RESEARCH ARTICLE

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DEVELOPMENT AND EVALUATION OF CEFPODOXIME PROXETIL GELLAN GUM BASED IN SITU GEL

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Abstract: Among oral dosage form, liquid dosage forms are more prone to low bioavailability because of their quick transit from the gastrointestinal tract. Sustained release liquid formulation with efficacy can be produced using approach of In situ gel. The purpose of the present work was to develop oral in situ gelling system using Gellan gum for in situ gelation of Cefpodoxime proxetill. Optimized formulations were prepared having desirability and evaluated for various parameter. The developed formulation was stable, non-irritant and provided sustained release over 8-hour period and it is a viable alternative to conventional dosage form.

Keywords: Cefpodoxime proxetil (CDP), Gellan Gum, In-situ Gel formation, Sustain release.

INTRODUCTION

Oral route is the most convenient and extensively used route for drug administration having high patient acceptability; primarily due to ease of administration.[1] High dosing frequency of drug with shorter half life can be avoided by sustained release formulation.[2] The drug profile data, such as absorption properties, half life determines the dose of drug in formulation.[3] Many attempts have been made to develop sustained release preparations with extended clinical effects and reduced dosing frequency. The present investigation concerns the development of In situ gelling system using Gellan gum[4] which after oral administration are designed to prolong release of drug, Increase the drug bioavailability, and diminish the side effects of irritating drugs.

As conventional drug delivery systems do not remain in the stomach for prolonged periods, they are unable to deliver the CDP to the site of infection in effective concentrations. Therefore, it is necessary to design drug delivery systems that not only alleviate the shortcomings of conventional delivery vehicles but also deliver (CDP) to the infected cell lines. Some researchers had prepared and reported new (CDP) formulations, such as floating tablets[5], mucoadhesive tablets[6], and mucoadhesive microspheres[7], which were able to reside in stomach for an extended period of time in stomach.

MATERIALS AND METHODS

Cefpodoxime Proxetil was obtained as a gift sample from Cadilla Pharmaceuticals Pvt. Ltd. All other Chemicals were used of analytical grade.

Methods

Gellan gum solutions with different concentrations were prepared by adding gellan gum to ultrapure water containing Sodium citrate and heating to 80 ^{o}C.

To above solutions different concentration of Calcium chloride was added while stirring upon cooling to 40 ^{o}C. In another beaker Cefpodoxime proxetil and propyl paraben were dissolved in Water (with the help of Tween 80). Mix it with above solution. Prepared solutions were finally

stored in amber colored bottles for further use.

Preliminary batches for selection of polymer and $CaCl_2$ Ratio

Preliminary batches were prepared using Gallan Gum and Calcium Chloride. Gels of gellan gum were prepared with trial and error methods and better consistency was achieved by adding $CaCl_2$.

Physical appearance and pH

All the prepared in situ solutions of CDP were checked for their clarity and the type of the solutions. The pH of each of the solution of Gellan gum based in situ solutions of CDP was measured using a calibrated digital pH meter at room temperature in triplicate.

Determination of viscosity

Viscosity of the samples was determined using a Brookfield digital viscometer at ambient condition. Increasing the concentration of a Gellan gum generally gives rise to increasing viscosity (i.e. thickening), and also as molecular weight of a solute increases viscosity.

***In vitro* gelling capacity**

The formulations for their *in vitro* gelling capacity were by visual method. The *in vitro* gelling capacity of prepared formulations was measured by placing five ml of the gelation solution (0.1N HCl, pH 1.2) in a 15 ml borosilicate glass test tube and maintained at 37±1 ºC temperature. One ml of formulation solution was added with the help of pipette in gelation solution. As the solution comes in contact with gelation solution, it was immediately converted into stiff gel like structure. The gelling capacity of solution was evaluated on the basis of time period for which formed gel remains as such. The *in-vitro* gelling capacity was graded in categories on the basis of gelation time and time period for which formed gel remains.[8]

Determination of drug content

The amount of CDP in each unit dosage form sample was determined by U.V. spectroscopy after sufficient dilution. The UV absorbance of the sample was determined at a wavelength of 263 nm. The drug content for batches was measured in triplicate and the average values are recorded.

Compatibility study

The FT-IR spectrum of the obtained sample of the drug was compared with the standard FT-IR spectra of the pure drug. FT-IR

spectroscopy was carried out to check the compatibility between drug and polymer.

