IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

"SUSTAIN RELEASE BEHAVIOR OF METFORMIN HYDROCHLORIDE THROUGH INCORPORATION OF STOMACH AND INTESTINE SPECIFIC SODIUM ALGINATE BEADS"

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ABSTRACT:

Ionic gelation was used to create sodium alginate and gum ghatti (GG) bio adhesive beads containing metformin HCl for orally usage. A 3^2 factorial design has been used to evaluate the effects of gum ghatti concentration and HPMC K100M concentration on the bead size (mm) and % Drug release after 12 hours (DR %) of ionotropic ally gelled sodium alginate and gum ghatti muco-adhesive beads containing metformin HCl. CCD is utilised for this, and response surface methodology (RSM) is used. The optimized sodium alginate beads had a bead size of 1.2mm to 1.45mm and a DR of 79 % to 91 % after 12 hours. The in-vitro release of metformin HCl from these ionotropic ally-gelled SA-GG beads lasted for 12 hours and followed a zero-order model. The improved mucoadhesive beads also have good muco-adhesive properties with biological mucosal membranes and follow pH-dependent swelling.

KEYWORDS: Metformin hydrochloride (MH), Gum Ghatti (GG), Mucoadhesion, Sustained release, alginate beads. Etc.

1. Introduction:

Diabetes mellitus is one of the most severe disorders that threatens global public health and is spreading quickly; according to study, up to 366 million people will be affected in the next ten years.[1] Metformin hydrochloride (MF) is an orally administered antidiabetic drug from the biguanide class that is used to treat type 2 diabetes as a first-line therapy. Its hypoglycemic effect involves a decrease in hepatic glucose generation and intestinal glucose absorption, as well as an increase in glucose metabolism, resulting in a decrease in plasma glucose levels. Additionally, MF lowers hunger and aids weight loss and lipid profile improvement while posing no risk

of hypoglycemia. While MF is water soluble, it only has a 50% bioavailability following oral administration in typical dosage formulations. [2]

Anogeissus latifolia produces a transparent amorphous form of Gum-Ghatti, a water soluble complex non-starch polysaccharide. It also serves as a release retardant polymer in oral controlled medication delivery systems due to its nontoxic and good emulsifying properties. Because GG is incapable of forming beads on its own, sodium alginate was added. GG has a gelling property and is employed in a variety of medicinal formulations, including microspheres, beads, and hydrogels, among others. In the presence of cations, GG can form gels, even though the presence of acetyl groups can interfere with the ions' bonding characteristics. They are discovered to be more stable at acidic pH than alkaline pH. This is owing to the fact that swelling happens faster quickly in alkaline pH than acidic pH. [3]

Another commonly utilised mucoadhesive polymer for the creation of various drug delivery systems is sodium alginate (sodium salt of alginic acid). It's a biodegradable and biocompatible linear anionic polysaccharide derived from brown algae.[4] Due to the presence of free carboxyl groups, it has high mucoadhesive properties, allowing the polymer to interface with mucin in the mucous membrane through hydrogen and electrostatic bonding .[5] It has been also used as matrix material in the development of sustained release formulation.[6] Due to its hydrogel forming properties, it deliver the drug over a prolonged period [7] In aqueous solution and in the presence of Ca2 + Al3 +, etc, both GG and sodium alginate have properties to undergo ionotropic gelation [8]. In pharmaceutical drug design, gel forming property of GG and mucoadhesive behavior of sodium alginate. [9] Are mainly used for controlled drug delivery applications. [10]

Due to its hydrophilic matrices, HPMC K100M is the most common cellulose ether used to create swellable-soluble matrices, which effectively extend the time of drug release to prolong therapeutic benefits. When HPMC K100M is applied, drug release may be dominated by swelling, with the polymer becoming slowly eroded and eliminated. , an attempt was made to formulate beads containing sodium alginate,GG, and hydrophobic HPMC K100M in various concentrations for controlled release in acidic and alkaline pH, which would eliminate the need for multiple dosing, thereby increasing patient compliance and minimizing the occurrence of drug adverse effects.[11]

2. Experimental:

Materials and methods:

2.1 Materials:

The active API MH ware purchase from Aarti Chemicals Mumbai. Sodium alginate and GG was purchased from BASF ltd, Mumbai. HPMC K100M and CaCl2 was purchased from Loba chemical Pvt. Ltd., Mumbai, India and all other chemicals were of analytical grade and used as provided.

2.2 Methods:

Preparation of sodium alginate beads containing Metformin Hydrochloride:

The mucoadhesive beads could be prepared via Ionic Gelation Method (IG).

a) The aqueous dispersions of sodium alginate, Gum Ghatti, and HPMC K100M were arranged separately using distilled water.

b) These dispersions were well blended using a magnetic stirrer for 10 minutes at 300-600 rpm, then mixed with the aqueous dispersion metformin hydrochloride drug solution.

b) The stirring is continued until a transparent dispersion forms, after which the dispersion is dropped into a calcium chloride (CaCl2) solution using a 21-G needle.

d) The additional droplets were kept for 15 minutes to allow the healing process to finish and hard beads to form.

e) The beads were filtered, rinsed with distilled water, and allowed to air dry.

