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"DESIGN AND ESTIMATION OF POLYMERIC NANOPARTICLES CONTAINING CELECOXIB FOR THE TREATMENT OF INFLAMMATORY BOWEL DISEASE"

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Abstract

Celecoxib (CXB) is a poorly aqueous solubility sulfonamide non-steroidal anti-inflammatory drug (NSAID). Hence, the formulation of CXB was selected for solubilization and bioavailability. To find out suitable formulation for colon targeted delivery of celecoxib for the treatment of crohn's disease. The prepared nanoparticles were evaluated for various evaluation parameters and formulated as SM1-SM7. The prepared nanoparticles were spherical with some looser aggregates. Thesize was in the range of 455.5 to 1338 nm and zeta potential in the range of -6.85 to -12.7 mV. The DEE was found to be in the range of 53.76 % to 71.62 %. As the concentration of polymer was increased in the nanoparticles, the DEE was decreased. The DSC and XRD analyses indicated the amorphous dispersion of drug in the nanoparticles. FTIR study indicated the stability of celecoxib within the nanoparticles. in vitro was tested for its integrity and transit in vivo in rabbits. The results indicated that the prepared formulation was intact up to 8 hours and transit was clearly seen. Drug release mechanism followed non-fickian transport.

Key words: *Celecoxib, Nanoparticles, In-vitro release, Crohn's disease*

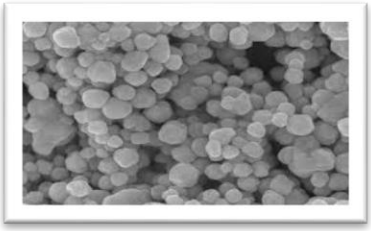
1. Introduction

1.1. Oral Route of Administration

The oral route of administration is the most commonly utilized method for drug administration because of its simplicity of administration, self-medication and patient compliance has gain the advantages over the other route of administration.[5] However the route has problem with controlled drug delivery system because of variable gastric emptying motility, further more gastric emptying time in humans is up to 2 – 5 hrs. A few endeavors are being made to create controlled medication conveyance framework. In the present investigation the endeavor had been made to plan the nanoparticles for oral medication conveyance as a result of its capacity to cross the mucosal hindrance accordingly. nanoparticles oral drug delivery system have slower transit time than larger dosage form which increase the concentration gradient across the absorptive cells and enhances the local and systemic delivery forfree and bound drug across gut.[5]

1.2. Nanoparticles

Nanoparticles are particles in the vicinity of 1 and 100 nanometer in estimate. In nanotechnology, a molecule is characterized as a little question that carries on overall unit with individual to its vehicle and properties.[6]



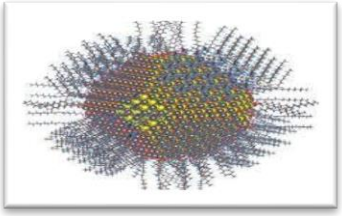


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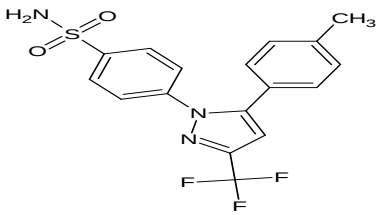
Figure 1: Photograph of nanoparticles Preparation of nanoparticles

2. Drug Profile

Celecoxib



Chemical Name: 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-pyrazol-1yl] benzenesulfonamide

Physicochemical properties

Molecular Formula: C17H14F3N3O2S

Molecular Weight: -Average- 381.4

Category: - celecoxib inhibits cyclooxygenase 2 (COX-2) enzymes**.**

Description: - Celecoxib is indicated for symptomatic treatment of adult osteoarthritis (OA) and adult rheumatoid arthritis (RA). Celecoxib is not a substitute for aspirin for cardiovascular event prophylaxis.

Melting point: - 157-159 ^{0}C

Solubility: - Celecoxib is insoluble in Water, soluble in Ethanol, methanol.

Pharmacodynamics

Celecoxib inhibits cyclooxygenase 2 (COX-2) enzymes, reducing pain and inflammation. It is important to note that though the risk of bleeding with celecoxib is lower than with certain other NSAIDS, it exists nonetheless and caution must be observed when it is administered to those with a high risk of gastrointestinal bleeding.

3. Mechanism Of Action

Unlike most NSAIDs, which inhibit both types of cyclooxygenases (COX-1 and COX-2); celecoxib is a selective noncompetitive inhibitor of cyclooxygenase-2 (COX-2) enzyme. COX-2 is expressed heavily in inflamed tissues where it is induced by inflammatory mediators The inhibition of this enzyme reduces the synthesis of metabolites that include prostaglandin E2 (PGE2), prostacyclin (PGI2), thromboxane (TXA2), prostaglandin D2 (PGD2), and prostaglandin F2 (PGF2). Resultant inhibition of these mediators leads to the alleviation of pain and inflammation. By inhibiting prostaglandin synthesis, non-steroidal anti-inflammatory drugs (NSAIDs) cause mucosal damage, ulceration and ulcer complication throughout the gastrointestinaltract.[9]

Conclusion

The drug delivery systems targeted to colon should not only protect the drug being released in the stomach and small intestine, but they should also release and sustain the drug release in the colon. Hence, in vitro drug release studies were performed in phosphate buffer pH 6.8 containing 4% rat ceacal contents. represent the drug release pattern in the presence of rat cercal content medium. The SM6 and SM7 formulations which showed satisfactory results were chosen for the study. A 33.09% and 36.52% of drug was released from SM6 and SM7 formulations at the end of 5th hour in the environment of stomach and intestine.

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