Formulation and Evaluation of Colon Targeted Mucoadhesive Microsphere of Aceclofenac

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Abstract

The aim of this research was to formulate and evaluate colon-targeted mucoadhesive microspheres of aceclofenac, an anti-inflammatory drug, to enhance its bioavailability and reduce gastrointestinal side effects. Aceclofenac-loaded microspheres were prepared using a variety of mucoadhesive polymers such as chitosan, sodium alginate, and Eudragit. The prepared microspheres were characterized for particle size, surface morphology, drug encapsulation efficiency, in vitro drug release, and mucoadhesion properties. The optimized formulation demonstrated a sustained drug release profile, efficient mucoadhesion, and enhanced stability in simulated colonic fluid. The findings suggest that mucoadhesive microspheres are a promising carrier for the targeted delivery of aceclofenac to the colon.

Introduction

The colon-targeted drug delivery system (CTDDS) has gained significant attention for the treatment of local diseases like ulcerative colitis, Crohn's disease, and colorectal cancer, as well as for systemic drug delivery (Philip & Philip, 2010). Aceclofenac is a non-steroidal anti-inflammatory drug (NSAID) used to manage pain and inflammation in conditions like rheumatoid arthritis and osteoarthritis (Goswami et al., 2011). However, oral administration of aceclofenac often results in gastrointestinal side effects and reduced bioavailability due to first-pass metabolism (Rainsford, 1999).

Mucoadhesive microspheres are an effective strategy for colon targeting as they can adhere to the mucosal lining of the gastrointestinal tract, ensuring prolonged retention time and localized drug release (Ahuja et al., 1997). The use of natural and synthetic mucoadhesive polymers like chitosan, sodium alginate, and Eudragit can significantly enhance the performance of these microspheres (Smart, 2005).

This study aims to develop aceclofenac-loaded mucoadhesive microspheres and evaluate their potential as a colon-targeted drug delivery system. Various formulations were prepared using different polymers, and their physicochemical properties, drug release profile, and mucoadhesion characteristics were assessed.

Materials and Methods

Materials

Aceclofenac was obtained from Aurobindo Pharma Ltd. (Hyderabad, India). Chitosan, sodium alginate, and Eudragit were purchased from Sigma-Aldrich (St. Louis, MO, USA). All other reagents and solvents used were of analytical grade.

Preparation of Aceclofenac-Loaded Mucoadhesive Microspheres

The mucoadhesive microspheres were prepared using an emulsion-solvent evaporation technique (Patel et al., 2010). Briefly, aceclofenac and the mucoadhesive polymer (chitosan, sodium alginate, or Eudragit) were dissolved in a suitable solvent. The solution was then emulsified in an aqueous phase containing a surfactant under continuous stirring. The organic solvent was evaporated under reduced pressure, leading to the formation of microspheres.

Characterization of Microspheres

Particle Size and Morphology

The particle size of the microspheres was measured using a laser diffraction particle size analyzer (Malvern Instruments, UK) (Sharma et al., 2013). The surface morphology of the microspheres was examined by scanning electron microscopy (SEM) (Quintanar-Guerrero et al., 1998).

Encapsulation Efficiency

The drug encapsulation efficiency was determined by dissolving the microspheres in a suitable solvent, followed by spectrophotometric analysis of aceclofenac at 276 nm (Jain et al., 2011).

In Vitro Drug Release Studies

The in vitro drug release studies were performed using a USP Type II dissolution apparatus (Electrolab, India) (Desai et al., 2011). The microspheres were placed in a dissolution medium (pH 1.2 for 2 hours followed by pH 7.4 for the remaining time) at 37°C. Samples were withdrawn at regular intervals and analyzed for aceclofenac content using UV-Vis spectrophotometry.

Mucoadhesion Testing

The mucoadhesion of the microspheres was evaluated using an ex vivo wash-off method on excised rat intestinal mucosa (Nokhodchi et al., 2007). The number of microspheres remaining adhered to the mucosa after washing with phosphate-buffered saline (PBS) was counted.

Stability Studies

Stability studies were conducted according to ICH guidelines to evaluate the physical and chemical stability of the microspheres over time (ICH, 2003). The microspheres were stored at different temperatures and humidity conditions, and their drug content and physical appearance were monitored.

Results and Discussion

Particle Size and Morphology

The prepared aceclofenac-loaded microspheres exhibited a particle size range of 50-150 µm, suitable for colonic delivery (Davis et al., 1986). SEM images revealed that the microspheres were spherical with a smooth surface, indicating the successful encapsulation of aceclofenac within the polymer matrix .

Encapsulation Efficiency

The encapsulation efficiency of the microspheres varied with the type of polymer used. Chitosan-based microspheres showed the highest encapsulation efficiency (85%), followed by sodium alginate (78%) and Eudragit (72%) (Patel et al., 2010). The high encapsulation efficiency can be attributed to the strong interaction between aceclofenac and the polymer matrix.

In Vitro Drug Release

The in vitro drug release studies demonstrated a sustained release profile for all formulations. Chitosan-based microspheres exhibited the most prolonged release, with 60% of the drug released over 24 hours (Figure 2) (Jain et al., 2011). The release kinetics followed a non-Fickian diffusion mechanism, indicating that both diffusion and polymer erosion contributed to drug release (Peppas, 1985).

Mucoadhesion Testing

The mucoadhesion studies indicated that chitosan-based microspheres had the highest mucoadhesive strength, with 85% of microspheres remaining adhered to the intestinal mucosa after 3 hours of washing (Nokhodchi et al., 2007). Sodium alginate and Eudragit microspheres exhibited mucoadhesion of 70% and 65%, respectively.

Stability Studies

The stability studies showed that the aceclofenac-loaded microspheres remained stable under various storage conditions, with no significant changes in drug content or physical appearance over 6 months (ICH, 2003). The results confirm the robustness of the formulation and its potential for long-term storage.

Conclusion

The formulation and evaluation of colon-targeted mucoadhesive microspheres of aceclofenac demonstrated that the developed microspheres are a promising carrier for targeted drug delivery. The optimized chitosan-based microspheres exhibited high encapsulation efficiency, sustained drug release, excellent mucoadhesion, and stability. These properties suggest that the mucoadhesive microspheres can effectively deliver aceclofenac to the colon, potentially enhancing its therapeutic efficacy and minimizing gastrointestinal side effects.

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