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In vitro release with C980 was found to be linear. Incorporation of carbopols resulted in mucoadhesion formulations and studies using sheep mucosa indicated bioadhesion of formulations on sheep mucosa (fig. 6). The comparative studies of nasal sprays indicated that VP6D gave constant shot weight of 110 mg when compared to VP7D and VP7 were the shot weight varied from 100-110 mg. Spray patterns also revealed that VP6D gave spherical and uniform spray pattern. The content uniformity per spray with VP6D valve was found to be 98-102%. All the intranasal formulations could be sprayed conveniently with uniform spray pattern using the above spray pumps. The in vivo studies are in progress to assess the intranasal deposition pattern of the developed formulations. Stable intranasal formulations of sumatriptan have been developed and evaluated. Thermoreversible microemulsion based intranasal delivery might be a promising approach for the rapid onset and controlled delivery of sumatriptan succinate.

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Preparation and Characterization of Chitosan Nanoparticles for Nose to Brain Delivery of a Cholinesterase inhibitor

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The blood brain barrier (BBB) is an insurmountable obstacle for large number of drugs including anticancer agents, antibiotics and variety of central nervous system (CNS) drugs, particularly the neuropeptides1. Nanoparticles are polymeric particles having a size range between 10-100 nm, and are employed to carry the drugs through absorption or incorporation12. Nanoparticles loaded with drugs show drug release at right rate and dose at specific sites in the body for a certain time to realize the accurate delivery, which enhances the therapeutic effect and reduces the toxicity and side effects. It is reported that nanoparticles over coated with polysorbate 80, hold great promise for the transport of agents across the BBB13,4. Since chitosan nanoparticles have been reported to extend circulation time in the blood and decreased uptake by the reticuloendothelial system, we decided to evaluate the efficiency of polysorbate 80 coated chitosan nanoparticles as brain delivery carriers5. Earlier studies have demonstrated the use of intranasal route as an alternative route of administration for rapid drug delivery to the brain as it is a practical and non-invasive route6. The objective of this investigation was to prepare cholinesterase inhibitor chitosan nanoparticles as a carrier system via nose-to-brain delivery. A further objective was to characterize and evaluate it on the basis of particle size, drug loading and drug entrapment efficacy, for the treatment of neurodegenerative diseases. It was hypothesized that mucoadhesive nanoparticles as intranasal formulation
is an alternative drug delivery systems which will result in nose-to-brain transport of cholinesterase inhibitor and greater drug transport and distribution into and within the brain. This can help to maximize the therapeutic index of the drug, reduce side effects, decrease the dose and frequency of dosing, and perhaps even the cost of the therapy.

MATERIALS AND METHODS

Cholinesterase inhibitor (derivative of piperidine) was received as a gift sample from Ranbaxy Ltd. (Gurgaon, India). Chitosan was purchased from Sigma Aldrich (New Delhi, India). Sodium tripolyphosphate (TPP) was purchased from Central Drug House (Delhi, India) and Tween-80 was supplied by S. D. Fine Chemicals (New Delhi, India). Water used was purified by reverse osmosis (MilliQ. Millipore, USA). All other chemicals were of analytical grade and used as received.

Preparation of chitosan nanoparticles:

Chitosan nanoparticles were prepared by ionic cross linking of chitosan solution (with or without drug) with TPP prepared in the presence of Tween 80 as a resuspending agent to prevent particle aggregation, at ambient temperature while stirring. Cholinesterase inhibitor-loaded chitosan nanoparticles were prepared as described above by dissolving 10 mg of cholinesterase inhibitor in 10 ml chitosan solution (0.1, 0.2, 0.3, 0.4 and 0.5% w/v) containing 0.5% w/v Tween 80 before adding TPP (0.25% w/v). The nanoparticle suspensions were centrifuged at 12 000×g for 30 min using C24 centrifuge (Remi Centrifuge, Mumbai, India). The supernatant was analyzed by UV spectrophotometry to calculate the % drug entrapment and drug loading.

RESULTS AND DISCUSSION

The cholinesterase inhibitor chitosan nanoparticles were prepared and characterized for the particle size, morphology and particle size distribution. The chitosan nanoparticles had a particle diameter ranging from 100-200 nm and the shape was spherical when analyzed by quasi electron laser spectrophotometer (QELS) and scanning electron microscopy (SEM), respectively. The nanoparticles showed a loading efficiency up to 92% and a loading capacity up to 50% (w/w). These studies showed that the submicron size range achieved for the chitosan nanoparticles, the mucoadhesive property of chitosan and ability of Tween 80 to cross BBB will provide effective delivery of cholinesterase inhibitors from nose-to-brain to cross BBB. Thus, chitosan nanoparticles possess a potential to deliver cholinesterase inhibitor through the nasal mucosa to reach the brain for the treatment of neurodegenerative disease.

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