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Formulation and Physical Characterization of Bio-Degradable Chitosan-Poloxamer Gel Base for Local Drug Delivery

Dahake Prasanna T.[1]*, Baliga Sudhindra M.[2], Punse Triveni[3], Biyani Dinesh M.[3], Raut Neha[3], Umekar Milind J.[3]

[1] Ph.D. Student, Pharmacology and Pedodontics, (Interdisciplinary Sciences), Datta Meghe Institute of Medical Sciences (Deemed to be University), Sawangi (M), Wardha, Maharashtra, India.
Pin code – 442001.

[2] Department of Pedodontics and Preventive Dentistry, Sharad Pawar Dental College and Hospital, Datta Meghe Institute of Medical Sciences (Deemed to be University), Sawangi (M), Wardha, Maharashtra, India. Pin code – 442001.
[3] Department of Pharmaceutics, Smt. Kishoritai Bhoyar College of Pharmacy, Kampti, Nagpur, Maharashtra, India. Pin code – 441002

ABSTRACT

Objective: Thermo-modulated in-situ hydrogel (TSHG) are formulated routinely utilizing poloxamer for extended drug release. However physical properties of such formulations may have some flaws, which can be rectified using a combination of polymers with better physical properties such as chitosan. The purpose of the present study was to fabricate biodegradable chitosan-poloxamer-based in-situ drug delivery systems and assessment of their physical properties.

Methods: The present chitosan-poloxamer gel base was formulated using a two-stage method. Initially, chitosan gel was prepared by dissolving 1% w/w chitosan in glacial acetic acid. The poloxamer gel was prepared using "cold method". The final chitosan-poloxamer gel base was prepared by mixing equal amounts of both solutions and evaluated for physical and mechanical properties.

Result and Discussion: The DSC thermogram demonstrated no obvious interactions among ingredients or micellization temperature. The gelation temperature of the gel was between 27 and 33^{0}C. The pH was 7 with slight clarity. The viscosity of the gel ranged from 15.14 to 41.19 pa.s. The gel was syringable between 4-30^{0}C and biodegradable under physiological conditions. The mean particle size of the gel under SEM was found in the range of 300-554 nm.

Conclusion: After the evaluation of the formulation, it can be concluded that all the ingredients in the gel showed good compatibility with each other, which could form a stable and homogeneous gel with favorable mechanical and physical properties.

Keywords: chitosan, drug delivery system, hydrogels, poloxamer

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***Address for Correspondence:**

Dahake Prasanna T., Ph.D. Student, Pharmacology and Pedodontics, (Interdisciplinary Sciences), Datta Meghe Institute of Medical Sciences (Deemed to be University), Sawangi (M), Wardha, Maharashtra, India. Pin code – 442001.

INTRODUCTION

Inventions, besides technological advancements in biogenic natural or synthetic polymers, have shown few promising results using targeted drug delivery systems. Among the recently proposed materials, linear aliphatic polyesters, polyanhydrides, poly (orthoesters), proteins[1], polylactic acid, polyglycolic acid, and copolymers have extensive applications in local drug-delivery systems.[2] The embodiment of microparticulate drug molecules in biodegradable polymers is a suitable alternative to some complex medical and dental procedures. Numerous synthetic microspheres are biocompatible, degradable, and easily convertible to three-dimensional matrixes of variable structures.[2] The polysaccharides recommended for such purposes include chitin, chitosan, poloxamer, carboxymethyl cellulose, agar, and alginate which are naturally occurring cationic biopolymer.

Apart from its derivation from crustaceans' shells, and the result of the diacylation of chitin[3,4]; chitosan exhibits several physicochemical properties like blending[5], Schiff base formation[6], compatibility with other bioactive agents[7], superior biocompatibility, nontoxicity, hemostatic and antimicrobial properties as well. Chitosan is utilized in a wide variety of medical applications such as in situ gels for

