ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 15, Issue 1, 2022

Online - 2455-3891
Print - 0974-2441

Original Article

DEVELOPMENT OF CIPROFLOXACIN LOADED THROAT PAINT FOR THE TREATMENT OF STREP THROAT INFECTION

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Received: 06 November 2021, Revised and Accepted: 12 December 2021

ABSTRACT

Objective: This study is to enhance the solubility and sustained release of ciprofloxacin (CPX) drug by amplifying the adhesive capability of formulation by forming throat paint for the Streptococcal pharyngitis, a sore throat infection.

Methods: Solid dispersion was prepared by solvent evaporation technique, in which three different ratios of Polyethylene glycol-6000 (PEG-6000) were selected, and the best ratio of solid dispersion was selected after characterization including Scanning electron microscopy (SEM) and Differential scanning calorimetry (DSC) with evaluation parameters including % yield, drug content, and drug solubility. In the case of throat paint, out of six different formulations, the best formulation was selected through viscosity, *in vitro* mucoadhesion, *in situ* release study, and spreadability parameters.

Results: The DSC and SEM data proved that solid dispersion has a different moiety than its ingredients but it is quite a stable form. Formulation MD-2 was selected as the best formulation which able to increase the solubility of the drug by more than 3.5 folds, at the same time it shows the highest rate of drug dissolution of 13.951 µg/ml with % yield (97.199±0.167%) and drug content (96.425%). Throat paint was formed by fusion and trituration process and out of all six formulations F3 was selected as the best formulation on the basis of Viscosity (11932 Centi poise), Spreadability (17.621), Mucoadhesion (3937.481 dyne/cm^2), and drug release (90.336±0.6%).

Conclusion: Solid dispersion was successfully prepared with 3.5 times of solubility enhancement capability in comparison with pure CPX drug. The throat paint releases the drug (≥3 h) in a sustained manner with high mucoadhesive force.

Keywords: Strep throat infection, Ciprofloxacin, Solvent evaporation technique, Polyethylene glycol 6000, Solid dispersion.

 DOI: http://dx.doi.org/10.22159/ajpcr.2022v15i1.42591 Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Whenever we deal with a disease that occurs in the buccal area, local drug delivery becomes our first choice, as it is easy to use and shows its benefits directly over the target. There are many diseases including bacterial and fungal infections for which some marketed preparation like creams and gels are available [1]. In the new era of research across the globe, various novel concepts of drug delivery such as *in situ* gels, modified films, and paints, etc. have been developed to overcome the problems related to different barriers present in the mouth These formulation-based approaches have been considered to be sufficient enough in achieving the maximum drug concentration at a specific site of the throat, buccal and sublingual reason for the local drug delivery. The main motive behind the development of the paint (highly viscous substance) is to improve the drug delivery of drugs and thereby improve the therapeutic efficacy [2].

It's a kind of inflammation of the pharynx, which is just present at the back of the throat. This kind of inflammation shows the symptom of a sore throat with a cough but as we know that sore throat is taken place because of viruses and only 5–10% of sore throat (pharyngitis) takes place because of bacterial infection, which is caused by *Streptococcus* bacteria, and disease caused by bacterial throat infection is called strep throat. This kind of disease is commonly found in school-going children (3–15 year) but it may occur to anyone, this disease mainly includes sore throat with high efficiency of pain with difficulty in swallowing, mild fever, and swollen neck glands. Sometimes patients may be found with nausea and headache [3].

Oral bioavailability generally depends on the drug solubility or dissolution in water or solvent, therefore efforts make to increase the solubility for which many methods are available like salt formation, micronization, and addition of solvent or surface-active agents [4]. However, one of the methods which is quite easy to prepare and much effective for increasing the solubility known as a solid dispersion. Solid dispersion is one that is formed in between drug and hydrophilic carriers and is able to enhance the dissolution rate when comes in contact with water because of change in surface area [5]. Solid dispersion may contain a mixture of polymers and surfactants to further enhance the solubility rate of the drug. In the current project, PEG-6000 is used as a hydrophilic carrier to enhance the solubility of a drug by forming solid dispersion. These types of dispersions have quite a high solubility when they make water contact. Solid dispersion can be prepared by different methods such as solvent evaporation technique, melting method and co-evaporation technique [6-8].

