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# Drug Discovery and Development

From Molecules to Medicine

*Edited by Omboon Vallisuta and Suleiman Olimat*



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## **Drug Discovery and Development - From Molecules to Medicine**

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## Chapter 13 OPEN ACCESS

### Intranasal Drug Administration — An Attractive Delivery Route for Some Drugs

By Degenhard Marx, Gerallt Williams and Matthias Birkhoff  
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Figure 1. Multi-dose spray pumps can be fitted onto the bottles using a crimp ferrule, screwed-on or simply snapped on (from left to the right). In the forefront different types of nasal spray actuators.

#### [2. Evolution of multi-dose spray pumps](#)



Figure 2. Components of a typical multi dose pump. For a fully functional system a dip tube, fixture and actuator need to be added.

#### [3. A short introduction on intranasal administration](#)



Figure 3. Anatomy of the nasal cavity.

#### [4. Which technology is on the market?](#)



Figure 4. Spray tips for syringes which are used for the intranasal administration of naloxone, midazolam or some influenza vaccines.



Figure 5. Examples of unit/bidose systems for liquids on the left with a glass vial which contains the one or two doses of the drug product and dry powder devices on the right.

#### [4.1. Bottles](#)

#### [5. First steps to identify the right delivery system](#)

#### [6. Formulation development](#)

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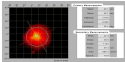


Figure 6. Typical display from a spray pattern test using laser imaging, which can give information about the ovality of the emitted spray.

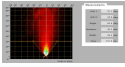


Figure 7. Typical display from a spray angle test using laser imaging, which can give information about the angle of the emitted spray.

[8. Trends for nasal drug administration](#)

[8.1. Use of preservatives in multi-dose products](#)

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[8.3. Side actuated spray pumps](#)



Figure 8. Example of a side actuated multi-dose spray pump

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## Intranasal Drug Administration — An Attractive Delivery Route for Some Drugs

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### 1. Introduction

Intranasal drug administration has a long tradition and was and is still used for medical as well as recreational purposes. The most common use is for treatment of local symptoms e.g. nasal congestion in the course of a common rhinitis or inflammation linked to allergic rhinitis. The medications intended for local activity are well established and can be found across the globe in every pharmacy and drug store. Examples for topical treatment of rhinitis are decongestants (oxymetazoline, xylometazoline, naphazoline), anti-histamines (azelastine, levocabastine, olopatadine) and glucocorticoids (e.g. mometasone, budesonide, fluticasone). For this particular indication, drugs should act fast and only locally while systemic absorption should be as low as possible; this to avoid systemic side effects which are linked with typical oral formulations of comparable drug substances.

As described earlier [[1](#)] intranasal administration has much more potential. The nasal mucosa can be used for non-invasive systemic administration of drugs. The surface of the nasal mucosa in humans is around 150 cm<sup>2</sup>, a tissue which is well supplied by blood vessels. This ensures a rapid absorption of most drugs, can generate high systemic blood levels and avoids the first pass metabolism which needs to be taken into account following oral administration. This bypassing of the gastrointestinal system even enables the delivery of peptide hormones [[1](#)]. Calcitonin and desmopressin are on the market for years now; insulin and glucagon were under clinical development for this administration route [[2](#)].

The rapid absorption of drugs via the nasal mucosa is also utilized for pain medications (e.g. fentanyl nasal sprays), rescue medications like naloxone for opioid overdosing or midazolam for seizures in children. An important aspect for such medications is that intranasal administration is considered a non-invasive administration route and easy to do for self-administration or for care-givers. It has a low potential for injuries or disease transmission (hepatitis B, HIV). This is of special importance if fast relief from severe symptoms is required and patient's ability to deal with injections is impaired. Intranasal triptanes for migraine treatment, fentanyl to stop cancer breakthrough pain and ondansetron to relieve nausea are examples for this trend. For these indications, single dose systems or multi-dose pumps with counting or lock-out mechanisms are available to reduce the risk of unintended overdosing or misuse [[1](#)].

Vaccines may also benefit from the intranasal route. Existing vaccines commonly utilize the intramuscular and oral administration route. While the respiratory and gastrointestinal tract is very immune competent and fights with microbes permanently, the muscle is not the first choice. Intramuscular vaccination primarily induces systemic immune response, mainly via formation of vaccine-strain specific circulating antibodies. Injections of vaccines were done since the early days and they are indeed effective. So for most people today vaccination is equal to getting an intramuscular injection which is linked to pain. For the health care professional it is linked to fears of needle stick injuries, risk of disease transmission and dangerous medical waste.

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