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Research Article

DESIGN AND DEVELOPMENT OF CURCUMIN FLOATING ORAL IN-SITU GEL CONTAINING PEANUT HUSK POWDER

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A B S T R A C T

The main objective of this study was to develop and evaluate novel oral in- situ gels of Herbal Curcumin to get sustain action for Peptic Ulcer treatment. The formulations are prepared by using sodium alginate as a natural biodegradable polymer, Calcium carbonate as a cross linking agent, and Peanut husk Powder as a floating agent. Initially the formulation is in sol form once taken orally it reacts with gastric pH and it changes to gel form. Various evaluation tests were conducted and from the results it was evident that formulation F4 containing 2.5 % of sodium alginate and 1% peanut husk powder has shown good viscosity, drug content 98.99%, pH, in vitro gelling capacity, better floating efficacy >12hrs and sustained drug release 98% for 14 hrs and it was found to be stable. Finally peanut husk powder can be used as a floating agent in in-situ preparations for getting sustained action due to its low density and its cost effectiveness.

INTRODUCTION

Peptic ulcer is the major problem observed now a days because of the food habits, excess spicy food, less water consumption, eating at odd times etc., To overcome this oral in-situ gels can be used.This can be consumed orally in solution form once it enters gastric system it changes into gel and becomes less dense than gastric fluid and floats on it[1]. And thereby the drug from this dosage form releases in a controlled manner for prolonged period and after the release of drug, the residual system is emptied from the stomach. By this the frequency of dosing can be reduced, Patient compliance will be more[2].

Peanut husk powder is used as a natural polymer (cellulose 35.7%, hemicelluloses 18.7%, lignin 30.2%) which is biodegradable, biocompatible, nontoxic, economically cheap cost, devoid of adverse and side effects and easy availability[3].

Curcumin the yellow pigment found in the rhizome of Curcuma longa, also known as turmeric, has both phenolic OH and CH_2 groups in β-diketone moiety which shows potent antioxidant property[4]. This will protect the patients from the adverse gastric side effects of many anti-inflammatory drugs, improves the quality of life of patients and decreases the treatment costs significantly.

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MATERIALS AND METHODS

Curcumin is obtained from Sehat Pvt Ltd, Himatnagar, Sodium Alginate, Calcium carbonate , Sodium citrate and D-Sorbitol from Lobachemie pvt Ltd, Peanut Husk Powder from Guntur Local market all the other chemicals used were of Analytical grade.

Pre-formulation Studies

FT-IR studies: Compatibility of Curcumin with formulation excipients was done by using FT-IR.

Preparation of Formulations: [5]

The polymers were dispersed in water heated at 60^0C with continuous stirring, cooled to 40^0C and other excipients were weighed accurately and formulated as per the Table 1.The formulations were finally stored in amber coloured bottles for further use.

Physical appearance and pH*[6]*: Formulations are physically checked for clear visibility. The time required for gel formation and type of gel formed was checked by keeping the solution in 0.1N HCL, pH 1.2. The pH was measured using a calibrated digital pH meter at 27^0C.

Viscosity*[7]*: It was determined by a Brookfield viscometer DV-III (Brookfield, USA) using spindle number 21 with cup and bob setting at 50 rpm.

Floating Behaviour*[8]*: The solution was poured in 0.1N HCL and the floating time was noted.

In-vitro gelling capacity [9]**:** It was measured by placing 5 ml of 0.1N HCL into a test tube which was maintained at 37ºC. 1ml of formulation was slowly transferred from pipette onto the surface of above solution. As the formulation comes in contact with gelation solution, it was immediately converted into stiff gel like structure. It was evaluated on the basis of stiffness and time period for which the formed gel remains as such. It graded in three categories:

1. Gels is formed after few minutes and dispersed rapidly
2. Gel is formed immediately and remains for <12 hours
3. Gel is formed immediately and remains for >12 hours**.**

Drug Content [10]

Ten ml of the solution was added to 900 ml of 0.1N HCl solution and stirred for 1 hour on a magnetic stirrer. The solution was filtered and the drug concentration was determined by using UV-visible spectrophotometer at 421nm against a suitable blank solution**.**

In-vitro Drug Release Studies

The studies were carried out using dissolution test apparatus USP Type II as shown in Table 2. Ten ml of the formulation was placed into a Petri dish which was kept into the dissolution vessel containing 0.1N HCL. At each time interval, 1ml of aliquot was pipette out and replaced with fresh medium and the concentration in the aliquot was determined by UV Spectroscopy [6]**.**

Drug release Kinetics: The *in-vitro* drug release data was fitted to Zero order, First order, Higuchi model and Peppas model to ascertain the kinetic modelling of the drug release.

