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# Nasal Systemic Drug Delivery

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# 1

# Anatomy and Physiology of the Nose

The bioavailability of a drug and hence its therapeutic effectiveness are often influenced by the route selected for administration. For a medication to achieve its maximal efficacy, a drug should be able to be administered easily so better patient compliance can be achieved; and it should be capable of being absorbed efficiently so greater bioavailability can be accomplished. The nasal route appears to be an ideal alternative to the parenterals for administering drugs intended for systemic effect in view of the rich vascularity of the nasal membranes and the ease of intranasal administration.

Several advantages can be achieved from delivering drugs intranasally: (a) avoidance of hepatic "first-pass" elimination, gut wall metabolism, and/or destruction in gastrointestinal tracts; (b) the rate and extent of absorption and the plasma concentration vs. time profile are relatively comparable to that obtained by intravenous medication; and (c) the existence of a rich vasculature and a highly permeable structure in the nasal membranes for absorption. These advantages have made the nasal mucosa a feasible and desirable site for systemic drug delivery.

However, there are some factors that should also be considered for optimizing the intranasal adminstration of drugs: (a) methods and techniques of administration; (b) the site of disposition; (c) the rate of clearance; and (d) the existence of any pathological conditions which may affect the nasal functions. These factors could potentially influence the efficiency of nasal absorption of drugs.

To study the intranasal delivery of drugs for systemic medication, it is important to first gain some fundamental understanding of the anatomy and physiology of the nose.

## 1.1 NASAL PASSAGE

The upper respiratory tract is constantly influenced by the inspired air. The nasal modification of the inspired air by filtration, humidification, and/or warming are considered to be prime functions of the nose in man (1). To carry out its functions, the nose must control the rate of air flow, remove noxious agents, and introduce large quantities of fluid into the air stream.

The nasal passage which runs from the nasal vestibule (i.e., nasal valve) to the nasopharynx has a depth of approximately 12-14 cm (2) (Figure 1.1). In this passage, the nasal cellular apparatus is in close contact with mucus which protects the mucosa from the inspired air. There are three distinct functional zones in the nasal cavities (3,4); namely, vestibular, respiratory, and olfactory areas, which are arranged anteroposteriorly in this sequence of order (Figure 1.2). (a) The vestibular area serves as a baffle system, and its surface is covered by a common pseudostratified epithelium where the long hairs may provide the function of filtering airborne particles. (b) The respiratory area has a surface lined by a pseudostratified columnar epithelium, and is normally covered by a dense layer of mucus that is constantly moving toward the posterior apertures of the nasal cavity by a powerful system of motile cilia. (c) The olfactory region is about 10 $cm^2$, as compared to 170 $cm^2$ in the German shepherd dog. The olfactory airway lies above the middle turbinate between the nasal septum and the lateral wall of the main nasal passage. The airway here is only about 1-2 mm wide and is contiguous to the cribriform plate above. This region is generally free of inspiratory air flow.

The nasal passage is composed of a horizontally skin-lined vestibule with the passages being directed upward and backward, and is separated by a cartilaginous, bony nasal septum (5). The lateral wall is convoluted with strategically placed turbinates that mold the air stream to their configurations and changing dimensions.

The anterior nares mark the beginning of the double nasal airway, which extends from the entrance at the nostrils to the beginning of ciliated mucosa at the anterior ends of the nasal septum and turbinates (5,6). The main

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