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Tailoring of clindamycin hydrochloride IPN hydrogel scaffold for periodontal plaques treatment

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Abstract

Periodontal disease is an oral infectious and inflammatory disease caused by microorganisms that determine the host-mediated destruction of soft and hard periodontal tissues, which ultimately leads to tooth loss. Clindamycin is a lincosamide antibiotic with a broad spectrum, has been used in periodontal treatment both systemically and locally. Interpenetrating polymer network (IPN) hydrogels are cross linked by two or more polymer networks, providing free volume space in the 3D network structure, and providing conditions for the sustained and controlled release of drugs. Clindamycin hydrochloride IPN hydrogel were prepared by chemical crosslinking method and optimized by 3^2 full factorial design. The gel was formulated by using different gelling agents (Chitosan, Sodium CMC and Sodium alginate) and with varying concentrations of PVA (3, 4, 5% w/v). The prepared hydrogel formulations were evaluated for physical appearance, grittiness, pH, spredability, % swelling, drug content, viscosity and *in-vitro* diffusion study. Drug-excipients compatibility studies were performed by DSC and FT-IR analysis. All gel formulations showed acceptable physico-chemical and rheological properties and results were found to be within the limits. Drug-excipients compatibility studies showed that there no interaction between the drug ad selected excipients. The optimized formulation with sodium alginate as polymer and 5% PVA concentration was prepared and evaluated. It produced desired viscosity, % swelling index and controlled drug release up to 8 hrs. These findings strongly suggested the great potential use of this IPN hydrogels in antibiotic delivery systems for successful periodontal treatment.

Keywords: Clindamycin Hydrochloride; IPN Hydrogel; Dental Plaques; Chemical Crosslinking; 3^2 Full Factorial Design; Optimization

1. Introduction

The word periodontal literally means "around the tooth". Periodontal disease broadly defines several diseases associated with the periodontium. Common oral diseases include caries, periodontitis, pulp necrosis, oral mucositis etc., In periodontal disease there is formation of periodontal pocket which is pathologically deepened sulcus. Advanced forms of periodontal disease have sub gingival bacterial plaque with colonies of *Porphyromonas gingivalis* and *Actinobacillus actinomycetemcomitans*. Dental caries also known as tooth decay or a cavity is an infection, bacterial in origin that causes demineralization and destruction of the hard tissues surrounding teeth. Caries may be characterized by the experience of pain, problem with eating, chewing, smiling and communication due to missing, discoloured or damaged teeth. Dental caries is affecting 60-90% of school children and the vast majority of adults. It is also a most prevalent oral disease in several Asian and Latin American countries. Nowadays, as a consequence of high prevalence of dental caries, the need for treatment is increased [1].

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Clindamycin hydrochloride is one of the most common antibacterial agents for dental infections. Clindamycin is an antibiotic originally derived from lincomycin with a wide range of actions, with a high activity against Gram-positive aerobic bacteria & a broad range of anaerobic bacteria, among which are pathogens that produce beta-lactamase. Clindamycin acts by enhancing the functional capacity of poly morphonuclear neutrophils (PMNs) and bacterial killing. Clindamycin reduces adherence of bacteria to host cells, increases intracellular killing of susceptible organisms. Clindamycin is active against most periodontopathogenic bacteria (Actinomyces, Eubacterium, Bacteroides, Prevotella, Porphyromonas, Fusobacterium, Veillonella sp.). It does not block the proangiogenic activity, thus having positive effect in the overall regenerative outcome. Clindamycin is a water- soluble weak base (pKa 7.72), which is mostly in ionized form at physiological pH, and it is usually classified in class III of the Biopharmaceutics Classification System (BCS), with good aqueous solubility and poor membrane permeability [2-4].

Hydrogels are colloids composed of a hydrophilic polymer with high water content and a three-dimensional (3D) cross-linked networks structure, formed by physical or chemical cross- linking of polymer chains[3]. It is widely used in tissue engineering, biomedicine and other fields. It is used for cell planting, adhesion, proliferation, and spatial distribution. Hydrogels can absorb a large amount of liquid and swell due to their fantastic hydrophilicity, with good viscoelasticity and longer residence time. It has good biocompatibility close to living tissue and biodegradability. It has soft texture, high water-holding capacity. Thus, hydrogels have attracted increasing attention as alternative materials for linear the treatment of bacterial infections. Traditional hydrogels have defects such as poor mechanical properties and single performance, and their application in biomedicine is significantly limited. In recent years, with the development of life sciences, various types of hydrogels are developed to fulfil customer needs [5-7].

Interpenetrating polymer network (IPN) Hydrogels are 3D polymers formed by combining 2 or more hydrophilic polymers with water molecules. This hydrogel network can be fabricated using a wide range of natural polymers, synthetic polymers, monomers as well as from the combination of natural and synthetic polymers. Natural polymers offer advantages of biocompatibility, biodegradability, low toxicity while synthetic polymers have tunable characteristics, capable of being moulded in wide range of shapes and possess improved mechanical properties and thermal stability. IPN hydrogels contain a 3D network structure, producing a free volume for the easy encapsulation of drugs, and provide conditions for sustained and controlled release of drugs [8,9].

The present research work aims to formulate and optimize clindamycin hydrochloride IPN hydrogel scaffold for treatment of periodontal plaques.

2. Materials and methods

Clindamycin Hydrochloride was procured from Yarrow chem products, Mumbai, Maharashtra. Sodium Carboxy Methyl Cellulose and Chitosan were purchased from Yarrow chem products, Mumbai, Maharashtra. Poly Vinyl Alcohol and Sodium Alginate were purchased from Himedia laboratories Pvt, Ltd., Mumbai and NICE Chemicals Pvt, Ltd, Kerala, India respectively. All other chemicals and solvents were of analytical grade satisfying pharmacopoeial specifications.