2.3. Experimental design for optimization:

In that central composite Design, DESIGN-EXPERT software was used for statistical experimental study. The 32 (three level-two factor) response surface methodology was utilised for optimization and identification of the impact of independent variables on responses. The concentrations of HPMC K100M (X1) and Gum ghatti (X2 %) were chosen as independent variables and varied at three levels: low (1) middle (0) and high (+1). Bead size (Y1) and % DR were chosen as dependent variables (Y2). The statistical design for dependent and independent variables that have been chosen. The significance (p 0.05) of the models, individual factors, and interactions of individual factors was determined using one-way ANOVA. The effect of independent factors on the measured responses was investigated using surface response plots and contour plots.

Table1: Formulation Composition of for Metformin hydrochloride loaded alginate beads.

	Independent variable		**Dependent variable**	
Code	**A:Hpmc K100m**	**B:Gum Ghatti**	**Beads Size (Y1)**	**Drug Release (Y2)**
	[mg]	**[mg]**	**[mm]**	**[%]**
F1	900	900	1.42	79
F2	650	650	1.34	86
F3	650	400	1.2	88
F4	650	900	1.4	86
F5	400	400	1.23	89
F6	400	900	1.45	90
F7	900	650	1.31	78
F8	400	650	1.36	91
F9	900	400	1.28	79.5

Independent variable	low level (-1)	medium level (0)	high level (+1)
A = conc. Of HPMC K100M	400 mg	650 mg	900 mg
B = conc. Of Gum Ghatti	400 mg	650 mg	900 mg

Number	HPMC K100M	Gum Ghatti	Bead Size	Drug Release
1	0.400	0.400	1.244 mm	91.000 %
2	0.400	0.400	1.200 mm	90.00 %

Error (%) = (difference between observed and predicted values)/predicted value × 100

2.4. Bead Size Measurement:

The average particle size of 100 dried beads from each batch was determined using an optical microscope and an optical microscopic method (Olympus). Previously, the stage micrometer was used to calibrate the ocular micrometer.

2.5. Surface Morphology Analysis by Scanning Electron Microscopy (SEM):

Beads containing medication were gold coated by mounting them on a brass stub using double-sided adhesive tape and sputtering a thin coating of gold (3–5 nm) for 75 seconds at 20 kV in an ion sputter to make them electrically conductive, and their morphology was examined using a scanning electron microscope (ZEISS EVO 40, Japan). [12]

2.6. Fourier Transform Infra-Red Spectroscopy:

The compatibility of the pure medication and the polymer was determined using FT-IR spectra. Using a Fourier transform-infrared (FTIR) spectroscope, samples were reduced to powder and examined as KBr pellets (Perkin Elmer Spectrum RX I, USA). Within the sample holder, the pellet was put. Spectral scanning was performed at a resolution of 4 cm1 with a scan speed of 1 cm/s in the wavelength range of 4000 to 400 cm^{-1}. [13]

2.7. **Evaluation of Swelling Behavior:**

In two different aqueous media, 0.1 N HCl (pH 1.2) and phosphate buffer, the swelling behavior of beads containing medication was investigated (pH 7.4). Dissolution apparatus (Campbell Electronics, India) vessels containing 500 ml equivalent media were filled with 100 mg beads. The experiment was carried out at 37°C and a paddle speed of 50 rpm. After drying the surface with tissue paper, the swollen beads were removed at regular intervals and weighed. Swelling index was resolved by using the following formula:

$$\text{Swelling index } (\%) = \frac{\text{wt. of beads after swelling} - \text{Dry Wt. of beads}}{\text{Dry wt. of beads}} \times 100$$

2.8. Determination of DEE:

In a mortar and pestle, 100 mg of beads were smashed. The crushed powders of drug-beads were added to a 250 ml volumetric flask, which was then filled with phosphate buffer (pH 7.4) and kept at 37 0.5 C for 24 hours with constant shaking. A magnetic stirrer was used to agitate the mixture at 500 rpm for 20 minutes after the necessary period had passed (Remi Motors, India). The polymer debris that generated when the bead disintegrated was filtered out using Whatman® filter paper (No. 40). A UV-Spectrophotometer (Shimadzu, Japan) was used to measure the drug content in the filtrate at 220 nm against an acceptable blank. [14] The DEE (%) of these prepared beads was calculated by the following formula,

$$\% \text{ Drug Entrapment Efficiency} = \frac{\text{Actual content of Drug in beads}}{\text{therotical content of drug}} \times 100$$

2.9. Ex- vivo Mucoadhesion Testing:

Ex vivo wash-off methods was used to assess the mucoadhesive characteristics of beads carrying medication. Thread was used to attach freshly cut portions of goat intestinal mucosa (2 cm x 2 cm) (taken from the slaughterhouse) on a glass slide (7.5 cm x 2.5 cm). The prepared slide was slung into a groove of the disintegration test instrument, and about 50 beads were unfolded onto the moist tissue samples. At 37 0.5 C, the tissue specimen was moved up and down in a tank containing 900 ml of 0.1 N HCl (pH 1.2) and phosphate buffer (pH 7.4), respectively.[15] The machine was halted at regular intervals, and the number of beads still adhered to the tissue was counted.[16]