The binary systems were prepared by a solvent evaporation method because this is one of the techniques with easy to use, cost-effective, and at the same time able to enhance the solubility of poorly water-soluble drugs up to 11 folds [7]. Here, polymer and drug both are dissolving in an organic solvent which evaporates and left behind a solid mass, which is further crushed and used as a complex, this complex is used to enhance the dissolution rate and also protect the drug from decomposition. In this project, PEG-6000 is used as a hydrophilic carrier for drug encapsulation and ethanol is used as an organic solvent [9].

MATERIALS AND METHODS

Materials

Ciprofloxacin (CPX) drug were purchased from Balaji Enterprise, thakordwar society, B/H spinning mill, Varchha road, SURAT-395011(GUJRAT). Polyethylene glycol-6000 (PEG-6000) and HydroxyPropyl Methylcellulose (HPMC) were purchased from CDH laboratory reagent, central drug house (p) Ltd. New Delhi-110002 and other excipients like Ethyl Cellulose (EC) and Chitosan were purchased from S.D fine Chem Limited, Narol, Ahmedabad, Gujarat, 380405.

Methods

Preparation of complex

Solvent evaporation method

The binary system of drug CPX (100 mg) with PEG6000 was prepared at three different weight ratios of 1:0.5, 1:1, and 1:2, shown in Table 1. PEG-6000 and the drug were mixed together in ethanol which is used as a common organic solvent with continuous stirring. At 50°C, solvent is fully evaporated and left behind a solid mass which is further crushed in a mortar pestle and passes through the sieve of 100 mesh size. The binary system was named MD-0.5, MD-1, and MD-2 [6,9].

Characterization of complex

Scanning electron microscopy (SEM)

Scanning electron micrographs of pure drug and drug-containing complex were determined by using the scanning electron microscopic technique (JEOL 5400, Jeol, Tokyo, Japan). Here, on one hand, took a small amount of drug and on another hand took complex preparation and then dispersed one by one over carbon tab and then finally drug and complex coated with a layer of gold by sputter coater unit (VG Microtech, West Sussex, UK). This helps to give a clear image of both the samples to test [10].

Differential scanning calorimetry (DSC)

DSC (DSC Q20 V24.4 Build 116, USIC, K.U. Dharwad, India) studies were performed by conducted with placing, measured weighed samples in the sealed pans of aluminum with the help of liquid nitrogen gas used as a coolant. Then, finally samples were scanned through a temperature range of 40–400°C, by maintaining the 10°C/min of rate. DSC thermograms of pure CPX drug, PEG6000 and complex of both formed were determined [11].

Evaluation of complex

Solid dispersion solubility

Solubility measurements of CPX were performed according to the given method [12]. Here in this method, a Solid dispersion weight of 100 mg of CPX was shaken in a conical flask with 10 ml distilled water by covering it by stopper in an orbital shaker for a total time period of 24 h at room temperature. Finally, the solution was filtered through the Whatman filter paper type No.1, and then the filtered solution was diluted properly with a given amount of distilled water. The diluted solution was then analyzed for the presence of CPX on a ultraviolet (UV) spectrophotometer at 274 nm.

Determination of percent yield

About 150, 200, 300 mg of solid dispersion of complex were weighed and the percent yield of the prepared different concentrations of the complex was calculated using the formula given below. After then crushed them properly and dried for 6 h. with the help of a desiccator and pass through sieve No. 120 for fully uniform size distribution, then with the help of the formula given below, find out the expression [13].

Percent yield = (Prepared solid dispersion total weight/weight of drug at individual level + weight of carriers at individual level) × 100

Table 1: The composition of the prepared binary systems of ciprofloxacin and PEG-6000

S. No.	Formulation code	Drug: PEG ratio	Method used
1.	MD-0.5	1:0.5	Solvent evaporation method
2.	MD-1	1:1	Solvent evaporation method
3.	MD-2	1:2	Solvent evaporation method

Determination of drug content

CPX content in solid dispersions was estimated. Accurately weight samples (10 mg) of the mixture were dissolved in 10 ml of dichloromethane and volume was made up to 10 ml with double distilled water. This solution was further suitably diluted with double distilled water if needed and the absorbance was measured at 274 nm using a UV/visible spectrophotometer [14].