2.1. Design of Clindamycin Hydrochloride IPN Hydrogels

9 formulations of 1% Clindamycin Hydrochloride gel were prepared with different polymers and their concentrations, adopting 3^2 Full Factorial Design (FFD) in Design Expert software (Version 13.0.5.0). Two critical process parameters were selected, Polymers Sodium alginate, Sodium CMC and Chitosan were used as Independent variable X1, the concentrations of PVA were Independent variable X2. Factors and Levels of 3^2 factorial designs are presented and quantitative compositions of prepared formulations are shown in table no.1 & 2 respectively.

Table 1 Levels and factors for of 3^2 Full Factorial design

Factors	Low	Medium	High
Polymer type (X1)	Sodium Alginate	Chitosan	Sodium CMC
% PVA Concentration (X2)	3	4	5

Table 2 Formulation table of Clindamycin Hydrochloride IPN Hydrogel

Formulation Code	Polymer	PVA Concentration (% w/w)
F1	Sodium Alginate	3%
F2	Sodium Carboxy methyl cellulose	5%
F3	Chitosan	4%
F4	Sodium Alginate	4%
F5	Sodium Carboxy methyl cellulose	3%
F6	Sodium Alginate	5%
F7	Sodium Carboxy methyl cellulose	4%
F8	Chitosan	3%
F9	Chitosan	5%

2.2. Preparation of Clindamycin Hydrochloride IPN Hydrogels:

A 3% w/v chitosan solution was prepared by dissolving in 0.1 M acetic acid by overnight stirring, for Sodium Alginate and Sodium CMC 5% w/v stock solutions were prepared by dispersing the polymer in distilled water, left to swell and hydrate overnight i.e., to form a homogenous dispersion without lumps. PVA 3%, 4%, 5% W/V aqueous solution were also prepared by dispersing PVA in distilled water and left to hydrate overnight. The polymer portion was mixed with PVA in equal ratio in an enamel dish with pestle until a homogenous dispersion was formed. The cross-linking agent gluteraldehyde was added drop wise to the dispersion to form IPN Hydrogel by chemical cross-linking. The drug loading was done by adding Clindamycin Hydrochloride aqueous solution to the formed IPN Hydrogels with mixing. The permeation enhancer and humectant i.e., PEG 600 & glycerine were added & mixed well. The triethanolamine was added to clindamycin hydrochloride IPN Hydrogel to neutralize the pH [9].

2.3. Drug-excipient compatibility studies:

2.3.1. Fourier transform infrared spectroscopic analysis (FTIR) studies:

FTIR spectroscopy was done to identify the functional groups present and interaction between drug and excipients. FTIR spectra were developed for pure drug and formulation by potassium bromide, the disk was prepared by compression of 10 tons pressure for 5 mins. Finally, disk was placed in a holder of FTIR machine (Agilent Cary-630) and a spectrum was recorded from 4000cm^{-1} to 500 cm^{-1} band width.

2.3.2. Differential scanning colorimetry (DSC) studies:

DSC is a thermo-analytical technique given an insight into the melting behaviour of substance. Generally, the temperature program for a DSC analysis is designed such that the sample holder temperature increases linearly as a function of time. The pure drug and formulation were subjected to DSC studies. DSC samples were sealed in 40µl aluminium pans an identical empty pan was used as a reference, and all the samples were scanned at 5°C/min with a 20 ml/min nitrogen purge from 20- 400°C.

2.3.3. Evaluation of IPN hydrogels:

Physical Characteristics

The prepared hydrogel formulations were inspected visually for their colour, homogeneity and presence of any aggregates [10].

Grittiness

Presence of any particulate matter in the formulations was observed microscopically [10].

pH measurement

The pH of hydrogel formulations was determined by digital pH meter. 1gm of gel was dissolved in 25 ml of distilled water and the electrode was then dipped into gel. formulation for 30 mins until constant reading obtained and constant reading was noted. The measurement of pH of each formulation was done in triplicate and average values were calculated [10].

2.4. Spreadability

Accurately weighed 1g the prepared hydrogel was applied to the glass plate. The formulation was covered with another plate, on the surface of which weight of 600 g was placed. The radii of the gels were measured after placing the weight. The results obtained allowed the area occupied by the prepared hydrogels to be calculated according to the following formula:

$$P = \pi r^2$$

Where, P - surface area occupied by the hydrogel (cm^2), r - radius of the hydrogel (cm)

Spreadability tests for hydrogels were carried out in triplicates at room temperature [11].

2.5. Swelling Behaviour

Swelling test was performed by immersing a tea bag containing hydrogels in PBS pH 6.8, at room temperature for 8 hrs to attain a constant weight. The swollen samples were weighted after wiping out excess water from the surface of the tea bag. The % swelling index was determined through the following equation:

$$\% \text{ Swelling Index } = \frac{(Ws - Ws)}{(Wd)} X\ 100$$

Where, Ws and Wd are the weights of the hydrogel at swelling state and dry state, respectively. The % swelling index of each hydrogel was calculated three times, and the average was taken to note the final reading. [12].

2.6. Drug Content

Accurately weighed equivalent to 1g of hydrogel was taken in beaker and added 50 ml of PBS pH 6.8. This solution was mixed thoroughly and filtered using Whatman filter paper no.1. This filtered solution was suitably diluted and analyzed using U.V-Spectrophotometer at λ max of 225 nm.

