PRINCIPLES AND SYSTEMS OF DRUG DELIVERY · SEMINARS 18–20

Mucosal routes: nasal, buccal, sublingual and pulmonary delivery

Educational program “Pharmacy” · 4th year · Al-Farabi Kazakh National University

The nose as a route of administration

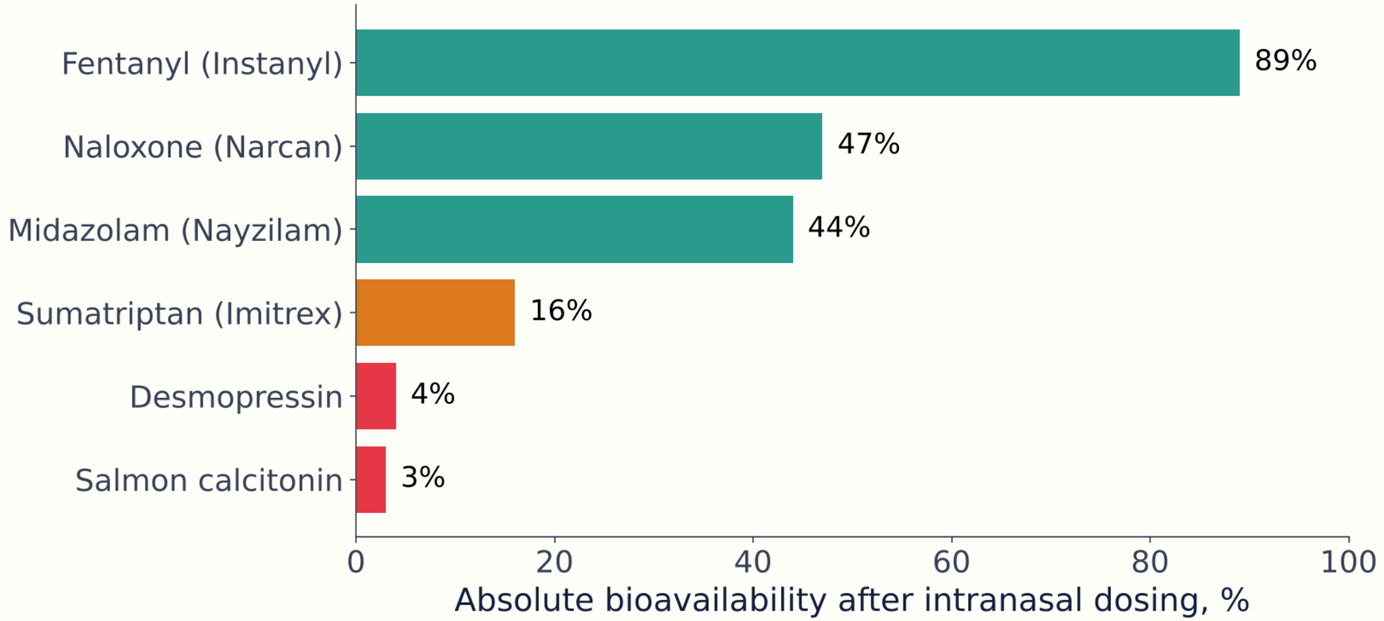
Advantages

- ~150 cm² highly vascular mucosa
- No first-pass; onset in minutes
- Needle-free, self-administered
- Olfactory region: route to the brain

Barriers

- Mucociliary clearance: ~15–20 min
- Small volume: 100–200 µL per nostril
- Enzymes (peptidases)
- Tight epithelium for molecules > 1 kDa

Nasal bioavailability falls with molecular size



Small lipophilic drugs: close to IV

Polar drugs: moderate

Peptides: a few %, need enhancers or high doses

Bioadhesive carriers keep the drug in place

Polymer	Mechanism	Effect
Chitosan	Cationic; binds mucin, opens tight junctions	Longer residence + enhanced absorption
Carbomer	Hydrogen bonds with mucin	Strong adhesion, viscous gel
HPMC, HPC	Swelling, chain entanglement	Moderate adhesion, gel layer
Thiolated polymers	Disulfide bonds with mucin cysteines	Very strong adhesion (Bernkop-Schnürch)
Starch microspheres	Absorb water, dehydrate cells	Slows clearance, opens junctions

Systemic nasal products and vaccines

Emergency

Naloxone (overdose), glucagon powder Baqsimi (hypoglycaemia), midazolam (seizures)

Pain, migraine

Fentanyl (Instanyl, PecFent with pectin gel), sumatriptan, zolmitriptan

Peptides

Desmopressin, oxytocin, nafarelin, calcitonin

Vaccines

Live attenuated influenza vaccine (FluMist / Fluenz): mucosal IgA

CNS

Esketamine (Spravato) for resistant depression

Devices

Metered pumps, unit-dose sprays, powder devices, bidirectional devices

Sublingual versus buccal

Feature	Sublingual	Buccal
Epithelium	Thin (100–200 µm), non-keratinised	Thicker (500–800 µm), non-keratinised
Permeability	High	Lower
Onset	1–3 minutes	Slower
Best for	Rapid action	Prolonged release from mucoadhesive forms
Limitation	Saliva washes drug away; short contact	Taste, swallowing of dissolved drug

Both avoid first-pass metabolism: veins drain into the jugular vein, not the portal vein.

