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Research Article

FORMULATION AND EVALUATION OF GASTRORETENTIVE FLOATING MUCOADHESIVE TABLET OF REPAGLINIDE

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ABSTRACT

Formulation of Gastroretentive floating mucoadhesive tablet which would remainin stomach for prolonged period of time thereby maximizing the drug release at the desired site for stipulated time. Repaglinide is having half life 60 min; to improve its half life by using excipient like HPMC k15M, HPMC k100M and Xanthan gum as polymer, Optimization using 3^2fullfactorial design to study stability testing of optimized formulation. **Method-** The tablet formulation prepared by direct compression method. Prepared formulation were evaluated in terms of their physical properties, hardness, % friability, weight variation, content uniformity, *in-vitro* release, floating properties, mucoadhesive strength and swelling index. The classical zero order release curve was found to be linear (R2 ≥ 0.90). For the Korsemeyer's Peppas release curves R^2 was found to be ≥ 0.90for all 9 formulations. **Result-** FTIR and DSC studies showed no evidence of interactions between drug, polymers, and excipients. The best *in-vitro* drug release profile was achieved with the formulation F7 is 95.96 % after 12 h, which contain10 mg drug, 25 mg HPMC K15M, 50 mg HPMC K100M and 25 mg Xanthan gum. The floating lag time of formulation F7 was found to be 78±0.04sec. to98±0.05sec. The *in-vitro* release kinetics studies reveal that all formulations show Zero order and anomalous or nonfickiandiffusion. The stability study and no change in anyphysical characteristics and drug content over a 2 monthsperiod at 40±2°C. **Conclusion-**Study concluded that successful stable formulation of Gastro retentive floating mucoadhesive drug delivery system of Repaglinide can be prepared to maximize drug release at desired site for stipulated time.

INTRODUCTION

Gastroretentive Floating Mucoadhesive Drug Delivey System

The Gastroretentive Floating Mucoadhesive Drug Delivery Systems are based on the two working principles of either floating and bioadhesion or swelling and bioadhesion. FDDS are formulated to persist floating on the gastric fluid when the stomach is full after a meal. However, as the stomach empties and the tablet reaches the pylorus, the buoyancy of the dosage form may be reduced. It may be that the dosage form will then pass through the pylorus into the small intestine. Thus, the buoyancy of an FDDS in the stomach may be limited to only 3-4 h. Furthermore, floating systems do not always release the drug at the intended site. In a bioadhesive drug delivery system, it is quite likely that the system becomes dislodged from the stomach mucosa wall when the system is full and the semiliquid contents are churning around due to the effect of peristalsis. A dual working system would overcome drawbacks associated with bioadhesive, swelling, and floating systems, and would have a significant effect on improving the therapeutic effect of the drug released. (Pawar VK *et al*. 2011)

Definition of mucoadhesion

Mucoadhesion can be defined as a state in which two components, of which one is of biological origin are held together for extended periods of time by the help of interfacialforces. Mucoadhesion is a complex phenomenon which involves wetting, adsorption and interpenetration of polymer chains.

Advantages

1. Improved patient compliance,
2. Improved Drug compliance,
3. Better control of disease condition,
4. Better control of plasma levels,
5. Decreasing in total amount of dose administered,
6. Short time require for disease treatment,
7. Reducing in health care costs.

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Several research groups have been reported different gastro-intestinal mucoadhesive dosage forms such as microspheres, matrix tablets, discs etc. (Zate SU *et al*. 2010)

Types of Bio Adhesion

The term bioadhesion refers to any bond formed between two biological surfaces or a bond between a biological and a synthetic surface. In case of bioadhesive drug delivery, the term bioadhesion is used to describe the adhesion between polymers, either synthetic or natural and soft tissues or the gastrointestinal mucosa. In cases where the bond is formed with the mucus the term mucoadhesion may be used synonymously with bioadhesion.

Type I: The bioadhesion is characterized by adhesion occurring between biological objects without involvement of artificial materials. Example: Cell fusion and cell aggregation

Type II: The bioadhesion can be represented by cell adhesion onto culture dishes or adhesion to a variety of substances including metals, woods, and other synthetic materials.

Type III: The bioadhesion can be described as adhesion of artificial substances to biological substrates such as adhesion of polymers to skin or other soft tissues. (Soni RP *et al*. 2001)

Mechanism of Mucoadhesion

Mucoadhesion is the attachment of the drug along with a suitable carrier to the mucous membrane. Mucoadhesion is a complex phenomenon which involves wetting, adsorption and interpenetration of polymer chains. Mucoadhesion has the following mechanism. (Gandhi RB *et al*. 1988)

1. Intimate contact between a bioadhesive and a membrane (wetting or swelling Phenomenon)
2. Penetration of the bioadhesive into the tissue or into the surface of the mucous membrane (interpenetration). (Andrews GP *et al*. 2009, Chowdary KPR *et al*. 2000)

Theories of Mucoadhesion (Gandhi RB et al. 1988)

Wetting Theory

Wetting theory is predominantly applicable to liquid bioadhesive systems. It analyzes adhesive and contact behavior in terms of the ability of a liquid or paste to spread over a biological system.

Electronic theory

The electronic theory depends on the assumption that the bioadhesive material and the target biological material have different electronic surface characteristics. Based on this, when two surfaces come in contact with each other, electron transfer occurs in an attempt to balance the Fermi levels, resulting in the formation of a double layer of electrical charge at the interface of the bioadhesive and the biologic surface. The bioadhesive force is believed to be present due to the attractive forces across this double layer. (Lee JW *et al*.2000, Derjaguin BV *et al*. 1996)

Fracture Theory

Fracture theory attempts to relate the difficulty of separation of two surfaces after adhesion.