2.7. Viscosity

The measurement of viscosity of the prepared hydrogel was done using Brookfield digital Viscometer (DS-53). The viscosity was measured using spindle no. 6 at 10 rpm and 25°C. The sufficient quantity of gel was filled in appropriate wide mouth container. The hydrogel was filled in the wide mouth container in such way that it should sufficiently allow to dip the spindle of the viscometer. Samples of the hydrogel were allowed to settle over 30 min at the constant temperature (25 $\pm 1^0$ C) before the measurements [10].

2.8. *In-vitro* diffusion study

An *In-vitro* release test of clindamycin hydrochloride from hydrogel formulations was performed in an apparatus, resembling a Franz diffusion cell. Briefly, a regenerated cellulose dialysis membrane (mean pore size 15,000 Da) was stretched over the open end of a glass tube containing the gel and made tight using a rubber band. The tube was immersed vertically in a beaker containing 100 ml of PBS pH 6.8 placed on a magnetic stirrer, set at 50 rpm. The test was performed at a room temperature of 25 °C. At predetermined time intervals for up to 8hrs, 5 ml aliquots of the dissolution medium were withdrawn for analysis and were replaced with an equal volume of medium to maintain a constant volume. The samples were filtered, and the absorbance was measured spectrophotometrically at 225 nm. The results were expressed as the mean values of three independent release experiments [4].

2.9. Development of optimized formulation

2.9.1. Analysis of formulation variables by design expert

This stage of Analysis is formed by entering the values of response variables into Design Expert software (Version 13.0.5.0). After entering the values into Design Expert, analysis of each variable was performed individually by fitting model till the ANOVA results are significant. The diagnostic and model graphs generated by software include perturbation, one factor, interaction graphs and 3D surface graphs.

The best fit model was selected based on comparison of several statistical parameters, including the coefficient of variation (CV), coefficient of determination and (adjusted R^2) coefficient of determination provided by Design Expert software. In addition, analysis of variance (ANOVA) was used to identify significant effects of factors on response regression co-efficient.