topical application, wound dressing, tissue engineering, and health-care food. It can enhance fibroblast growth, macrophage activation, and hemostasis secondary to wound sealing properties.[7] Poloxamer 407 (P407), also termed as Pluronic F127, is a routinely utilized polymer to formulate thermo-modulated in-situ hydrogel (TSHG) for extended drug release.[8] It can harbor both hydrophilic and hydrophobic drug molecules.[9] Hence, such a polymer can be effectively utilized for stabilizing single-dose macromolecular formulations. P407 is a commercially available member of the poly(ethylene oxide-b-propylene oxide-b-ethylene oxide) triblock copolymer family.[10] It has been utilized as a controlled release vehicle for many macromolecular drugs with variable molecular weights. The methods to prepare drug-loaded TSHGs relatively is modest, utilizing the mixing of ingredients only and sidestepping farthest settings such as heating, the addition of organic solvents, or chemical crosslinking agents. There are experimental studies that have evaluated the effect of individual polymers as drug delivery systems.[11] Very few experimental studies have attempted to evaluate poloxamer-modified chitosan gels as biologically acceptable bases to improve retention and harmonize their controlled release domain via in-situ ionotropic gelation.

Consequently, the present study was purposed to formulate a biodegradable chitosan-poloxamer in-situ gel base system for local drug delivery.

MATERIALS AND METHODS

The present in vitro study was conducted at the Department of Pediatric and Preventive Dentistry in association with the Department of Pharmaceutics after gaining clearance from the Institutional Ethical Committee, letter no. DMIMS(DU)/IEC/2015-16/1744, Dated: 31/12/2015.

Materials used for the formulation of the gel base: All materials and chemicals were used in the present experiment were of analytical grade. The quantity and names of various suppliers are mentioned in Table 1.

Table 1: Ingredients used in the gel formulation

Ingredients	Quantity	Supplier
Chitosan	1% w/w	HiMedia Laboratories, Mumbai, India.
Poloxamer 407	15% w/w	Sigma-Aldrich Mumbai.
Carbopol 940	0.5 % w/w	Akhil Healthcare Private Limited, Gujarat, India.
Triethanolamine	2 drops v/v	Merck Specialities Pvt. Ltd, Mumbai.
Methyl paraben	0.15% w/w	Sigma Aldrich, Mumbai.
Hydrochloric acid	0.1% w/w	Merck Specialities Pvt. Ltd, Mumbai.
Propylene glycol	10% w/w	Merck Specialities Pvt. Ltd, Mumbai.
Polyethylene glycol-200	10% w/w	Merck Specialities Pvt. Ltd, Mumbai.
Isopropyl alcohol	10% w/w	Sigma-Aldrich, Mumbai.
Glacial acetic acid	2% w/w	Fisher Scientific India, Pvt. Ltd, Mumbai.

Preparation of chitosan-poloxamer-based gels:

A two-stage formulation was utilized to prepare the chitosan- poloxamer gel base. Initially, chitosan gel was prepared by following the method mentioned in a previously sited literature report.[12] Chitosan (1% w/w) was dissolved gradually in aqueous glacial acetic acid (2% w/v) continuously with slow stirring until complete dissolution. Carbopol 940 (0.5% w/w) was precisely measured and thawed slowly in double de-ionized distilled water through continuous magnetic stirrer mixing at 200 rpm. Both solutions were further blended with continuous stirring. Once the carbopol chitosan solution was prepared, PEG 200 (10% w/v), propylene glycol (10% w/v), isopropyl alcohol (10% w/v), and 2 drops of triethanolamine were added gradually[12] to achieve a clear solution. To prepare the poloxamer gel, the "cold method" was used as stated by Matthew et al. For this purpose, the precisely measured amount of polymer was poured into a flat bottom flask followed by the addition of distilled water and 0.9% NaCl to wet it completely with nonstop magnetic stirrer agitation at 100 rpm for 1 h at room temperature to give partially dissolved solutions. PEG (10%) was added to this solution with constant magnetic agitation at 100 rpm. This solution was further stored at 4ºC for 24 h until the entire polymer was completely dissolved to obtain a clear solution.[13] The refrigerated chitosan gel was utilized as a solvent for poloxamer dispersion. The final solution of chitosan-poloxamer was prepared by adding an equal amount of both solutions with a continuous stirring mode of 200 rpm for 1 h. At last, methylparaben was incorporated as a preservative. The gel pH was adjusted by adding 0.1% HCl (w/v) to 7.0. The solution thus derived was partially dissolved hence refrigerated again at 4^{0}C for 24 h until a clear solution was achieved. This procedure gave a clear tacky solution at the end of 4^{0}C.