Adsorption theory

This theory states that the bioadhesive bond formed between an adhesive substrate and the tissue is due to the weak van der waals forces and hydrogen bond formation. It is one of the most widely accepted theories of bioadhesion. (Good RJ, Tabor D *et al*. 1977)

Need of Study

The future associated with the development of the controlled or sustained drug delivery system to using bioadhesive molecules in the Gastroretentive floating mucoadhesive tablet of Repaglinide to improved the dosage form parameters its include,

- Bioavailability
- Therapeutics efficiency and
- Possible reduction of the dose.
- Maintenance of constant therapeutic levels over a prolonged period and thus reduction in fluctuation in the therapeutic levels
- Reduce drug wastage
- Improves solubility of drugs that are less soluble at high pH environment (e.g. weakly basic drug like domperidone, papaverine)

The Potential use for mucoadhesive systems as drug carriers lies in its prolongation of the residence time at the absorption site, the bioadhesive molecules, it is possible to retain the preparation at the action site or tissue.

MATERIALS AND METHODS

Drug sample of Repaglinide were obtained from Swapnroop Laboratoriesand Pharmaceuticals, Aurangabad, India. HPMC K15M, HPMC K100M, Xanthan gum, Sodium Bicarbonate, Citric Acid, Magnesium Stearate, Talc and Lactose.

Ingredients use in formulations

Table 1 Ingredients use in formulations

Sr.No	Name of Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Repaglinide	9	9	9	9	9	9	9	9	9
2	HPMC K15M	25	25	25	25	25	25	25	25	25
3	HPMC K100M	30	30	30	40	40	40	50	50	50
4	Xanthan Gum	25	30	35	25	30	35	25	30	35
5	Sodium bicarbonate	40	40	40	40	40	40	40	40	40
6	Citric acid	10	10	10	10	10	10	10	10	10
7	Mg Stearate	5	5	5	5	5	5	5	5	5
8	Talc	5	5	5	5	5	5	5	5	5
9	Lactose	51	46	41	36	36	31	31	26	21

Preformulation Studies (Agarwal G et al. 2018)

Preformulation studies on the obtained sample of drug for identification and compatibility studies were performed.

A. Organoleptic properties

The sample of Repaglinide was studied for organoleptic properties such as colour, odor and appearance.

B. Melting point

The meltingpoints of Repaglinide were determined by melting point apparatus. Observed value was compared with the reported value.

C. Solubility

Solubility of the drug was determined as per IP.

D. UV spectroscopy study

Stock solutions (100µg/ml) Repaglinide was prepared in 0.1N HCL. These solutions were appropriately diluted with the respective solvents to obtain a suitable concentration. The UV spectrum was recorded in the range 200-400 nm by using UV spectrophotometer. The wavelength of maximum absorption (λ max) was determined. (Chatwal GR *et al*. 2009)

E. Drug excipient compatibility study

Drug excipient compatibility was performed by FTIR. It was performed by mixing drug with excipient in equal proportion and then IR spectrum was noted for mixture using NaCl cell. Small amount of the mixture was placed on the sample cell, the cell was then filtered in sample holder and spectra were scanned over a frequency range 4000-400 cm^{-1}. (Shewartz TB *et al*. 2008)

F. Differential Scanning Calorimetry

Thermal analysis of drug was carried out using Differential Scanning Calorimetry

Evaluation Parameters (Agarwal G et al. 2018)

1. General appearance

Morphological characters like shape, color and texture were determined visually.

2. Hardness

The hardness of prepared tablets was determined by using Monsanto hardness tester and measured in terms of kg/cm2.

3. Thickness

Thickness of prepared tablets were tested using vernier calipers. The test was done in six time and average was determined.

4. Weight variation

Twenty tablets were selected randomly from the lot and weighed individually to check for weight variation as per IP limit.

5. Friability

Friability of the tablets was determined using Veego friabilator.

$$F = (1- W_0 / W) \times 100$$

Where,
W_0 is the weight of the tablets before the test and
W is the weight of the tablet after the test.

6. Swelling studies

The extent of swelling was measured in terms of %of weight gained by the tablet. One tablet from each formulation was weighed and kept in Petridish containing 50 ml of 0.1N Hydrochloric acid solution. At the end of specified time intervals tablets were withdrawn from Petri dish and excess buffer blotted with tissue paper and weighed. The% of weight gained by the tablet was calculated by using following formula:

$SI = (Wt – W_0)/W_0$

Where,
Mt – weight of tablets at time 't';
M_0 –weight of tablets at time '0'

7. Buoyancy lag time and Total floating time

The *in vitro* buoyancy was determined by the Buoyancy lag time. The tablets were placed in a 100 ml beaker containing 0.1N HCL. The time required for the tablet to rise to the surface for floating was determined as the Buoyancy lag time and further floating duration of all tablets was determined by visual observation.

8. Mucoadhesive strength

Mucoadhesive strength of the tablet was measured on the modified physical balance. The apparatus consist of a modified double beam physical balance in which the right pan has been replaced by Teflon with copper wire and additional weight, to make the right side weight equal with left side pan. Goat or rat stomach mucosa was used as a model membrane and buffer media pH 1.2 was used as moistening fluid. The addition of weights was stopped when mucoadhesive tablet was detached from the goat or rat stomach mucosa. The weight required to detach mucoadhesive tablet from stomach mucosa was noted as mucoadhesive strength in grams. (Yadav VD *et al*. 2013)

9. Uniformity of drug content

The drug content was carried out by weighing 10 tablets from each batch and calculated the average weight. Then the tablets were triturated to get a fine powder. From the resulting triturate, powder was weighed accurately which is equivalent to 100 mg of Repaglinide and dissolved in a 100 ml volumetric flask containing 50 ml of 0.1N hydrochloric acid (HCl) and volume was made up to 100 ml with same solvent. The volumetric flask was shaken for 15 min and after suitable dilution with 0.1N hydrochloric acid, the drug content was determined using UV-Visible Spectrophotometer at 285 nm.(Agarwal G *et al*. 2018)

