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RESEARCH ARTICLE

SLN approach for nose-to-brain delivery of alprazolam

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Abstract In the present study, alprazolam-loaded solid lipid nanoparticles were prepared and characterized. They were evaluated for their efficiency in nose-to-brain targeting and biodistribution in a suitable animal model after intranasal delivery. Solid lipid nanoparticles may offer an improvement to nose-to-brain drug delivery since they are able to protect the encapsulated drug from biological and/or chemical degradation. The distribution of the drug to different organs was recorded through biodistribution studies in male Wistar rats and gamma scintigraphy imaging in New Zealand rabbits by tagging the formulation with radioactive substance ^{99m}Tc. The radioactivity count of various organs was taken as a function of the drug concentration. The study reveals that alprazolam can be rapidly transferred to the brain via intranasal route, bypassing the blood–brain barrier and a direct nose-to-brain transfer. The enhanced rate and extent of transport may help in reducing the dose and dosing frequency, thereby providing ease for ambulatory patients.

Keywords Brain targeting · SLN · Gamma scintigraphy · Lipoidal · Nanoparticles

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Background

Despite enormous advances in brain research, central nervous system (CNS) disorders remain the world's leading cause of disability. Since the brain is the most important organ of the body, nature provides various barriers to protect it from the outside environment. Unfortunately, the same barriers prevent the entry of drugs and other chemicals into the brain, which makes it a great challenge to deliver any drug to the brain. Among the various obstacles like blood–brain barrier (BBB), blood cerebrospinal fluid barrier, and efflux mechanism, BBB plays a major role. Thus, various approaches like BBB disruption (osmotic and biochemical); drug manipulation (prodrug, lipophilic analogues, chemical drug delivery, carrier-mediated drug delivery, and receptor/vector-mediated drug delivery); and alteration in the route of administration like the intracerebroventricular, intrathecal, and olfactory pathways are used for the targeting of drugs to the brain [1, 2].

Alprazolam, 8-chloro-1-methyl-6-phenyl-4H-[1,2,4] triazolo[4,3-a][1,4]benzodiazepine, is approved as an anti-anxiety drug [3]. It belongs to the chemical class of benzodiazepines and is available for oral delivery as tablets. However, repeated dosing is required for maintaining constant plasma profiles. Alprazolam acts by enhancing the effect of GABA in the brain. After oral drug delivery, the drug first gets distributed systemically and a small portion is able to reach the brain through the blood. Specific clinical complications associated with a high systemic concentration include respiratory disturbance, skin rashes, nausea, vomiting, and musculoskeletal disorder. Moreover, alprazolam is a habit-forming drug; a smaller dose would be more suitable for a patient. The drug is 70–80 % bound to plasma proteins, thereby affecting oral bioavailability [4].