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Formulation & evaluation of colon targeted drug delivery system of omeprazole

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ABSTRACT

The purpose of the present study was to formulate colon delivery tablets of Omeprazole, an Anti-ulcer agents. Omeprazole tablets were prepared by direct compression method employing rate controlling the synthetic polymer Eudragit RSPO, Eudragit RLPO The Prepared granules were subjected for pre compressional and drug excipient compatibility studies and tablets were evaluated for post compressional parameters such as weight variation, hardness, friability, drug content, and *Invitro* dissolution studies. It was concluded that the out of all the formulations F12 was the best formulation as the extent of drug release was found to be 96 % upto 24 hrs and the kinetics of drug release was follows first order kinetics with the 'n' value of more than 0.5 indicates that non-fickian mechanism. % Cumulative drug release from all the prepared formulation was found to be in following order F12>F11>F10>F9>F8>F7>F6>F5>F4>F3>F2>F1 The kinetics of optimized formulation F12 was found to be follows first order kinetics and the 'n' is more than 0.5 indicates that it follows non-fickian mechanism. Endured super case II release, during the dissolution study, which indicated that polymer relaxation, had a significant role in the drug release mechanism. Drug release mechanism was case II non-Fickian (anomalous) release ($0.5 \leq n \leq 0.89$).

Keywords: Omeprazole, Eudragit RSPO, Eudragit RLPO, Non-fickian mechanism

INTRODUCTION

Oral drug delivery is the most desirable and preferred method of administering therapeutic agents for their systemic effects. Colon specific drug delivery system should be capable of protecting the drug en route to the colon i.e. drug release and absorption should not occur in the stomach as well as in the small intestine, but the drug only released and absorbed once the system reaches to the colon [1].

Colonic delivery offers numerous therapeutic advantages like drugs, which are destroyed by the stomach acid and metabolized by pancreatic enzymes are minimally effected in the colon.

Colon targeted drug delivery systems have been gaining significant attention not just for providing more effective therapy to colon related disease, but also as a potential approach for systemic delivery of therapeutic proteins and peptide drugs. Colon is also a potential site for treatment of disease

sensitive to circadian rhythms such as asthma, angina, arthritis [2] etc.

Various colon specific drug delivery systems are being developed by taking advantages of the luminal pH in the ileum and microbial enzymes in the colon. In general, four primary approaches have been proposed for colon-specific delivery namely prodrugs, pH- dependent, time dependent and microflora-activated systems. Most recently new colon specific delivery system are developed .These are pressure controlled colon delivery capsule, CODESTM, osmotically controlled drug delivery system, pulsincap system, time clock system etc. significant milestone in oral NDDS is the development of the osmotic drug delivery system, an innovative and highly versatile drug delivery system. Osmotic drug delivery system (ODDS) differ from diffusion- based system in that; the delivery of active agent (s) is driven by an osmotic gradient rather than the concentration of drug in the device [3].

MATERIALS AND METHODS

Materials

Omeprazole, Eudragit RSPO, Eudragit RLPO were obtained from Yarrow chemicals, Vadodara and all other chemicals/ solvents used were of analytical grade.

Method

Preparation of Omeprazole of Colon tablets

Weigh all the ingredients properly and pass it through sieve no 40 except talc and magnesium stearate. Weigh talc and magnesium stearate and pass it through sieve no 60 and was blended uniformly and was compressed using a tablet compression machine in 6 mm punch.

Table.1: Formulation table for preparation of omeprazole Colon specific drug delivery systems

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Omeprazole	20	20	20	20	20	20	20	20	20	20	20	20
Eudragit RSPO	5	10	15	20	25	30	-	-	-	-	-	-
Eudragit RLPO	-	-	-	-	-	-	5	10	15	20	25	30
Microcrystalline cellulose	66.5	61.5	56.5	51.5	46.5	41.5	66.5	61.5	56.5	51.5	46.5	41.5
Magnesium stearate	2	2	2	2	2	2	2	2	2	2	2	2
Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
PVP K 30	5	5	5	5	5	5	5	5	5	5	5	5
Total	100	100	100	100	100	100	100	100	100	100	100	100

COATING OF TABLETS

The prepared tablets were coated with shellac solution using spray coating technique

