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Original Article

Combined Raft Formation-Interpenetrating Complex Approach to Reconstitutable Sustained-Release Suspension Development

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ABSTRACT

Background: The foundation of this work is the use of raft formation and Interpenetrating Polymeric Network (IPN) complexation techniques to create a reconstitutable sustained-release suspension of Diltiazem Hydrochloride (DZH) for elderly patients. **Materials and Methods:** Xanthan gum and chitosan were used in combination to prepare IPN complexes of DZH. A central composite design was used to optimize the raft-forming *in situ* gelling system. The concentrations of HPMC K4M and sodium alginate were the independent variables. **Results:** *In vitro* dissolution, X-ray powder diffraction, and differential scanning calorimetric studies were conducted to examine the IPN complexes. The optimized batch (ratio of sodium alginate to HPMC K4M, 1500:100) exhibited gelation properties for an extended time period, as well as the desirable floating duration (>12 hr). A desirable drug release of 97.39±0.97% in up to 12 hr was achieved. The release kinetics of the DZH obeyed the Higuchi order of release following the Fickian diffusion mechanism with an n value of 0.366. **Conclusion:** The *in vitro* study suggested that a reconstitutable sustained-release suspension was successfully prepared using the raft forming formulation approach and the IPN complex of DZH. The optimized formulation exhibited sustained release of the water-soluble drug over 12 hr due to the combined effect of the RFGS and the IPN complex.

Keywords: Sustained Release, IPN Complex, *In situ* gel, Reconstituted Suspension.

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INTRODUCTION

Several kinds of drug delivery systems have been developed to release drugs in a controlled fashion. Administration of a drug formulation by the oral route is a more acceptable mode.[1] The oral route is the first choice for most patients, because of its simple nature, ease of administration, safety, acceptability, and good absorption through the gastrointestinal tract.[2] Tablets and capsules are the most favored dosage form, but swallowing these is a difficult task for geriatric patients. Hence liquid dosage is the preferred choice of drug administration in geriatrics.[3] Repeated administration, missing of doses, and burst-releases of the drug are the major issues in the administration of conventional liquid formulations. Sustained drug delivery formulations are the alternative for addressing the issues of conventional liquid formulations, because of their ability to deliver drugs at slower rates for prolonged periods within the body, which makes them beneficial for geriatric patients.[4]

The patient-compliance of sustained-release suspensions is better, they have fewer side effects, and their bio-availability is better,[5] However, they have drawbacks, including increased drug solubility due to pH changes brought on by chemical degradation,[6] high solubility in liquid formulations,[7] incompatibility of ingredients, changes in viscosity, conversion between polymorphic forms, crystal growth. The use of polymer complexes is another approach to overcoming the physical stability problem, frequently encountered, in conventional suspensions and to reducing the solubility of a highly soluble drug. An association of various polymers that mix well is called a polymer complex. The comparatively high intermolecular interactions (stereo-match effect) between polymer chains cause the miscibility.[8] A drug-polymer complexation is an ionic interaction between a drug and a polymer. In interactions of this kind, the drug and polymers have opposite ionic charges. These

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opposite charges have an attraction towards each other, and the drug-polymer complex is formed. The complex gives sustain release action within the formulation.[9,10]

A Reconstituted Suspension (RS) can be used to avoid the issue of drug release during the storage of a liquid suspension. RSs are dry mixtures to which water must be added at the time of administration.[11] The preferred formulation in cases where drugs stability is a significant concern is a reconstituted system. Because the drug is spread when administered, it has a higher bioavailability than tablets and capsules. This system's drugs stability is sufficient for the duration of its shelf life. The weight of the final product is less also.[12,13]

Thus, the focus of this research work was to develop an RS based on a combination of the Raft-Forming Gelling System (RFGS) and Interpenetrating Polymeric Network (IPN) complex approaches in order to extend the release of Diltiazem Hydrochloride (DZH), which is highly soluble in water, in geriatrics.

MATERIALS AND METHODS

Materials

Swapnroop Laboratories Ltd., in Aurangabad, Maharashtra, India, provided the DZH. Loba Chemie Pvt. Ltd., in Mumbai gave the Sodium Alginate (SA), Xanthan Gum (XG), and Hydroxypropyl Methylcellulose K4M (HPMC K4M). The provider of Chitosan (CS) was Research-Lab Fine Chem Industries in Mumbai. Every chemical and reagent utilized in the investigation was of pharmaceutical grade.

Preparation of DZH-Polymer Complex

A DZH-polymer complex was made by combining various polymers with powdered DZH in a 1:2 ratio. These polymers included gellan gum, XG, and pectin. All the ingredients were physically mixed and triturated with drop-wise addition of distilled water until the formation of a homogeneous paste. An oven set to 50°C was used to dry the mixture, and the product obtained was ground using a mortar and pestle and passed through sieve no. 60.[14,15]

Preparation of IPN Complex

CS and the DZH-XG complex were physically combined in a 1:2 ratio to XG. The mixture was triturated with drop-wise addition of distilled water, which was ended when a paste was formed. The paste was placed in an oven and maintained at a temperature of up to 55°C until it was completely dry. The dry mixture was passed through sieve no. 60, as described in the previous section.[14-16]

Evaluation of DZH-Polymer and IPN Complexes

Drug Content

A sample of an IPN complex, equivalent to 30 mg of the drug, was dispersed in a 500 mL solution of pH 1.2 buffer. This dispersion was thereafter sonicated for 1 hr and then agitated for 24 hr at a temperature of 37±0.5°C. Following a 48-hr agitation, the mixture was filtered, and the drug concentration was quantified using a UV-visible spectrophotometer at a wavelength of 238 nm.[17]

Studies on the *In vitro* release of DZH

The DZH releases from the DZH-polymer and IPN complexes were examined over 8 hr in 0.1 N HCl. A USP-II apparatus (Inspire 08 ETC-15, Electrolab, Navi Mumbai) was used. A quantity of each complex (weighed) equivalent to 30 mg of DZH was mixed in 500 mL of 0.1 N HCl. A temperature of 37±0.5°C was consistently maintained. 5 mL aliquots were extracted at 1, 2, 3, 4, 5, 6, 7 and 8 hr, and the volume was adjusted using the fresh medium. The DZH concentration was analysed utilizing a UV spectrophotometer (UV-2401, Shimadzu, Japan) at a λ_{max} value of 238 nm,[17,18] All of the release studies were carried out in triplicate, with the average values and standard deviation in order to minimize experiment variability.