2.10. In Vitro Drug Release Studies:

Dissolution apparatus USP was used to assess the release of medication from a variety of beads (Campbell Electronics, India). To prevent the beads from seeping out, the baskets were lined with dialysis membrane. At 37 1 C and a speed of 50 rpm, the dissolution rates were measured. Beads containing Metformin Hydrochloride equivalent to 100 mg were accurately weighed and added to 900 ml of 0.1 N HCl (pH 1.2). After 2 hours, the test was repeated in phosphate buffer (pH 7.4) for another 8 hours. At regular intervals, 5 mL of aliquots were collected, and the same amount of new dissolution medium was put in the dissolution vessel to maintain the sink condition throughout the experiment. [17] The obtained aliquots were filtered and diluted to evaluate the absorbance against an appropriate blank using a UV–vis spectrophotometer (Shimadzu, Japan). [18]

2.11. Drug release kinetics parameter studies:

Mathematical models such as zero-order, first-order, Hixson-Crowell, Higuchi, and Korsmeyer– Pappas were employed to fit the in vitro DR data of the VLG formulation. Q = kt + Q0, where Q is the amount of pharmaceuticals released over time (t), Q0 is the initial value of Q, and k is the rate constant, in the Zero-order model. Q = kt + Q0, where Q is the amount of medication released in relation to time (t), Q0 is the initial value of Q, and k is the rate constant, represents the Zero-order model. Q = kt0.5, where Q is the amount of medication released as a function of time (t) and k is the rate constant in the Higuchi model. For the Korsmeyer–Pappas model, use the following formula: Where Q is the amount of medication released as a function of time (t), k is the rate constant, and n is the release exponent, Q = ktn (R. Jayachandra Babu et al 2010) the accuracy and prediction abilities of these models were calculated using the squared coefficient of correlation (R^2).

2.12. Stability studies of MH beads:

The stability studies performed for one month at room temperature place optimized formulation in Desiccator and further tested for physical Changes, bead size and in-vitro drug release.

3. Results and discussion

3.1. Optimization of sodium alginate beads containing Metformin Hydrochloride

Design-Expert 13.1.0.0 software performs a statistical analysis of the data acquired from the experiment. Additionally, there is a central composite design. After implementing certain limits on beads size and drug release, the best Metformin Hydrochloride sodium alginate beads formula was created. The acquired optimum formula was then manufactured and analyzed for additional characterization such as bead size, DEE, Swelling index, mucoadhesive research, stability study, in vitro drug release, and SEM characterization. A 32 response surface methodology was utilised to estimate the effects of independent factors (X1, X2) on dependent variables (Y1; Y2). The impacts of independent factors were investigated using 2D and 3D counter plots. The three-dimensional (3D) response surface graph is particularly useful for interpreting the main and interaction effects of the independent variables. HPMC K100M concentration (X1) and Gum ghatti concentration (X2) were the independent factors in this study, whereas Beads size (mm) and DR were the dependent variables (%) The beads size was predicted to rise when the concentration of HPMC K100M (X1) was decreased and the concentration of Gum ghatti (X2) was raised by the 2D and 3D plots for beads size. However, increasing the concentration of HPMC K100M (X2) and the concentration of Gum ghatti (X2) had no influence on the % DR.The size of the beads was between 1.12mm and 1.39mm in all 9 experimental runs, and the % DR was between 77 and 80 %, as shown in Table 1. Polynomial equations and counterplots are used to study the mathematical relationship between the dependent and independent variables. The correlation coefficient (R2) values for the Linear model for both Y1 and Y2 responses were 0.8684 and 0.8976, respectively, indicating satisfactory fit. The following equations were obtained for the Bead size (Y1), EE (Y2), and DR (Y3) responses.

$$Y1 = + 1.102 - 0.0200\ A + 0.3733B \quad \text{..... (Equation 1)}$$

$$Y2 = + 100.33 - 22.33A - 1.00B \quad \text{..... (Equation 2)}$$

Positive and negative values in the above equations represent synergistic and antagonistic effects, respectively. The quadratic equation predicts that the independent variables A, B had an impact on the size of the beads (Y1). Similarly, and % DR response, it also denotes a quadratic equation, which was influenced by independent variables A; B. At P 0.05, the effects of these independent factors on the size of the beads, % EE, and % DR were significant. The models were significant at F values of 27.40 and 36.08 at P 0.05, with a smaller difference between actual and projected values, implying that the model was **significantly fit.**

ANOVA for Linear model:

Table 2. Summary of ANOVA for linear model.