Table.2: Ingredients of coating pan

S.NO	Ingredient	Quantity
1.	Cellulose acetate phalate	40 mg
2.	Triethyl citrate	6
3.	Isopropyl alcohol	q.s
4.	Dichloromethane	q.s

Pan Charge - 3.5 Kg
Pan speed -14 rpm
Inlet Temperature -52-58^{o}C
Exhaust air temperature - 40-42^{o}C
Bed Temperature -35-40^{o}C
Spray rate -50 g/min
Distance Between spray gun and tablet bed -15 cm
Coating time min -160

POST COMPRESSIONAL PARAMETERS

Evaluation of tablets

Weight variation

Twenty tablets were selected at random and average weight was determined. Then individual tablets were weighed and the individual weight was compared with an average weight. The results are shown in Tables –3.

Hardness and Friability

Friability of the tablets was checked by using Roche Friabilator. The device subjects a number of tablets to the combined effect of abrasions and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets from a height of 6 inches with each revolution. Pre-weighed sample tablets were placed in the friabilator, which was then operated for 100 revolutions. Tablets were dusted and reweighed. The results are shown in Table – 3.

Content uniformity test

Ten tablets were weighed and powdered, a quantity of powder equivalent to 10 mg of omeprazole was transferred to a 25 ml volumetric flask and 15 ml water is added. The drug is extracted in water by vigorously shaking the stoppered flask for 15 minutes. Then the volume is adjusted to the mark with distille water and the liquid is filtered. The Hydrochlorothiazide content was determined by measuring the absorbance after appropriate dilution. The drug content was calculated using the standard calibration curve. The mean percent drug content was calculated as an average of three determinations.

In vitro drug release study

The *in vitro* dissolution study of omeprazole tablets were determined using USP XXIII type II (paddle) dissolution apparatus. The paddle rotation speed of 100 r/min and temperature of 37 ± 0.5˚C was maintained. Aliquots (5 ml) of the solution were collected at predetermined time intervals from the dissolution apparatus and samples were replaced with fresh dissolution medium. Firstly the dissolution medium was 0.1N Hcl for 2 hrs then it was replaced with 7.2pH phosphate buffer.Absorbance of these solutions was measured Cumulative percentage drug release was calculated using equation.

Release kinetics

Data obtained from *in-vitro* release studied was evaluated to check the goodness of fit to various kinetics equations for quantifying the phenomena controlling the release from microspheres. The kinetic models used were zero order, first order, and HiguchiandKorsmeyer-peppas model. The goodness of fit was evaluated using the correlation coefficient values (R2)

Mechanism of drug release

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model [139-146].

Zero order release rate kinetics [137]

To study the zero–order release kinetics the release rate data are fitted to the following equation.

$$F = K_o t$$

Where ‘F’ is the drug release at time‘t’, and ‘K’ is the zero order release rate constant. The plot of % drug release versus time is linear.

First order release rate kinetics

The release rate data are fitted to the following equation

$$\text{Log } (100 - F) = kt$$

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

Higuchi release model

To study the Higuchi release kinetics, the release rate data were fitted to the following equation,

$$F = k\,t^{1/2}$$

Where 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to korsmeyer-peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight line.

$$M_t/M_\infty = Kt^n$$

Where, M_t/M_∞ is fraction of drug released at time '*t*', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process.

RESULTS AND DISCUSSIONS

Table 3: Omeprozole tablets characterization

F.Code	Hardness (kg/cm^2) †	Thickness (mm) ‡	Weight (mg) ‡	Friability (%)	Drug content * (%)
F1	5.50 ±0.44	3.22±0.17	100.8±1.48	0.36	98.25±1.37
F2	5.50±0.31	3.37±0.25	101.4±0.54	0.39	95.28±0.80
F3	5.58±0.40	3.14±0.80	99.6±0.41	0.43	99.12±2.47
F4	5.66±0.55	3.20±0.20	102.8±1.64	0.12	101.22±0.88
F5	4.25±0.57	3.08±0.66	102.6±1.14	0.54	100.24±1.25
F6	4.08±0.30	3.33±0.25	100.2±0.83	0.58	99.53±1.87
F7	4.25±0.57	3.24±0.71	99.9±0.67	0.64	93.28±1.99
F8	4.41±0.60	3.32±0.89	98.0±0.43	0.37	95.35±1.14
F9	5.00±0.44	3.38±0.73	102.5±0.80	0.77	96.34±2.18
F10	5.00±0.31	3.00±0.68	101.2±0.83	0.42	91.29±0.98
F11	5.08±0.37	2.98±0.88	102.1±0.93	0.48	97.35±0.43
F12	5.41±0.70	3.11±0.36	101.2±0.97	0.15	99.88±0.88