Characterization of IPN complex

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR (84005, Shimadzu Asia Pacific Pvt. Ltd., Singapore) studies were carried out using the KBr disc method. The functional groups, chemical bonding, and existence of DZH-polymer interactions were identified by recording the spectra of DZH, a DZH-polymer physical mixture, and the IPN complex. After mixing, each sample (corresponding to 10 mg of DZH) was pressed into KBr discs. It then was scanned over the 4000 to 400 cm^{-1} range (Figure 1).[19,20]

Differential Scanning Calorimetric (DSC)

The thermal examination of the IPN complex was conducted using a differential scanning calorimeter (DSC-60, Shimadzu, Japan). The specimen was weighed and examined in the perforated DSC aluminum pan (Aluminium Standard 40 µl) at the rate of heating of 10°C/minute under an atmosphere of nitrogen with an average flow rate of 50 mL/min and a temperature range of 25-400°C. (Figure 2) depicts the obtained thermograms.[20,21]

X-ray powder diffraction study

An X-ray diffractometer (XRD-7000 Maxima, Shimadzu, Japan) was used to analyze the samples in order to determine if the DZH powder and the IPN complex were crystalline or amorphous, with a diffraction angle 2 theta with the voltage set at 40 kV and the current at 30 mA (Figure 3).[20]

Formulation of RFGS

RFGSs was prepared using different concentrations of highly viscous SA, HPMC K4M, and Calcium Carbonate ($CaCO_3$) (Table 1). A solution of SA (1.2-1.8%, w/v) was prepared by dissolving the polymer in deionized water. HPMC K 100 (0.05-0.150%, w/v) was added. Finally, 7.5% (w/v) $CaCO_3$ was dispersed well in the

mixture with continuous stirring. The volume of the dispersion was adjusted to 100 mL with distilled water. The RFGS prepared was reconstituted with the IPN complex equivalent to 600 mg DZH at the time of administration and evaluation.[22]

Design of Experiments

A methodical, scientific approach-particularly an experimental design-can be employed to examine the interaction and relationship between dependent and independent variables. The selected design, which can offer a sufficient degree of freedom, can be used to ascertain the effects and interactions of the independent variables. A central composite design was used to codify the RFGSs. Two independent factors (variables), SA (A) and HPMC K4M (B), were selected and evaluated at three levels: a higher level (-1), a medium level (0), and a lesser level (+1). The dependent variable was the drug release. The process variables, their levels, and the experimental values are reported in (Table 2).[23,24]

Evaluation of RFGS

Measurement of the viscosity of RFGS

The viscosity of the RFGS was determined using a Brookfield CAP Viscometer (CAP 2000+, Brookfield Engineering Laboratories, Inc., USA). Two or three droplets of the RFGS sample were placed on the temperature-sensitive plate at 20±1°C at varying shear rates. Cone number 1 was utilized to assess the viscosity of the RFGS while it was resting on the plate.[25]

In vitro gelation Study

The RFGS's gelation in a beaker with 500 mL of hydrochloric acid solution (0.1 N, pH 1.2) was examined. To prevent breaking of the gel, 10 mL precisely measured of the formulation were added to 0.1 N HCI (pH 1.2) under mild agitation. The gelling was assessed qualitatively and visually.[25] All the samples were analyzed in triplicate, with the average values and standard deviation.

In vitro floating study

An *in vitro* floating investigation was performed in a USP class II dissolution equipment using 500 mL of 0.1 N HCl (pH 1.2). The medium was preserved at 37±0.5°C in temperature. 10 mL of the *in situ* gel formulation produced were taken out with a disposable syringe and then placed in a Petri dish with an internal diameter 4.5 cm. The Petri plate was then carefully placed in the dissolving reservoir with least disturbance. Recorded were the times it took for the formulation to surface on the medium (floating lag time) and the times it took for the formulation to float continuously on the surface of the dissolution medium (floating duration).[25,26] All the samples were checked in triplicate, with the average values and standard deviation.

Assessment of *in vitro* DZH release

The release of DZH from the RFGS loaded with the DZH-IPN complex was measured. A USP-II dissolution apparatus (Inspire 08 ETC-15, Electrolab, Navi Mumbai) was used, with a speed of 50 rpm. This speed was just low enough to shatter the gel. The dissolution medium was 0.1 N HCl (500 mL, pH 1.2), and 37±0.5°C was the constant temperature. Using a disposable syringe, a 5 mL of RFGS was drawn up. The syringe was cleaned and wiped, and the excess RFGS from the tip was removed. A 5 mL sample was extruded directly into the dissolution medium by slowly depressing the plunger of the syringe. At 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12 hr, the dissolving medium was sampled exactly (5 mL), and the volume was adjusted using fresh medium. A UV spectrophotometer set to measure absorbance of DZH at 238 nm (UV 2401 PC, Shimadzu, Japan) was used to filter the extracted samples.[27] Each experiment was performed in triplicate, and the average values and standard deviations are reported.

