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Research Article

FORMULATION AND EVALUATION OF COLON TARGETED DOSAGE FORM OF PREDNISOLONE TABLET USING STERCULIA GUM

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ABSTRACT

Matrix tablets of Prednisolone were prepared by wet granulation method using various proportions of Sterculia gum with Carbopol 934P and Sterculia gum with Ethyl cellulose at 1:1, 1: .5 and 1:2 ratio were used. Coating was carried out by using 1:1 ratio of Eudragit L100 and Eudragit S100. All the preparation were evaluated for Pre compressional properties, Post compressional properties and in-vitro Dissolution study in different pH buffer of 0.1N HCL ,pH 7.4 , pH 6.8 in order to mimic GIT condition. Formulation shows good results with good percentage yield.

KEY WORDS: Colon targeted, Ethyl Cellulose, Carbopol 934p, Sterculia gum, wet granulation, Crohn's disease.

INTRODUCTION

Colon Targeted Drug Delivery System (CTDDS) may be follow the concept of Controlled or Sustained drug Delivery System. For CTDDS oral route of administration has received most attention. Local delivery allows topical treatment of inflammatory bowel disease. Colon is highly desirable for local treatment of a variety of bowel diseases such as ulcerative colitis, Crohn's disease, amebiosis, colonic cancer, local treatment of colonic pathologies, and systemic delivery of protein and peptide drugs [1, 2]. For effective and safe therapy of these colonic disorders, colon specific drug delivery is necessary i.e. drug release and absorption should not occur in the stomach as well as the small intestine, and neither the bioactive agent should be degraded in either of the dissolution sites but only released and absorbed once the system reaches the colon [3]. Today, colon specific drug delivery is challenging task to pharmaceutical technologist. The colon is believed to be a suitable absorption site for peptides and protein drugs for the following reasons, (i) less diversity, and intensity of digestive enzymes, (ii) comparative proteolytic activity of colon mucosa is much less than that observed in the small intestine, thus CDDS protects peptide drugs from hydrolysis, and enzymatic degradation in duodenum and jejunum, and eventually releases the drug into ileum or colon which leads to greater systemic bioavailability [4]. The concentration of drug reaching the colon depends on formulation factors, the extent of retrograde spreading and the retention time [5]. Coating of the drugs with pH-sensitive polymers provides simple approach for colon-specific drug delivery [6]. The bioactive agent should be degraded in either of the dissolution sites but only released and absorbed once the reaches the colon. Because the colon has a long residence time 72 hours and high water content it favors absorption of poorly absorbed drug molecule may have an improved bioavailability, CDDS has been employ to achieve following objectives i) Sustained delivery to reduce dosing frequency ii) Delay delivery of drug to achieve high concentration in treatment of disease of

distal gut iii) to delay deliver to a time appropriate to treat acute phase of disease iv) Deliver drug to that region that is less hostile metabolically, drug which is acid and enzyme labile such as proteins [7]. The upper part of GIT, i.e. the stomach and the duodenum has a microflora of less than 10^3 - 10^4 CFU/ml. The microflora of colon on the other side is in the range of 10^{11}-10^{12} CFU/ml consisting mainly of anaerobic bacteria, e.g. Bacteroides, Bifidobacteria, Eubacteria, Clostridia, Enterococci, Enterobacteria, etc.

This vast microflora fulfils its energy needs by fermenting various types of substrates that have been left undigested in the small intestine, e.g, di and trisaccharides, polysaccharide etc. For this fermentation, the microflora produces a vast number of enzymes like glucuronidase, xylosidase, arabinosidase, galactosidase, nitroreductase, azoreductase, deaminase and urea dehydroxylase. Because of the presence of these biodegradable enzymes only in the colon, the use of bacterial degradable polymers for colon specific drug delivery seems to be a more site specific approach as compared to other approaches. This study given the idea to evaluate the usefulness of Sterculia gum as carrier using Prednisolone as drug. Sterculia gum is a complex polysaccharide of high molecular weight. A molecular weight as high as 9,500,000 and viscosity of 1% solution is CPS >1100 has been reported. On hydrolysis it yields Galactose, Rhamnose, and Galacturonic acid. The present research work aimed to develop the sterculia gum colon specific tablet in combination with carbopol 934 P and ethyl cellulose at various proportions by wet granulation technology. To study the physical integrity up to 24 h and the *in vitro* dissolution to explore the application of sterculia gum as drug carrier in colon matrix tablet.

MATERIALS AND METHODS

2.1 MATERIAL

Prednisolone as gift sample obtained from Emcross pharmachem, Roorkee. Sterculia gum Carbopol 934 P, Ethyl cellulose, magnesium sterate and talc obtained from Central drug house Pvt Ltd. New Delhi.

2.2 Method of preparation of Prednisolone tablet for colon

The ingredients required to prepare a batch of tablets as given in formula (table 1) were weighed accurately and passed through # 120 mesh sieve and uniformly blended in a mortar. Starch pastes were prepared. The powder blend was taken in a mortar and was thoroughly triturated with starch paste to produce wet mass. Then wet mass was passed through mesh # 14. Granules so obtained were dried at 40°C for 2 h. Dried granules again passed through mesh # 18. Later, talc and magnesium sterate were added as required and blended. Then the granules are evaluated for rheological characteristics. The dried granules were compressed into tablet using a 10 station Tablet pilot press.