3. Results and discussion

3.1. Drug Excipients Compatibility Studies

3.1.1. FTIR Studies

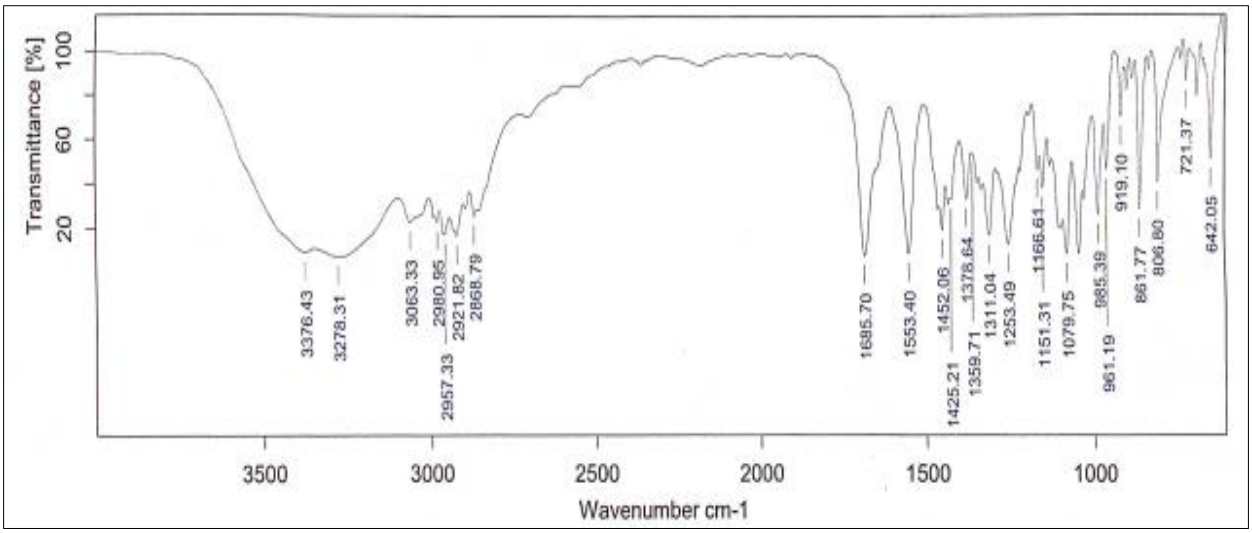

Figure 1 FTIR Spectrum of Clindamycin Hydrochloride

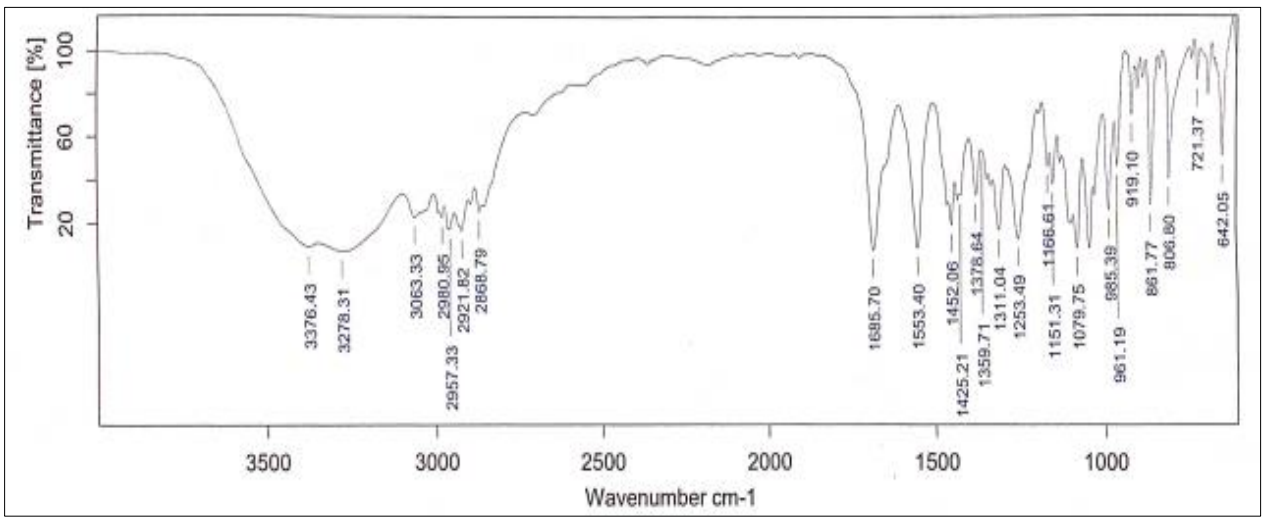

Figure 2 FTIR Spectrum of formulation (drug + excipients)

The characteristic peaks obtained from FTIR spectrum of pure drug and formulation are depicted in Fig no. 1 & 2 respectively. All the major drug characteristic peaks like C-H alkane bending, C-Cl alkyl halides stretching, C-N amine stretching, C=O carbonyl stretching are observed at 1378.66 cm^{-1}, 642.00 cm^{-1}, 1311.12 cm^{-1}, 1685.43 cm^{-1} in formulation, with in actual frequency ranges, indicating compatibility between drug and excipients.

3.1.2. DSC studies

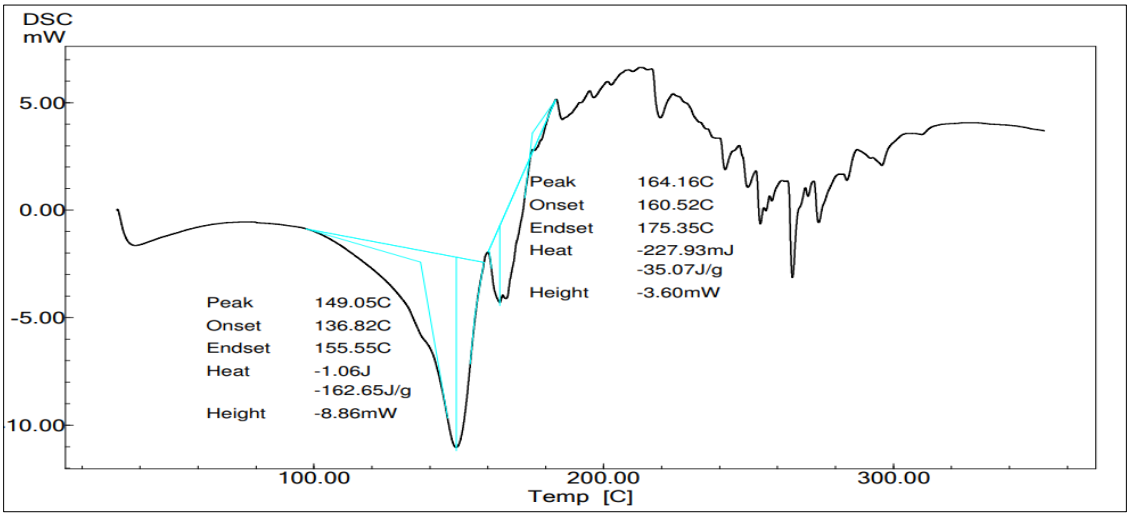

Figure 3 DSC thermogram of Clindamycin Hydrochloride

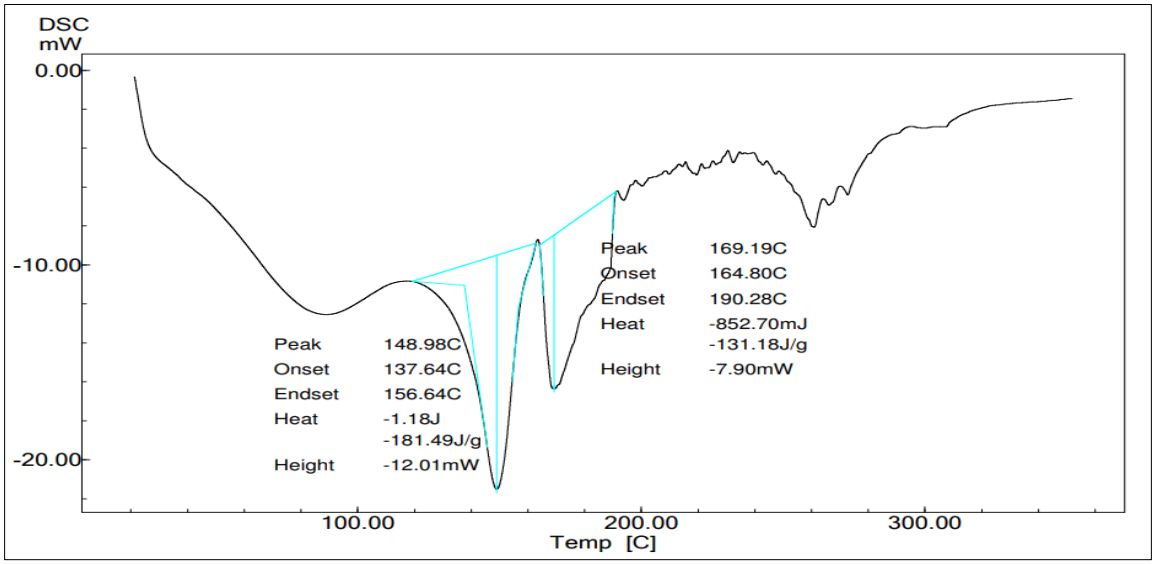

Figure 4 DSC thermogram of formulation (drug + excipient)