Study of physical interaction between ingredients by differential scanning calorimetry (DSC) study: 3-5 mg of the gel formulation was loaded in an aluminum pan carefully for calorimetric analysis. The pan was carefully sealed by crimping the lid. An empty crimped aluminum pan was used for standard reference. DSC analysis of the gel was performed on a DSC-25 Mettler Toldo system equipped with a refrigerated cooling system and Star^e software apparatus (Mettler Toledo, DSC 823^e, Greifensee, Switzerland). The experimental and reference pans were heated at predetermined temperature modules in a nitrogen atmosphere at 10ºC/min, between 20 and 400^{0}C. Nitrogen was released at 20 ml/min flow rate at 2 bars. The scans

were documented, and heat flow-temperature plots were obtained.[14] The recorded thermogram was verified with individual excipient thermograms to analyze the compatibility and interaction of the excipients with each other.[15]

Physical appearance and pH: The formulations were assessed through visual examination for clarity in front of black and white backgrounds to categorize them as: very clear [+++], clear [++], and turbid [+].[16,17] Before estimating the pH of the gel formulation, the equipment was standardized in the range of 4-9 using standard buffer solutions. Later pH of the gel was estimated by plunging the glass electrode entirely into the gel.[16]

Measurement of gelation temperature and time: The gelation temperature of the gel was measured utilizing the process designated by Garala et al.[18] A volume of 3-4 mL gel was transported in a test tube and sealed with paraffin wax. The assembly was dipped in a water bath maintained at 4 °C. The bath temperature was increased incrementally by 2°C per minute for 25 mins (range 4^0C-54^0C). The gelation temperature of the formulation was noted at the point where the meniscus no longer moved by tilting the test tube by more than 90^0 angles.[8,19] To calculate the gelling time, 5ml sol maintained at 4^0C was added to a transparent vial with a magnetic stirrer and placed immediately in a water bath (37^0C). The stirring rate of the bar was set at 50 rpm. The time when the sol was converted into the gel and the magnetic bar lost movements due to loss of fluidity was considered as the gelation time.[8]

Measurement of viscosity: To determine the viscosity of the gel, 1ml of the sample was added to a coaxial cylinder viscometer (RST-CC Rheometer, Brookfield Engineering Labs, Inc. Middleboro, USA) that contained a cone with an angle of 1^0, inverted on a stainless-steel cylinder. The viscosity of the gel was estimated at room temperature (range 25-27^{0}C) with a constant shear rate of 6.5/s at a time interval of 4 s (range 4–40 s), in ascending and descending manner.[8]

Texture profile analysis (TPA): Texture profile analysis (TPA) was assessed in vitro utilizing a CT3 Texture Analyzer (with Texture-Pro CT Software, Brookfield Engineering Labs, Inc. Middleboro, USA) in TPA mode, as recently portrayed.[11,20] Sample (35 g) was added to 50-ml bottles, dodging air incorporation into the sample. The analytical probe (10 mm diameter) was twofold trampled into the formulation at a predetermined rate of 0.5 mm/s to a specified depth of 4 mm. A delay period of 15 s was permitted amid two compressions at room temperature (range 25-27 ^{0}C). From the subsequent force-time plots, the hardness, compressibility, adhesiveness, cohesiveness, stringiness, fracturability, and springiness were estimated.[20]

Measurement of Spreadability: The spreadability of the gel was estimated with a CT3 Texture Analyzer (with Texture-Pro CT Software, Brookfield Engineering Labs, Inc. Middleboro, USA) in TPA mode. For that, a set of matched male and female Perspex cones was utilized. All the procedures were followed as explained in the company manual to set up machine assembly precisely, before testing. A conical analytical probe sample holder (30 mm diameter, 60^0) was filled with the gel using a spatula, and its surface was leveled with a flat knife. The conical probe was enforced into the sample holder at a pretest speed of 1 mm/s. At a trigger force of 10 g, the probe pierced the gel at 2 mm/s test speed for 25 mm depth. After penetration at a specified depth, the probe was retracted from the sample at 2 mm/s posttest speed. The subsequent force-time plot thus derived, was the spreadability of the gel.[17]