10. In-vitro dissolution studies

The *in-vitro* dissolution study was performed according to parameters. Aliquot (5 ml) of the solution was collected from the dissolution apparatus (from a zone midway between the surface of dissolution medium and the top of rotating paddle not less than 1 cm apart from the vessel wall) at the time interval of one hour and was replaced with fresh dissolution medium. The withdrawn samples were analyzed by an UV spectrophotometer at 285 nm using 0.1N HCl as a blank. Drug content in dissolution sample was determined using calibration curve.(Agarwal G *et al*. 2018)

Table 2 *In vitro* drug release studies details

Dissolution Parameters	USP Type II dissolution test apparatus
Dissolution medium	0.1 N HCL
Dissolution medium volume	900 ml
Temperature	37± 0.5°c
Speed of basket	50 rpm
Sampling intervals	1hrs
Sample withdraw	5 ml
Absorbance measured	285 nm

Optimization By 3^2 Factorial Designs (Bele MH et al. 2012)

Optimization is the key parameter in the development of any product factorial designs used to evaluate two or more factors

simultaneously interactions can be determined in the factorial design. A study in which two factors and three levels are involved is called as 3^2factorial design. For the present work 3^2 factorial design selected and 2 factors were evaluated at three possible levels by formulating all possible 9 formulation combination which are shown in table

Formulation code assigned to the batches

X_1 = HPMCK100 M
X_2 = Xanthan gum

Table 3 Design summary

Factor	Name	Unit	Type	Min.	Max.	-1 actual	+1 actual	Mean	Std. Dev.
A	HPMC K100M	%	Numeric	30	50	-1.00	1.00	40	12.18
B	Xanthan Gum	%	Numeric	25	35	-1.00	1.00	30	11.25

HPMC K100 M and Xanthan gum are independent variable used in the formulation. The HPMC K100 M are Sustained Released Polymer as well as it's a floating behavior to use in floating mucoadhesive tablet formulation. Xanthan gum are used as a mucoadhesive polymer to adhesion of tablet to the wall of the mucosa in the stomach, to increase the residence time of formulation in gastrointestinal tract and also show their effect on mucoadhesive strength, swelling index, and in vitro drug release.

Independent variable

X_1= HPMC K100 M
X_2= Xanthan gum

Dependent variable

Y1= Drug release
Y2= Swelling index
Y3= Mucoadhesive strength

RESULT AND DISCUSSION

Preformulation studies

Preformulation studies of the obtained sample of the drug for identification andcharacterization of the drug and compatibility studies were performed.

Identification and Characterization of the Drug

Organoleptic properties

The sample of Repaglinide was studied for organoleptic properties such as appearance, color and odor.

Table 4 Identification Test of Repaglinide

Sr.No	Identification Test	Observed Results	Reported Standard
1	Appearance	Crystalline Powder	Crystalline Powder
2	Color	White	White
3	Odour	Odorless	Odorless

Melting point

The meltingpoints of Repaglinide was determined by melting point test apparatus by capillary method the Observed value is compared with the Standard value the melting point was found to be

Table 5 Melting Point of Repaglinide

Parameter	Standard Value	Observed Value
Melting point	128^0C – 132^0C	132^0C -135^0C

Solubility Determination

Table 6 Determination of drug solubility in various solvents

Sr. No	Solvents	Solubility Determination
1	Distilled water	Insoluble
2	Methanol	Freely soluble
3	HCL 0.1 N	Soluble

Determination of λ max of Repaglinide in 0.1 N HCL by ultra violet spectroscopy

The UV spectrum of Repaglinide solution 10µg/ml scanned between 400-200 nm using UV spectrophotometer. Repaglinide showed maximum absorption wavelength 285nm in 0.1 N HCL.

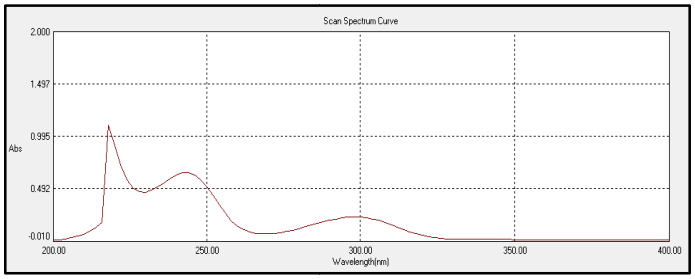

Figure 1 UV spectrum of drug in 0.1 N HCL

Compatibility Study

Infra-red spectrum

The FTIR spectrum of pure Repaglinide showed peaks in wave numbers (cm-1) which corresponds to the functional group present in the structure of the drug. FT-IR spectrum of Repaglinide is shown in figure. And interpretation of FTIR spectrum is given in Table. From the below observation we conclude that the given sample was Repaglinide.

Repaglinide

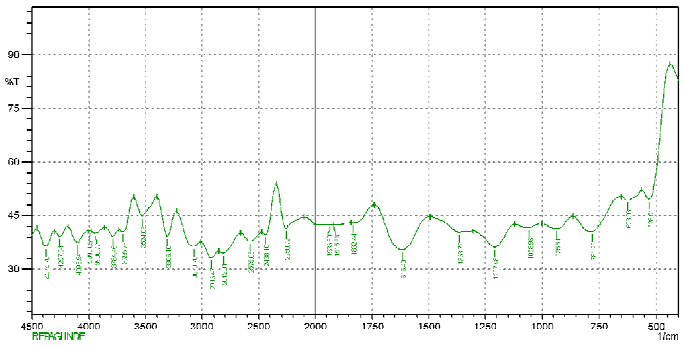

Figure 2 FTIR Spectrum of Repaglinide

Fourier Transform Infra-Red Spectroscopy (FTIR)

Infra-red spectra of drug and polymers showed matching peck with the drug spectra. The data obtained from the IR spectra showed no evidence of the interaction between the drug and the polymer studies. All the major characteristics peckes of the

drug were present in the drug polymer combination spectra which indicate compatibility of drug with the polymers.