DSC thermogram of pure drug Clindamycin hydrochloride and formulation are shown in Fig. 3 & 4 respectively. The DSC studies start from a temperature of 0°C and extends up to 400°C. Pure drug as showed sharp endothermic peak at 149.05°C. The formulation DSC thermogram exhibited drug peak at 148.98°C, without significant shift indicating absence of incompatibility between drug and excipients.

3.1.3. Physical Characteristics

All the prepared Clindamycin hydrochloride hydrogel were inspected visually for their colour, homogenisity and grittiness, the observations are mentioned in table no.3. Hydrogels were pale yellow, amber and pale white coloured, depending on the use of different types of polymers. All the formulations showed good homogenisity with absence of lumps and grittiness.

3.1.4. pH measurement

The pH values are in the range from 6.40 to 7.07 which corresponds to the physiological pH of the buccal cavity and indicates that formulations can be applied without causing irritation during application.

Table 3 Evaluation results of Clindamycin Hydrochloride IPN Hydrogels

Formulation Code	Physical Characteristics			pH*
	Color	Homogenisity	Grittiness	
F1	Pale yellow	Homogenous	Absence of grittiness	6.40±0.01
F2	Pale white	Homogenous	Absence of grittiness	6.80±0.03
F3	Amber	Homogenous	Absence of grittiness	7.07±0.04
F4	Pale yellow	Homogenous	Absence of grittiness	6.78±0.02
F5	Pale white	Homogenous	Absence of grittiness	6.95±0.03
F6	Pale yellow	Homogenous	Absence of grittiness	6.80±0.05
F7	Pale white	Homogenous	Absence of grittiness	6.57±0.08
F8	Amber	Homogenous	Absence of grittiness	6.99±0.06
F9	Amber	Homogenous	Absence of grittiness	6.95±0.09

*n=3, pH values are Mean ± S.D

3.1.5. Spreadability

Spreadability measures the increase in surface area of the hydrogel under applied pressure. The ease of spreading the gel enables patient compliance and facilitates it's even application. The diameters of the spredability in circles ranged from 3.6 cm to 9.1 cm. It was found that hydrogels based on Sodium CMC had the highest spreadability and the ones based on Sodium Alginate had the lowest spreadability. The results revealed that as the concentration of PVA is increased, spredability of the gel decreased due to formation of rigid interlocking hydrogels.

3.1.6. Swelling behaviour

The % swelling index values for hydrogels ranged between 521% to 783%. The order of polymers is in relation to swelling is Sodium Alginate > Sodium CMC > Chitosan. The swellability increased with increase in PVA concentration. Sodium Alginate may act as a pore expander of gel network leading to increased water penetration and thus better swelling ability. This overall increase in water absorbency of Sodium Alginate could be attributed to the presence of carboxylate group on polymer, assists ionization may cause increased electrostatic repulsion leading to expansion of hydrogel network.

3.1.7. % Drug content

All the formulations exhibited fairly uniform drug content. The percentage of Clindamycin hydrochloride in the IPN hydrogel formulations ranged from 95.211% to 98.289% of the desired drug content, which indicates that the IPN hydrogel formulations were made by an adequate method of preparation with minimal or no drug loss. The % drug content increased with increase in PVA concentration. This can be attributed to formation of highly packed, rigid and compact IPN hydrogel structure which entraps more amount of drug with in polymeric network.

3.1.8. Viscosity

The viscosity of IPN hydrogels was obtained by using Brookfield digital viscometer was in the range of 8294 to 9637 cps. The order of polymers in relation to viscosity is Chitosan > Sodium Alginate > Sodium CMC. The viscosity increased with increase in PVA concentration. This may be due to formation of rigid polymeric structure, intense entanglement in the network as more functional sites is available for crosslinking reaction with polymer at higher concentration.

Table 4 Evaluation results of clindamycin hydrochloride IPN Hydrogels

Formulations	Spreadability* (cm)	% Swelling Index*	%Drug Content*	Viscosity* (cps)
F1	6.1±0.02	750±0.02	95.211±0.01	8768±0.02
F2	8.2±0.05	656±0.01	98.276±0.04	8513±0.04
F3	3.9±0.03	551±0.03	95.956±0.08	9548±0.02
F4	5.4±0.01	768±0.06	96.482±0.01	8852±0.03
F5	9.1±0.02	616±0.04	97.341±0.02	8294±0.04
F6	5.1±0.06	783±0.05	98.289±0.06	9084±0.05
F7	8.9±0.03	637±0.02	98.256±0.05	8453±0.08
F8	4.1±0.04	521±0.08	95.299±0.06	9416±0.06
F9	3.6±0.05	566±0.05	96.414±0.03	9637±0.03

