Development and Optimization of Colon Targeted Drug Delivery System of Ayurvedic Churna Formulation Using Eudragit L100 and Ethyl Cellulose as Coating Material

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Abstract—The purpose of this study was to prepare time and pH dependent release tablets of Ayurvedic Churna formulation and evaluate their advantages as colon targeted drug delivery system. The Vidangadi Churna was selected for this study which contains Embelin and Gallic acid. Embelin is used in Helminthiasis as therapeutic agent. Embelin is insoluble in water and unstable in gastric environment so it was formulated in time and pH dependent tablets coated with combination of two polymers Eudragit L100 and ethyl cellulose. The 150mg of core tablet of dried extract and lactose were prepared by wet granulation method. The compression coating was used in the polymer concentration of 150mg for both the layer as upper and lower coating tablet was investigated. The results showed that no release was found in 0.1 N HCl and pH 6.8 phosphate buffers for initial 5 hours and about 98.97% of the drug was released in pH 7.4 phosphate buffer in total 17 Hours. The in vitro release profiles of drug from the formulation could be best expressed first order kinetics as highest linearity ($r^2 = 0.9943$). The results of the present study have demonstrated that the time and pH dependent tablets system is a promising vehicle for preventing rapid hydrolysis in gastric environment and improving oral bioavailability of Embelin and Gallic acid for treatment of Helminthiasis.

Keywords—Embelin, Gallic acid, Vidangadi Churna, Colon targeted drug delivery.

I. INTRODUCTION

VIDANGADI Churna used as Cakradatta for the treatment of Krimiroga in a high dose of 3-5 gm daily mentioned in Ayurvedic formulary. It contains Vidang fruit which constitutes of active ingredient *Embelin*. In modern medicine Embelin is used as anthelmintic, antibacterial antifungal etc. Vidangadi Churna has more frequency of administration. Embelin cannot be absorbed in upper GIT track, hence making overall incompatible dosage form in terms of dose remembrance and bulk. Hence, we aim to formulate novel drug delivery system which will reduce the dose, dosing frequency and increasing the bioavailability of Embelin in Vidangadi Churn [1].

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II. MATERIALS AND METHODS

A. Materials

Vidangadi Churna was prepared in laboratory and its individual components were procured from, Ms. Sanjivani Ausadhalay, Bhavnagar. The Embelin and Gallic acid were obtained from department of Pharmacognosy SKPCPER, Ganpat University, Mehsana, Gujarat, India.

B. Methods

Preparation of stock solution and determination of absorption maxima of Embelin and Gallic acid in 7.4 Phosphate buffer solution.

10mg of each Embelin and Gallic acid was dissolved in 1ml of methanol and q.s. to 10ml with 7.4 Phosphate buffer solutions. 1ml of this solution was further diluted to 10ml in volumetric flask with 7.4 Phosphate buffer solutions. This was serving as a standard stock solution (100µg/ml). The spectrum of the Embelin and Gallic acid was obtained by scanning this solution in the range of 200nm- 400nm against 7.4 Phosphate buffer solution as blank to fix absorption maxima.

C. Calibration Curve

Calibration curve were established with six dilutions of standard prepared from standard stock solution using further dilution, at concentration range from 2 to 12 µg/ml. Each concentration was measured in triplicate. The corresponding absorbance was plotted against the concentration of the marker. The reference substance employed was Embelin for Vidang and Gallic acid for Harade. The graph so obtained was shown in Figs. 1 and 2.

D. Preparation of Core Tablets by Direct Compression Method

The core tablets were prepared by direct compression method. The extract was dried, powdered and properly mixed with diluents in pestle. Then the mixture was moistened with a granulating agent (starch paste 5% w/v in water) until a coherent but not too damp mass was produced. The coherent mass was passed through sieve number 22 & 44. The resulting granules were dried in oven at not more than 60°C. The dried granules were mixed with talc and magnesium stearate (4%) and compressed into tablet using 6mm punches on 8 station rotary tablet compression machine.