***In vitro* Drug release study**

Apparatus: USP Dissolution Testing Apparatus-II

Dissolution medium: Dissolve 56.5 gm of glycine and 42.6 gm of sodium citrate in 500 ml of water in 1000ml flask.cautiously add with swirling,14.2 ml of Hydrochoric acid and allow to cool. dilute with water and mix .Transfer 50 ml of this stock solution into flask and dilute with water to 900 ml to obtain the solution having the pH of 1.2 ± 0.2

Volume: 900ml

Temperature: 37±0.5 ^{0}C

Speed: 75 RPM

RESULTS AND DISCUSSION

Appearance and pH

Clarity of all the formulations was found to be satisfactory. The pH of the formulations was found to be satisfactory as depicted in table 2 and was in the range of 6.5 -7.5. The formulations were liquid at room temperature and at the pH formulated.

***In vitro* Gelation Studies[9]**

Table 3 shows the gelling capacity of all formulations and is depicted as + (gels after few minutes and dissolves rapidly), ++ (gelation immediate, remains for few hours only) and +++ (gelation immediate, remains for extended period).

Drug content

Figure 1 and Table 3 **s**hows the percent drug content for formulations. The drug content was found to be in acceptable range for all the formulations indicating uniform distribution of drug.

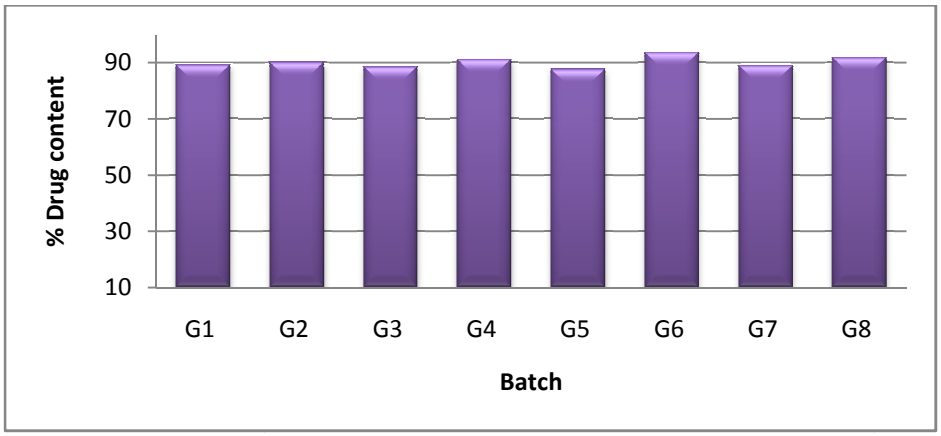

Figure 1. % drug content analysis

Viscosity[11]

The formulation should have an optimum viscosity that will allow ease of administration as a liquid (drops), which would undergo a rapid sol-to-gel transition. Table 3 also shows the viscosity (cp) of formulations from G1 to G8. The viscosity increased in proportion with gelling agent. This may be attributed to the higher viscosity of Gellan gum.

Compatibility study

The IR spectrum of the pure Cefpodoxime proxetil sample was recorded by FTIR spectrometer. Preformulation studies were carried out to study the compatibility of pure drug CDP with the polymer Gellan gum and other excipients. The individual IR spectra of the pure drug and combination with polymers are shown in the Figure 2-3.