Table. No 1

Ingredient	F_1	F_2	F_3	F_4	F_5	F_6
Drug	50	50	50	50	50	50
Sterculia gum	150	150	200	200	100	100
Carbopol 934p	150		100		200	
Ethyl cellulose		150		100		200
Talc	25	25	25	25	25	25
Mg. Sterate	25	25	25	25	25	25
Total	400	400	400	400	400	400

COATING: Composition of coating

Table. No 2

Eudragit S100 and Eudragit L 100	1:1 , 1: 0.5 , 1:2

3. Evalution of pre compressional characteristics of Prednisolone

3.1 BULK GRANULAR DENSITY:

Bulk density (LBD) were determined. A quantity of 50 g of powder from each formulation was introduced into a 100 ml measuring cylinder. Initial volume was observed, the cylinder was allowed to tap. The tapping was continued until no further change in volume was noted. Bulk density is calculated by using formula:

Bulk density (ρb) = Bulk volume of the powder/Weight of the powder

3.2 TAPPED GRANULAR DENSITY:

Tapped granular density determine by tapping method, here 50g of the granules (W) was introduced into a 100ml measuring cylinder, The cylinder was allowed to fall under its own weight onto a hard surface from the height of 1 inch at 2 sec intervals. The tapping was continued until no further change in volume was noted. The bulk density and tapped density were calculated using the following formulae.

Tapped density (ρt) = Tapped volume of the powder/ Weight of the powder

3.3 CARR'S INDEX [COMPRESSIBILITY INDEX] AND HAUSNER'S RATIO:

The carr's index of the powder was determined by using formula:

Carr's index (%) = Tapped Granular density – Bulk Granular density × 100/ Tapped density

Hausner's ratio = Tapped Granular density / Bulk Granular density.

Table. No . 3

S.NO	HAUSNER'S RATIO	PROPERTY
1.	0-1.2	FREE FLOWING
2.	1.2-1.6	COHESIVE POWDER

TABLE.NO . 4

S.NO	CARR'S INDEX	PROPERTIES
1.	5-12	FREE FLOWING
2.	12-16	GOOD
3.	18-21	FAIR
4.	23-35	POOR
5.	33-38	VERY POOR
6.	>40	EXTREMELY POOR

3.4 ANGLE OF REPOSE:

The angle of repose of blend was determined by the funnel method. The accurately weight power was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the power. The powder was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation

$$\emptyset = \tan^{-1} h/r$$

Table. No. 5

S.NO	ANGLE OF REPOSE (Ø)	TYPE OF FLOW
1.	<25	Excellent
2.	25- 30	Good
3.	30-40	Passable
4.	>40	Very poor

4. Evaluation of compressional characteristics of the Prednisolone tablets

4.1 Weight uniformity

Twenty tablets were taken and weighed individu-ally. Average weight was calculated standard deviation and percent coefficient of variance was computed.

4.2 Thickness test

The tablets were evaluated for their thickness using a micrometer (Mitutoyo, Japan). Average of three readings were taken and the results were tabulated (n = 3).

4.3 Diameter test

The tablets were evaluated for diameter using a micrometer (Mitutoyo, Japan). Average of three readings were taken and tabulated (n = 3).

4.4 Hardness test

The tablets were evaluated for their hardness using Pfizer hardness tester. Average of three reading were taken and tabulated (n = 3).

4.5 Friability test

The friability of the tablets was determined in Roche Friabilator. Five tablets were weighed accurately and placed in the tumbling chamber and rotated at 25 rpm for a period of 4 min. Tablets were taken and again weighed. The percentage weight loss was determined by using formula given below. The experiment was repeated for three times and average was noted. % **Friability=Initial wt of tablets−Final wt of tabletsInitial wt of tablets X 100**

4.6 Determination of drug content

Five prednisolone tablets were crushed into powder in a mortar and powdered equivalent to prednisolone dose was taken in a volumetric flask containing distilled water and kept aside with constant shaking on a rotary shaker for 7-10 h to extract the total drug present in the tablet. Then the absorbance of the solutions was measured after suitable dilution at 245 nm against distilled water as blank. Averages of triplicate readings were taken. The content of drug was calculated using slope from calibration curve.

4.7 In vitro dissolution study

The *in vitro* dissolution study was performed in three different buffers of pH 0.1N HCL for 2 h and pH 7.4 for 3 h and pH 6.4 for 10 h in order to mimic from mouth to colon. The drug release study were carried out in pH O.1N HCL in USP dissolution test apparatus of 900 ml fluid (Apparatus 1, 100 rpm, 37°C) at regular interval sample is withdrawn and suitable dilutions are made and estimated for amount of drug release by measuring absorbance of sample in UV spectropho-tometer at the λmax of 245 nm. At the end of study dissolution medium were replaced with Sorenson phosphate buffer of pH 7.4 and continued the drug release study for 3 h. The samples were withdrawn at regular intervals and diluted with respective dissolution medium and estimated the drug release by measuring the sample absorbance at λ max of the drug in UV spectrophotometer.