World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:7, No:12, 2013

E. Preparation of Coating Granules Using Different Polymers in Equal Ratio

The coating layer compositions containing Eudragit L100 and ethyl cellulose in equal ratio. The Eudragit L100 and ethyl cellulose mixture were properly mixed in pestle. Then the mixture was moistened with a granulating agent (Acacia mucilage 1% w/v in water) until a coherent but not too damp mass was produced. The coherent mass was passed through sieve number 22 & 44. The resulting granules were dried in oven at not more than $60^{\circ}C$.

F. Preparation of Compressed Coated Colon Targeted Tablet [2], [3], [6]-[17]

Weight accurately about 150mg of prepared coating granules of Eudragit L 100 and ethyl cellulose filled in 12mm punch and place prepared core tablet in centre, again filled 150mg of coating granules and punched on 8 station rotary tablet compression machine. The optimized formula was given in Table I.

G. Evaluation of Granules and Tablets [5]

The granules were evaluated for bulk density, tapped density, carr's index, Hausner's ratio and angle of repose. The tablets were evaluated for hardness thickness, friability, weight variation test and in-vitro dissolution studies. The result so obtained was shown in Tables II & III.

H. In-vitro Dissolution Studies

In-vitro release profile of the compressed coated colon targeted tablets was evaluated using rotating basket dissolution apparatus, in 900ml of 0.1 N HCl, for initial 2 hrs, than in 900 ml of 6.8 PBS for 3 hrs and then final in 7.4 PBS for 12 hrs until maximum released achieved. The temperature maintained at $37\pm0.50C$ for dissolution media respectively, and the basket was rotated at a constant speed of 50 rpm. The tablet was placed in the baskets. Aliquots of samples were withdrawn at the interval of 1 hour for 17 hrs. The samples withdrawn were filtered, diluted suitably and analyzed at 307.5nm and 341nm spectrophotometrically for drug release. The result so obtained was shown in Table IV.

I. Model Dependent Parameters [4]

To study the release kinetics, the data obtained from *in vitro* drug release studies were plotted in various kinetic models.

J. Zero Order Model

As cumulative amount of drug released vs. time, describes concentration independent drug release rate from the formulation

$$C = k_0 t$$

where ko is the zero-order rate constant expressed in units of concentration/time and t is the time in hours. The graph so obtained was shown in Fig. 3 and the results so obtained were shown in Table V.

K. First Order Model

As log cumulative percent drug remaining vs. time, describes concentration dependent drug release from the system.

$$LogC = LogC0 - kt/ 2.303$$

where C0 is the initial concentration of drug and k is the first order constant. The graph so obtained was shown in Fig. 4 and the result so obtained was shown in Table V.

L. Peppas Model

A simple semi empirical model relating exponentially the drug release to the elapsed time (t):

$$Qt/Q\alpha = K_k t^n$$

K_k is a constant incorporating structural and geometric characteristic of the drug dosage form and in is the release exponent, indicative of the drug release mechanism. The graph so obtained was shown in Fig. 5 and the result so obtained was shown in Table V.

M. Higuchi Model

As cumulative percentage of drug released vs. square root of time, described the release of drug based on Fickian diffusion as a square root of time dependent process from swellable insoluble matrix.

$$Q = kt1/2$$

where k is the constant reflecting the design variables of the system. The graph so obtained was shown in Fig. 6 and the result so obtained was shown in Table V.

III. RESULTS AND DISCUSSION

The major objective of the present investigation was carried out to develop a time dependent and pH dependent colon drug delivery system for targeting the drug into the colon. In this study, the core tablets were prepared using equal mixture of dried drug extract and Lactose using 5% w/v starch paste in water. The coating layer compositions containing Eudragit L100 and ethyl cellulose in equal ratio were prepared using 1% w/v Acacia mucilage in water. The prepared tablets were evaluated for physicochemical parameters as hardness, thickness, friability, % weight variation and % drug content they all are within the limit as per standard. In-vitro dissolution studies reveal that the % drug release at the end of 17 hrs was found to 98.97 % respectively. The in vitro release profiles of drug from the formulation could be best expressed first order as the plots showed highest linearity ($r^2 = 0.9561$) and it is concluded that formulation follows the first order kinetics of drug release which is best fitted for the pharmaceutical dosage form that release the drug in a way that is proportional to the amount of drug remaining in its core, in such a way that the amount of drug released by unit of time diminish.

