Research Article

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Dexamethasone Matrix Tablet for Colon Specific Drug Delivery

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ABSTRACT:

There is increasing awareness that the human gut micro flora plays a critical role in maintaining host health, both within the gastrointestinal tract and, through the absorption of metabolites, systemically. An 'optimal' gut micro flora establishes an efficient barrier to the invasion and colonization of the gut by pathogenic bacteria produces a range of metabolic substrates which in turn are utilized by the host (e.g. vitamins and short chain fatty acids) and stimulates the immune system in a non-inflammatory manner. Although little is known about the individual species of bacteria responsible for these beneficial activities, it is generally accepted that the bifidobacteria and lactobacilli constitute important components of the beneficial gut micro flora. A number of diet-based micro flora management tools have been developed and refined over recent decades including probiotic, prebiotic and synbiotic approaches. Each aims to stimulate numbers and/or activities of the bifidobacteria and lactobacilli within the gut micro flora. The aim of this article is to examine how prebiotics are being applied to the improvement of human health and to review the scientific evidence supporting their use.

KEYWORDS: dexamethosone, colonic diseases, matrix tablet, corticosteroids

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INTRODUCTION:

Delivery of drugs to the colon is useful in the treatment of several colonic diseases (ulcerative colitis and crohn's disease). Corticosteroids have traditionally formed the basis of treating inflammatory bowel disease. However chronic treatment of inflammatory bowel disease with steroids, while often effective, is plagued by a number of serious side-effects (e.g. acne, moonface, striae, hypertension, peptic ulcer, impaired glucose tolerance and mood disturbances. If these undesired side-effects could be overcome or markedly reduced in both subchronic and chronic dosing regimes. Corticosteroids would have the potential of being ideal therapeutic treatments of inflammatory bowel disease.

A potential matrix material for colonic drug delivery is guar gum. Owing to its high viscosity this polysaccharide may carry certain drugs to the large intestine without appreciable release in the stomach or small intestine. Once in the large intestine, the guar gum matrix will be degraded by specific enzymes produced by the gut microflora (i.e, α-galactosidases and β-mannanase) to initiate drug release [1].

The anti-inflammatory property of dexamethasone is useful in the treatment of

inflammatory bowel diseases (IBD). 75mg of dexamethasone is equivalent in anti-inflammatory activity to about 5mg of prednisolone for inflammatory bowel diseases (IBD) [2].

The aim of this study was to develop guar gum based colon targeted drug delivery systems of dexamethosone for the prevention of inflammatory Bowel Disease (IBD).

MATERIALS AND METHODS

Materials

Dexamethasone (Arbro pharmaceuticals Ltd, New Delhi, India), Microcrystalline cellulose (Avicel, PH-105), Guar gum (Loba chemie Pvt. Ltd., Mumbai, India), Sodium starch glycollate (CFL Pharmaceuticals Ltd., Goa, India), Absolute ethanol-99% (S.D. Fine chem. Limited, Mumbai, India), Magnesium stearate and talc were of pharmacopoeia quality (USNF).

Preparation of tablets

Tablets were prepared by direct compression of the mixture of dexamethasone, guar gum (in matrix tablets), sodium starch glycollate (in immediate release tablets), microcrystalline cellulose. Magnesium stearate and talc (1:2) was used as lubricant. Tablets were compressed using 10mm round, flat and plain punch on a manual hydraulic press. Thickness of tablet was between 3.19 to 3.62mm. Composition of the formulation is given in Table 1.

Table 1 Composition of the tablet formulation (mg)

	DX-40	DX-50	DX-60	DX-IR
DEX	9	9	9	9
GG	140	175	210	….
Na s gly	….	….	….	17.5
MCC	190.5	155.5	120.5	313
Talc	7	7	7	7
Mg St	3.5	3.5	3.5	3.5

In vitro release of Dexamethasone with and without rate caecal content

The matrix tablets of dexamethasone were evaluated for their integrity in the physiological environment of stomach and small intestine under mimicking mouth to colon transit. These studies were carried out using a USP XXIII dissolution rate apparatus (apparatus 1, 100 rpm, 37º C). drug release studies in 0.1N HCl (2h), pH 7.4 sorenson's phosphate buffer (3h) and pH 6.8 phosphate buffered saline with rat caecal contents and without rat caecal contents (control study). Release studies for immediate release tablets were carried out in 0.1 N HCl (2h).

Samples of 1ml were taken from the medium at time intervals without a prefilter and replaced with respective dissolution medium. The sample were diluted, sonicated, filtered through G-5 bacteria proof filter and assayed for dexamethasone at 242 nm using UV spectrophotometer (Shimadzu UV-1201). The cumulative percent of dexamethasone released from formulations at different time periods with and without rat caecal contents (control) was compared. The statistical significance was teste by using student's T-test. A value of $P < 0.05$ was considered statistically significant [3].

RESULT AND DISCUSSION

Release of dexamethasone with and without rat caecal contents (control) in the pH 6.8 PBS from formulations containing different percentage of guar gum (DX-40, DX-50, DX-60) and immediate release formulation (DX-IR) is shown in Fig 1. Formulated immediate release dexamethasone tablets used as reference formulation to find the difference in the *in vitro* release profile of the drug, released entire quantity of drug with in 2 hour (about 95.5%). The matrix formuation DX-40 released almost the entire quantity of the drug with in 18 h of dissolution study. The formulation DX-50 and DX-60 released 99.47% and 61.53% respectively of its drug content at the end of 24 h of dissolution study.

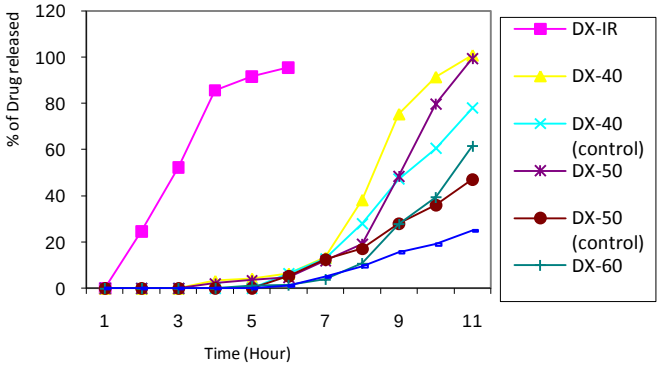

Figure 1.Drug Release Profiles of Formulations

CONCLUSION

It is clear from the results that DX-50 could target dexamethasone to colon because as at released almost the entire quantity at the end of 24 h of the study. The DX-60 tablets are also considered as potential formulation for targeting of dexamethasone to colon because of the fact that the human caecal content would be far more than what was used in the present study.

References

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