Preparation of bromocriptine loaded Nanoparticles for Treatment of Parkinsonism: In vitro evaluation

Shadab Md., Sanjula Baboota, Jasjeet Kaur Sahni and Javed Ali

Department of Pharmaceutics, Faculty of Pharmacy, Jamia Hamdard, New Delhi-110062, India

Email address: shadabmd1982@gmail.com, jali@jamiahamdard.ac.in

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Abstract: Objectives: Bromocriptine (BRC) is a dopamine agonist with low oral bioavailability (10-20%) due to first pass effect used in the treatment of Parkinsonism. The scope of this research is to administer the drug directly to the targeted site by means of nasal route to avoid distribution to non-targeted site and first pass metabolism. The investigation also aims to develop mucoadhesive polymeric nanoparticles of bromocriptine, as these nanoparticles are expected to increase nasal residence time and release the drug at slow and constant rate.

Methodology: Chitosan nanoparticles (CS NPs) and bromocriptine (BRC) loaded CS NPs were prepared by ionic gelation method using tripolyphosphate (TPP) and in vitro characterization was done for particle size, particle size distribution, zeta potential, polydispersibility index by Zetasizer Nano ZS, (Malvern Instruments Ltd, Worcestershire, UK). The entrapment efficiency, loading capacity and in vitro release studies were also performed. TPP solution 0.175% w/v (3 ml) was added drop wise to 10 ml of CS solution with constant stirring (600 rpm) at room temperature for 30 min. and the resultant formulation was centrifuged at 15000 rpm at 10°C for 45 min. The supernatant was analyzed at λmax 305 nm to determine the entrapment efficiency and loading capacity. The pellets were washed with distilled water and then freeze dried. The in vitro drug release studies was performed by redispersing separated nanoparticles (5 mg) in 4 mL freshly prepared phosphate buffer pH (7.4), in a dialysis membrane bag (molecular weight cut off at 5 kDa). The amount of drug in the released medium was evaluated from the HPLC.

Results: Particle size distribution analysis confirmed the average particle size as 147.3±3.97 nm and 161.3±4.73 nm for CS NPs and BRC loaded CS NPs respectively. The formulation with the initial BRC concentration of 0.5 mg/ml provided the highest entrapment efficiency (84.26±3.56) and the highest extent of release (75% at 24 h) suggesting the possibility to achieve a therapeutically effective calculated dose.

Conclusions: The bromocriptine (BRC) nanoparticles can be formed by controlling the key processing parameters such as CS concentration and CS/TPP mass ratio. According to the data obtained, this chitosan-based nanotechnology opens new and interesting perspectives for the treatment of Parkinson disease via intranasal route.

References
Figures:

(a) Effect of CS concentration on particle size and entrapment efficiency of BRC loaded CS NPs, (BRC concentration 0.5mg/ml and CS/TPP mass ratio 3.33/1)

(b) Effect of drug concentration on entrapment efficiency of BRC loaded CS NP

Fig 3. Particle size, particle size distribution and polydispersibility index of optimized formulation