World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:7, No:12, 2013

IV. CONCLUSION

The present study was carried out to investigate the ability of polymers for targeting the drug release in colon. From results it is obtained that in the present study, the in vitro studies showed that compressed coated tablets were successfully deliver the maximum amount of drug in intact form to the colon. The coating material Eudragit L100 and Ethyl cellulose used in equal ratio for both upper layer as well as lower layer which, prevents the drug release in the stomach and intestine so we can solve the problem of side effect of anti inflammatory drug in this area & also prevents ulcerative colitis.

TABLE I
OPTIMIZED FORMULA FOR COMPRESSED COATED COLON TARGETED TABLET

For core tablet		For coating granules		Total Weight of tablet in mg
Dried extract in mg	Lactose in mg	Eudragit L100 in mg	Ethyl cellulose in mg	
72	78	75	75	450

TABLE II
EVALUATION PARAMETER FOR GRANULES

Bulk density (g/cc)		Tapped density (g/cc)		Carr's index (%)		Hausner's Ratio		Angle of Repose (θ)	
Core Tablet	Coating Granules	Core Tablet	Coating Granules	Core Tablet	Coating Granules	Core Tablet	Coating Granules	Core Tablet	Coating Granules
0.638	0.533	0.595	0.599	9.11	9.21	1.4	1.6	25.22	24.72

TABLE III
EVALUATION PARAMETER FOR TABLET

Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	%Weight variation	% Drug contents
4.2	2.7	0.470	+1.8	99.55

TABLE IV
IN VITRO DISSOLUTION STUDIES

Time (Hours)	Absorbance		Conc. µg/ml	Conc. µg/5ml	Conc. µg/900ml	Cumulative Drug Release (in mg)	% Cumulative Drug Release
	307.5	341					
1.	0	0	0	0	0	0	0
2.	0	0	0	0	0	0	0
3.	0	0	0	0	0	0	0
4.	0	0	0	0	0	0	0
5.	0	0	0	0	0	0	0
6.	0.005	0.003	2.91	14.55	2619	2.62	3.64
7.	0.009	0.006	4.72	23.6	4248	4.26	5.92
8.	0.012	0.009	7.50	37.5	6750	6.77	9.41
9.	0.015	0.011	9.12	45.6	8208	8.25	11.45
10.	0.021	0.017	14.16	70.8	12744	12.79	17.76
11.	0.039	0.031	25.82	129.1	23238	23.31	32.37
12.	0.045	0.039	32.49	162.45	29241	29.37	40.79
13.	0.055	0.046	37.4	187	33660	33.82	46.98
14.	0.082	0.07	58.25	291.25	52425	52.61	73.07
15.	0.098	0.089	74.15	370.75	66735	67.03	93.09
16.	0.11	0.092	76.63	383.15	68967	69.34	96.30
17.	0.15	0.1	78.75	393.75	70875	71.26	98.97

TABLE V
MODEL DEPENDENT PARAMETERS

Zero order (R^2)	First order (R^2)	Korsmeyer Peppas Model (R^2)	Higuchi's Model (R^2)
0.8402	**0.9561**	0.8169	0.718
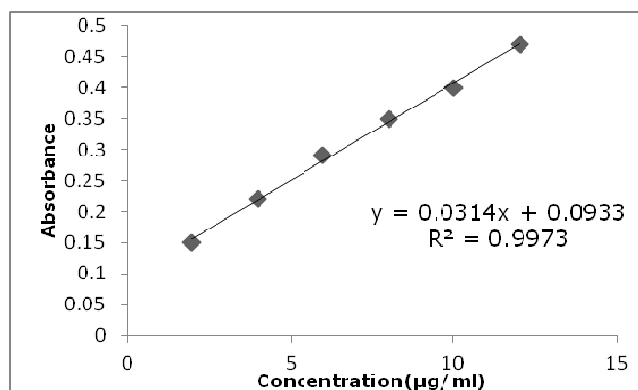
Fig. 1 Calibration curve of Standard Embelin in 7.4 PBS at 341 nm