*n=3, values are Mean ± S.D

3.1.9. In-Vitro Diffusion Studies

In-Vitro diffusion results of Clindamycin hydrochloride IPN hydrogels was represented in table no.6.7. and figure no.6.7. It was found that amount of drug diffused from all formulations ranged from 99.667 to 74.111% during 8 hrs study. Formulations F2 and F7 containing sodium alginate showed complete drug release in 5 hrs. The drug release from formulations F1 and F5 extended up to 6 hrs and for formulations F4 and F8 extended up to 7 hrs. Formulations F3, F6 and F9 have extended drug release up to 8 hrs. Amongst the prepared formulations maximum sustained release up to 8 hrs was found in Formulation F6 containing Sodium alginate as polymer and 5% PVA concentration. Formulations F3 and F9 containing chitosan as polymer showed incomplete drug release up to 8 hrs. Drug diffusion study results illustrated that drug release from IPN hydrogels was influenced by polymer type and concentration of PVA used. The release rate of drug was found to decrease drastically with increase in viscosity as proven by formulations F3 & F9. Increase in PVA concentration may have promoted intra and inter-molecular cross linkage resulting in formation of highly dense, viscous & low porous structure, thus hindering the movement of drug molecules and promoted controlled release up to 8 hrs.

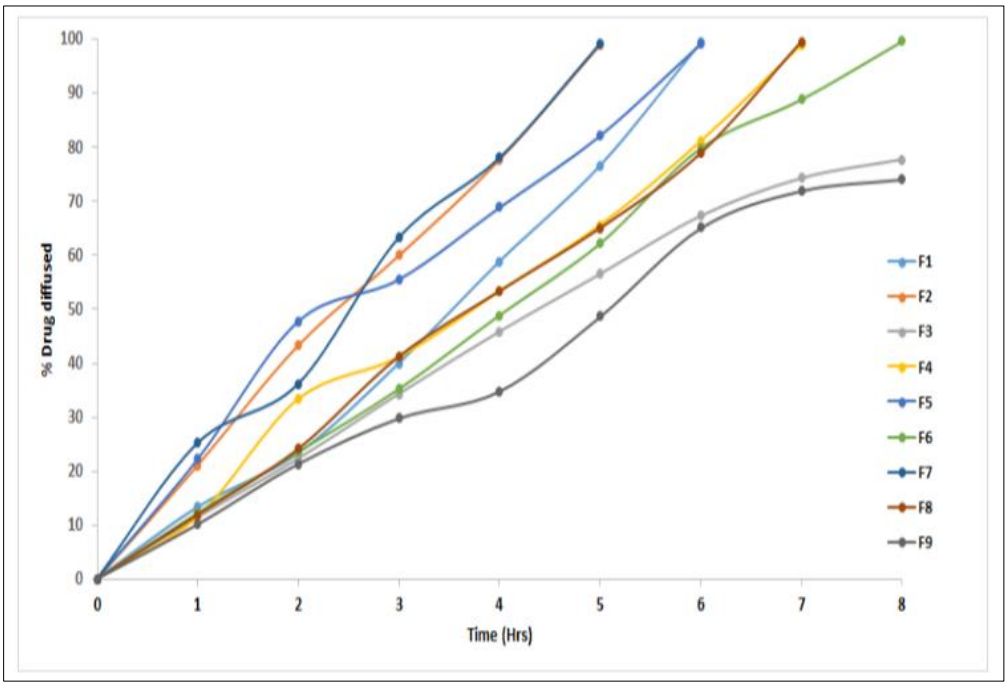

Figure 5 *In-vitro* diffusion plots of Clindamycin Hydrochloride IPN Hydrogels

3.2. Statistical analysis

Viscosity and % swelling index were selected as critical quality attributes. ANOVA with multiple regression analysis of the Response-1 (Viscosity), Response-2 (% swelling index), using Design Expert software were implemented for statistical analysis of 3^2 FFD formulations. The effects of these factors on the responses were displayed in 3D response surface plots as illustrated in Figure no.6 & 7. The estimated factors effects with p-values on the responses were presented in Table no.5 & 6.

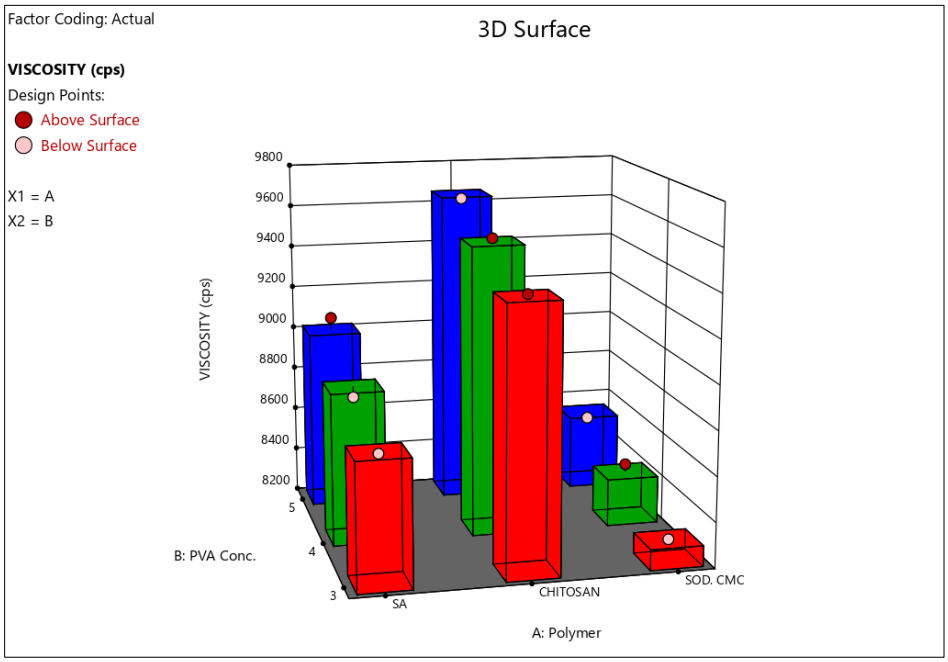

Figure 6 3D Surface of response – 1 (Viscosity)

The above 3D surface plots of response 1 (Viscosity) in relation to factor A (Polymer type), and factor B (PVA concentration). Fig no.6.8. illustrates that high viscosity of 9637 cps is attained by formulation containing chitosan as polymer and PVA 5% concentration, it is indicated as blue bar graph. Least viscosity of 8294 cps is attained by formulation containing sodium CMC as polymer and PVA 3% concentration, it is indicated as red bar graph.