RESULT

5. RESULTS AND DISCUSSION

5.1 PREFORMULATION PARAMETERS

1. **Melting Point –** 235 – 238 Degree Celsius (Reported M.P 235)
2. **Solubility's -** 1g dissolves of drug
   In 30ml of Methanol
   In about 50ml of Acetone solution
   Partial soluble in Water
   Partial soluble in Phosphate buffer
   Partial soluble in 0.1 N HCL

3. Table. No.6

PARAMETER	PREDNISOLONE G
Bulk Granular Density (gm/cm^2)	0.43±0.01- 0.67±0.06
Tapped Granular Density (gm/cm^2)	0.49±0.03-0.71±0.09
Compressibility Index	5.3±0.40-14.38±2.97
Hausner's Ratio	1.20±0.08-1.24±0.21
Angle of repose	24.87±0.3-27.22±0.20

Based on the result of Pre – compression tests, all the formulation showed angle of repose ranging from 36.30^0 to 27.5^0 indicating a good flow property and carr's index ranging indicating compressibility of the granules is fairly passable.

5.2 Post formulation parameters

TABLE.NO 7

Formulation parameter	Core tablet of Prednisolone
Weight Variantion (mg)	502.24±0.02-502.65±0.57
Hardness (kg / cm^2)	6.8±0.18 – 7.4±0.14
Thickness (mm)	35.3±0.04-5.9±0.11
% Friability	0.40±0.04-0.58±0.15
Drug content uniformity	93±0.12-98±.14

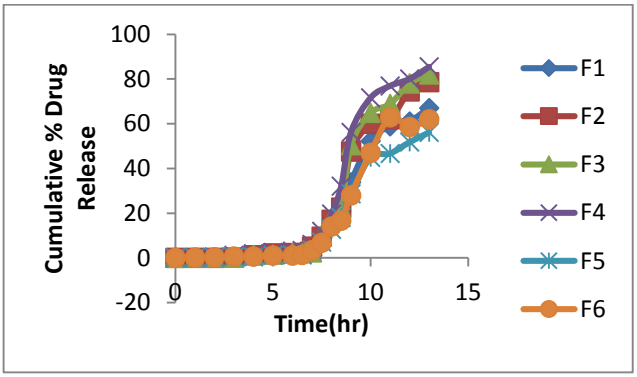
5.3 *IN- VITRO* RELEASE STUDIES

TABLE.NO 8

S.NO	Time	%CDR F1	%CDR F2	%CDR F3	%CDR F4	%CDR F5	%CDR F6
1	0	0	0	0	0	0	0
2	1	0.147	0.124	0.06	0.08	0.04	0.02
3	2	1.254	1.234	1.212	1.20	1.19	1.14
4	3	2.25	2.223	2.18	2.15	2.09	2.01
5	4	3.28	3.25	3.22	3.17	3.15	3.11

6	5	3.42	3.40	3.35	3.29	3.25	3.16
7	6	4.81	4.43	3.64	4.09	4.08	4.11
8	6.5	5.22	4.16	4.12	5.28	4.19	4.26
9	7	5.48	5.09	6.23	6.11	5.65	5.41
10	7.5	7.12	9.43	10.25	11.9	6.98	6.77
11	8	15.23	17.14	17.85	19.62	12.79	14.08
12	8.5	21.07	22.49	22.37	32.06	18.07	16.66
13	9	33.85	47.54	50.43	56.19	28.64	28.01
14	10	52.27	60.04	64.85	71.59	45.01	46.94
15	11	58.94	62.09	68.84	76.95	46.74	62.91
16	12	61.03	74.49	78.09	80.08	51.79	58.64
17	13	67.04	78.59	82.03	85.46	56.14	62.05

PDR^{1-} % Drug release of formulation F_1 , PDR^2- Drug release of formulation F_2 ,PDR^3- Drug release of formulation F_3 , PDR^4- Drug release of formulation F_4, PDR^5 - Drug release of formulation F_5 ,PDR^6 - Drug release of formulation F_6.



In-vitro drug release profile

CONCLUSION

Colon targeted matrix tablet are developed by using carrier sterculia gum, ethyl cellulose and carbopol along with coating (Eudragit S100 and Eudragit S100). Granules are evaluated for rheological properties. The formulation prepared has a ratio in 3 different ways. The formulation of F1 and F2 is 1:1, F3 and F4 is 1:0.5 and F5 and F6 is 1:2. The ratio difference is between Natural Polymer and Synthetic Polymer. Based on *In vitro* drug release study, formulation F4>F3>F2>F1>F6>F5, the drug release found to be 85.46, 82.03, 78.59, 67.34, 62.05 and 56.14 respectively. According to Drug release profile founded that drug release is highest in F4 formulation. The optimized formulation show First Order Kinetics with R^2 value 0.957- 0.965 , Peppas –Korsmeyer release with a regression coefficient value between 0.657-0.908 and N value between 1.661- 1.972. So the drug release mechanism is found to be through super case II transport.

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