Kinetic Model of drug release

Drug release kinetics were analysed using first-order, zero-order, Higuchi, and Korsmeyer Peppas models. To simulate and compare the drug-release profiles, DDSOLVER, an ad in application for Microsoft Excel, was utilized. The best-fitting model was determined to be the one with the highest coefficient of determination (R^2).[28]

RESULTS AND DISCUSSON

Preparation of IPN complex

A DZH-IPN complex was prepared from XG and CS using the kneading technique. DZH and XG form ionic complexes because of the positive (+) and negative (-) charges on them, respectively. CS is a positive charge polymer form partially interlaced IPN with XG.[14]

Evaluation of complexes

XG exhibited more sustained release behaviour compared with the other two anionic polymers, GG and PC, to form a complex with the cationic DZH. But the DZH release was not sustained for more than 4 hr. So, the cationic polymer CS was added to develop an IPN Complex in which the drug release would be restricted. Owing to the higher solubility of DZH, the release of the drug from the IPN complex was not sustained up to 12 hr. The DZH release was sustained up to 7 hr. In order to extend the sustained-release effect, we decided to incorporate IPN complex of DZH in an RFGS. In FTIR Spectra (Figure 1), XG's Carboxylate ($-COO^-$) stretching vibrations at 1600-1650 cm^{-1} (asymmetric) and 1400-1450 cm^{-1} (symmetric) were significantly reduced and slightly displaced in the IPN spectrum. CS's amide II and amino ($-NH_2$) bands about 1550-1650 cm^{-1} exhibited modest changes and decreased intensity. These spectrum alterations point to significant ionic interactions between the anionic carboxylate

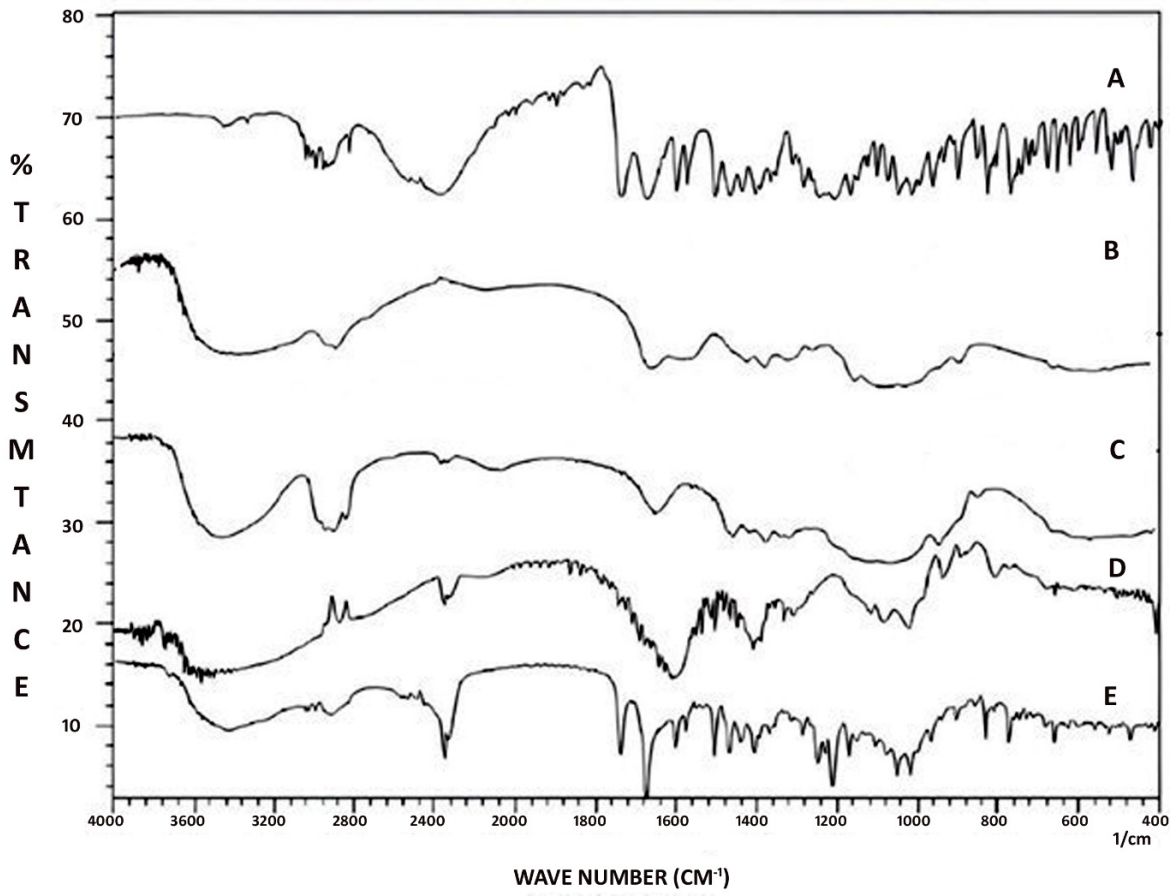

Figure 1: FTIR spectra of A. DZH, B. XG, C. CS, D. Physical mixture of DZH, XG and CS polymers E. IPN Complex.

Table 1: Amount of drug, sodium alginate, calcium carbonate, HPMC K4M, deionized water, gelation, floating lag time, floating duration.