In vitro mucoadhesive strength: The mucoadhesive quality of the gel formulation was assessed in vitro through the force essential to detach it from goat cheek mucosa[11], utilizing a CT3 Texture Analyzer (with Texture-Pro CT Software, Brookfield Engineering Labs, Inc. Middleboro, USA).[20] The gel was packed into a 30 mm diameter tube and centrifuged to remove the entrapped air from it, creating a smooth surface. A fresh piece of goat cheek mucosa was obtained and trimmed to dimensions of (20 × 20 mm). It was cleaned with a phosphate buffer solution (pH 6.8). The mucosa sheet was secured onto the tissue holder, with the orifice of the lid open to expose a small section of the mucosa in a 500 mL beaker with simulated saliva at 37 ± 0.5^{0}C through a thermostat. The tissue holder was kept in a beaker with stirring to equilibrate at this temperature for 15 mins. The gel was positioned on the mucosal surface through the holder orifice, followed by lowering of the probe assembly on the gel surface at 0.1 mm/s continuous speed and, of 7 g contact force. After 120 s of contact, the probe was uplifted with 1.0 mm/s speed. The area under the curve (AUC) was considered from the force-distance plot as a function of mucoadhesion.[21]

Measurement of Tensile strength: The mechanical properties of the gel formulation were estimated with a CT3 Texture Analyzer (with Texture-Pro CT Software, Brookfield Engineering Labs, Inc. Middleboro, USA), armed with 7 g of a load cell. The gel was positioned in a 30 mm tube after freeing from air bubbles and inadequacies, and a 10 mm analytical probe was twofold trampled into the gel at a predetermined rate of 0.5 mm/s to 4 mm depth at room temperature. A delay period of 15 s was allotted for two cycles. The subsequent force-time plots for tensile strength for percentage elongation were measured when the gel broke.[22]

Syringability study: The flowability of the gel was analyzed through their syringeability and injectability by utilizing needles like clinical situations or small lab animals like rats or mice.[23] Through the procedure of withdrawing 1ml of the refrigerated gel employing 25G (0.5mm×19mm) and 22G (0.65mm×25mm) needles, was utilized to evaluate the syringeability of the chitosan-poloxamer gel. Similarly, the gel injectability was estimated by regulating it through the same gauge needles affixed to a standard 1ml syringe with a Luer-Lok system (DISPOVAN, Faridabad, U.P., India).[24] The criteria followed were classified as (i) injectable suspension (a free-flowing suspension of fine suspended particles that passes easily through a 25G needle without noticeable resistance); (ii) injectable gel (a solution that passes through a 25G needle with some resistance and emerges as a stream of coagulated gel); (iii) administrable gels (a solution that is difficult to push through a 25G needle and emerges in the form of gel droplets rather than a stream); or (iv) semisolid gel (a gel solution that cannot be injected through a 25G needle but passes easily through a 22G needle, emerging as a thick gel).[24] The gel was stored at 4-8^{0}C before syringeability/injectability testing.

Biodegradability test: The biodegradability of the gel formulation was reviewed as per previously published literature.[25,26] Momentarily, 100 mg sample was transported and incubated into a glass tube comprising 10 mL of phosphate buffer solution (pH 7.0) followed by supplementation with 13 mg/L lysozyme solutions (like in human serum). The blends were kept at 37^{0}C with continuous agitation at 60 rpm for various time intervals (1, 2, 4, 6, 8, and 10 days). The lysozyme solution was

replenished every day. Toward the finish point of every degradation period, the sample was gathered from the medium, washed with deionized distilled water, and dried at 50^{0}C in a heated vacuum chamber until consistent weight. The test was repeated in triplicate, and the weight loss (%) was determined by the accompanying equation.

$$\text{Weight loss } \% = \frac{w_i - w_f}{w_f} \times 100$$

Wi is the initial weight of the sample and *Wf* is the final weight of the sample after degradation.

SEM Analysis of the gel: The gel formulation sample was kept at room temperature for 48 h in a vacuum desiccator to expel any leftover solvent. After mounting the gel sample formulation on the holding device and Au-Pd sputtering, its morphology was imaged at 15 keV under a scanning electron microscope Zeiss EVO-50XVP, (Carl Zeiss SMT, Inc., Peabody, MA, USA). The structural arrangements of the polymeric contents, their orientation, and average particle diameter were determined based on two distinctive SEM micrographs and in all 3 estimations utilizing an image analysis program.[24,25]