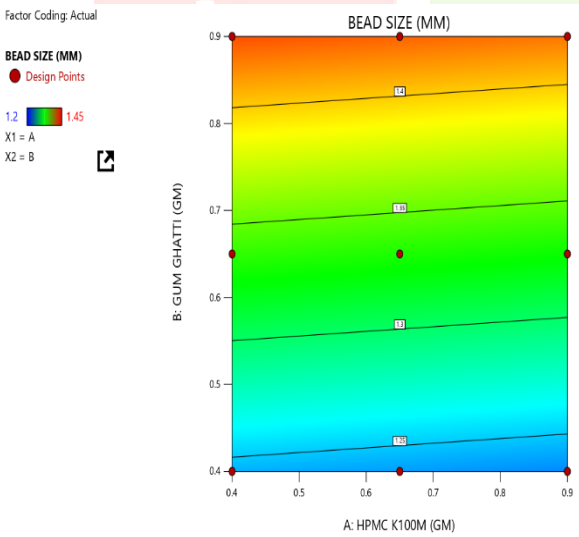
Response 1: BEAD SIZE

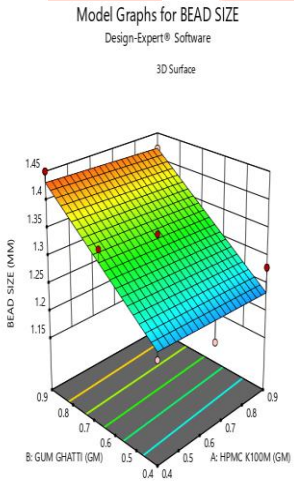
Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	0.0524	2	0.0262	27.40	0.0010	**significant**
A-HPMC K100M	0.0001	1	0.0001	0.1568	0.7058	
B-GUM GHATTI	0.0523	1	0.0523	54.64	0.0003	
Residual	0.0057	6	0.0010			
Cor Total	0.0582	8				

Response 2: DRUG RELEASE

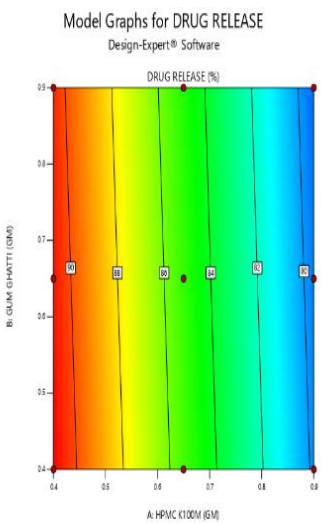
Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	187.42	2	93.71	36.08	0.0005	**significant**
A-HPMC K100M	187.04	1	187.04	72.02	0.0001	
B-GUM GHATTI	0.3750	1	0.3750	0.1444	0.7170	
Residual	15.58	6	2.60			
Cor Total	203.00	8				

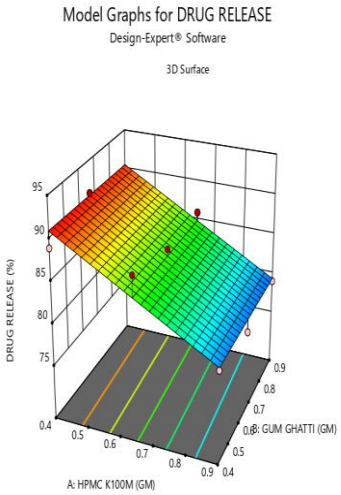
A **B**





C **D**





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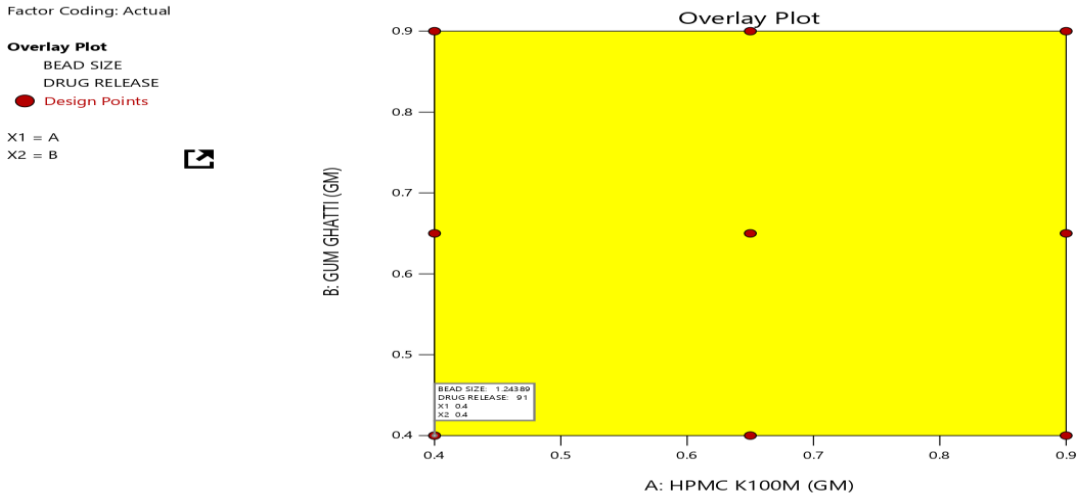


Fig. 1. (A) 2D contour graph showing the effects of concentration of Gum Ghatti and HPMC K100M on Bead size; (B) 3D response surface graph showing the effects of concentration of Gum Ghatti and HPMC K100M on Bead size (c) 2D response surface graph showing the effects of concentration of Gum Ghatti and HPMC K100M on % Drug release (C) 2D response surface graph showing the effects of concentration of Gum Ghatti and HPMC K100M on % Drug release (E) the overlay plot indicating the region of optimal process variable settings (yellow area).