In vitro dissolution rate study

The *in vitro* dissolution profile of pure CPX, formulations of solid dispersions of CPX were studied using USP XXIII dissolution rate test apparatus TYPE II employing paddle method. 900 ml of double distilled water was used as dissolution medium maintained at 37±0.5°C and stirred at 50 rpm [15,16]. The solid dispersion containing 100 mg of CPX was taken in a muslin cloth and tied with a rotating paddle kept in a basket of dissolution apparatus. Five milliliters of the sample were withdrawn at specific time intervals and the CPX content was assayed at 274 nm using UV/visible spectrophotometer. Cumulative percent CPX release versus time plots was plotted.

Preparation of solid dispersion loaded throat paint

The throat paint was prepared by fusion and trituration process in which polymers like HPMC, EC, and Chitosan were used in two different types of concentration with ethanol and glycerine mixed together and kept for 24 h for hydration. Then, the drug was dissolved in 20 ml of ethanol and added to the above prepared hydrated base then volume was made by the glycerol and the mixture was stirred for 30 min at 50 rpm to get a homogenous dispersion of the drug, CPX 1% [17]. The composition of all ingredients used in throat paint preparation is shown in Table 2.

Evaluation of throat paint

Clarity and pH

We can visually check the clarity of the throat paint by a place down the formulation behind a black and white background, which shows the presence of different small particles, and also find the pH of the developed throat paint formulations, using a Digital pH meter belong to the model No. of 111 E (HICON®, New Delhi, India) [18].

Measurement of viscosity

Throat paint viscosity was measured using cone and plate geometry viscometer with 40 number of spindle (Brookfield, Massachusetts, USA). While measuring angular velocity up to 1000 rpm of spindle we can easily measure the viscosity of throat paint while maintaining the temperature of 37°C [19]. Mean values were calculated after finding the three back-to-back values.

Spreadability

The spreadability was determined as the excess amount of formulation (throat paint) was added in between two glass slides and compressed by keeping them under 1000 g weight over it for up to 10 min. Now

Table 2: Composition of the throat paint

S. No.	Ingredients	F1	F2	F3	F4	F5	F6
1.	Ciprofloxacin (gm)	1	1	1	1	1	1
2.	HPMC (% w/v)	-	-	-	-	1	2
3.	Chitosan (% w/v)	1	2	-	-	-	-
4.	EC (% w/v)	-	-	1	2	-	-
5.	Ethanol (ml)	20	20	20	20	20	20
6.	Propylene glycol (ml)	20	20	20	20	20	20
7	Glycerol	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

HPMC: Hydroxypropyl methyl cellulose

weight 50 g was added over the pan which is used here. Note down the time required to separate the slides, that is, when the upper glass slide move from the surface of the lower glass slide [20].

S=M×L/T,

Where,
M = is a weight tide over upper slide,
L = length of slide over the another glass slide,
T = time taken.

***In vitro* mucoadhesion**

With the help of the mucoadhesive force measuring device shown in Fig. 1 given below, we can measure the mucoadhesive force of throat paint [21], for this, the throat mucosa of goat wash with buffer saline solution that should have pH 7.4. Then, same throat mucosa was dipped into a ringer salt solution for at least 15 min at room temperature. Now this goat throat mucosa (F) is first attached with the balance pan, after then, over the sample holder (G) adhere to the film with a water bath (C). Finally, add different amounts of weight over (A) to confirm the contact between film and goat buccal mucosa at last add water drop by drop manner into the beaker which is arranged to the right pan (Y), and water comes out through burette (J). Measure the stress over the skin by applying the formula given below.

$$\text{Detachment stress} = m \times \frac{g}{A}$$

Where,
m= weight on balance
g = acceleration force due to gravity
A = tissue area over gel applied

***In situ* release studies**

To find out *in situ* release behavior of drug through throat paint, also to determine the duration of bioadhesion/erosion of paint with a flow-through apparatus [22] which was designed on the basis of modification in "flow-through device cell." The flow-through cell was made of glass material and a length of 10.5 cm with a diameter of 2.1 cm. Its mouth is close from one end but open at the other end. The cavity at the lower base was 1.6 cm in length and has a depth of 1.5 cm for proper placement of the goat throat mucous membrane. The dissolution medium for the drug was selected as of pH 6.8 (phosphate buffer) which was pumped with a constant flow rate of 0.6 ml/min (corresponding to mean resting salivary flow rate) using flow regulators. The paint was added from the top open tube whole which is then come in contact with phosphate buffer. Then paint settled on the throat mucous membrane and shows the mucoadhesive property. The sample (2 ml) is withdrawn at different time intervals from the reservoir, up to a level when the whole paint will erode. The cumulative percent drug release was determined by measuring the absorbance at 274 nm.