RESULTS AND DISCUSSION

Preparation of chitosan-poloxamer-based gels: This study aimed to develop a biodegradable chitosan-poloxamer gel base for sustained release using chitosan, carbopol as the primary ingredients. Whereas, P407 as a polymer additive to achieve high performance in situ thermo-reversible matrix gel. Previous reports have elaborated on the poloxamer gel's restricted ability to dissolve quickly in biological and functional environments.[27] Chitosan harbors very good mucoadhesive properties and augments the gel strength when added at a proper ratio. In the existing study, polymers were added as a second system based on the investigations and reports from previous literature.[28]

Study of physical interaction between ingredients DSC: DSC (Differential Scanning Calorimetry) was utilized in the pharmaceutical field to establish the identity and purity of solid-state systems. It is also used to detect the interaction of the ingredients used in a formulation, and hence, can be utilized for the selection of suitable and chemically compatible ingredients. The thermogram of the gel with all polymers and other ingredients is presented in Figure 1. Chitosan demonstrated a single, defined endothermic peak onset at 124.54°C, and the peak was obtained at 157.21^{0}c. While poloxamer demonstrated an endothermic peak at 53 °C, however, characteristic peaks of other excipients were unobserved in this figure. Secondly, there was no evidence of any new peak with any of the individual content, suggesting no evidence of excipients and polymer interactions. In this study, DSC was used to study the effects of chitosan and carbopol on the micellization of poloxamer through the critical micellization temperature of the gel. Both the major ingredients, chitosan, and poloxamer, showed typical and clear endothermic peaks, indicative of micellization. This peak is the result of P407 hydrophobic polypropylene oxide (PPO) block dehydration, through the passage of their micellization, as mentioned in previous reports.[29,30] The thermogram obtained from poloxamer shows lower values of T_{onset}, T_{peak}, and T_{endset} compared to chitosan. Carbopol and other additives did not disclose significant peaks or changes in the present thermogram. Similarly, the effects of chitosan and carbopol addition on the micellization of P407 were relatively tangible and did not cause any visible alteration in the critical micellization temperature of any ingredient.

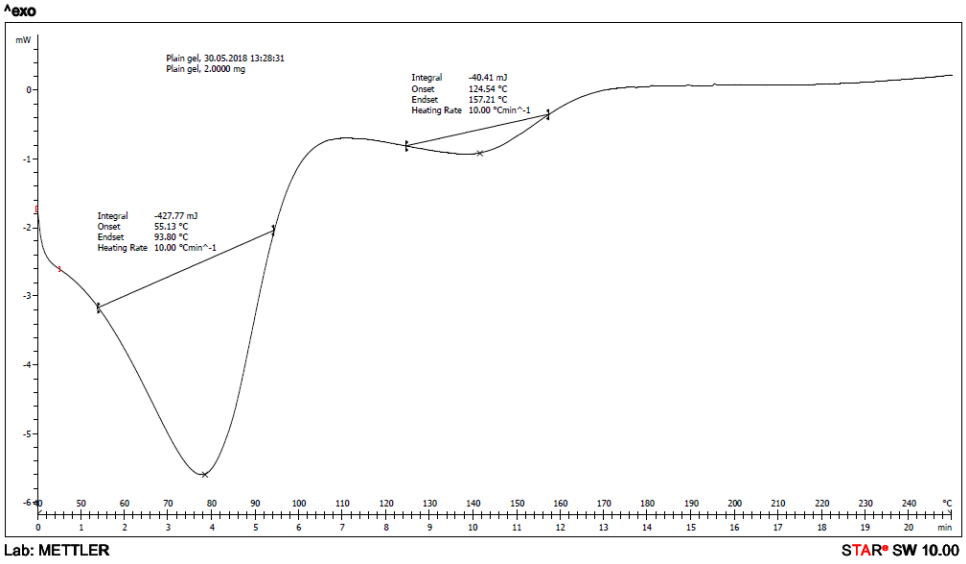


Figure 1: DSC thermogram of the gel formulation

Physical appearance and pH: The physical appearance of the gel was graded clear with a mean value of ++. The clarity of the gel formulation can be attributed to the non-presence of drug molecules at this phase of a formulation. Likewise, it was not very clear and transparent due to few excipients having different refractive indices, altering the gel clarity slightly. The mean pH of the present gel was found 7 (with a range of 6.9–7.1) [Table 2].