3.3. Bead size:

The sodium alginate beads containing metformin HCl were between 1.2-1.45 mm in diameter. The increase in bead size with increasing Gum Ghatti concentration in polymer-blend solution from 400 mg to 800 mg may be explained using the hydrodynamic viscosity idea. With the addition of Gum Ghatti in increasing Concentration, the viscosity of the polymer-blend solution may increase, resulting in larger droplets of polymer-blend solution flowing through the needle to the cross-linking solution containing Ca2+ ions. When concentrated CaCl2 solution was utilised as the crosslinking solution, however, the size of sodium alginate beads decreased. This could be due to the formation of more rigid polymeric network by the high degree of cross-linking.

3.4. SEM analyses:

Metformin Hydrochloride with alginate beads has a highly hard surface with enormous creases and fissures, as seen in SEM images. The partially collapsing of the polymeric gel-like network after drying causes these fissures and wrinkles. The production of drug crystals is caused by the migration of beads and water to the surface during drying.

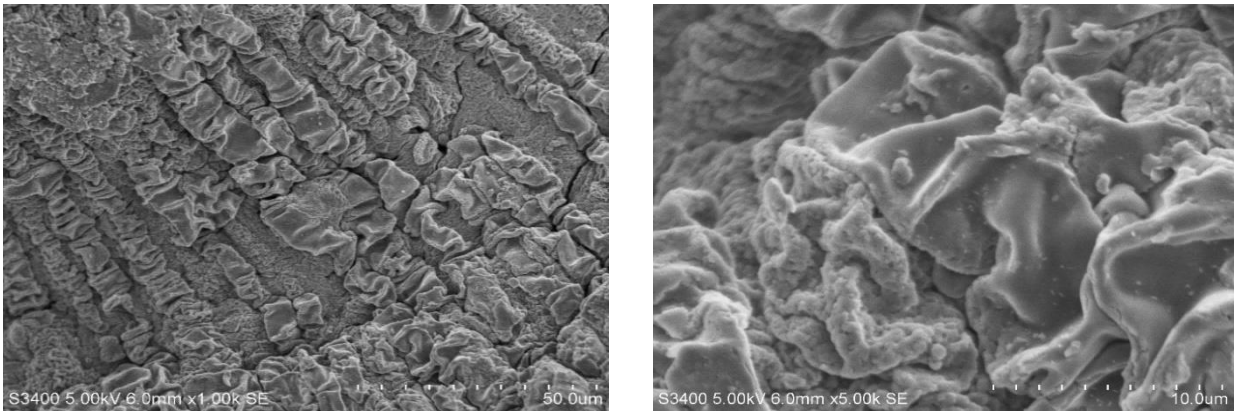


Fig.2. Surface morphology study of optimized formulation of sodium alginate beads containing metformin hydrochloride.

3.5. Fourier Transform Infra-Red Spectroscopy:

The principal absorption peaks of metformin HCl were seen at 3169 cm1 due to N H stretching of the primary amine group (NH2) and at 1063 cm1 due to C N stretching, with a peak at 1584 cm1 due to N H bending vibrations of the primary amine group. These peaks were present in the optimized beads containing metformin HCl as well, with no notable changes or shifts. This showed that the medicine (in this case metformin HCl) retained its identity after being formed into beads using sodium alginate-GG and HPMC K100M polymeric-blends utilizing the ionotropic gelation process.