***** All values represent mean ± Standard Deviation (SD), n=3

† All values represent mean ± Standard Deviation (SD), n=6

‡ All values represent mean ± Standard Deviation (SD), n=20

All the formulations were evaluated for various parameters like hardness, friability, drug content, disintegration time and *In-vitro* drug release values are given in Table No. 3. All the tablets passed evaluation tests and were within the pharmacopoeial limits

Invitro dissolution studies

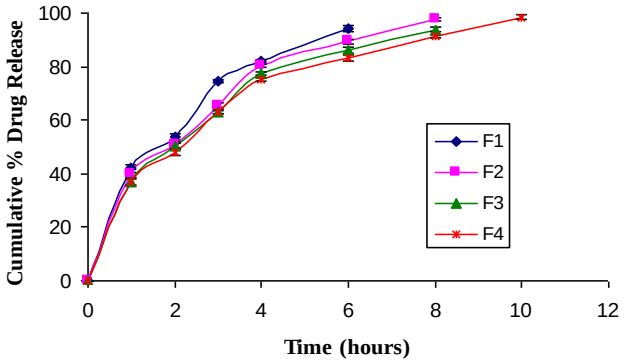

Fig no: 1 *In vitro* drug releases of F1, F2, F3 and F4 formulations

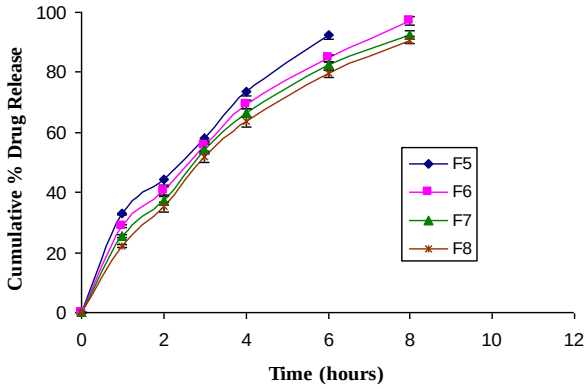

Fig no: 2 *In vitro* dissolution graph for F5-F8

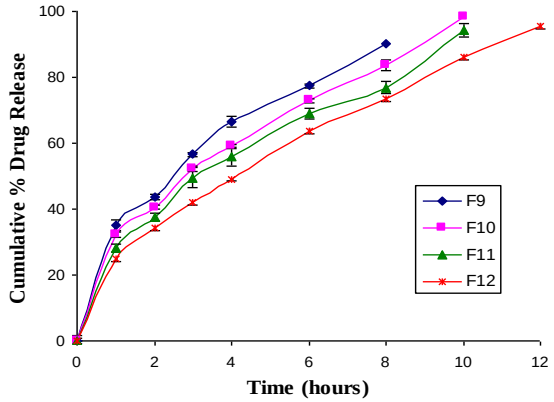

Fig no: 2 *In vitro* dissolution graph for F9-F12

CONCLUSION

Omeprazole is the preferred drugs used in treatment of Peptic ulcer. The project was intended to formulate and evaluate Omeprazole enteric coated tablets, as the drug is a potent drug used in peptic ulcer but is unstable in acidic environment. The angle of repose, compressibility index and sieve analysis results shown that the formulation is suitable for direct compression.

This study have been showed that Omeprazole could be efficiently colon targeted It, provides extended duration of action in therapeutic range without reaching toxic levels as in the case of conventional dosage forms. These dosage forms have the ability to reduce the dosing frequency and increasing.

The technique employed in the preparation of matrix system i.e. Direct compression, is highly practical and economical from the industry point of view.The tablets were entric coated using Shellac solution by spray coating technique. The sustainability of the drug with Eudragit RLPO with 30 mg (i.e) F12 was found to show good Targetted site controlled drug delivery, as it showed 96% drug release for 24 hrs. Success of the *In vitro* drug release studies recommends the product for further *In vivo* studies, it may improve patient compliance.

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