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FORMULATION AND EVALUATION OF CIPROFLOXACIN COLON TARGETED TABLETS BY COMPRESSION COATING TECHNIQUE

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ABSTRACT

The aim of the present study is to develop colon targeted drug delivery system for ciprofloxacin using various proportions of guargum and HPMC K4M to treat the crohn's disease. The compression coated tablets of ciprofloxacin were prepared and were evaluated for hardness, thickness, friability, diameter, drug content, weight variation and *invitro* drug release studies. The amount of ciprofloxacin released from tablets at different time intervals was estimated by UV visible spectroscopy. From these evaluations it is observed that release of the drug was comparatively less in gastric and intestinal fluids and increased in colonic fluids. When the dissolution study was continued in simulated colonic fluids, the compression coated tablets with 175 mg of HPMC K4M coat released 96.07% (F8) and 99.02% (F9) of ciprofloxacin after degradation by colonic bacteria at the end of 24 h of the dissolution study. The compression coated tablets with 175mg of guar gum: HPMC K4M coat released about 98.09% (F14) of ciprofloxacin, respectively, in simulated colonic fluids indicating the susceptibility of the guar gum formulations to the rat caecal contents. The mean percentage of ciprofloxacin released at various time intervals was calculated and plotted against time. The mechanism of drug release with the formulations F8 and F9 was dominantly case-2 transport diffusion and followed zero order kinetics, where as the formulation F14 followed Korsemeyer peppas equation. The ciprofloxacin compression coated tablets showed no change either in physical appearance, drug content or in dissolution pattern. Based on the R^2 values obtained F9 is considered as the best formulation.

KEYWORDS: Ciprofloxacin, Guar gum, HPMC, Crospovidone, Colon targeted drug delivery, Compression coating tech.

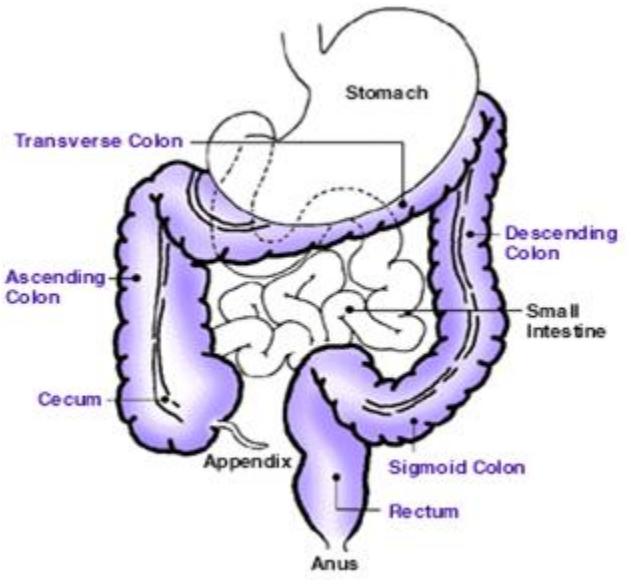
INTRODUCTION

COLON

Colon was considered as most of the drugs were absorbed from upper part of GI tract. It has also been suggested that colonic delivery of orally administered protein and peptide drugs might be possible, because enzyme activity is low in the colon. Besides these low hostile environment, the colonic transit time is long (20-30 hours) and the colonic tissue is highly responsive to the action of absorbtion enhancers Analgesic peptides, oral vaccines, growth hormone and insulin are candidates for use of the colon as a site for absorption. Various diseases that exhibit diurnal rhythms might also be treatable using colon-specific formulations.

Anatomy of colon

It is a 6-foot long muscular tube that connects the small intestine to the rectum. The large intestine is made up of the ceacum, the ascending (right) colon, the transverse (across) colon, the descending (left) colon, and the sigmoid colon, which connects to the rectum. It is about 1.5m long, the transverse colon being the largest and most mobile part, and has an average diameter of about 6.5cm, although it varies in diameter from approximately 9cm in the ceacum to 2cm in the sigmoid colon. The appendix is a small tube attached to the ceacum. The large intestine is a highly specialized organ that is responsible for processing waste so that emptying the bowels is easy and convenient.



Advantages: Colon is an ideal site for the delivery of agents to cure the local diseases of the colon.

Local treatment has the advantage of requiring smaller drug quantities.

Reduce gastric irritation caused by many drugs (e.g. NSAIDS).

Bypass initial first pass metabolism.

Extended daytime or nighttime activity.

Improve patient compliance.

Targeted drug delivery system.

Disadvantages

For poorly soluble drug as the fluid contents in colon is much lower and it is more viscous than in upper part of GI tract, for successful delivery through this site, drugs require to be in solution form before it arrives to colon and/or it should dissolve in luminal fluid of colon.

The resident microflora could also affect colonic performances via metabolic degradation of drug.

Lower surface area and relative 'Tightness' of the tight junction in the colon can also restrict drug transport across the mucosa and into the systemic circulation.

COMPRESSION COATING OF TABLETS

Compression coating is an old concept, which has been recently renewed as a novel technology due to advances in tablet press technologies. Compression coated tablets have two layers, an inner core and an outer shell.