Oromucosal products

Nitroglycerin sublingual

Angina relief in 1–3 min; oral bioavailability would be very low

Buprenorphine / naloxone film

Opioid dependence; naloxone inactive orally, active if injected

Fentanyl buccal tablet

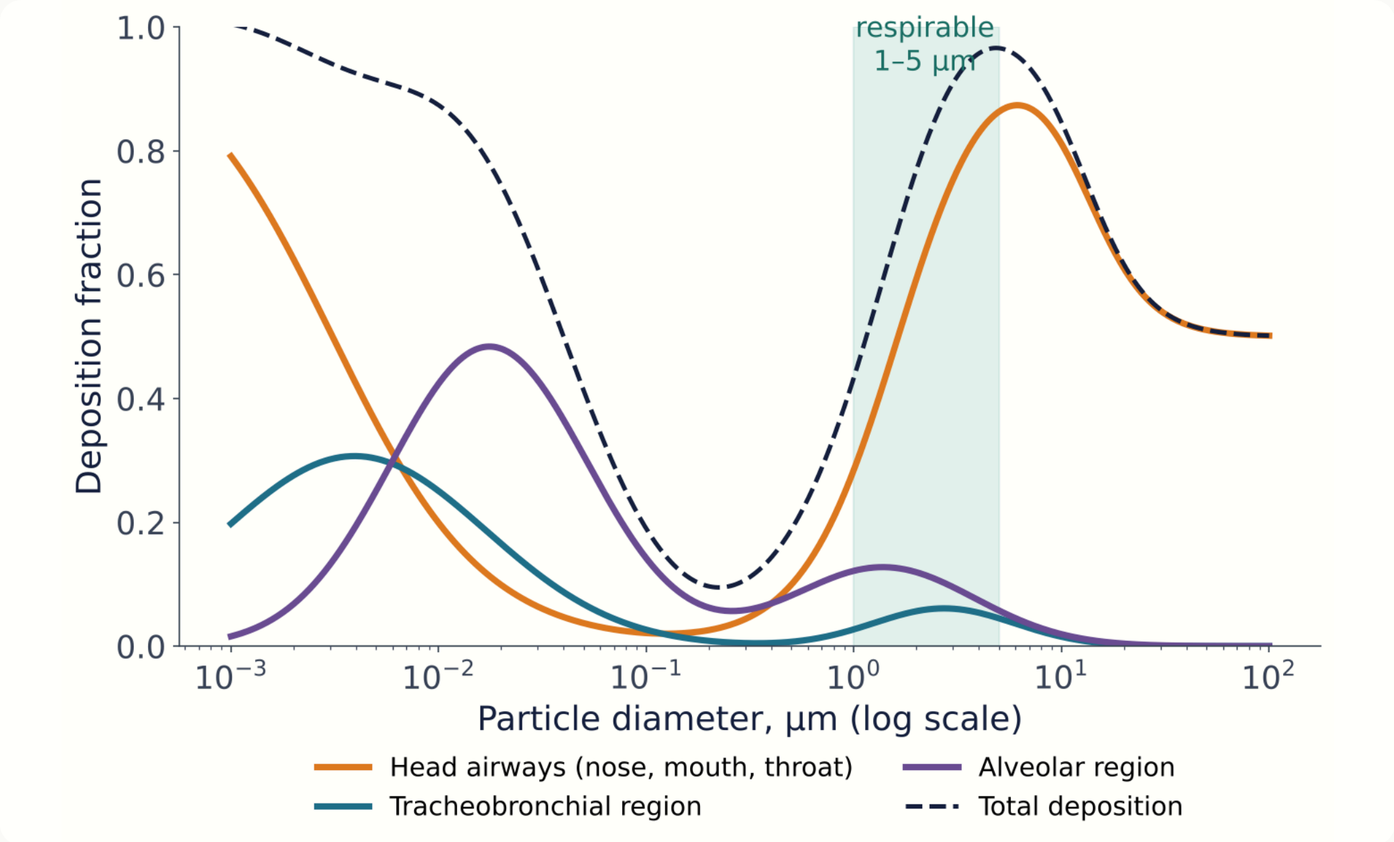
Effervescent: local pH change raises absorption

Midazolam oromucosal solution

Buccolam: seizures in children, given by carers

Formats: sublingual tablets, orally dissolving films, mucoadhesive buccal tablets and patches, sprays.

Lung deposition depends on particle size



> 5 µm: impaction in throat

1–5 µm: sedimentation in airways and alveoli

< 0.1 µm: diffusion; 0.3–0.5 µm mostly exhaled

Four inhaler families

Device	Energy	Strength	Limit
pMDI	Propellant (HFA)	Cheap, portable	Coordination; spacer helps
DPI	Patient’s breath	Breath-actuated, no propellant	Needs 30–90 L/min flow
Nebulizer	Air jet, mesh	Any age, high doses	Slow, bulky
Soft mist (Respimat)	Spring	Slow mist ~1.5 s	Device handling

Quality: delivered dose uniformity and aerodynamic size by cascade impactor (Ph. Eur. 2.9.18).

SYSTEMIC DELIVERY THROUGH THE LUNG

About 100 m² of alveoli and a 0.1–0.2 µm barrier make the lung a needle-free route for insulin, levodopa and loxapine

Exubera (2006) was withdrawn in 2007; Afrezza (2014) and Inbrija (2018) remain on the US market.

Questions for discussion

1. Why is nasal bioavailability of desmopressin so much lower than of fentanyl?
2. How does chitosan increase nasal absorption?
3. Why is nitroglycerin given sublingually and not swallowed?
4. Why does buprenorphine/naloxone discourage injection misuse?
5. Which particle size targets the alveoli?
6. Which inhaler suits an elderly patient with weak inspiration?

References

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