Drug + HPMC K 15M

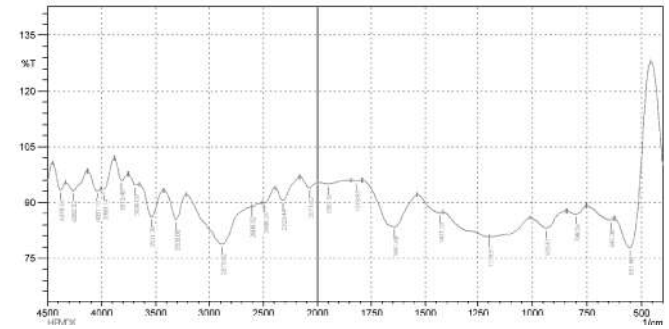

Figure 3 FTIR Spectrum of Drug + HPMC K 15M

Drug + HPMC K 100 M

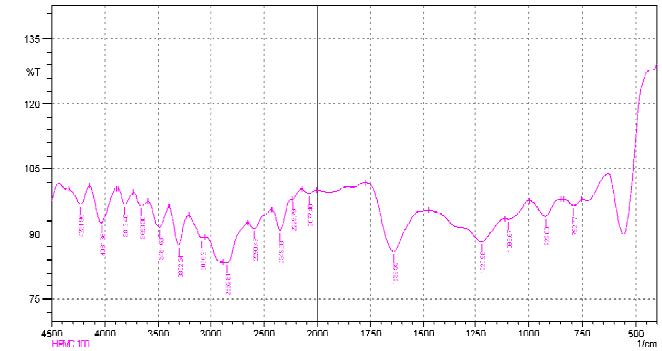

Figure 4 FTIR Spectrum of Drug + HPMC K 100 M

Drug + Xanthum gum

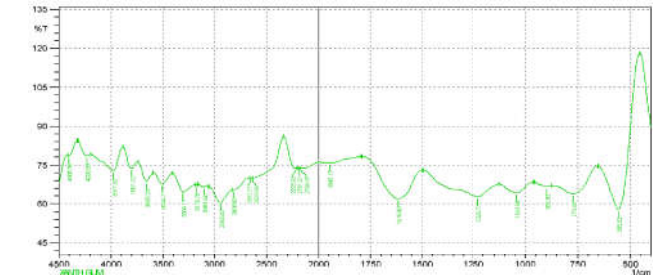

Figure 5 FTIR Spectrum of Drug + xanthan gum

Differential Scanning Calorimetry

Thermal analysis of drug was carried out using DSC. The DSC curve of Repaglinide profile a sharp exothermic peak at 134^0 C corresponding to its melting, and indicating its crystalline nature and purity of sample. The DSC thermogram is shown in figure

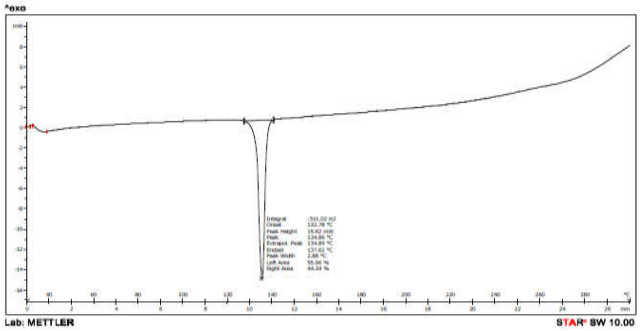

Figure 6 DSC Thermogram of Repaglinide

Evaluation Parameters

The prepared powder mixtures were evaluated for the physical properties like bulk density, tapped density, Carr's index, Angle of repose and Hausner's ratio. Results obtained are shown below (Table 7.)

Table 7 Pre compression parameters for GR- Floating Mucoadhesive tablet of Repaglinide

Formulation code	Angle of repose(^{0}) Mean ±S.D*	Bulk density(g/ml) Mean ±S.D*	Tapped density(g/ml) Mean ±S.D*	Carr's index (%) Mean ±S.D*	Hausner's ratio Mean ±S.D*
F_1	33.98±1.08	0.70±0.011	0.80±0.010	12.5±0.44	1.14±0.018
F_2	34.04±0.85	0.70±0.010	0.8±0.011	12.5±0.37	1.14±0.018
F_3	33.39±1.53	0.63±0.012	0.75±0.010	16.0±0.60	1.19±0.010
F_4	32.00±0.93	0.73±0.013	0.80±0.011	8.75±0.31	1.09±0.011
F_5	33.42±0.84	0.66±0.010	0.80±0.010	17.5±0.80	1.21±0.018
F_6	33.68±0.73	0.75±0.015	0.85±0.010	11.76±0.60	1.13±0.008
F_7	31.52±0.50	0.68±0.010	0.78±0.027	12.82±0.47	1.14±0.011
F_8	32.82±0.55	0.70±0.013	0.81±0.010	13.58±0.33	1.15±0.010
F_9	32.57±0.67	0.65±0.013	0.76±0.012	14.47±0.70	1.16±0.007

*n=6

The powder characteristics of drug affect formulation of tablet. The results shown in above table indicated that the physical properties of powder has good flow property.