Table 2: Gelation temperature, time pH, and physical appearance of the gel

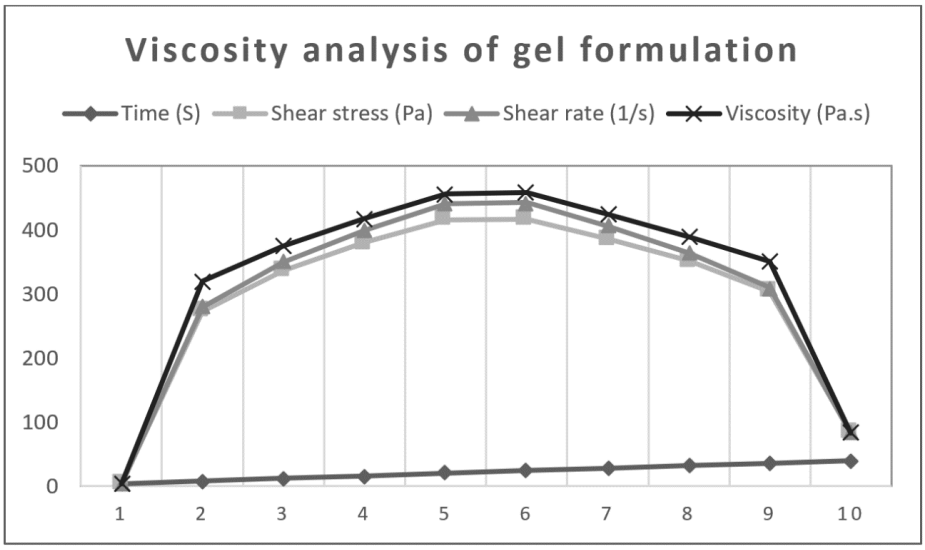
Sr. No.	Parameter	Readings
1.	Gelation temperature	33^{0}C
2.	Gelation time at 37^{0}C	25 secs
3.	pH	7
4.	Physical appearance	++

Measurement of gelation temperature and time: The gelation temperature of the gel was between 27 and 33^{0}C. The gelation time of the present formulation at 37^{0}C was found to be 25 s (Table 2). Certain external triggers alter the gelation temperature and time of such preparations, like a solvent exchange, ionic cross-linkage, pH change, or UV radiation. The internal triggers that alter gel behavior are the concentration of the ingredients, as mentioned in previous literature.[12]

Measurement of viscosity: In general, an essential factor for an in-situ gel is the gelation temperatures and viscosity whenever applied at the target site for a prolonged stay. Gelation temperature in the range of 25–37 °C is appropriate as the internal temperature ranges between 36-38^{0}C. Hence, the study was aimed to prepare an injectable/insertable thermo-reversible in-situ gel system with a gel-sol transition temperature range of 27-33^{0}C. As presented in Table 3 and Graph 1, the viscosity of the formulation decreased with an increase in shear stress and shear rate. The viscosity of the gel ranged from 15.14 to 41.19 pa.s.

Table 3: Viscosity analysis of the gel formulation at room temperature

Sr. No.	Time (s)	Shear stress (Pa)	Shear rate (1/s)	Viscosity (Pa.s)
1	4	00.00	0.00	0.00
2	8	264.29	6.47	40.82
3	12	324.61	12.97	25.03
4	16	363.63	19.46	18.69
5	20	395.01	25.94	15.23
1	24	392.68	25.94	15.14
2	28	357.71	19.45	18.39
3	32	319.24	12.97	24.62
4	36	267.07	06.49	41.19
5	40	42.98	0.000	00.00



Graph 1: Viscosity analysis of the gel formulation.

Texture profile analysis: Texture profile analysis of the present in-situ gel formulation at a peak load of 32 g showed hardness up to 3.97 mm, adhesiveness of 0.4mJ, stringiness of 1.97 mm, fracture deformation at 0.03 mm (7 g load), the cohesiveness of 0.98, and springiness of 3.08 mm (Table 4). These outcomes demonstrated the relevance of gels to target sites or adhesion capacity revealing the retainability of the gel there. Hardness values affirmed the immovability of the gel, while cohesiveness demonstrated better consistency. This will be helpful in cohesion resistance of the formulation in function.