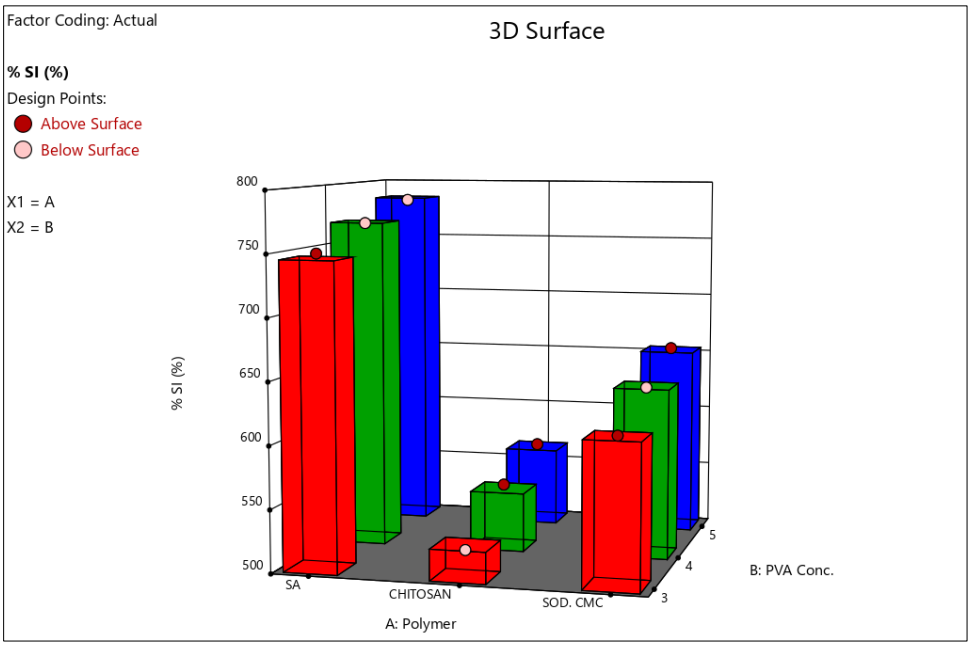

Figure 7 3D surface plots of response – 2 (% Swelling Index)

The above 3D surface plots of response 2 (% Swelling Index) in relation to factor A (Polymer type), and factor B (PVA concentration). Fig no.6.9. illustrates that high % Swelling Index of 9637 cps is attained by formulation containing sodium alginate as polymer and PVA 5% concentration, it is indicated as blue bar graph. Least % Swelling Index of 8294 cps is attained by formulation containing chitosan as polymer and PVA 3% concentration, it is indicated as red bar graph.

Table 5 ANOVA Table for response-1 (Viscosity)

S. No.	Source	F-value	p-value	
1	Model	227.05	< 0.0001	Significant
2	A-Polymer	432.12	< 0.0001	
3	B-PVA Conc	21.99	0.0069	
4	R^2	---	---	0.9956
5	Adequate Precision	---	---	39.3703

The Model F-value of 227.05 implies the model is significant. P-values less than 0.0500 indicate model terms are significant. In this case A & B both factors are significant model terms. Values greater than 0.1000 indicate model terms are not significant. Higher proximity of R2 value towards 1, highlights the model strength, R2 value for designed model system was recorded as 0.9956 confirming higher interdependence of model parameters. Adequate Precision ratio greater than 4 is desirable. Obtained ratio of 39.3703 indicates this model can be used to navigate the design space.

Table 6 ANOVA Table for response-2 (% Swelling Index)

S. No.	Source	F-value	p-value	
1	Model	1420.99	< 0.0001	Significant
2	A-Polymer	2754.85	< 0.0001	
3	B-PVA Conc	87.13	0.0005	
4	R^2	---	---	0.9993
5	Adequate Precision	---	---	95.2565

The Model F-value of 1420.99 implies the model is significant. P-values less than 0.0500 indicate model terms are significant. In this case A & B both factors are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. Higher proximity of R2 value towards 1, highlights the model strength, R2 value for designed model system was recorded as 0.9993 confirming the higher interdependence of the model parameters. Adequate Precision ratio greater than 4 is desirable. Obtained ratio of 95.2565 indicates this model can be used to navigate the design space.

3.3. Mathematical modelling of experimental data

Depending on the analysis of the observed values of the responses; a mathematical model for each response was generated and presented in the form of equations.

3.3.1. Quadratic equation for response-1 (Viscosity)

$$\text{Viscosity (R1)} = 8951.67 + 582.00A + 125.67B + 48.67AB$$

(A=Polymer type, B= PVA concentration)

The equation in terms of coded factors can be used to make predictions about the response for given levels of each factor. The coded equation is useful for identifying the relative impact of the factors by comparing the factor coefficients. In the above equation factor- A i.e. Polymer type has +ve sign. This indicates that all 3 types of polymers have increased viscosity in formulations. Factor-B is PVA concentration has a +ve sign. This indicates as PVA concentration increases viscosity increases. For interaction effect AB, the sign is +ve indicating a synergistic interactive effect on viscosity.