Accelerated Stability Studies of optimized formulation [12]**:**As per ICH guidelines the optimized formulation was kept in amber coloured bottle and it was placed in the accelerated stability chamber at an elevated temperature and humidity of 40^0 C or 75% relative humidity and a control sample was placed at an ambient condition for a period of 1 month. Sampling was done at a predetermined time of initial 0,1,2,3 and 4 weeks interval respectively. At the end of study, samples were analyzed for the appearance, pH and drug content.

Table 1 Formulation of Floating *in situ* gel

S.no	Ingredients (g)	F1	F2	F3	F4	F5
1	Curcumin	0.5	0.5	0.5	0.5	0.5
2	Sodium alginate	1.5	2	2.5	2.5	2.5
3	Peanut husk Powder	-	-	-	1	0.5
4	Calcium carbonate	0.5	0.5	0.5	0.5	0.5
5	Sodium Citrate	0.5	0.5	0.5	0.5	0.5
6	Methyl paraben	0.18	0.18	0.18	0.18	0.18
7	D-Sorbitol	2	2	2	2	2
8	Purified water(ml)	100	100	100	100	100

Table 2 Dissolution data for floating i*n situ* Gel

Dissolution medium	900 ml of (0.1N HCL,1.2 pH) solution
Temperature	37 ^{0}C±0.2 ^{0}C
RPM	50
Volume withdrawn	10 ml every 1 hour.
λ max	421nm
Sol. taken	Ten ml sol. (known drug content)

Table 3 pH, Viscosity, Floating behaviour, Gelling capacity and Drug content of formulations

Formulation code	F1	F2	F3	F4	F5
pH*	8.2 ±0.16	8.4 ±0.12	8.6 ±0.07	8.7 ±0.09	8.5 ±0.13
Viscosity(cps)* at 27^{0}C	221±0.23	240±0.19	258±0.07	272±0.12	265±0.15
Buoyancy lag time (sec)*	69±0.24	72±0.13	76±0.16	61±0.34	67±0.22
Floating time (hr)	>10	>12	>12	>12	>12
Gelling capacity	++	+++	+++	+++	+++
Drug Content (%)*	97.03±0.18	98.28±0.42	98.62±0.17	98.99±0.12	97.63±0.38

*All values represent mean ± standard deviations (SD), n=3

Table 4 In-vitro Drug release of Formulations (F1- F5)

Time(min)	F1	F2	F3	F4	F5
0	0	0	0	0	0
5	28.65±0.12	21.37±0.23	18.26±0.26	14.21±0.21	16.12±0.27
10	37.98±0.48	32.14±0.71	25.25±0.14	20.32±0.64	21.45±0.38
15	43.64±0.23	35.07±0.20	29.23±0.20	23.78±0.29	26.32±0.24
20	49.32±0.16	38.11±0.13	32.21±0.42	28.67±0.20	30.54±0.36
30	55.54±0.03	39.61±0.28	37.96±0.05	34.21±0.39	35.98±0.67
60	61.29±0.05	46.19±0.19	41.32±0.01	38.61±0.25	40.14±0.19
120	68.32±0.09	53.16±0.13	46.35±0.19	42.31±0.18	44.31±0.82
180	72.32±0.14	58.12±0.09	50.84±0.42	45.98±0.70	48.65±0.28
240	79.32±0.54	65.94±0.21	57.32±0.11	51.94±0.18	54.56±0.18
300	85.32±0.34	73.19±0.27	62.48±0.56	56.78±0.14	59.84±0.25
360	91.12±0.23	75.29±0.28	68.65±0.32	62.45±0.29	64.87±0.13
420	95.81±0.32	78.45±0.39	71.54±0.51	65.98±0.23	69.54±0.14
480	98.64±0.24	82±0.18	76.12±0.20	70.32±0.29	72.34±0.38
540	100±0.02	93.43±0.21	82.34±0.15	75.16±0.91	78.49±0.63
600		96.21±0.29	87.39±0.29	79.95±0.12	82.46±0.54
660		100±0.08	92.87±0.35	82.68±0.36	87.34±0.02
720			96.25±0.28	88.49±0.61	92.31±0.07
780				93.21±0.21	97.81±0.26
840				98.01±0.42	

*All values represent mean ± standard deviations (SD), n=3

Table 5 Release kinetic data of the optimized formulation

Formulations	Zero order (R2)	First order (R2)	Higuchi (R2)	Erosion (R2)	Korseymeyer peppas
F4	0.863	0.929	0.977	0.480	0.975

Table 6 Accelerated stability study of Optimized Formulation

Temp(40^{0}C) RH 75%	Appearance& Clarity	pH	% Drug Content
Initial	No Change	8.9	98.62
First week Ambient	No Change	8.9	98.62
Second week Ambient	No Change	8.9	98.62
Third week Ambient	No Change	8.9	98.62