Table 4: Texture profile analysis (TPA) test method of the gel

Test Type	**TPA (Texture Profile Analysis)**	
Pre-Test Speed	2.0 mm/s	
Test Speed	0.5 mm/s	
Post-Test Speed	0.5 mm/s	
Target Type	Distance – Gel	
Target Value	4 mm	
Trigger Force	7 g	
Peak load	32 g	
Deformation at peak load	1.49 mm	
Parameters	**Work cycle performed**	**Test results**
Hardness	Deformation	3.97 mm
	Recoverable deformation	1.06 mm
Adhesion	Adhesiveness	0.4 mJ
	Resilience	0.22
Stringiness	Length	1.97 mm
	Stringiness	0.1 mJ
Fracturability	Peak load	7 g
	Fracture deformation	0.03 mm
Cohesion	Cohesiveness	0.98
	Recoverable deformation	1.19 mm
	Recoverable work	0. 1 mJ
Springiness	Springiness	3.08 mm
	Springiness index	0.77

Measurement of Spreadability: Spreadability characterizes the scope of the gel to spread easily during application. Mucoadhesive polymers, by viscosity, demonstrate such properties. Gel spreadability is inversely proportional to its viscosity. Such properties are always desirable for an in-situ gel formulation to deliver active drugs for an ailment.[24]

In vitro mucoadhesive strength: Table 5 shows the mucoadhesion values of the experimental gel. The present gel demonstrated mucoadhesive strength to pick the goat cheek mucosa up to 3.61 mm. This mucoadhesive property is required for retention of the drug-containing gel in situ for better drug release with minimal wastage of the drugs. For the present formulation, mucoadhesion was seen up to 3.61 mm.

Table 5: Mucoadhesion, spreadability, tensile strength of the gel

Test Type	**Spreadability**	**Mucoadhesion**	**Tensile strength**
Pre-Test Speed	2.0 mm/s	2.0 mm/s	2.0 mm/s
Test Speed	0.5 mm/s	0.01 mm/s	0.5 mm/s
Post-Test Speed	0.5 mm/s	4.5 mm/s	0.5 mm/s
Target Type	Distance – Gel	Distance – Gel	Distance – Gel
Target Value	1.5 mm	4 mm	1.5 mm
Trigger Force	13 g	7 g	7 g
Peak load	19 g	19 g	25 g
Deformation at peak load	1.49 mm	3.61 mm	3.92 mm

Measurement of tensile strength: Table 5 reveals the tensile strength of the gel formulation. When a peak load of 25 g was applied to the gel at a speed of 0.5 mm/s, the gel could bear a tensile strength deformation of up to 3.92 mm. The internal factors modulating the tensile strength of a gel are the percentage distribution of individual composition, adhesion of unlike molecules, and cohesion of like molecules from the ingredients. However, some extrinsic inducements can alter the tensile strength as, the variabilities in force, temperature, and environment.[22]

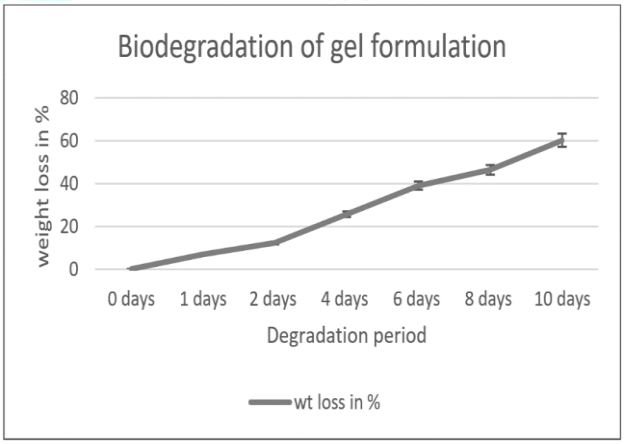
Syringability study: Table 6 reveals the syringeability of the present gel formulation in detail. When present chitosan-poloxamer gel formulation was refrigerated, it maintained its sol form, while at room temperature of 25-27^{0}C, it lost syringeability within 2-3 mins. At 25^{0}C, the gel could be easily withdrawn through a 25G and 22G needle. Between 25-27^{0}C, gel exhibited some resistance to the 25G needle but extruded easily from the 22G needle. Hence, the formulation can be considered as "easily injectable suspensions" in refrigerated conditions as a sol, suitable for parenteral application. After 27^{0}C, the particles started coagulating, requiring the application of little force to inject the solution through the 25G needle and can be termed as injectable gels. Between 27-30^{0}C, it was difficult to extrude the gel from the 25G needle but could be expressed easily through a 22G needle. Beyond 30^{0}C, it was difficult to extrude the gel through a 25G needle, but from a 22G needle requiring extra pressure and emerged as droplets. Beyond 33^{0}C gel did not extrude from the 22G needle also.