y = 0.0314x + 0.0933
R² = 0.9973

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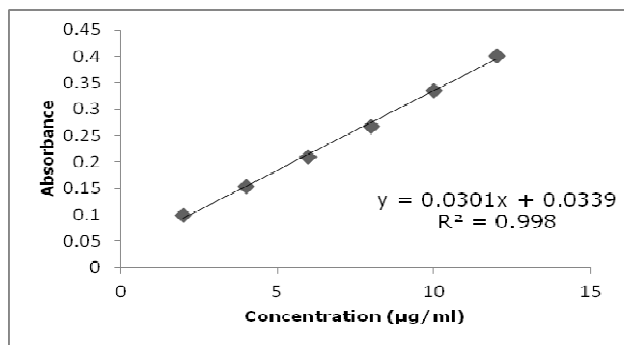Vol:7, No:12, 2013

Fig. 2 Calibration curve of Standard Gallic acid in 7.4 PBS at 258 nm
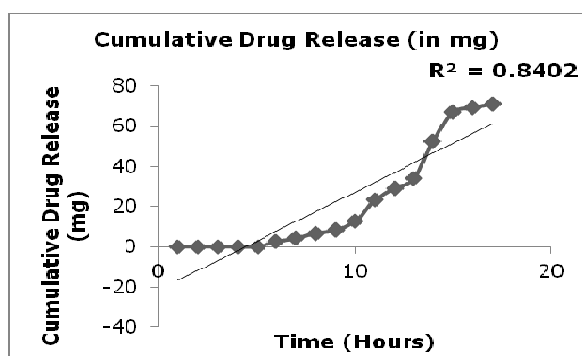
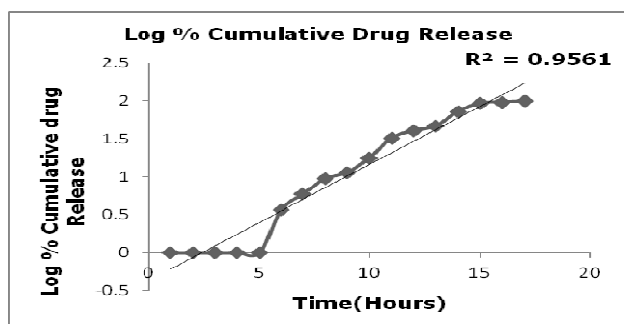Fig. 3 Zero order model for drug release pattern

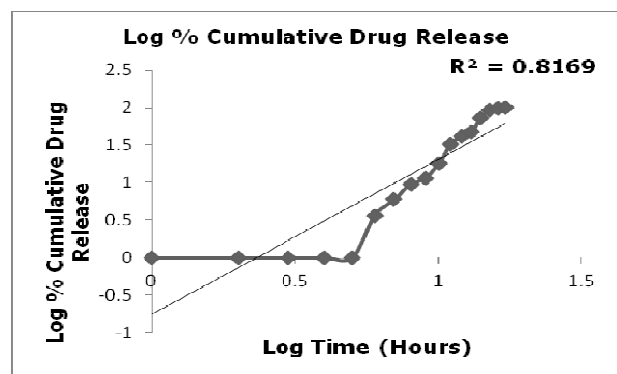Fig. 4 First order model for drug release pattern

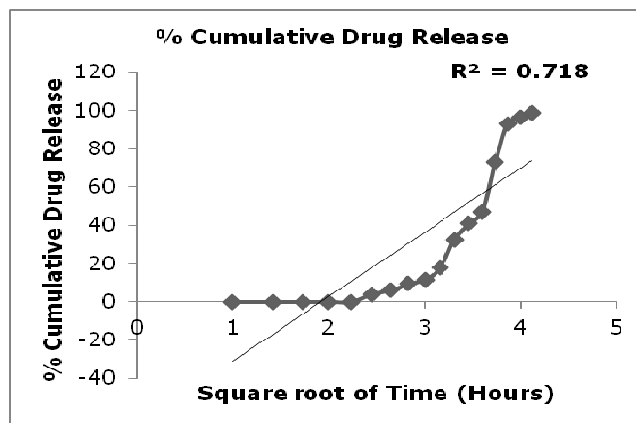Fig. 5 Korsmeyer Peppas model for drug release pattern

Fig. 6 Higuchi's model for drug release pattern

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