RESULTS AND DISCUSSION

Characterization of complex

SEM

SEM helps to study the morphologic changes at the surface of the formulation. Here, scanning electron microphotographs of a drug (CPX) and its complex called CPX-PEG complex are shown in two different figures (Fig. 3.3 and 3.4). Here in Fig. 3.3, it is found that CPX appeared as a regular smooth surface but irregular in shape and size but are present in three-dimensional crystals, but in Fig. 3.4 a major morphological change has been noticed in the complex formation, in this image the original morphology of the raw materials disappeared as the surface is seen to be porous in nature and it is impossible to differentiate the two components as the solid dispersion looks like matrix particles. Furthermore, the crystalline nature of CPX has totally disappeared (Fig. 3.4) and amorphous agglomerate is found after complex formation. This kind of drastic change in particle shape and aspect in binary complexes was indicative of the presence of a new solid phase which is formed during the solvent evaporation technique.

DSC

DSC is always associated with measuring the heat which is either evolved and or absorb, so this technique was carried out to find the interaction between drug and polymer in which result revealed that in Fig. 3.8 image of a drug is having three peaks, at 155°, 165° and at 315°C. in which we found that the endothermic peak at 155°C which is very sharp proven the drug crystalline nature were as exothermic peak at 165°C proven that the drug is melted down and at the 315°C drug was degrade whereas in the peak of PEG-6000 which is used as excipient shown a peak at 165°C also proven that the polymer was meltdown here. Whereas in case of drug-polymer complex proven that the endothermic peak of drug which is observed at the 60°C is now shifted this means the drug crystalline behavior is changed whereas the peak at 120°C proven that the melting point of a drug is also changed, which further proves that drug lost its crystalline nature also with its morphologic nature, which is fully changed because of the method which is utilized for the complex formation.

Evaluation of complex

Solid dispersion solubility studies

After solid dispersion preparation, its solubility was analyzed and compared with the solubility result of pure drug, through which, it is found that the ratio of 1:3 of drug and polymer shows the highest solubility among all types of different ratios of drug and polymer and having nearby four-time increment in the solubility of the drug when it forms a complex with the polymer in ratio 1:3. The result of solid

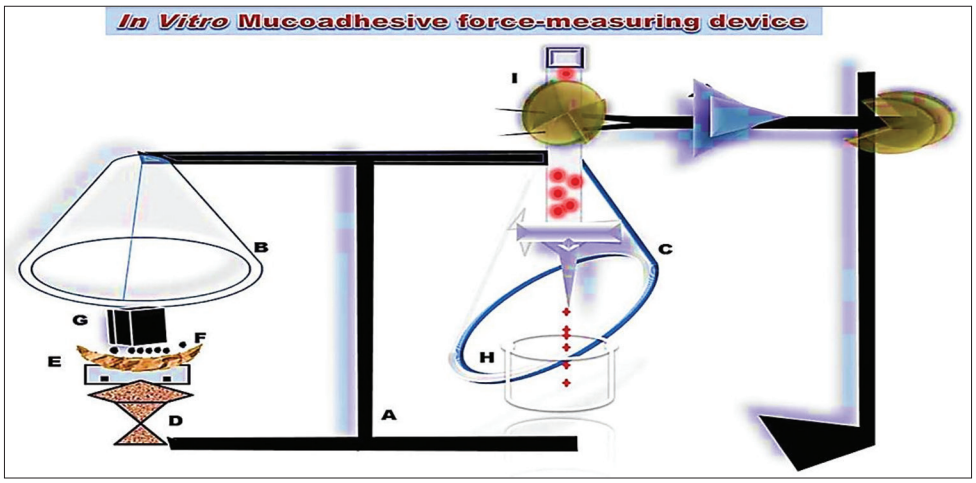

Fig. 1: Schematic representation and assembly arrangement for mucoadhesive force system

dispersion solubility study of CPX drug in different ratios, including drug alone solubility as shown in Table 3 in which the solubility of a drug in the ratio of 1:0.5, 1:1, and 1:2 was found to be 9.545, 11.397, 13.951 µg/ml.