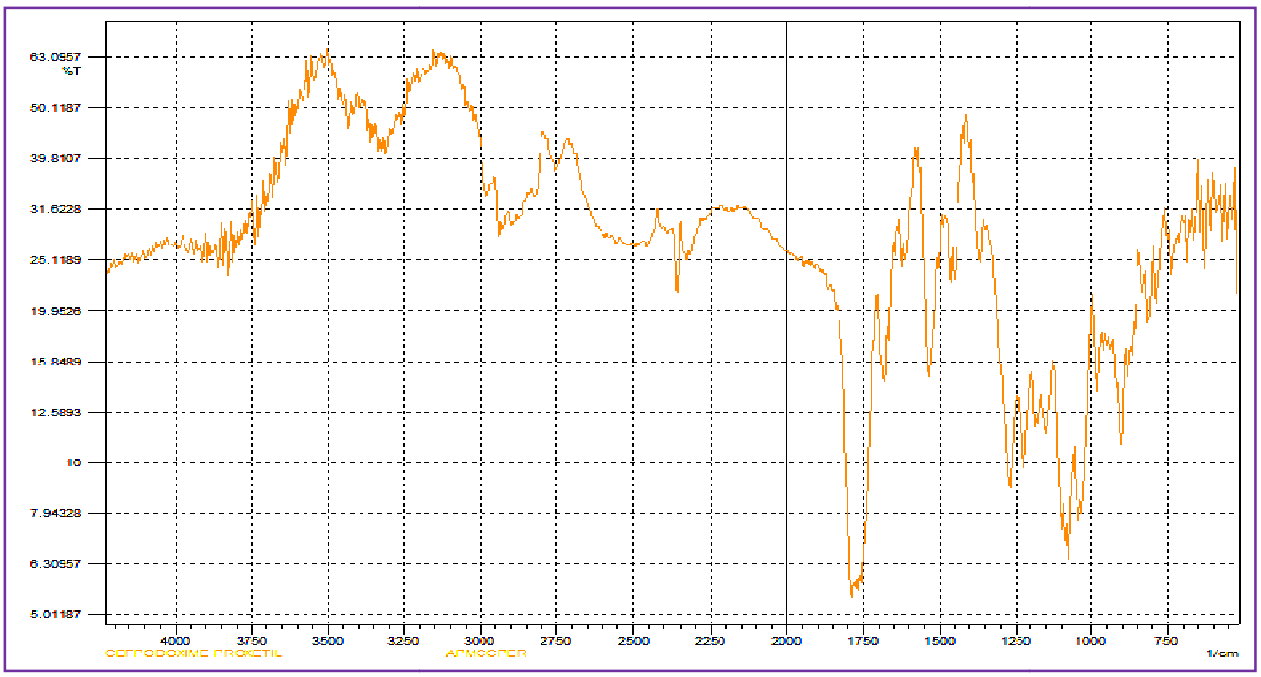

Figure 2. FTIR of Cefpodoxime Proxetil

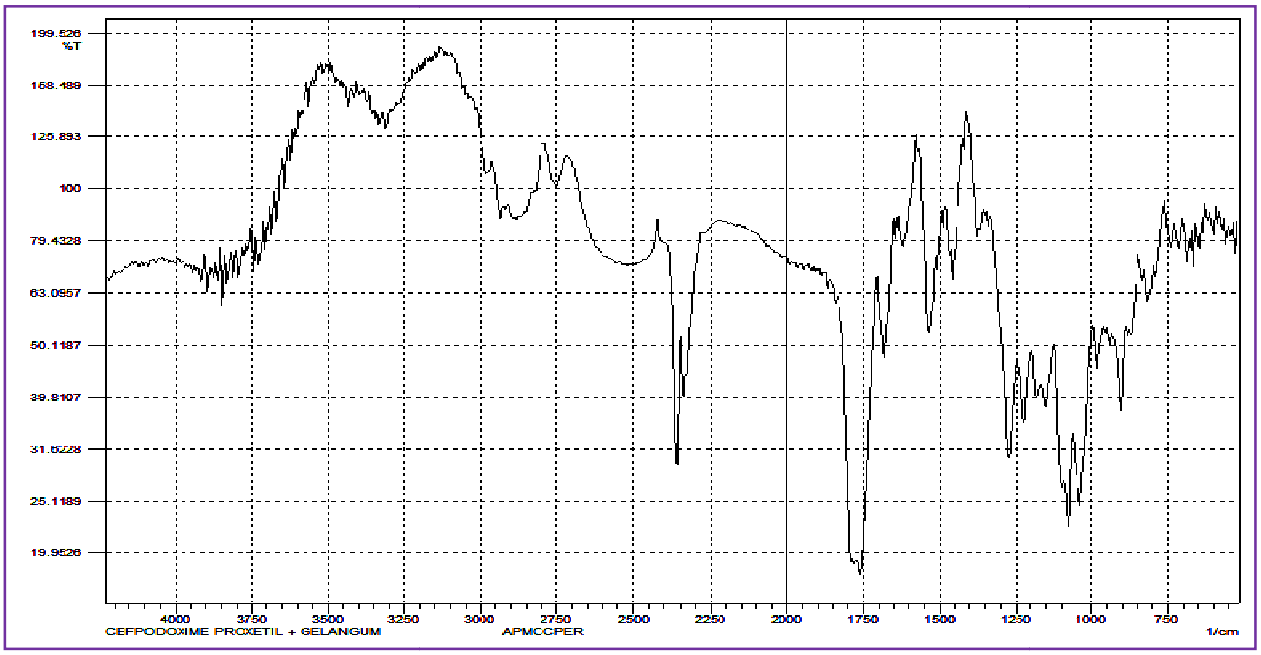

Figure 3. FTIR of CDP and Gellan Gum

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***In Vitro* drug release study**[12]

Optimization of batch was done by observing the evaluating physical parameter and *In vitro* drug release study of preliminary batches.