Sl. No.	Batches	Ingredients					Gelation (pH1.2)	Floating Lag Time (Sec)*	Floating Duration (Hrs.)
		Amount of drug (mg)	Sodium alginate(mg)	Calcium Carbonate(mg)	HPMC K4M(mg)	Deionized water			
1	F1	600	1200	750	50	Q.S Up to 100 mL	++	14±1	≥12
2	F2	600	1800	750	50		+++	21±1	>12
3	F3	600	1200	750	150		+++	17±2	≤12
4	F4	600	1800	750	150		+	22±2	>12
5	F5	600	1075.74	750	100		++	19±1	≥12
6	F6	600	1924.26	750	100		+++	28±2	>12
7	F7	600	1500	750	29.289		++	31±2	>12
8	F8	600	1500	750	170.71		+++	36±3	≥12
9	F9	600	1500	750	100		+++	28±1	≥12

*Each value represents mean±Standard deviation(n=3).+: Gelatin after few second.++:Immediate gelatin, remain for few hours.+++: Immediate gelatin, remain for extended period.

Table 2: Variable level with experimental value.

Sl. No.	Independent Variable	Level		
		-1	0	1
1	Sodium Alginate (mg)	1200	1500	1800
2	HPMC K4M (mg)	50	100	150

groups of XG and the cationic amino groups of CS, resulting in the creation of a crosslinked polymeric network. Loading DZH into the IPN resulted in spectrum alterations, particularly in the fingerprint region (600-1500 cm^{-1}), where drug-specific peaks dropped or moved. This suggests that DZH molecules are partially interlaced inside the polymeric network through ionic interactions and hydrogen bonding, which improves drug-polymer compatibility and stabilizes the complex.

The DSC thermogram of pure DZH showed a prominent endothermic peak at 217°C, which corresponds to its melting temperature, indicating its crystalline form. The thermograms of XG and CS displayed large endothermic transitions between 80-120°C, attributable to the loss of bound water and polymeric relaxation. In the physical mixing of DZH, XG, and CS, the characteristic melting peak of DZH remained evident, although slightly expanded and lowered in intensity, indicating partial interaction without major disruption of the drug's crystalline structure. However, in the thermogram of the DZH-loaded semi-IPN, the strong melting endotherm of DZH was completely absent, indicating that the drug was no longer in crystalline form. The absence of a melting peak indicates that DZH was molecularly disseminated inside the polymeric matrix rather than just physically blended (Figure 2). The X-ray diffractogram of pure DZH revealed several crisp and powerful diffraction peaks, indicating its crystalline structure. Similarly, the physical mixture of DZH with the polymers (XG and CS) revealed the majority of DZH's distinctive peaks, showing that the medication maintained its crystallinity in the simple blend and that no substantial interaction occurred during physical mixing. In contrast, the XRD pattern of the DZH-loaded IPN complex revealed a considerable reduction in the number and strength of DZH's distinctive crystalline peaks. While a few weak reflections of DZH could still be seen, many of its unique peaks were absent or significantly reduced. This decrease in crystallinity indicates that DZH got partially amorphized and distributed inside the interpenetrating polymer network as it formed (Figure 3). The elimination of various drug-specific peaks can be attributed to DZH's molecular dispersion in the semi-IPN structure, as well as potential interactions (ionic or hydrogen bonding) with XG and CS.[19-21]

Formulation of RFGS

The composition of the RFGS is presented in Table 1. In order to create RFGS, there are two crucial requirements, the optimal viscosity and the optimal gelling capacity, which refer to the extent and speed of gelation. The produced RFGT exhibited immediate gelation and floating behavior in the stomach's acidic environment. The transformation to a gel state from a solution occurred when the *in situ* polymers came into contact with divalent or monovalent cations present in gastric fluids. Upon reaction with an acid, the $CaCO_3$ in the formulation, which was present as an insoluble dispersion, dissolved and let out carbon dioxide. The liberated calcium ions subsequently contributed to the creation of a gel raft that buoyed.[25]

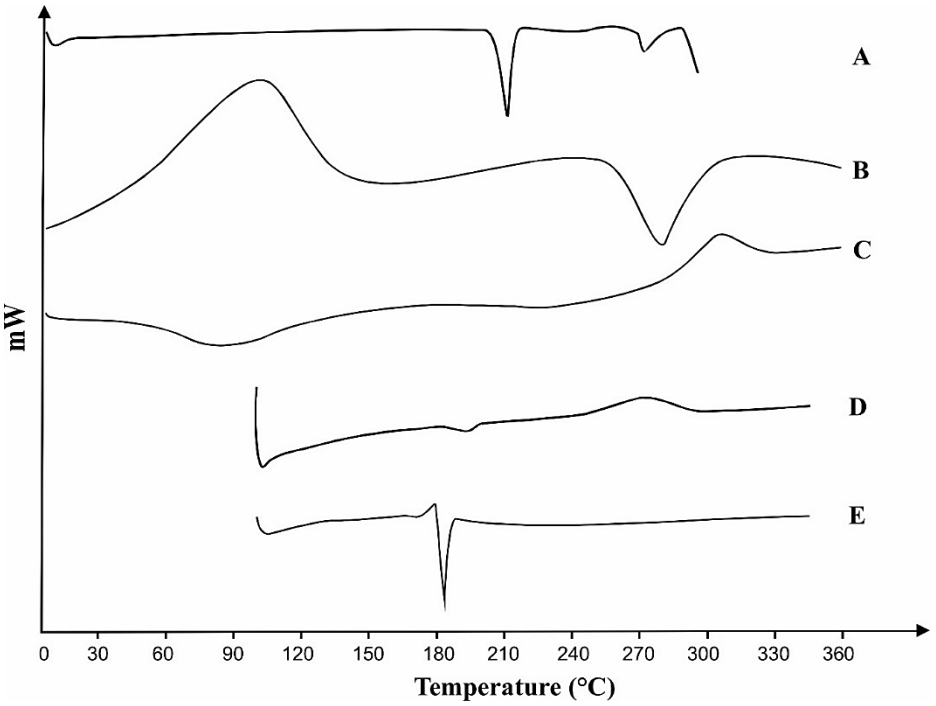

Figure 2: DSC thermograms of A. DZH, B. XG, C. CS, D. Physical mixture of DZH, XG and CS polymers E. IPN Complex.

