Microemulsions for Nasal Drug Delivery Systems: An Overview

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Received July 28, 2012; accepted October 26, 2012

ABSTRACT
Most drugs cannot be given orally because of significant degradation in the GIT or first pass metabolism in the liver. Nasal route for the delivery of some drugs offers an alternative in the pharmaceutical industry. The present review deals with the utility of the nasal route for the delivery of drugs to the brain as a microemulsion system in the treatment of a number of ailments like migraine, epilepsy, and hypertension. The nasal route could be important for drugs that are used in crisis treatments, such as for pain, and for centrally acting drugs where the pathway from nose to brain might provide a faster and more specific therapeutic effect. The purpose of the article is to provide an overview of the concept of microemulsion, selection of surfactant, co-surfactant, oils, formulation of microemulsion, phase diagram study, and evaluation of microemulsion. The review also focuses on the excipients available for formulation of microemulsions for nasal delivery and describes the investigations reported for the various classes of therapeutic agents. The interesting features of microemulsion such as spontaneity of formation, ease of manufacturing, high solubilization capacity and self-preserving properties make them the vehicle of choice for nasal delivery.

KEYWORDS: Microemulsion; nasal delivery; mucoadhesion; drug delivery; solubilization.

Introduction
Nasal drug delivery is increasingly important as an alternative to the oral and parenteral routes for systemic drug delivery. There has been increasing interest in using the nose as a route for administration of systemically active drugs. There are number of research and review articles on nasal drug delivery. This interest arises from the different possible advantages presented by the nasal cavity such as: vascularized epithelium, large surface area available for drug absorption, lower enzymatic activity compared to the gastrointestinal tract and liver and the direct transport of absorbed drugs into the systemic circulation, thereby, avoiding hepatic first-pass metabolism and irritation of gastrointestinal membrane. Also, the nasal route is non-invasive, therefore produces reduced risk of infection, ease of convenience and self medication resulting in improved patient compliance (Ugwoke et al., 2001). Although nasal administration of drugs has many disadvantages, one of the most important is the nasal mucociliary clearance that limits the time allowed for drug absorption to occur (Martinac et al., 2005). To overcome the rapid clearance mainly two approaches have been utilized. Use of penetration enhancers (surfactants, bile salts, cyclodextrins, phospholipids and fatty acids), which can promote the absorption of poorly absorbable drugs and use mucoadhesive systems (bioadhesive liquid formulations, mucoadhesive microemulsion, microspheres, powders and liquid gelling formulations) that decrease the mucociliary clearance of drug formulation and thereby increase the contact time between the drug and the site of absorption. The world market has seen an increasing number of systemically acting drugs being marketed as nasal formulation, including a range of antimigraine drugs such as sumatriptan from GlaxoSmithKline, zolmitriptan from AstraZeneca, ergotamine from Novartis and butorphanol from BristolMyersSquibb, as well as a range of peptides, such as calcitonin marketed by Novartis, desmopressin from Ferring and buserelin from Aventis (Majithiya et al., 2006). Intranasal drug delivery also offers advantages such as drugs being able to be administered simply, cost effectively, and conveniently (Liu et al., 2001). Direct transport of drugs to the brain circumventing the brain-barriers following intranasal administration provides a unique feature and better option to target drugs to the brain (Lisbeth, 2003; Vyas et al., 2005).

Microemulsions, by virtue of their lipophilic nature and low globule size, are widely explored as a delivery system to enhance uptake across mucosa (Hu et al., 2001). Evidences of intranasal drug delivery systems formulated using mucoadhesive agents and their benefits in enhancing nose-to-brain drug transport have been reported by various scientists in literature (Alpar et al., 2005; Gavini et al., 2005). It was hypothesized that