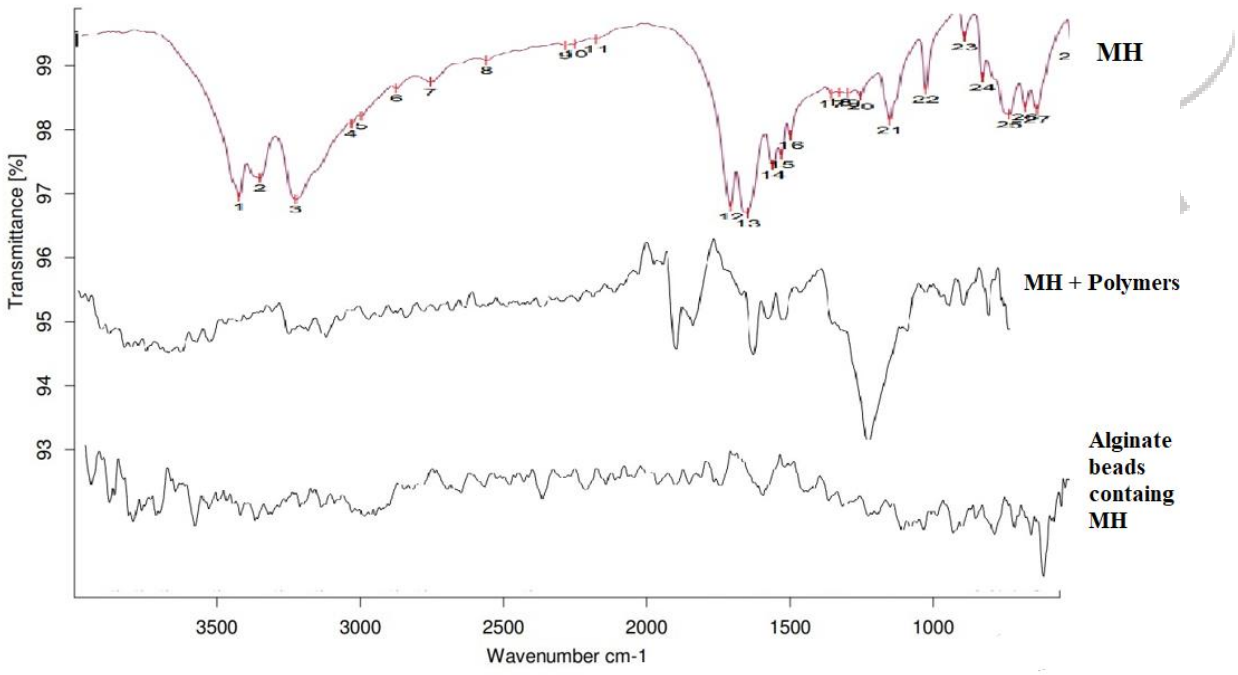
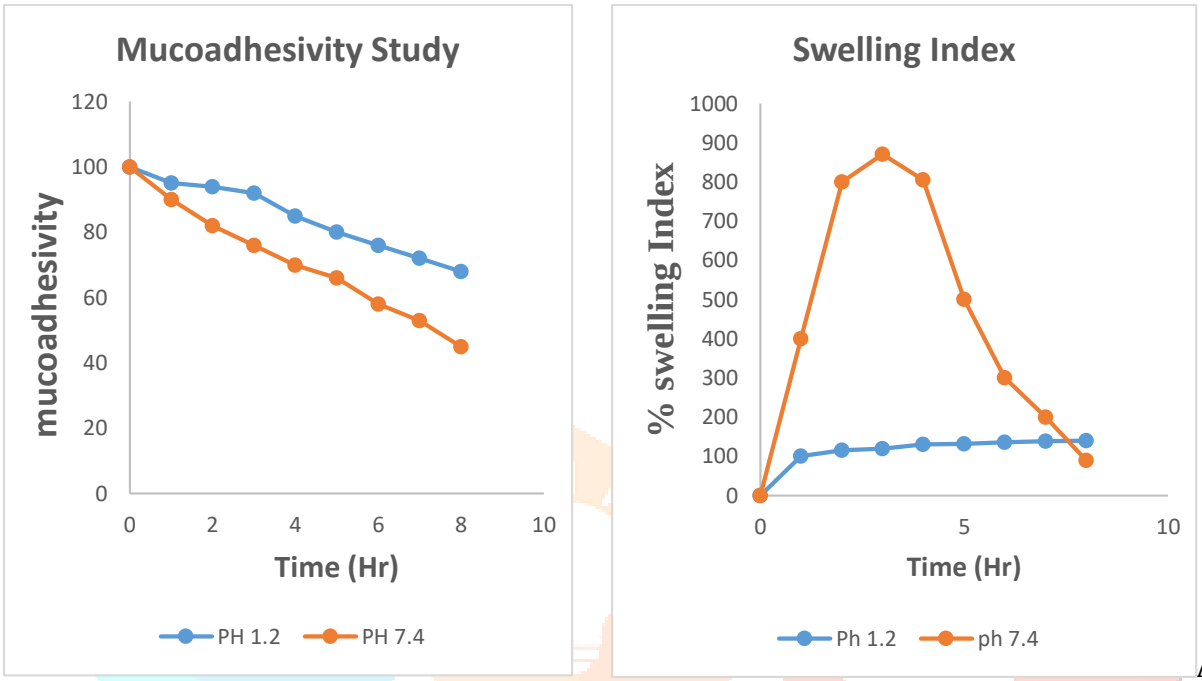


Fig. 3. FTIR spectra of (A) Pure Metformin Hydrochloride, (B) Metformin Hydrochloride with Polymer, (c) sodium alginate beads containing metformin HCl.

3.6. Swelling behavior:

The swelling behavior of optimized alginate beads-GG beads carrying metformin HCl (F-O) was investigated in both acidic (0.1 N HCl, pH 1.2) and alkaline (0.1 N HCl, pH 1.2) gastric pH and alkaline (0.1 N HCl, pH 1.2) intestinal pH. (Phosphate buffer, pH 7.4). The pH of the test medium has an effect on the swelling of optimized alginate beads-GG beads. In stomach pH (0.1 N HCl, pH 1.2), the swelling index of the optimized beads was found to be lower than in intestinal pH (phosphate buffer, pH 7.4). . After 2–3 hours in an alkaline pH (pH 7.4), the optimized beads swelled the most, followed by erosion and dissolution. pH affects the conformation of anionic GG chains in acidic medium by increasing the shielding effect of carboxyl group

repulsion, which is also enhanced by the addition of cross-linking cations and change of anionic nature of GG determined by the dissociation of carboxyl group , whereas in alkaline medium GG has hi anionic nature . Ion exchanging between Ca2+ ions of Ca2+-ion cross-linked alginate beads-GG beads and Na+ ions present in phosphate buffer due to the action of Ca2+-sequestrate phosphate ions could explain the swelling behavior of Ca2+-ion cross-linked alginate beads-GG beads in alkaline pH (pH 7.4). This could cause disaggregation of the ionotropically-gelled alginate beads-GG matrix structure, resulting in matrix erosion and dissolving of the swollen beads at alkaline pH (phosphate buffer, pH 7.4), thus speeding up drug release.