Post compression parameters

The average weight of the tablet was found to be 198 mg to 202 mg with the maximum % deviation ± 0.80 for all nine formulations. The tablet showed thickness in the range of 3.15 to 3.23 mm with the maximum % deviation 0.81.standard specification. All the results shown in below

Table 8 Post compression parameters for GR- Floating Mucoadhesivetablet of Repaglinide

Formulation code	Hardness (Kg/cm2)	Thickness (mm)	Friability (%)	% Weight variation (mg)	Floating lag time (s)	Total floating time (h)
1	4.8±0.22	3.23±0.019	0.95±0.013	198.34±0.78	96±0.05	>12
2	4.3±0.22	3.15±0.020	0.65±0.013	199.56±0.75	78±0.06	>12
3	4.7±0.16	3.18±0.016	0.67±0.012	201.08±0.73	75±0.06	>12
4	4.8±0.10	3.20±0.016	0.89±0.010	200.12±0.81	58±0.05	>12
5	4.2±0.12	3.21±0.018	0.69±0.012	199.76±0.71	69±0.08	>12
6	4.6±0.18	3.23±0.016	0.70±0.010	202.16±0.92	57±0.04	>12
7	4.6±0.13	3.23±0.015	0.84±0.012	198.94±0.072	78±0.04	>12
8	4.8±0.08	3.21±0.017	0.64±0.010	200.48±0.90	94±0.05	>12
9	4.7±0.07	3.20±0.019	0.60±0.015	201.62±0.94	98±0.05	>12

***n=6**

Drug content

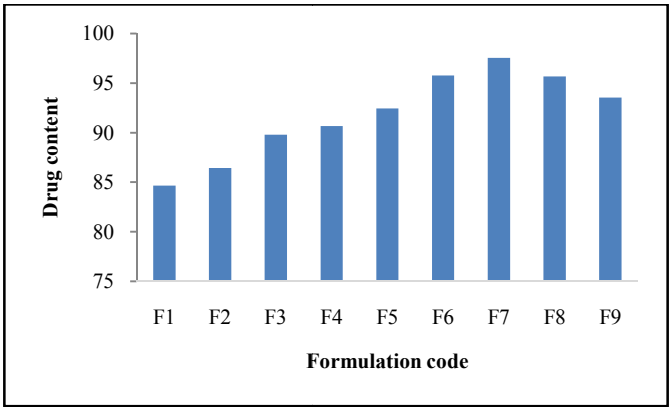

Figure 7 Graphical presentation of drug content

The uniformity of drug content in the range 90.43% to 97.56% which were within pharmacopoeial specifications. Hence, all

the formulations complies the test for uniformity of drug content.

In-vitro dissolution study

The *In-Vitro* drug Release Studies of GR- floating mucoadhesive tablets of Repaglinide were determined using USP type II apparatus. The drug release was found to vary according to the ratio of different polymers.

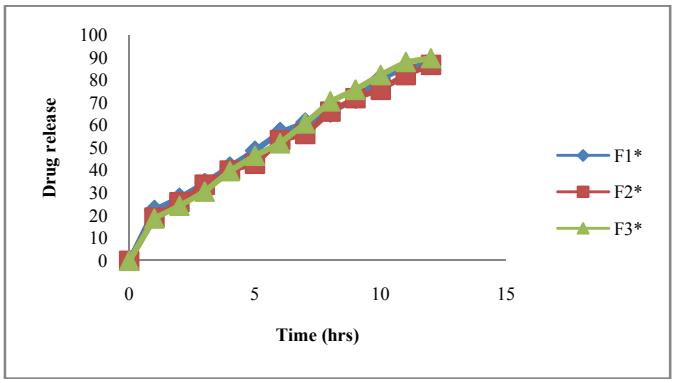

Figure 8 Graphical presentation of In-vitro drug release F1- F3

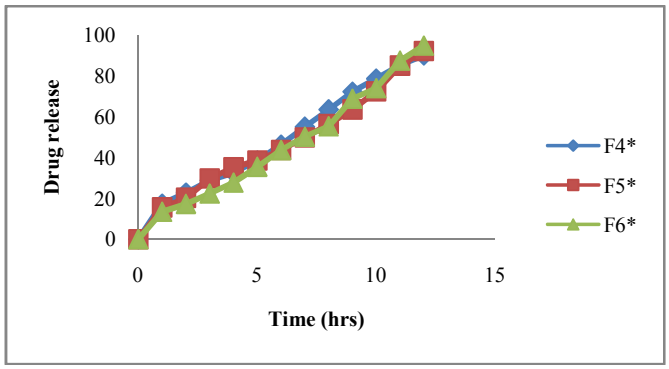

Figure 9 Graphical presentation of In-vitro drug release F4- F6

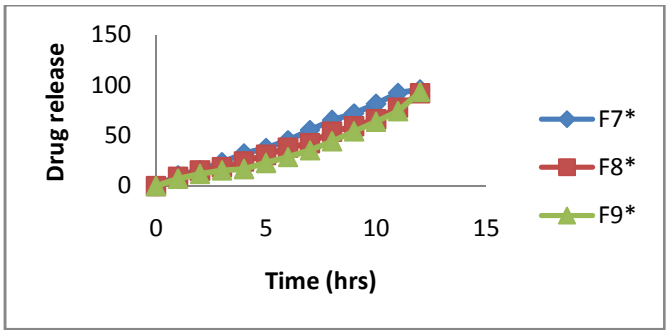

Figure 10 Graphical presentation of In-vitro drug release F7- F9

The designing of GR- floating mucoadhesive tablet of Repaglinide. Using the combination of the various mucoadhesive and sustained release polymer having the different ratio. The F1, F2 and F3 showed 87.08%,86.58% and 89.58% drug release within 12 hrs. F4, F5 and F6 showed 90.02%, 92.66% and 94.91% drug release within 12 hrs. & F7, F8 and F9 showed 95.96%, 92.00% and 93.23% drug release within 12 hrs. From the above comparison the F7 formulation shows good *in vitro* drug release.

The combination of the various mucoadhesive polymer having the ratio 1:2:1as the polymer HPMC K15M, HPMCK100M and Xanthan Gum respectively, it shows the good mucoadhesion along with in vitro drug release. (Singh SK *et al*. 2010)

From the study of different batches, batch F7gave good result in dissolution study as compared to other batches, the optimization was done on the basis of percent drug released within 12 hrs.

