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Colloidal properties of montelukast sodium nasal spray

Montelukast sodium (MTL) is leukotriene receptor antagonist indicated for prophylaxis and treatment of asthma and is widely used treatment for systemic and local diseases of the upper respiratory tract. However, MTL has many adverse effects including cough, fever, bronchitis, agitation, aggression, anxiousness, hallucinations, depression, insomnia, restlessness, suicidal ideation and liver dysfunction. Therefore administration of MTL locally can result in significant reduction in dose and possibly avoid systemic side effects. In this study, we reported MTL nasal spray formulation prepared as a colloid solution using hydroxypropyl cellulose (HPC) and Carbomer 934 (C934) as a mucoadhesive agent. Colloidal systems are dispersed systems which the size of dispersed phase is less than 1 μm. MTL nasal sprays were formulated by dissolving the polymers i.e., HPC from 0.01% to 0.5% w/v and C934 from 0.005% –0.15% w/v with MTL to form a colloidal system followed by the adjustment of pH. The colloidal system can enhance binding between the drug and the receptor at the nasal epithelial cell. The dose of MTL was calculated to be 240 ng for single administration. The prepared formulations were evaluated for colloidal properties using zetasizer. Other properties including pH, viscosity, particle size and droplet size were also determined. The MTL formulations containing HPC was clear whereas the formulations with C934 was clear to cloudy which depended on the polymer concentration. The particle size and polydispersity index was found to be 167 nm and 0.34, respectively for MTL solutions. The particle size of the MTL with C934 was 800 –2,500 nm with the size being related directly to the concentration of the polymer. On the other hand, the particle size of the formulations with HPC was 80 –400 nm showing an inverse relation with the concentration of HPC. The particle size of all formulations was larger than the pore size of the nasal epithelial tight junction (20 Å). It is unlikely that the particles will enter the blood circulation via paracellular pathway and avoid systemic side effects. The particle charge of all formulations was negative. The zeta potential of the formulations with HPC was in the range 1 –6 mV whereas it was 40 –60 mV for formulations with C934. Due to the higher value of zeta potential of C934 formulations as compared to HPC formulations, the formulations with C934 would be more stable than formulations with HPC with less chances of particle aggregation. pH of all formulations was in the range of 7 to 8. The viscosity of the formulations with C934 was found to be 2 –5 cPs which was suitable for sprays whereas in case of HPC, it was 2 –80 cPs which was found to depend on the concentration. The the formulations with HPC at concentrations 0.3 and 0.5% w/v were unsuitable for efficient spray formulation. The average droplet size of the formulations with C934 was in the range of 50 –80 μm that is suitable for nasal spray whereas the droplet size of the formlations with HPC was in the range 40 –400 μm. The HPC concentrations at 0.1 –0.5 % w/v produced the droplet size larger than 100 μm indicating that the concentration was influenced by the droplet size. Overall physicochemical properties of all formulations met the requirement for optimum nasal drug delivery. However, the stability of the formulations need to be evaluated further in a long term basis.

Key words: montelukast sodium, hydroxypropyl cellulose, Carbomer 934, colloidal

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