Here increase in the solubility of the drug when we increase the concentration is proven that the wettability of the drug in increasing when we increase the concentration of the polymer and it decreases the interfacial tension which is present between the drug and the medium [23,24]. The PEG works as a hydrophilic polymer and increases the hydrophilic behavior upon the hydrophobic CPX particles by enhancement in the wettability of the drug particle and finally increasing dissolution of CPX particles [13].

Determination of percent yield

The percent yield of various CPX containing solid dispersion ratios was determined by preparing three batches of PEG-6000 and CPX at different ratios of 1:0.5,1:1 and 1:2% under a similar set of conditions to check the reproducibility of the method and express as mean± S.D. solid dispersions percent yield was within the range of 89.04±0.937 to 97.199±0.167%, in which we found that the percent yield of CPX-6000 having ratio of 1:2 is better than the other two solid dispersion ratio this is because of the reason that PEG-6000 particles make drug particle more soluble in higher ratio or amount in comparison with lower ratio or amount. All formulations show a high percent yield, which indicated that the drug is uniformly dispersed in the polymer. The percent yield depends upon the agglomeration and sticking to the surface of the container during the preparation of solid dispersion. So the loss of drug during the percent yield depends on the sticking to the surface of the container and transfer of solid dispersion from one to another container.

Table 3: Solubility data of ciprofloxacin in distilled water in the presence of different concentration of PEG 6000

Sample composition	Ratio of carriers	Solid dispersion solubility (µg/ml)
CPX	------	3.642±0.0589
CPX+PEG	1:0.5	9.545±0.0496
CPX+PEG	1:1	11.397±0.061
CPX+PEG	1:3	13.951±0.078

PEG = PEG-6000, CPX: Ciprofloxacin

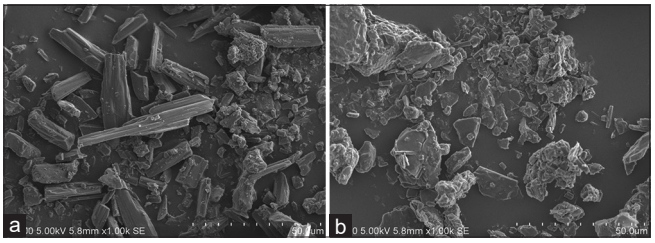

Fig. 2: Scanning electron microscopy photomicrograph of (a) pure drug (b) Ciprofloxacin-polyethylene 6000 complex

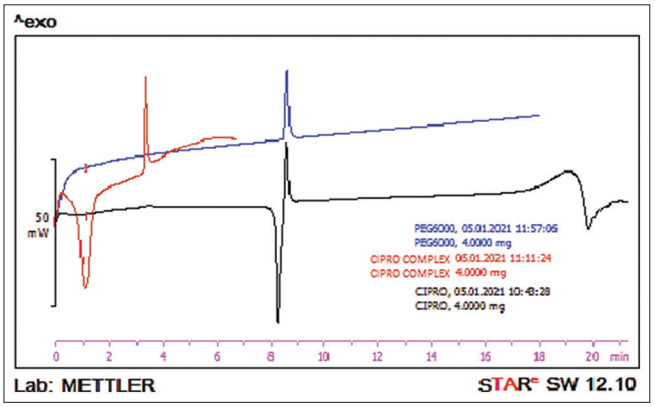

Fig. 3: Differential scanning calorimetry overlay of drug ciprofloxacin, PEG-6000 and Ciprofloxacin-PEG-6000 complex

Drug content

The solid dispersion drug content was found in a range of 89.597–96.425% which proven the high content uniformity and the maximum drug content in percent was found to be 96.42% which is present in ratio 1:2 in between drug and polymer as we found when we increase the concentration of polymer the drug content is also increased, this is because drug content provides high drug uniformity and distribution in the polymer network during its preparation [25], also the high drug content depends on the type and nature of the polymer and the method which is used to prepare the solid dispersion this further proof that we selected one of the best methods for drug loading, and there was less chance of drug loss from polymer network.