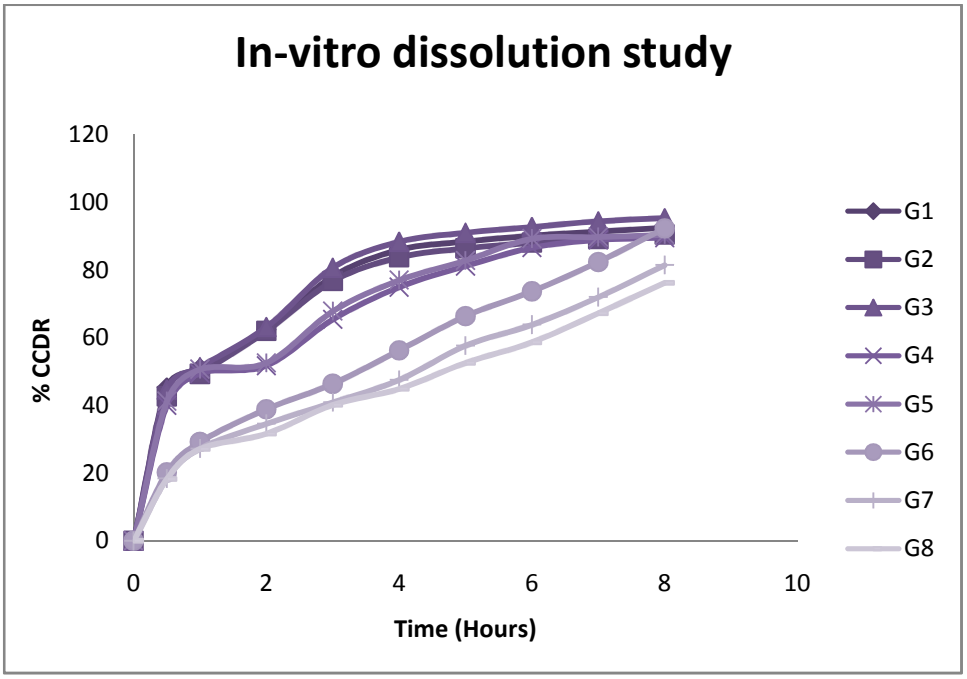

Figure 4. *In vitro* drug release study of gellan gum based in situ gelling system

CONCLUSION

Gellan gum based in situ gelling system undergoes sol-gel transition under influence of acidic pH in presence of calcium ion. After observing all the physical parameter and In-vitro drug release study the G6 formulation is optimized formulation. Sodium citrate helps maintain fluidity before administration by complexation of calcium chloride which becomes free at acidic pH. Very little concentration of divalent cation was required for formulation.

Table 1.

Formulation of various batches of in situ gel.

Ingredients	Formulations batch Code							
	G1	G2	G3	G4	G5	G6	G7	G8
Cefpodoxime proxetil(mg)	150	150	150	150	150	150	150	150
Gellan Gum (%)	0.1	0.25	0.25	0.25	0.25	0.5	1	1.5
Sodium Citrate (%)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Calcium chloride (%)	0.01	0.01	0.02	0.03	0.04	0.02	0.02	0.02
Sodium propyl paraben (%)	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Menthol (%)	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Sodium Saccharin (%)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

Table 2.

Physical evaluation Parameter of In situ gel

Batch	Gellan Gum	Calcium Chloride (%)	Gel Characteristic	Physical appearance
G1	0.1	0.01	No gel formation	Very Low Viscosity
G2	0.25	0.01	Very weak gel formation	Low Viscosity
G3	0.25	0.02	weak gel formation	Low Viscosity
G4	0.25	0.03	weak gel formation	Low Viscosity
G5	0.25	0.04	Outside gel	Very High Viscosity
G6	0.5	0.02	Stiff gel formation	Medium Viscosity
G7	1	0.02	Stiff gel formation	Medium Viscosity
G8	1.5	0.02	Stiff gel formation	Very High Viscosity

Table 3.

% Drug content, Viscosity and *In vitro* gelation Study parameter

Batch	pH	% Drug Content	Viscosity (cp)	*In vitro* gelation
G1	7.0 ± 0.06	89.25 ±0.16	124	+
G2	7.1 ± 0.06	90.12 ± 0.12	138	+
G3	6.9 ± 0.12	88.54 ± 0.08	149	++
G4	7.2 ± 0.06	91.21 ± 0.012	228	+
G5	6.9 ± 0.06	87.65 ± 0.14	256	+
G6	7.1 ± 0.08	93.65 ± 0.14	347	+++
G7	7.1 ± 0.06	88.98 ±0.12	215	+
G8	7.2 ± 0.10	91.85 ± 0.10	296	++

(+: poor, ++: good, +++: excellent)

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