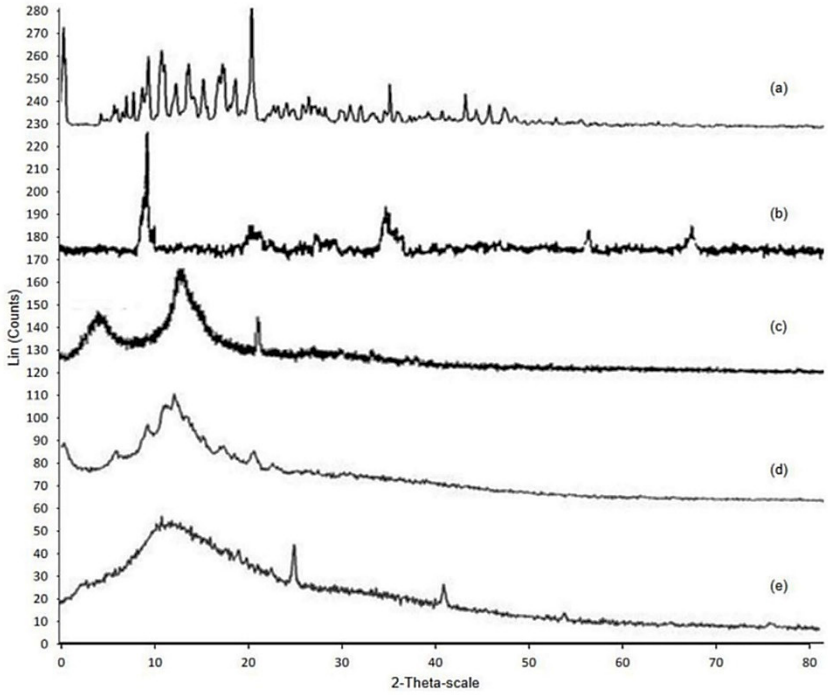

Figure 3: X-ray diffractograms of (a) DZH, (b) XG, (c) CS, (d) Physical Mixture of DZH, XG and CS, (e) IPN Complex.

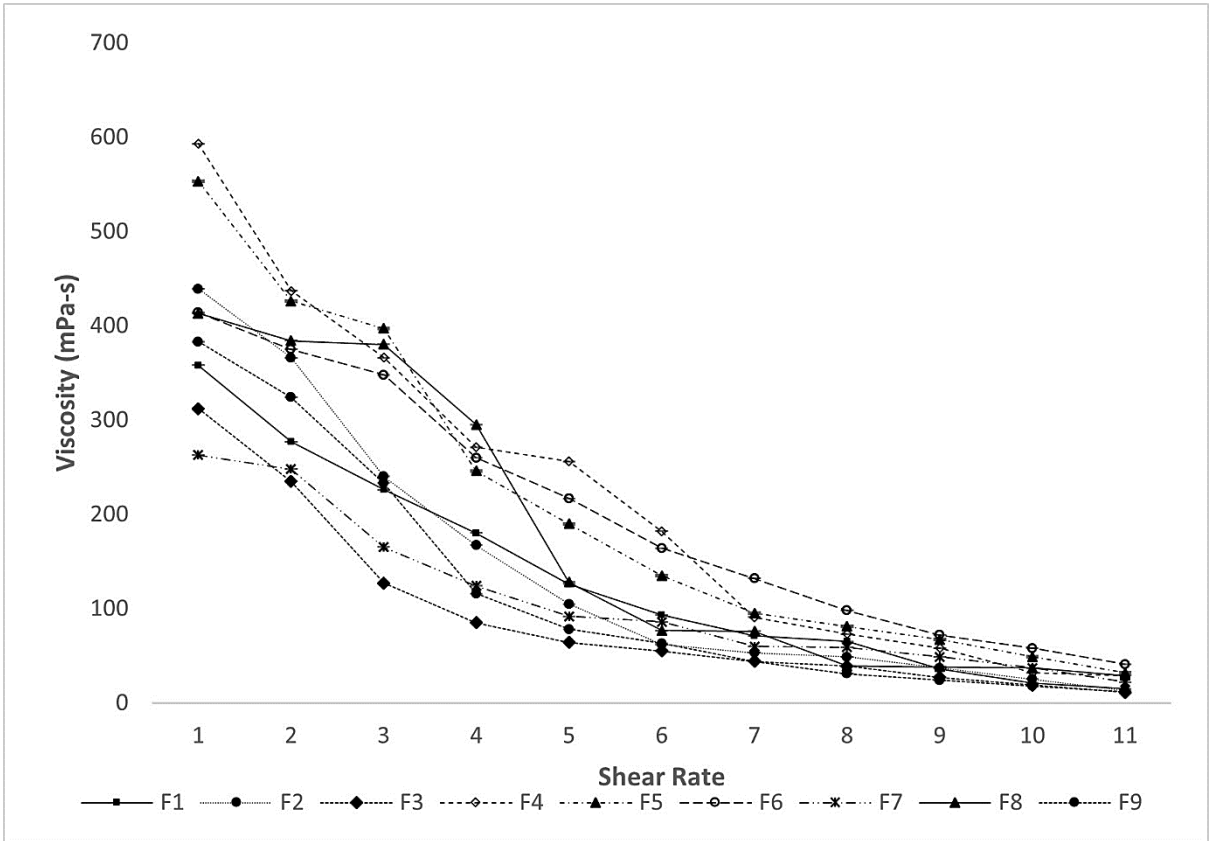

Figure 4: Viscosity Study of formulation batches F1-F9.