Swelling study

Xanthan Gum is used to produced directly compressed matrices that display a high degree of swelling due to water uptake and small amount of erosion due to polymer relaxation, this property is essentials for the dosage form to produce sustained released action. (Raymond CR *et al*. 2009)

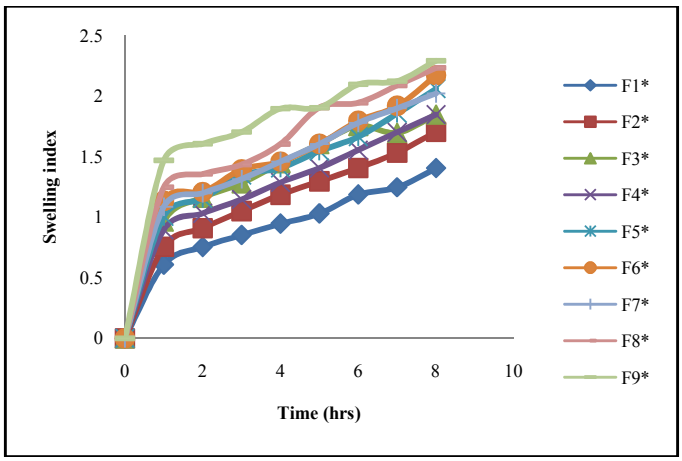

Figure 11 Graphical presentation of Swelling Index

The Property of hydrophilic polymer come in contact with water to start the swelling, the Xanthan Gum is the high degree of swelling due to water uptake.

The swelling index of formulation batch F_5 to F_9 observed a good swelling index than the other formulation. The swelling index of the dosage form increases with increase in the concentration of the polymer.

Mucoadhesive strength

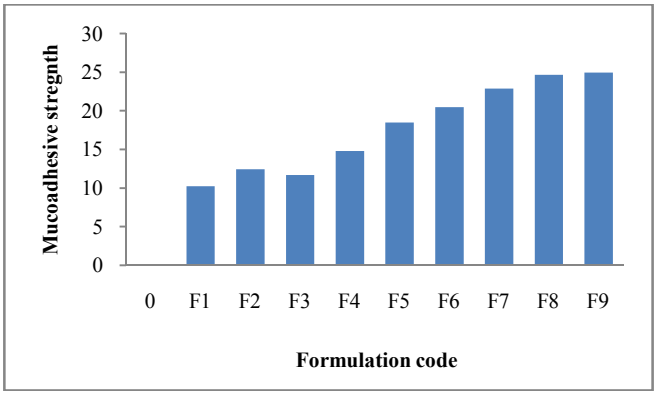

Figure 12 Graphical presentation of Mucoadhesive strength

The good bioadhesion strength was possessed by theformulationcontaining HPMC K15M, HPMC K100M and Xanthan gum, at the 1:2:1 ratio it shows good mucoadhesion. From the study formulation F5to F9have a good mucoadhesive strength than the other formulation, the concentration of polymer increases bioadhesion strength of the formulation is also increases.

Optimization (Design expert software 7.0)

A 3^2 full factorial design was selected and 2 factors were evaluated at 2 levels, respectively. The percentage of HPMC K100M (X1) and Xanthan Gum (X2) were selected as independent variables and dependent variables drug release, swelling index, mucoadhesive strength. The data obtain were treated using design expert software and analyzed statistically using analysis of variance (ANOVA).

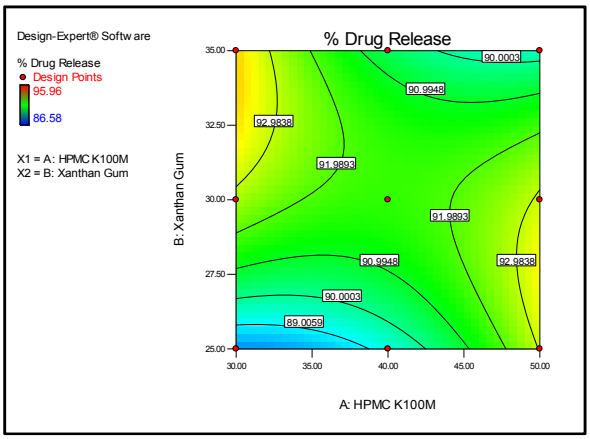

Figure 13 Surface response plot showing effect of HPMC K100M and Xanthan Gum on drug release

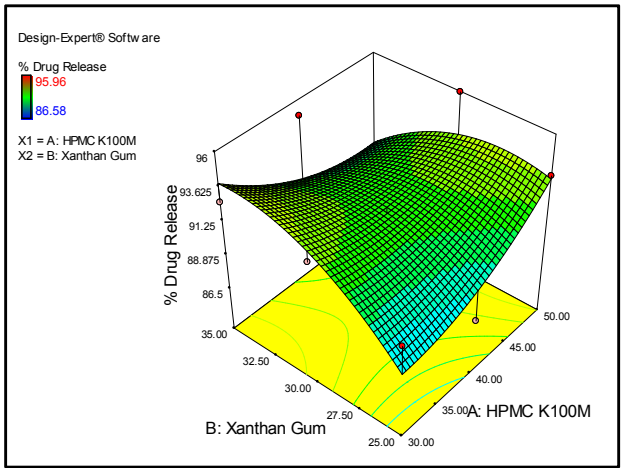

Figure 14 Counter plot showing effect of HPMC K100M and Xanthan Gum on drug release

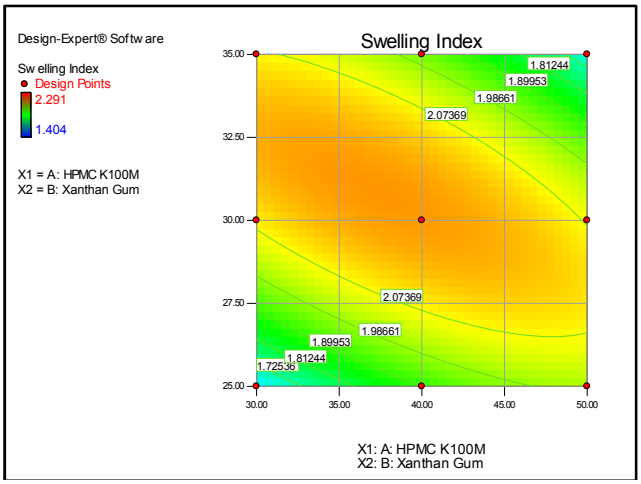

Figure 15 Surface response plot showing effect of HPMC K100M and Xanthan Gum on swelling index