***In vitro* dissolution rate studies**

The solid dispersion is followed by the solvent evaporation method, which shows a double fold increment in the dissolution rate of the drug. This is because of two reasons first is increased wettability of the drug and the second is the dispersibility of the drug by the hydrophilic carrier called PEG6000. The reason behind the hydrophilic carrier will help to improve the wetting property of the drug by decreasing the interfacial tension between the hydrophobic nature of the drug and the dissolution medium that's why the drug dissolution rate increase which was found in the order of the drug and polymer ratio 1:2> 1:1> 1:0.5 [26]. On the basis of these results which are shown in Fig. 4, we can say that when the concentration of polymer increases the rate of drug release also increase which proven a simple fundamental that higher the carrier amount we found a higher rate of drug release as higher amount of polymer not only work as a hydrophilic carrier but also reduce the interfacial tension between the hydrophobic nature drug particle and dissolution medium which can easily help to increase the wetting ability of drug by helping early stage of the dissolution process in the microenvironment surrounding drug particle and conversion of drug crystalline to amorphous form which finally help in better and faster solubilization and this is found in the ratio of 1:2 which shows highest dissolution rate or *in vitro* release 95.529% after one hour in comparison with other solid dispersion ratio or with drug alone, which is only 47.096% after 1 h [27,28].

Selection of optimized formulation

On the basis of percent yield, drug content and *in-vitro* drug release data complex having a ratio (Drug: PEG) 1:2 was selected as best among all other formulation, on the basis of % yield was reported as 97.199, drug content was reported as 96.425% also *in-vitro* drug release was reported as 95.529% within 30 min of the time period, which is highest among all different ratio formed in between the CPX and PEG6000.

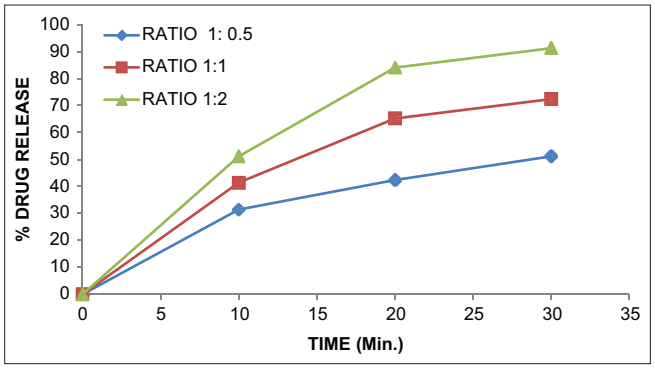

Fig. 4: *In vitro* drug release profiles of solid complex containing ciprofloxacin and PEG -6000 in different concentration in distilled water

Further work of throat paint has proceeded on the basis of the 1:2 ratio of complex only.

Preparation of throat paint

Here, the paint is prepared with glycerin as a base and includes three different kinds of polymers for increasing mucoadhesive property of throat paint, and property to form film type layer over mucus layer only in presence of water or saliva not only this they also provide sustained release for a formulation which is based on their polymer concentration. These agents or polymers have water loading and gel-forming property to which provide flexibility for entanglement with mucus [29]. These polymers also help in increasing the viscosity and adhesive nature which is very much needed in paint formation and their drug release behavior but these polymers do not affect the drug solubility in paints. Hence, all paint systems are ready for further evaluation parameters and have great progress in paint formation for future needs.

Evaluation of throat paint

Clarity and pH

For the development of throat paint, clarity and pH become the important prerequisite parameters. Thus, the formed paint should be clear and should not cause any kind of irritation in the throat area. As for a successful throat paint pH of the paint should be such that allows easy instillation and is easy to apply over the affected area. All the formulations were found to be clear, there was no residue present, which can irritate buccal and throat tissue. The pH of all formulations was found to be toward the acidic side (6.22±0.03–6.95±0.03) (Table 4). This confirmed the ability of paint for instillation. Moreover, formulations within the pH range were within ±0.5 units of the neutral pH were expected safe and acceptable for buccal and throat reason for drug delivery also no mucosal irritation were expected and ultimately achieve patient compliance.

Viscosity

The Viscosity value for the throat paint ranged from 11680.66 to 12900.33 cp as shown in Table 4; result found in viscosity data are based on their polymer type and amount, as we increase the amount of particular polymer then we found its viscosity will also rise and vice versa, in addition there was a noticeable difference in viscosity shown by the different types of polymer concentration as in case of formulation F1 and F2 which shows optimum viscosity of throat paint and higher level of viscosity shown by the one which have higher concentration of HPMC in F2 but in case of formulation F3 and F4 they show high rate of viscosity, which is totally depend on the type of polymer (EC) as in case No. 3 we found in formulation F5 and F6 shows the higher viscosity content which proven that the formulation formed by the chitosan shown the best adhesive capacity over the oral mucosal route in paint formulation, also concentration-dependent variation in velocity was found here also.