Analysis of the *in situ* gelling system

Viscosity measurement

All the RFGS formulations, prepared with different polymer concentrations, exhibited shear thinning, with a more pronounced effect observed at greater concentrations (Figure 4). This observation revealed a significant increase in viscosity as one raise polymer concentration. This change has been documented previously for SA and has been attributed to increased chain interactions with increasing polymer concentration.[29]

In vitro gelation analysis

The gelation properties of the RFGT were assessed on an ordinal scale ranging from + to +++ (Table 1). The RFGT batches F1, F3, and F5 were prepared with small amounts of SA, 1200, 1200, and 1075.74 mg, respectively. These formulations formed gels immediately, but the integrity of the gels was not retained for 12 hr. RFGT batches F2, F4, F6, F7, F8, and F9 were prepared with large amounts of SA, 1800, 1800, 1924.26, 1500, 1500, and 1500 mg, respectively. There was immediate formation of gels with these formulations, and the structural integrity of the gels was retained for more than 12 hr.[30]

After ingestion, the polymeric solution quickly converts from a sol to a gel via ionic gelation. During gelation, a double helical junction zone emerges, which eventually leads to the aggregation of double helical segments that form a three-dimensional network by the complexation of Ca^{2+} ions and hydrogen bonding.

In vitro buoyancy evaluation

The RFGTs of all the batches were found to have good floating properties (Table 1). The floating lag times for RFGS F1, F2, F3, F4, F5, F6, F7, F8, and F9 are 14±1, 21±1, 17±2, 22±2, 19±1, 28±2, 31±2, 36±3, and 28±1 sec, in that order. The released CO_2 in the formulation became entrapped within the gel network, which caused the formulation to become buoyant. Then, because of the small number and size of pores in the 3-D gel network, the calcium ions and SA reacted to establish a cross-linked three-dimensional gel network and expanded structure, which may have decreased the diffusion of CO_2 and the drug and led to longer floating and drug release periods, respectively.[31] As the formulation factors changed, so did the buoyancy lag time. Formulation F8 exhibited the longest floating lag time, whereas formulation F1 demonstrated the shortest. As the SA concentration rose, so did the floating lag time. It rose from 14±1 to 36±3 sec with the increase in polymer content.[32,33]

Studies on *In vitro* DZH release

For the *in vitro* release, every formulation batch was examined. Batches F1, F2, F3, F4, F5, F6, F7, F8, and F9 (containing SA of different concentrations loaded into the XG-CS IPN complex) exhibited cumulative drug release values of 96.69±0.38% at 9 hr, 89.36±0.85% at 12 hr, 92.54±0.94% at 12 hr, 85.73±0.63% at 12 hr, 96.28±0.68% at 12 hr, 83.97±0.18% at 12 hr, 92.70±0.64% at 12 hr, 87.25±0.78% at 12 hr, and 97.39±0.97% at 12 hr, respectively, as shown in (Figure 5). It was shown that when the concentration of polymers rose, the rate and magnitude of DZH release from *in situ* gels decreased. Not all of the batches were found to be connected to burst releases. This could be because of the barrier that the gel structure provides. According to this study, the drug might be retained by the *in situ* gel for extended periods of time.[34]

In any formulation, the drug's release is crucial. We are aware that the quantity of polymer utilized in the formulation has a major impact on the drug's release from a dosage form. At 12 hr, the drug release from batches F1-F9 ranged from 83.97±0.18% to 97.39±0.97%. The drug release of formulation F9 was greatest (97.39%) and that of formulation F6 was least (83.97%). The following polynomial equation was proposed from the model as determined using ANOVA, as per the provision of Design Expert

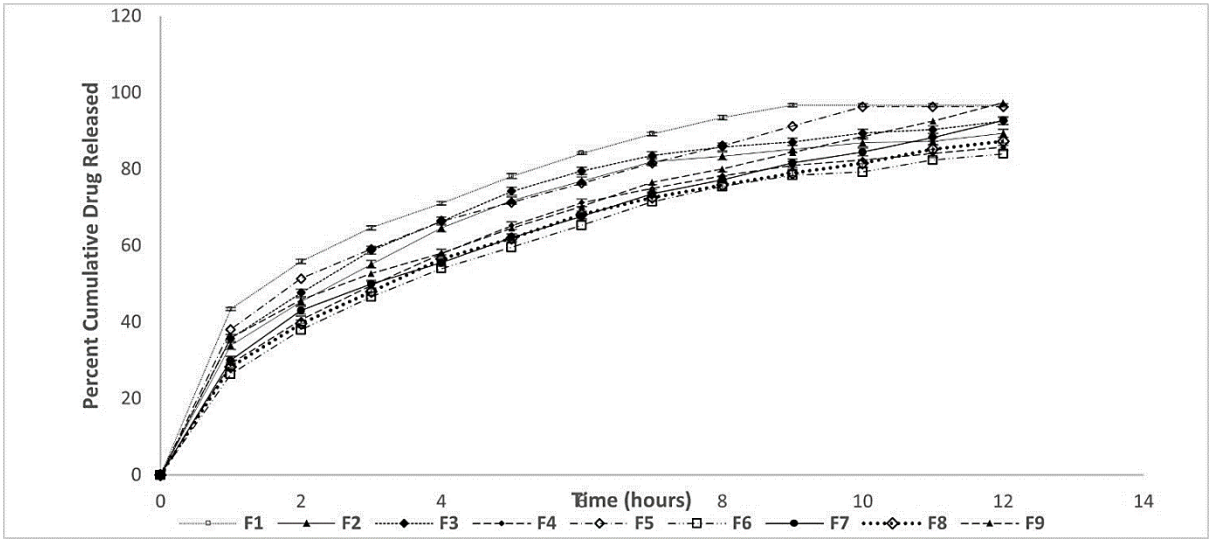

Figure 5: *In vitro* dissolution profile of DZH from formulation batches F1 to F9 in 0.1 N HCl.