3.3.2. Quadratic equation for response-2 (% Swelling Index)

% Swelling Index (R2) = 649.78+ 117.22A +20.78B+4.22AB

(A=Polymer type, B= PVA concentration)

The equation in terms of coded factors can be used to make predictions about the response for given levels of each factor. The coded equation is useful for identifying the relative impact of the factors by comparing the factor coefficients. In the above equation factor- A i.e. Polymer type has +ve sign. This indicates that all 3 types of polymers have exhibited higher swelling Index in formulations. Factor-B is PVA concentration has a +ve sign. This indicates as PVA concentration increases swelling Index increases. For interaction effect AB, the sign is +ve indicating a synergistic interactive effect on swelling Index.

3.4. Optimization of clindamycin hydrochloride IPN Hydrogels:

The resultant experimental data of all prepared formulations F1 to F9 were used to develop an optimized clindamycin hydrochloride IPN Hydrogel with optimum viscosity and % Swelling Index by using 3^2 FFD in Design Expert software. The suggested optimized formulation has Sodium alginate as polymer (X1) and 5% PVA concentration (X2). To validate these values, the optimized clindamycin hydrochloride IPN Hydrogel formulation was prepared and evaluated.

Optimized IPN Hydrogel was pale yellow coloured, showed neutral pH (6.8), good homogenisity with absence of lumps and grittiness. The observed responses of this formulation were spreadability of 5.2 cm, % swelling index of 786.21%, Drug content of 99.156%, Viscosity of 9029.78 cps and gave 99.556% drug release for 8 hours as depicted in Fig.no.8. These observed values are in a close agreement with the predicted values as shown in table no.7. This proved the feasibility of the optimization procedure using FFD in developing a new clindamycin hydrochloride IPN Hydrogel formulation with controlled release.

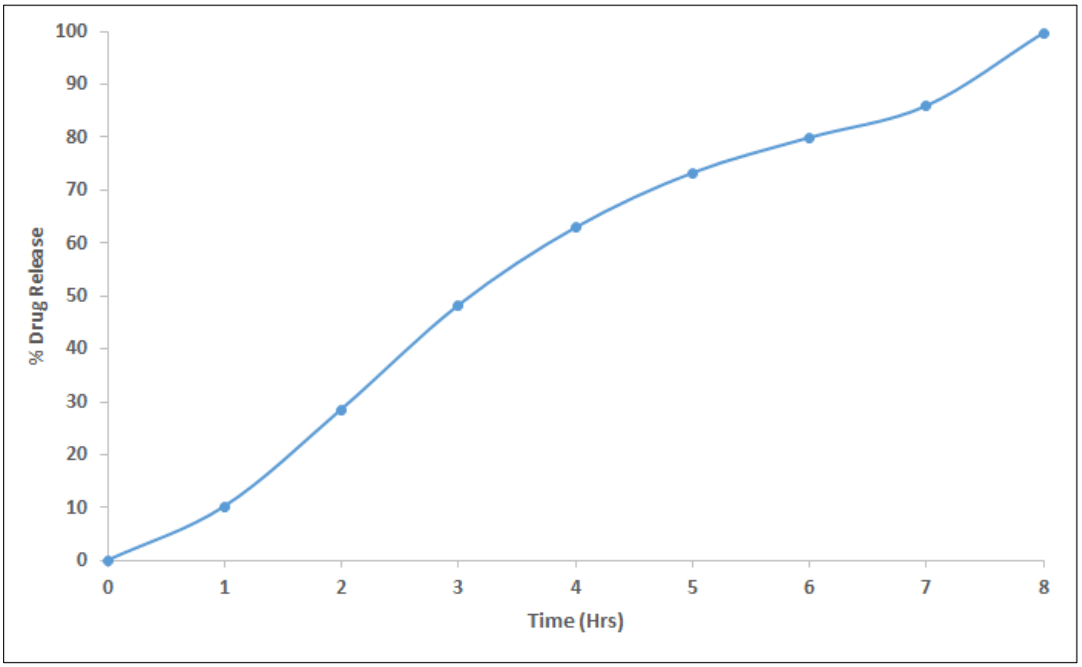

Figure 8 *In-vitro* diffusion plot of optimized Clindamycin Hydrochloride IPN Hydrogel

Table 7 Predicted Vs Observed Results

Parameters	Predicted Mean	Observed mean	S. D
Viscosity	9027.67 cps	9029.78 cps	1.491
% Swelling Index	785.556 %	786.21 %	0.462

4. Conclusion

In the present study, we have successfully developed an innovative, antibacterial and biocompatible Clindamycin hydrochloride IPN hydrogels. 9 formulations were prepared with different polymers Sodium alginate, Sodium CMC, Chitosan and with different PVA concentrations using 3^2 FFD for optimization. All prepared IPN hydrogels showed acceptable physical properties like colour, homogeneity, spreadability and pH value. Drug content, viscosity and % swelling index parameters showed satisfactory results and were found to be with in prescribed limits. The optimized formulation with sodium alginate as polymer and 5% PVA concentration was prepared and evaluated. It produced desired viscosity, % swelling index and controlled drug release up to 8 hrs. From the above results, it can be concluded that Clindamycin hydrochloride IPN hydrogels can be reliable antibiotic option in periodontal plaques therapy, with an excellent antimicrobial effect.

Compliance with ethical standards

Disclosure of conflict of interest

No Conflict of interest statement to be disclosed.

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