Spreadability

The spreadability value of the CPX throat paint was found in ranged from 10.106 to 18.845 as shown in Table 4; this result indicates that spreadability use shear force in small amount and it is not much variate by the amount of polymer and is only affected by the viscosity level of the dosage form as viscosity decreases which finally increase spreadability rate and it all depend on polymer concentration and low rate of spreadability show that it covers small area or diameter to spread over the membrane. This was given in Table 4, that polymer HPMC shows a higher rate of spreadability but has a poor viscosity level in comparison with other polymers. Here, highest spreadability value is shown by formulation F1 which is formed by HPMC and the lowest spreadability value is shown by formulation F6 which is formed by chitosan polymer. All this can be observed from the evaluation data compiled in the Table below [30].

***In vitro* mucoadhesion**

Mucoadhesive strength of throat paint was found in a range of 3090.32–7145.01 dynes/cm^2 shown in Table 4, results of mucoadhesion were revealed that a variable amount of polymers affected the mucoadhesion and its strength. The mucoadhesive strength depends on the wetting and swelling of polymers; in general, mucoadhesion is considered to occur in three stages, namely, wetting, penetration of media, and mechanical interlocking which takes place in between polymer and mucus membrane [31]. We found here that mucoadhesive polymer could interact with the mucus glycoprotein which forms physical and chemical entanglement, followed by a hydrogen bond that results in a highly strengthened mucous gel network which allows the formation of adhesive force for an extended time period [32]. When we increase the HPMC concentration, then results in mucoadhesion increased [33]. HPMC kind of mucoadhesion is like to form of physical bond with mucus component and finally possess a large number of hydroxyl groups which causes adhesion over the surface. Unlike other bioadhesive polymers, chitosan is positive charge by free amino groups and capable to develop additional attractive force by electrostatic interaction with negatively charged mucus surface and form network [34], whereas chitosan forms a weaker gel with the fractured surface because of low molecular weight and low rate of swelling, This result in low mucoadhesive strength. Whereas other formulation which contains ethylcellulose show a controlled rate of hydration and form an optimum level of entanglement with the mucus layer with strong bonding with the mucus layer, this may prevent the paint from quick over hydration and paint cannot be easily removed from the surface in case of EC-containing polymers. As in result all three types of polymer show optimum mucoadhesive force which is enough to remain to adhere over the surface of the mucus layer in the throat but the highest mucoadhesive force was found in the case of HPMC polymer Thus, it can be concluded that the formulation could achieve desirable residence in the throat area due to higher mucoadhesive strength.

***In situ* release studies**

Drug release of different dosage forms was performed in phosphate buffer Ph 6.8 as a dissolution medium. In which different dosage forms of throat paint containing the three different kinds of polymers (HPMC, EC, Chitosan) through which we found a different kind of drug release pattern of the drug. It was found that those formulations contain HPMC, show gel kind layer after swelling when coming in contact with saliva or water that's why the molecule of the polymer was easily eroded and allowed easy release of drug as compared to other formulations containing the other polymers [34,35]. In the case of the formulation containing chitosan, which cannot easily dissolve in phosphate buffer pH 6.8 as it is only able to dissolve in acidic pH that's why it takes more time to dissolve in saliva [36], which is nearby neutral and late drug release mechanism was found in this case as it can only easily dissolve in pH which is slightly acidic that's why it takes more time to dissolve in phosphate buffer pH 6.8 or in saliva and slow drug release was found within 3 h [37], in case of EC where optimum gel barrier was formed around the throat paint through which swelling of

Table 4: Characterization of solid dispersion containing throat paint (F1-F6)

Formulation code	pH	Viscosity (Centi poise)	Spreadability	Mucoadhesion (dyne/cm^2)
F1	6.58	11680.66	18.845±0.676	3090.32±36.85
F2	6.95	12511.33	14.886±1.205	3505.638±51.813
F3	6.22	11932	17.621±2.335	3937.481±95.187
F4	6.87	12703	12.936±0.380	5677±77.272
F5	6.18	12177.66	16.078±1.217	6010±64.629
F6	6.81	12900.33	10.106±0.398	7145.01±288.77

Table 5: *In vitro* drug release of solid dispersion containing throat paint (F1-F6)

