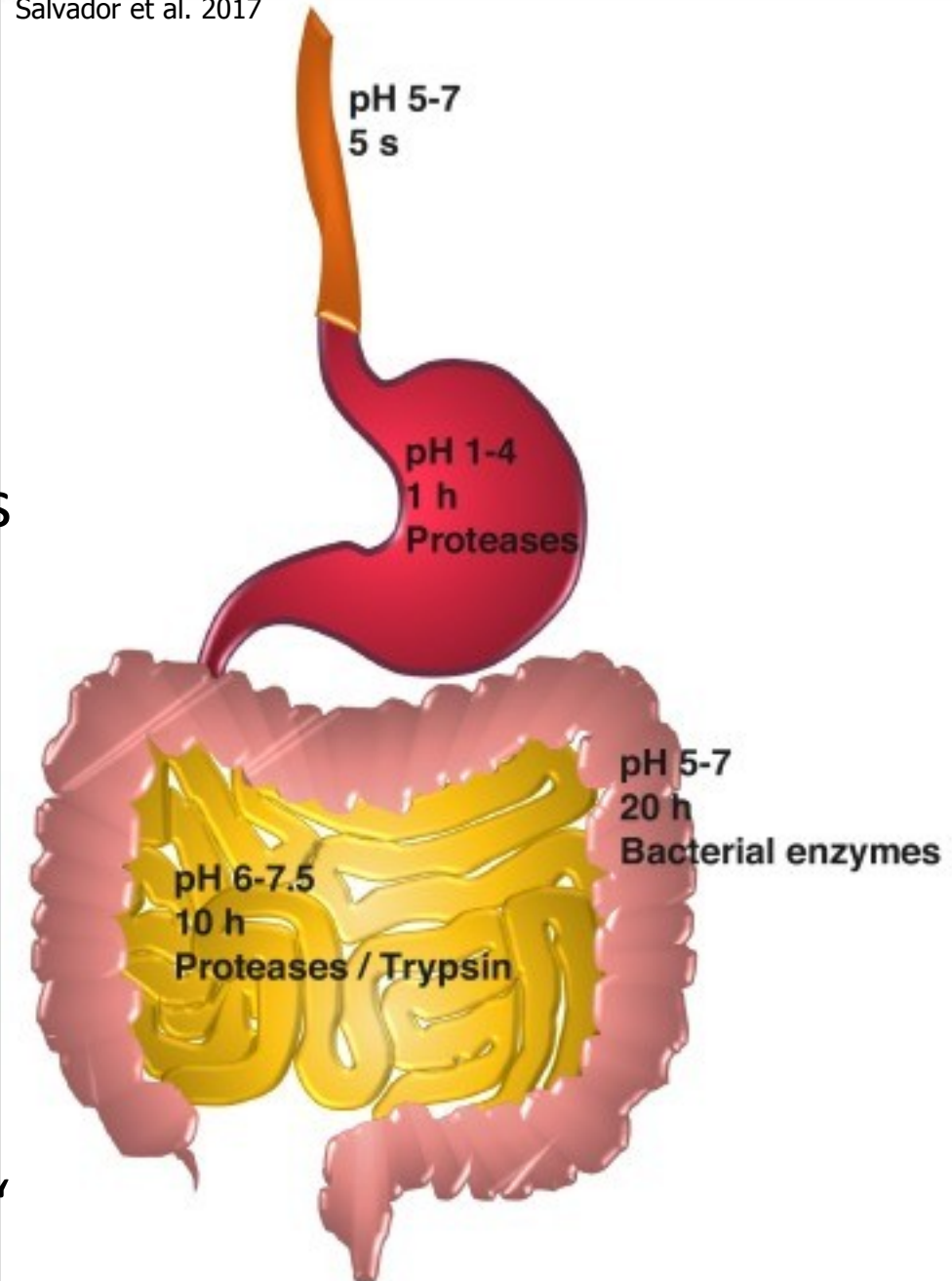
1. for local effect

- 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



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