Table 6: Syringeability of the gel formulation at various temperatures

Temperature	Extrusion from 25 G needle	Extrusion from 22 G needle
< 25^{0}C	Easily - as sol	Easily - as sol
25 – 27	Some resistance - as gel	Easily - as sol
27 – 30	More resistance - as coagulated drop	Some resistance - as gel
30 – 33	Extreme resistance – no extrusion	More resistance as - coagulated drop
> 33	Extreme resistance – no extrusion	Extreme resistance – no extrusion

Biodegradability test: Graph 2 demonstrates the biodegradation profile of the gel formulation, due to the loss of poloxamer, chitosan, and other crosslinking agents due to high water solubility respectively, in the presence of lysozyme. The results revealed that the developed gel was biodegraded due to the liberation of reduced sugar from it.[26] The degradation rate for the experimental gel gradually increased from 1st to 10th day, ranging from 7% to more than 60% of the total volume. However, this property is favorable for the intended use of the gel in situ. The present observation can be justified by the presence of all the hydrophilic water-soluble ingredients, and their high biodegradability. The lysosomal adsorption by this gel is attributed to the presence of several functional hydrophilic NH_2, OH^-, and COOH groups in these agents.[25,31]

SEM Analysis of the gel: Figure 2 represents the SEM analysis of the gel formulation. It represents a three-dimensional interconnected meshwork of all the ingredients used, without phase separation. The structural arrangements of the polymeric contents look like a blend of polymeric molecules; their orientation is unidirectional, suggesting good adhesion and cohesion of the polymers at 1000X magnification. The average particle diameter was found to be between 300 and 554 nm.



Graph 2 – Biodegradation of the gel formulation in lysosome solution

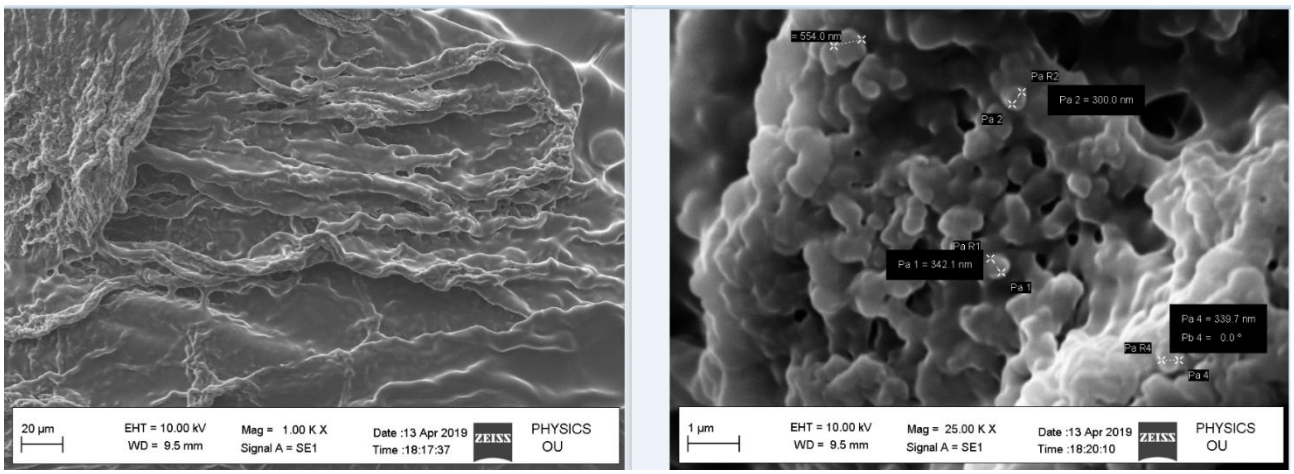


Figure 2: SEM analysis of the gel formulation

CONCLUSIONS

After the evaluation of the formulation, it can be concluded that all the ingredients in the gel showed good compatibility with each other, which could form a stable and homogeneous gel with favorable mechanical and physical properties. This biodegradable gel base can be used as a carrier for various drug moieties with prolonged residence time. However, further in vitro and in vivo studies are recommended in the future for bringing this formulation in practical use.

CONFLICT OF INTEREST: Declared none.

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