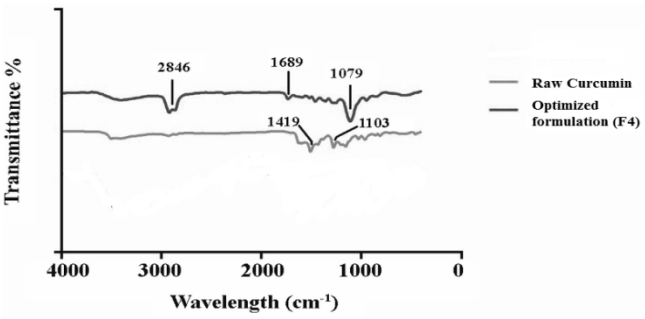

Figure 1 FT –IR spectrumof Curcumin and optimized formulation(F4)

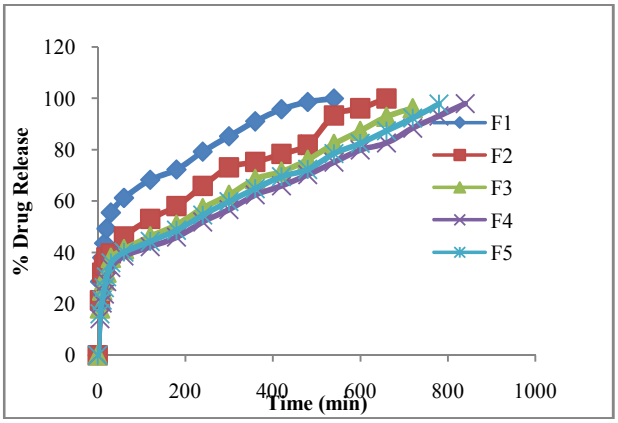

Figure 2 The drug release of formulations (F1-F5)

RESULTS AND DISCUSSIONS

Compatibility studies of Drug by FTIR: The peaks obtained in the spectra of pure drug correlates with the peaks of official spectrum of British Pharmacopeia which confirms the purity of drug as shown in figure: 1 and remained unaltered in the optimized formulation, which indicates that there is no interaction between the functional groups of drug with other excipient in the formulation.

Physical Appearance and pH: All the solutions are light yellow in appearance, showed no visible particles or lumps and are within the required pH range which was suitable for absorption as shown in Table 3.

Viscosity: The viscosity of the formulations increased with an increase in sodium alginate and calcium carbonate concentration and finally F4 shows high viscosity as shown in the table 3.

Floating Behaviour: The buoyancy lag time varied with the formulation variables as shown in Table 3.Formulation F4 exhibited the least buoyancy lag time (61 sec) while formulation F3 exhibited the highest lag time (76 sec). The decrease in the buoyancy lag time of a formulation F4 may be due to the availability of an increased concentration of peanut husk powder which was entrapped in the formed gel to give rapid buoyancy and more floating time i.e., > 12 hours.

Gelling Capacity: Gel was formed immediately as shown in Table 3.

Drug Content: The Drug content values ranges between 97.03% - 98.99% as shown in table 3. The values are acceptable as per united state pharmacopeia standards.

In-Vitro **Drug Release study:** The drug release data from 0 to 14 hours of (F1-F5) formulations are shown in the Table 4. The drug release plots are shown in (Fig. 2). The results indicate that the formulation F1 with less sodium alginate concentration has shown fast drug release i.e.,100% within 9hrs while F4 formulation with high sodium alginate concentration and 1% Peanut husk powder showed drug release evenly and completely in >14 hours. Thus F4 is the optimized formulation and shown sustained release.

Release Mechanisms: By incorporating the release data in Higuchi and erosion models, the R^2 values of all the formulations were found to be greater for Higuchi model. So, all the formulations in this study were best expressed by Higuchi's classical diffusion equation and the release process was diffusion controlled.

To further confirm the exact mechanism of drug release, the data was incorporated into Korsmeyer Peppas model and for all the formulations the release exponent 'n' value found to be between 0.696 to 0.7 as shown in the table 5. This indicates that the drug release followed non-fickian diffusion mechanism.

Accelerated Stability Studies: As the result shown in table 6 it was observed that there was no change in physical and chemical properties as well as in drug release profile even after storage at 40^0 C and 75 % relative humidity for 1month.

CONCLUSION

This method was very simple and sodium alginate which was used as gum has increased the viscosity, duration of action and drug release by increasing the concentration, whereas Peanut husk powder has shown good floating time i.e., more than 12 hours. The study reveals that the *in-situ* gel shows better therapeutic efficacy, enhanced bioavailability, longer gastric residence time and its ability to sustain the drug release over 14 hours period. More over the optimised formulation is cost effective, more Patient acceptance for treating peptic ulcers.

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