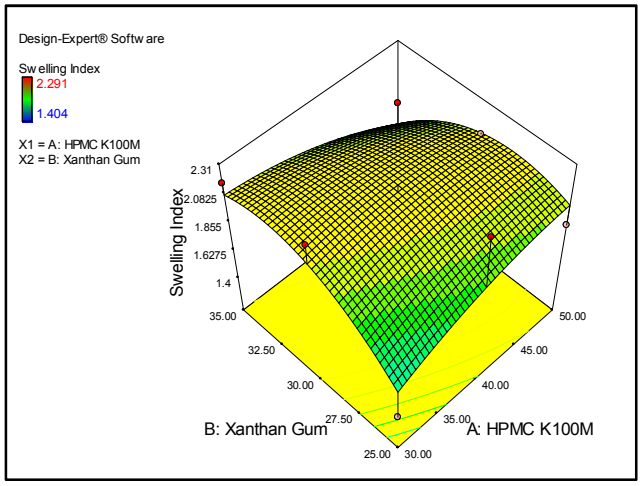

Figure 16 Counter plot showing effect of HPMC K100M and Xanthan Gum on swelling index

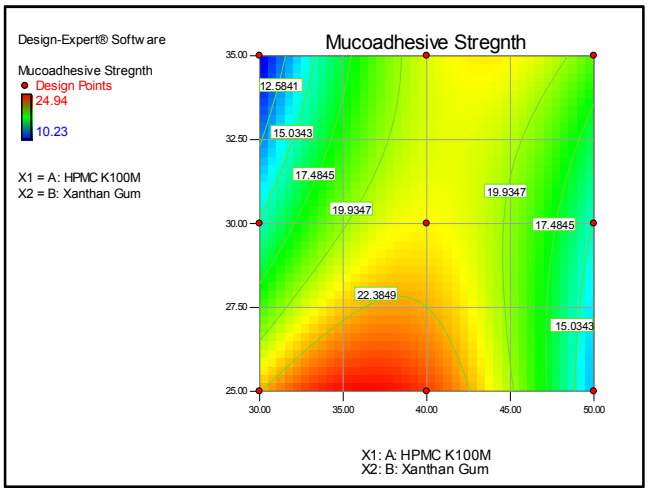

Figure 17 Surface response plot showing effect HPMC K100M and Xanthan Gum on mucoadhesive strength

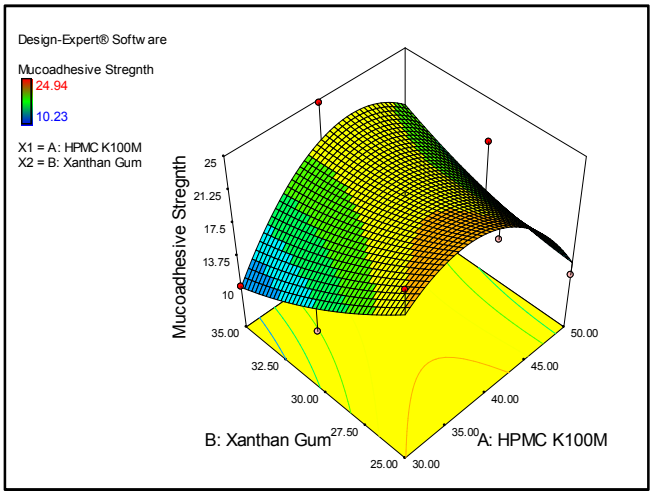

Figure 18 Counter plot showing effect of HPMC K100M and Xanthan Gum on mucoadhesive strength

From design expert optimum batch of HPMC K100M and Xanthan Gum was found to be optimized. From this data F7 was selected as optimized formulation.

Kinetic Study (Chime SA et al. 2013, Dash S et al. 2010)

Table 9 R^2 values of zero order release kinetics

Batch	F1	F2	F3	F4	F5	F6	F7	F8	F9
R^2	0.928	0.980	0.996	0.907	0.959	0.979	0.974	0.934	0.988

Table 10 R^2 values of Korsemayer'speppas model kinetics

Batch	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
R^2	0.959	0.972	0.938	0.988	0.974	0.909	0.970	0.908	0.912

The classical zero order released curved was found to be linear the curve plotted according to first order and Highuchi to be linear respectively. For the Korsemeyer's Peppas released curves r^2 was found to be ≥ 0.90 for all formulation and n value was found to be ≥ 0.5 which indicate that all the formulation show anomalous or non-fickian diffusion. The drug release occurs probably by diffusion, erosion and dissolution follows.

Stability studies of GR- floating mucoadhesive tablet of Repaglinide

Table 11 Stability study of optimized formulation

Sr. No	Observations	BeforeStability	Stability testing interval days	
			1 months	2months
	General appearance			
1.	Color	No change	No change	No change
	Odor	No change	No change	No change
2.	% Drug release	95.96	95.23	94.78
3.	% Drug content	97.56	97.18	96.47

Optimized formulation F7at 25 ^{0}c temperature was found to be stable up to 2 months. There was no significant change in appearance, drug release, drug content.