A B

Fig 4. (A) Swelling behavior of optimized formulation in pH 1.2 and pH 7.4; (B) Mucoadhesivity of optimized formulation in pH 1.2 and pH 7.4.

3.6. Drug Entrapment efficiency:

Drug entrapment efficiency ranges from 81 to 94.5 %. When the proportion of sodium alginate to gum ghatti in the polymer blend was raised, the DEE % increased. The viscosity fluctuations in the polymer blend are to blame for this. The medication would not be drained into the polymeric solution during the cross-linking method. When HPMC K100M concentrations are increased from 400 mg to 800 mg, entrapment efficiency remains constant.

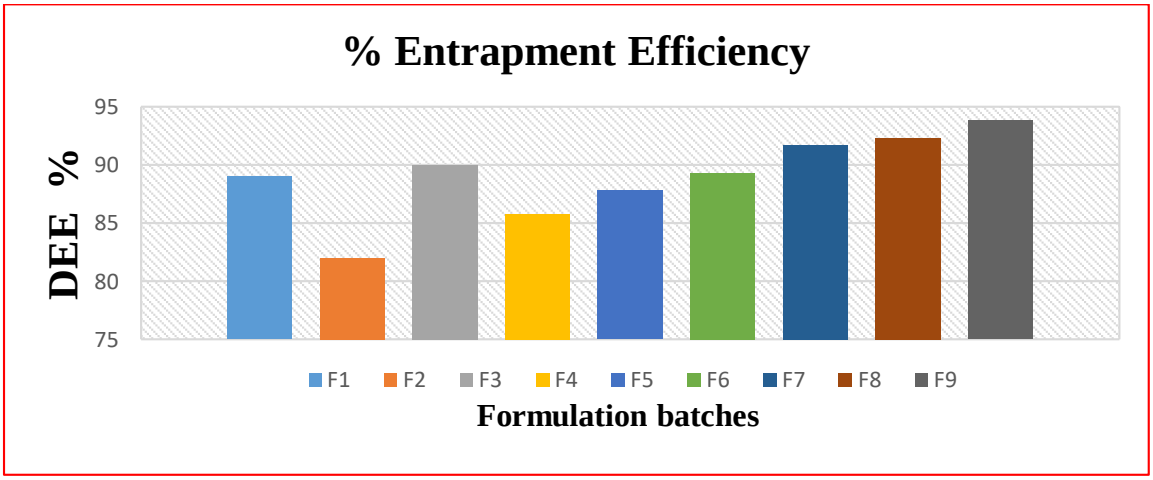


Fig 4. Determination of DEE of sodium alginate beads containing metformin hydrochloride

3.7. Mucoadhesivity:

Ex vivo wash-off tests employing goat intestinal mucosa in acidic stomach pH (0.1 N HCl, pH 1.2) and alkaline intestinal pH (0.1 N HCl, pH 1.2) were used to assess the mucoadhesivity of optimized alginate beads containing metformin HCl (F-O) (phosphate buffer, pH 7.4). The ex vivo wash off of these newly designed alginate beads was found to be faster in an alkaline pH environment than in an acidic environment. Ionization of carboxyl and other functional groups of the Gum Ghatti matrix structure could increase their solubility with lower adhesive strength, resulting in quick ex vivo wash off at alkaline pH. The wash off test revealed that optimized alginate beads-GG beads carrying metformin HCl have good mucoadhesive capability, which could result in enhanced bioavailability of the encapsulated drug due to extended stomach residence duration and closer contact between the absorptive membrane and these beads. This could also enable for medication release over longer periods of time, minimizing the necessity for dosage form read ministration. The inclusion of hydroxyl groups in both the hydrophilic polymers utilized as polymer-blend, which have the potential to create hydrogen bonds with mucous membranes, could explain the mucoadhesive behavior of these beads. Hydrophilic polymers like GG and alginate beads, on the other hand, can create non-covalent connections such as van der Waals forces or ionic interactions, leading in mucoadhesion.

3.8. In Vitro Drug Release Studies:

The in vitro metformin HCl release of Metformin HCl was released for 12 hours using sodium alginate beads. The release of metformin HCl from these beads was observed to be slower in the acidic dissolving liquid (0.1 N HCl; pH, 1.2) than in the alkaline dissolution medium (phosphate buffer; pH, 7.4). The surface attached drug could be to blame for the trace amount of drug released from these beads during the in vitro drug release study's first stages. Following that, alkaline dissolving medium (pH 7.4) released metformin HCl more quickly than acidic dissolution medium (pH 7.4). (pH, 1.2). This pattern could be explained by the fact that these beads inflated more quickly in alkaline dissolution liquid than in acidic dissolution medium, resulting in higher drug release in the alkaline dissolution medium. Electrostatic repulsion between the ionized carboxylic acid groups of the Gum Ghatti -backbone presumably caused a considerable swelling force in alkaline dissolution liquid. Actually, when exposed to phosphate buffer (pH 7.4), the gel structure may become loose and soluble, since the Ca2+ ions engaged in the ionotropically-gelled GG-based network might be displaced by Na+ ions as well as sequestered by phosphate ions present in phosphate buffer (pH, 7.4After 12 hours, the cumulative drug release from sodium alginate beads containing metformin HCl (R12hr, %) was in the range of 78.00 % to 90%, and this was shown to be decreasing as the concentration of HPMC K100M was increased.