Table 3: ANOVA and fit statistics for linear model.

Source	Sum of squares	Mean square	F-value	*p*-value	Significance
Model	296.87	59.37	103.19	<0.0001	Significant
A-Sodium Alginate	132.43	132.43	230.15	<0.0001	
B-HPMC K4M	26.24	26.24	45.60	0.0003	
Residual	4.03	1.34			
Fit statistics					
Std. dev.	0.7586				
R^2	0.9866				
Adjusted R^2	0.9771				
Predicted R^2	0.9048				
Adeq Precision	24.6432				

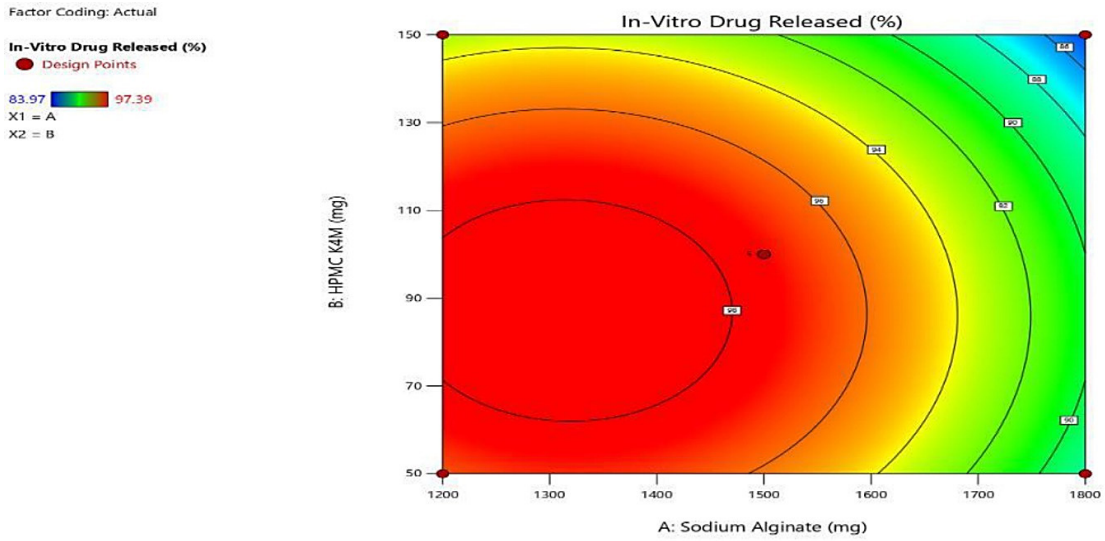

Figure 6: Contour plot showing the effect of the amount of polymers i.e. SA and HPMC K4M on *in vitro* DZH released from formulations.

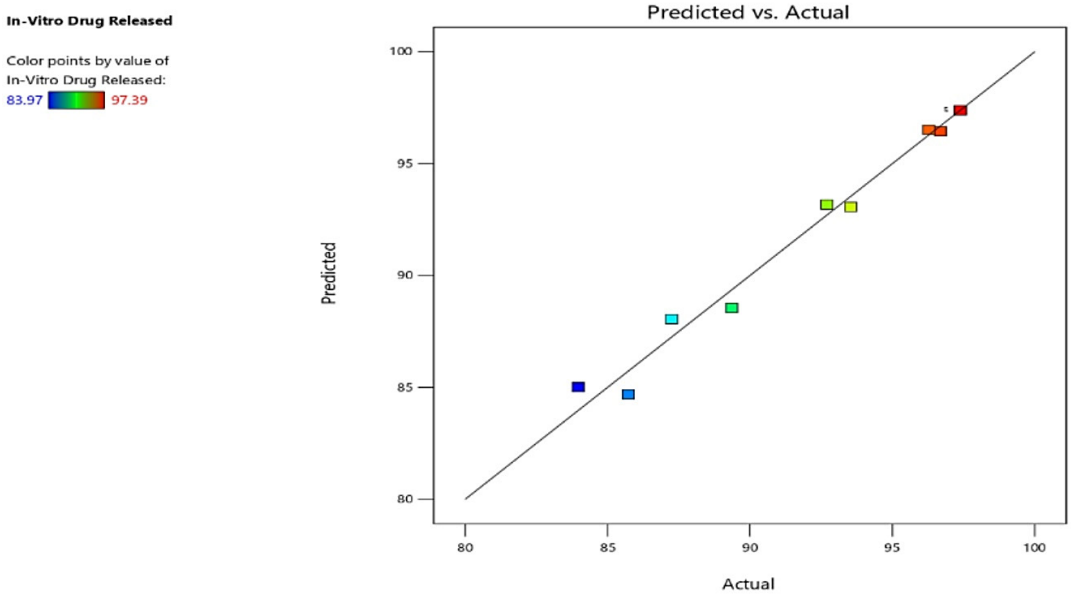

Figure 7: Predicted v/s Actual showing the effect of the amount of polymers i.e. SA and HPMC K4M on *in vitro* DZH released from formulations.