S. No.	Formulation code	% Drug release
1.	F1	91.947±0.346
2.	F2	78.126±0.133
3.	F3	90.336±0.6
4.	F4	65.393±0.55
5.	F5	85.392±0.282
6.	F6	58.951±0.263

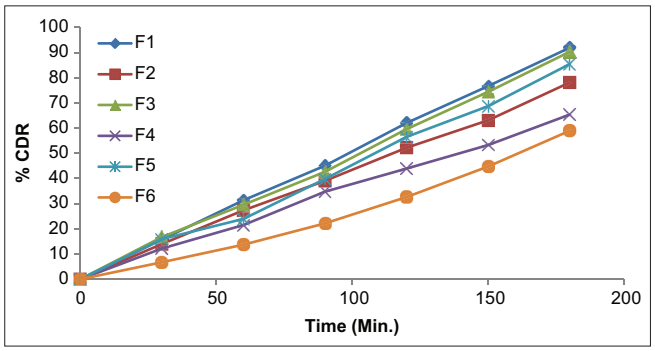

Fig. 5: *In vitro* drug release data of ciprofloxacin from developed throat paint formulations (F1-F6) in phosphate buffer, pH 6.8

paint takes place insight gel-type formation through which drug erode and it also depends on the viscosity of gel which formed when the paint comes in contact with any kind of liquid form(saliva) [38].

Here, we notice that the mechanism of drug release depends on the swelling of polymer and breakdown of the bond of a polymer chain, which only takes place when liquid enters into polymer chain and paint get diluted which cause loose entanglement of the paint and finally the release of the drug takes place which also increases the drug release, so finally the drug release depends on the time required for swelling of different polymer which finally converts into gel kind layer. We found that HPMC formed a loose gelling network of a polymer chain in presence of media if we compare with the other two polymers, that's why it shows the highest drug release 91.947% in giving time interval whereas EC show optimum drug release at giving time interval 90.336 but in case of chitosan which forms a strong network of the polymer chain, release the drug in a slow manner. In the end, we found that when we increase the concentration of all three formulations then the drug release rate decrease this may be due to the fact that although polymers swell rapidly, but their erosion may not have started so soon because formation strong gel layer around paint takes place because of high concentration of polymers and finally affect the overall drug release [39].

CONCLUSION

Here, solubility of CPX drug-enhanced by the formation of solid dispersion in presence of PEG- 6000 at three different ratios, solubility enhancement was noticed at all different ratios, but highest solubility enhancement was reported at a ratio of 1:2 of drug and PEG which is able to enhance the solubility up to 3.5 times than the pure drug. At the same ratio, solid dispersion was able to increase the dissolution rate up to 95%, in 1 h with the highest percent yield and drug content, the same complex was encapsulated inside the throat paint and formulation F3 was selected as the best among the rest because it was able to show second-highest drug release data of about 90% whereas remaining parameters such as Viscosity, Spreadability, and mucoadhesion value was found to be 11932 cp, 17.621 and 3937.481 dyne/cm^2 and all these values are found the second or third highest among all six formulations, so we can say that throat paint formed is able to provide the sustained release drug and also able to decrease the dosing frequency and dose-related side effect because of increasing the solubility. We can definitely decrease the dose of a drug. Finally, the SEM result proof that a complex was formed in which the drug was properly and uniformly distributed and DSC results prove that there was no interaction reported in between the complex formed. Hence, the problem arises with the drug, and the other dosage form to target strep throat disease is solved after throat paint preparation.

ACKNOWLEDGMENTS

We are highly thankful and are wished to acknowledge Balaji chemicals Ltd., Surat for providing CPX drug on time. The authors are also grateful to Diya labs Navi Mumbai for providing the excellent facilities of DSC and SEM studies.

AUTHORS' CONTRIBUTION

All the authors have contributed substantially to the design, performance, analysis, or reporting of the work. Mr. Amit K. Dubey and Mr. Rahul K. Singh have contributed to designing the project and literature survey and conduct drafting, editing, and revising the manuscript. Mrs. Sunaina has carried out the bench-work, laboratory analysis and Mr. Narendra Yadav has conducted data collection and drafted the manuscript.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest in this article.

AUTHORS FUNDING

The research work is funded by Rajiv Academy for Pharmacy, G.L. BAJAJ Group, Mathura an autonomous institute affiliated by Abdul Kalam Technical University, Uttar Pradesh, India.

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