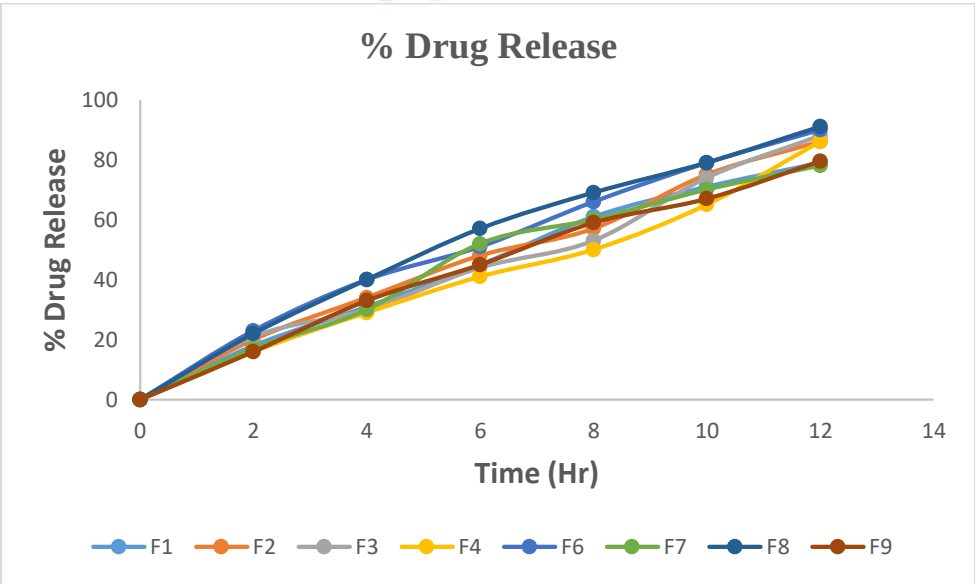


Fig. 5. In vitro drug release of sodium alginate beads containing metformin HCl

3.8. Drug release kinetics parameter studies:

The result of fitting the curve into various mathematical models, such as zero-order, first-order, Higuchi, Hixson-Crowell, and Korsmeyer–Peppas. When the squared correlation coefficients (R^2) of these ionotropically-gelled ALGINATE BEADS-GG beads containing metformin HCl were examined using various mathematical models, it was discovered that the drug release followed the zero-order model (R^2 = 0.983–0.983) over a 12-hour in vitro drug release period. To determine the DR kinetics, release data was fitted to kinetic models. In-vitro DR was shown to be substantially better at fitting Zero order kinetics, as seen by the plot, with a higher maximal linearity regression coefficient (R^2) than others.

Table 3. Result of fitting of in vitro drug release kinetic parameter of sodium alginate beads containing metformin hydrochloride.

Kinetic Model	**F0**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Zero Order Model	**0.988**	0.974	0.9729	0.9711	0.9741	0.972	0.9736	0.9714	0.9752	0.9774
First Order Model	**0.984**	0.879	0.861	0.847	0.8406	0.8323	0.8276	0.847	0.8889	0.8215
Higuchi Model	**0.987**	0.7045	0.717	0.7303	0.7492	0.7507	0.7387	0.7521	0.7165	0.7364
Hixon Crowell Model	**0.985**	0.843	0.8417	0.8403	0.8689	0.8647	0.8606	0.8728	0.8417	0.857
Korsmeyer-Peppas Model	**0.983**	0.792	0.7165	0.7259	0.7444	0.7449	0.7334	0.7475	0.7168	0.7325

3.9. Stability Study:

The stability studies performed for 1 month at RT further tested for physical Changes, bead size and in-vitro drug release

Formulation	Physical change	Bead size	% Drug Release
F1	No	1.178 mm	80%

After 1 months of stability study there was no any alteration physical change in case of color occurs. The bead size found to be 1.178 mm and in-vitro drug release was 80%. Showed that there was no significant difference in results indicating that the formulation was stable.

4. Conclusion:

The ionic gelation process was used to generate sodium alginate, Gum ghatti, and HPMC K100M mucoadhesive beads containing metformin HCl for oral drug delivery, which were then optimized using response surface methodology based on a 3^2 factorial design. These sodium alginate beads with metformin HCl were spherical in shape and ranged from 1.2mm to 1.45mm in diameter. The in vitro release of metformin HCl from these sodium alginate beads lasted for 12 hours and followed a zero-order drug release kinetic model. The optimized sodium alginate mucoadhesive beads containing metformin HCl had a DEE of 82 to 94 % and a drug release of 78.00 % to 90 % after 12 hours. The metformin HCl-containing optimized beads also showed pH-dependent swelling and good mucoadhesivity.

Acknowledgements:

I am kindly grateful to AICTE for providing financial assistance to carry out this work and our respected principal sir and my Guide Dr.K.B.Burade and our Head of department Dr.M.S.Charde Sir given all kind of help related research work.

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