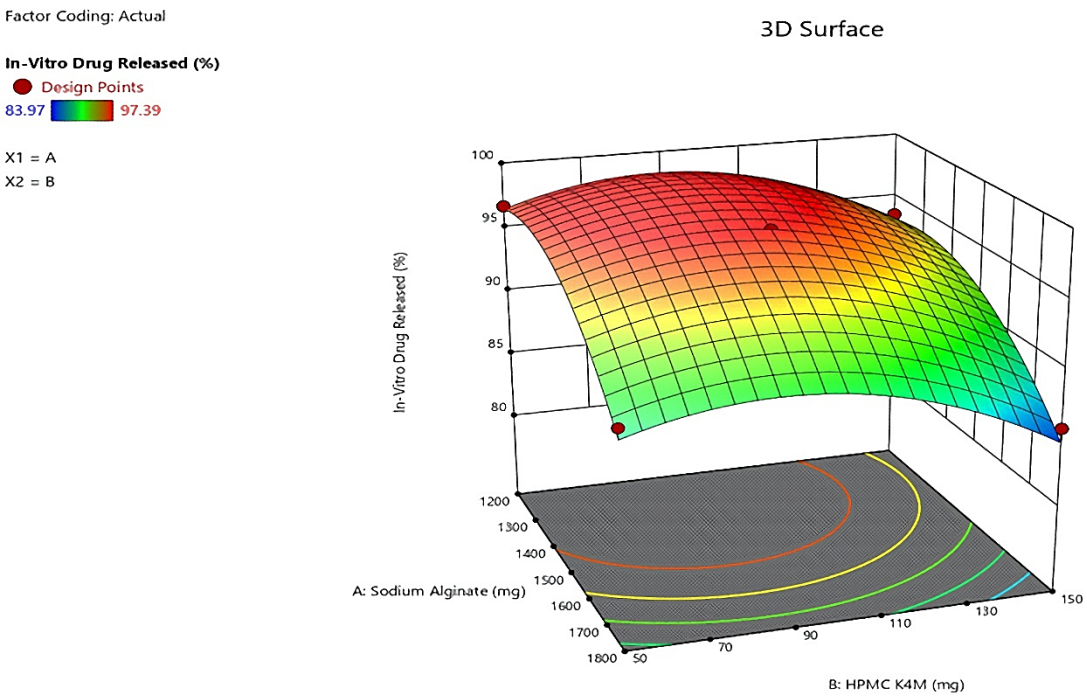

Figure 8: 3D surface plot showing the effect of the amount of polymers i.e. SA and HPMC K4M on *in vitro* DZH released from formulations.

software for drug release.[35,36] *In vitro* drug release = 97.39 - 4.068 A -1.81 B - 0.119 AB -3.312 A^2 - 3.387 B^2

Contour, predicted vs actual and 3-D surface plots showing the relationship between the lag time and the independent variables are shown in (Figures 6-8). The model is significant based on its F-value of 103.19 and its p-value, less than 0.0001 (Table 3). The difference between the expected R^2 value of 0.9048 and the adjusted R^2 value of 0.9771 is less than 0.2. The signal-to-noise ratio, which Add Precision measures, was found to be greater than 4. The ratio of 24.643 indicates a sufficient signal, and the model can be employed to explore the design space.[37]

Release Kinetics Study

It was concluded that Higuchi's equation offered the best explanation for the *in vitro* drug release because the Figure for the optimized formulation batch (F9) showed the best linearity (R^2=0.983). The Korsemeyer Peppas equation was applied to the release profile of batch F9. The Fickian diffusion mechanism was indicated by the value of n, which was found to be 0.366 ($n \leq 0.5$).[38]

CONCLUSION

The study focused on developing an oral liquid sustained-release formulation to address challenges faced in administering solid dosage forms, particularly to geriatric patients. The formulation utilized a RFGS loaded with a DZH-IPN complex. The objective was to reduce the dosing frequency, prolong the duration of drug action, and provide sustained drug release.

The initial development involved preparing a DZH-loaded IPN complex using XG and CS. The IPN complex released a large amount of the drug but exhibited a burst effect. However, it was selected for further investigation. Subsequently, RFGSs were prepared by incorporating the IPN complex into SA and HPMC K4M at various concentrations. The optimized formulation, batch F9, showed desirable properties such as good gelation, a floating ability, a suitable viscosity, and sustained drug release (97.39% over 12 hr). Fickian diffusion was identified as the drug release mechanism.

During three months of accelerated conditions, stability testing on the optimized formulation, batch F9, revealed no appreciable changes in the drug-release pattern, indicating that the formulation remained stable during this study period.

The sustained-release oral suspension developed using the RFGS loaded with the DZH-IPN complex demonstrated promising characteristics for addressing challenges in administering medications to geriatric patients. It has the potential to provide prolonged drug action, bring down dosing frequency, and improve patient adherence and treatment results.

ABBREVIATIONS

DZH: Diltiazem Hydrochloride; **XG:** Xanthan Gum; **CS:** Chitosan; **IPN:** Interpenetrating Network Complex; **HPMC:** Hydroxypropyl Methylcellulose; **FTIR:** Fourier Transform Infrared Spectroscopy; **DSC:** Differential Scanning Calorimetry; **XRD:** X-Ray Powder Diffraction; **KBR:** Potassium Bromide; **CCD:** Central Composite Design; **HCL:** Hydrochloric Acid.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

An IPN complex laden with DZH was created and assessed in this study using a floating *in situ* gel. The interaction and crystallinity of IPN complexes were examined. *In situ* gel generated with SA and HPMC K4M was used to reconstitute the chosen interpenetrating complex. The produced formulations' *in vitro* gelation, *in vitro* floating behavior, viscosity, and *in vitro* release properties were examined. According to the *in vitro* tests, formulation F9, which contains 1500 mg of SA and 100 mg of HPMC K4M, showed the desired gelation property, floating ability, and sustained drug release over a 12 h period. Formulation F9 can therefore release DZH in a consistent and controlled manner over a 12 hr period, and it has shown properties that address difficulties in administering drug to elderly individuals.

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