CONCLUSION

It was planned in this investigation to formulate and evaluate Gastroretentive floating mucoadhesive tablet of Repaglinide for extended period of time in order to reduce the dosing frequency and to improve the patient compliant. The tablet is formulated was compressed in a 8 station rotary machine using 8 mm diameter punch. Repaglinide was characterized by studying its absorbance, melting point and solubility in methanol and various solvent. Experiments were conducted to investigate the influence of polymer like HPMC grade polymer and Xanthan gum bioadhesion strength and release kinetic of mucoadhesive tablet of Repaglinide. In vitro dissolution studies were conducted in apparatus II at 50 rpm for 12 hr. The data was statically analyzed and mechanism of release kinetic studied.
From the experimental results it can be concluded that,

- A suitable method of analysis of drug by UV spectrophotometry was developed. Repaglinide showed maximum absorption at a wavelength 292 nm in pH 1.2 buffer (0.1NHCl). The value of regression coefficient (r2) was found to be 0.999, which showed linear relationship between concentration and absorbance.
- The weight uniformity of tablets ranged from198.34± 0.78 to 202.16± 0.92 mg.
- The hardness of all formulations was in the range of 4.2± 0.12 to 4.8± 0.22 kg/cm2.
- The values of friability of all formulations ranged from 0.60 to 0.95%.
- The % drug content of all the formulated tablets were found within the limit. % drugcontent value of Repaglinide was within 90.43± 0.62% to 97.56± 0.64%.
- % cumulative drug release after 12 hrs for F7showed 95.96± 0.78.
- The all formulation swelling index was in the range 1.404± 1.12 to 2.291± 1.08.
- The F7 formulation show good mucoadhesion strength of 10.23± 0.26.
- The combination of the various mucoadhesive polymer having the ratio 1:2:1as the polymer HPMC K15M, HPMCK100M and Xanthan Gum respectively, it shows the good mucoadhesion along with in vitro drug release.
- From the study of different batches, batch F7gave good result in dissolution study as compared to other batches, the optimization was done on the basis of percent drug released within 12 hrs.
- The results of accelerated stability study showed that there was no change in theformulation after two month.

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References

1. Pawar VK, KansalS, GargG, AwasthiR, Singodia D, KulkarniGT, Gastroretentive dosage forms: A review with special emphasis on floating drug delivery systems, Drug Delivery, 2011, 18:2, 97-110.
2. Zate SU, Kothawade PI, Mahale GH, Kapse KP, Anantwar SP, Gastroretentivebioadhesive drug delivery system: A review. *International journal of pharmatech research*. 2010; 2 (2): 1227-35.
3. Soni RP, Patel AV, Patel RB, Patel MR, Patel KR, Patel NM, Gastroretentive drug delivery systems: A review. *International journal of pharma world research*. 2001; 2(1): 1-24.
4. Gandhi RB, Robinson JR, Bioadhesion in drug delivery. Ind. J. Pharm. Sci, 1988, 50(3):145-152.
5. Andrews GP, Laverty TP, Jones DS, Mucoadhesive polymeric platforms for controlled drug delivery, *Eur. J. Pharm. Bio pharm*, 2009, 71: 505–518.
6. Chowdary KPR, Srinivas L, Mucoadhesive drug delivery systems: A review of current status. Indian Drugs.2000, 37(9): 400-406.
7. Lee JW, Park JH, Robinmson JR, bioadhesive based dosage forms: the next generation, *J Pharm. Sci*, 2000, 89: 850-866.
8. Derjaguin BV, Toporov YP, Muller VM, Aleinkova VM, On the relationship between the molecular component of the adhesion of elastic particles to a solid surface, *J Colloid Interface Sci*, 1966, 58: 528-533.
9. Good RJ, Surface energy of solids and liquids, Thermodynamics, molecular forces and structure, *J Colloid Interface Sci*, 1977, 59: 398-419.

10. Tabor D, surface forces and surface interactions, *J Colloid Interface Sci*, 1977, 58: 2-13.
11. Chatwal GR, AnandSk, Instrumental methods of chemical analysis, 5th edition, Himalaya publishing house; reprint 2009, 2.49-2.51
12. Shewartz TB, Oconnor RE, Schnaare RE, Schanaare RL, Optimization techniques in pharmaceutical Formulation and Processing In: Banker GS, Rhodes CT, Modern pharmaceutics New York; Basal Marcel Dekker:2008; 4thed.vol 21, 609-610.
13. Agarwal G, Agarwal S, Goyal S, Formulation & Evaluation of Sustained Release Matrix Tablet of Repaglinide. Open Acc Biostat Bioinform. 2018, 1(2). OABB.000509. 1-9.
14. Yadav VD, Gaikwad VD and Gaikwad PV, Development and in-vitro evaluation of mucoadhesive gastroretentive matrix tablets of cephalexin, IOSR-JPBS Vol-7, Sep.-Oct. 2013,25-31.
15. Bele MH, pharmaceutics formulation and processing of conventional dosage form, carrier publication 2012, 1st ed,48-55,128-131.
16. Singh SK, Bhothara SB, Singh S, Patel R, Dodia R, Formulation and evaluation of Mucoadhesive tablet: influence of some hydrophilic polymer on the release rate and in vitro evaluation. IJPSN, Oct-Dec 2010, vol-3, 1111-1121.
17. Raymond CR, Paul JS, Marian EQ, Handbook of Pharmaceutical excipients 6th ed, PhP. 2009, 181-785.
18. https://www.google.com/search?q=DX7Trial.enc&rlz=1C1GCEK_enIN825IN826&oq=DX7Trial.enc&aqs=chrome..69i57.37508j0j7&sourceid=chrome&ie=UTF-8
19. Chime SA, Onunkwo GC, Onyishi LL, Kinetic and mechanisms of drug release from swellable and Non swellable Matrice: A review, *Research journal of Pharmaceutical, Biological and chemical sciences* April- June 2013 Vol-4, 97.
20. Dash S, Murthy PN, Nath L, Chowdhury P, Kinetic Modeling on Drug Delivery Release from Controlled Drug Delivery System, APPDR, 2010, Vol.67 No.3 217-223.

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