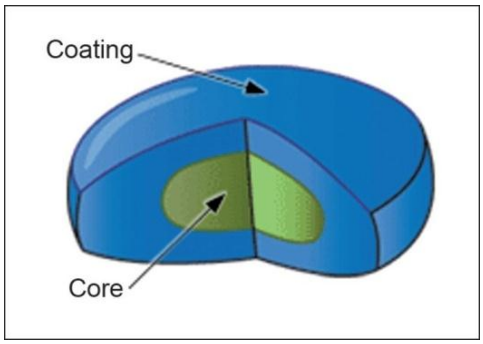


Illustration of Compression coated tablet

First the inner core is compressed as a small tablet, and then the inner core tablet is dry coated with rate controlling materials such as controlled release polymers and fillers. The

drug release rate is dependent on various factors such as thickness and porosity of the outershell, types of material used for inner core and outer shell, particle size of the excipients, compression used to compress both the layers and the position of the inner core in the tablet.

Up on contact with dissolution media or physiological liquids these materials forms gel like matrix. Erosion and diffusion of the swollen coating control the drug release rate.

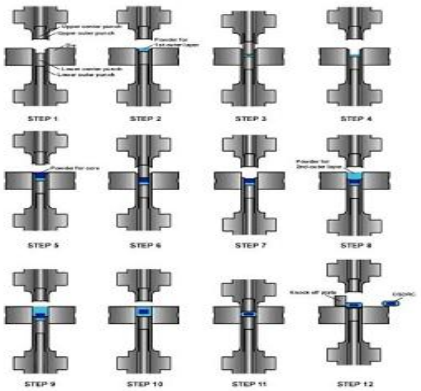


Diagram of Compression coating press

Penwest's Syncro Dose ^{TM} technology is a classical example of compression coated tablets. These tablets contain an immediate release inner core and compression coating outer layer of xanthum gum and locust bean gum. The lag time and rate of drug release is controlled by modulating the concentrations of two polysaccharides.

Advantages

Include the capability to physically separate two incompatible drugs with in the same dosage form.

Positive control of the weight of the coating can be maintained with in the close tolerences.

Uniform coatings with in the specified tolerences are reproducible from batch to batch.

Disadvantages

Position of the core tablet may alter during the transfer from one die cavity to other.

Pharmaceutical aspects of compression- coating tablets in dosage form development are;

To protect hygroscopic, light-sensitive, oxygen labile or acid- labile drugs.

To separate incompatible drugs from each other and achieve sustained release.

To modify drug release pattern (delayed, pulsatile and programmable release for different drugs in one tablet).

AIM AND OBJECTIVE

Aim

To formulate and evaluate Ciprofloxacin colon targeted tablet by compression coating technique.

Objective

The main objective is to estimate the drug content available in the colon region for the effective treatment of colon diseases like Crohn's disease for a long period of time with controlled infections.

- To select the drug suitable to target the colon for the treatment of Crohn's disease.
- To coat the core tablets using Compression coating technique.
- The formulated coated tablets were again subjected to physicochemical characters.
- To carry out *invitro* release studies and compare the dissolution values for formulations.
- To evaluate Drug release Kinetics.
- To evaluate accelerated stability tests.

MATERIALS AND METHODS

Materials Used

List of materials used in the formulation

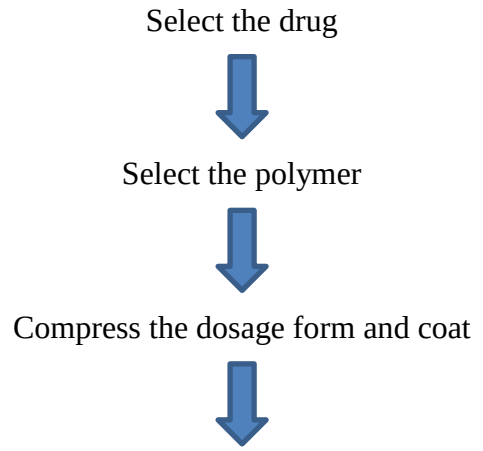
Ingredient	Category	Supplier
Ciprofloxacin	Drug	Granules India Ltd, Hyderabad, India.
Guar gum	Polymer	Nutriroma, India
HPMC different grade: K4M,	Polymer	Colorcon Asia Pvt. Ltd, India.
Microcrystalline cellulose	Diluent	S. D. Fine Chemicals Ltd., India.
Crospovidone	Disintegrant	Savvy spechems pvt Ltd, Hyderabad.
Magnesium stearate	Lubricant	S. D. Fine Chemicals Ltd., India.
Talc	Glidant	S. D. Fine Chemicals Ltd., India.

List of Equipments Used

Equipment	Company
Weighing balance	Shimadzu, AX200, Japan.
Tablet compression machine	Cadmach.
Friabilator	Roche ltd.
Hardness tester	Pfizer
UV-Spectrophotometer	Beckman and Coulter (DU 520series) spectrophotometer.
Dissolution apparatus	Erweka DT 700
Fourier transform infrared radiation spectrophotometer	Shimadzu, Japan.

PLAN OF WORK

- To review the literature suitable for the selection of drug, polymers and method
- Procurement of drug
- Preformulation studies must be conducted
  - ❖ Analysis by UV Visible spectrophotometer
  - ❖ Solubility
  - ❖ Fourier Transform Infra Red Spectrophotometer
- Formulation
  - ❖ To select the suitable method
  - ❖ To select the suitable polymers
  - ❖ Optimize the formulated compressed coated tablets
- Evaluation
  - ❖ To perform Hardness, Friability, Thickness, Drug content, *invitro* dissolution studies.
  - ❖ To perform accelerated stability studies.



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