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FORMULATION AND *IN-VITRO* CHARACTERIZATION OF MOXIFLOXACIN HYDROCHLORIDE FILM FORMING GEL FOR TOPICAL DELIVERY

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ABSTRACT

Film forming systems can function as both semisolids and patches and can provide topical as well as transdermal delivery as desired. Film Forming Systems creates super saturated systems immediately after application to the skin, overcoming the problem of instability. Thus it improves the drug permeation through skin compared to other dosage forms. The main objective of the present study is to prepare film forming gel of Moxifloxacin Hydrochloride a topical antibiotic agent to improve its delivery across the skin. By changing the concentration of gelling agents a total of 8 formulations were prepared. The prepared film forming gels were evaluated for physical appearance, pH, spreadability co-efficient, drying time, drug content, film properties, stickiness and *in-vitro* drug release. All the formulations were physically stable with the pH values within the range and have shown good spreadability coefficient. The films were formed within 5mins and were uniform and flexible enough which would not cause discomfort to the patient upon its application. *In-vitro* diffusion studies were carried out using phosphate buffer pH 6.8 and formulation F4 (Guargum 1%) has shown best results among all the developed formulations.

KEYWORDS

Film forming gel, Transdermal delivery, Moxifloxacin hydrochloride and Guargum.

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INTRODUCTON

Topical drug delivery is application of drug via the layers of the skin. These systems are generally used for local skin infection like fungal infection or in place where other routes of the drug administration fails. Skin of an average adult body covers a surface of about $2m^2$ and receives around one-third of the blood circulating through the body. Skin due to its lipophilicity is a barrier to allow materials allowing

only small quantities of drug molecules to penetrate over a period of time and its transport is facilitated by dissolution into intercellular lipids around the cells of *stratum corneum*. Absorption into the skin layers can occur through the pores of the hair follicles or sebaceous glands but the relative surface area of these pores is barely 1% of the total skin surface, but once the drug crosses the stratum corneal barrier, systemic uptake via the dermal layers occurs relatively quickly and easily[1,2].

In general, once drug molecules cross the stratum corneal barrier, passage into deeper dermal layers and systemic uptake occurs relatively quickly and easily. Drugs with the lipophilic character, are better suited for topical delivery. Topical route favours safe and effective delivery of drug molecules with lower doses as compared to the conventional system. Drugs via skin reach the desired area in optimum concentration, dropping the chances of side effects leading to increased bioavailability and increased patient compliance[3-5].

Film forming system (FFS) is a novel approach to conventional topical and transdermal formulations. It is defined as non-solid dosage form that produces a film *in-situ*, i.e. after application on the surface of skin or any other body surface. These systems contain the drug and film forming excipients in a vehicle which, upon contact with the skin, leaves behind a film of excipients along with the drug upon evaporation of the solvent. The formed film can either be a solid polymeric material that acts as matrix for sustained release of drug to the skin or a residual liquid film which is rapidly absorbed in the stratum corneum[6-8].

Moxifloxacin hydrochloride is an antibiotic, used in the treatment of various bacterial infections. In this study it has been formulated into gel system, which on application to the skin surface gets converted into film and remains at the site of application for longer duration thereby enhancing its penetration in the layers of the skin and increasing its availability and therapeutic effectiveness.

MATERIAL AND METHODS

Materials

Drug and chemicals used were analytical grade and procured either as gift samples or purchased. Moxifloxacin was received as a gift sample from K P labs and HPMC K4M, HPMC K100M, sodium CMC, guar gum, sodium alginate are purchased from horizon Chemicals Limited. Tween 80, propylene glycol, methyl paraben were purchased from S.D fine Chemicals Limited, Mumbai India. Ethanol was purchased from Jiangsu Huaxi International Trade Co. Limited.

Methods

Method of preparation[9-11]. The ingredients were taken as per the details mentioned in Table No.1.

Step-1

The Gel in formulations were prepared by dispersing polymer in purified water with constant stirring at a moderate speed then the pH are adjusted to 6 to 6.8 using Tri Ethanol Amine (TEA).

Step-2

Dissolve Moxifloxacin hydrochloride, Methyl paraben and Polyethylene glycol in ethanol. Similarly dissolve the film forming polymer i.e, HPMC K4M in water.

Step-3

Mix the Drug solution with the prepared gel formulations and continue stirring, until the solution is uniformly distributed throughout the gel phase.

Step-4

Add the solution of film forming agent to the above dispersion and stir to obtain the desired consistency of the formulation. Finally the pH of the formulation is adjusted using triethanolamine.

EVALUATION OF FORMULATION

Characterization of Gel

Physical appearance

The prepared gel formulations are inspected visually for their color, homogeneity and consistency after 24 h of preparation.

pH

The pH values of 1% aqueous solutions of the prepared gels were measured by a calibrated pH meter.

Spreadibility

The spreadability of the gel formulations was determined 48 h after preparation, by measuring the spreading diameter of 0.5g gel which was placed within a circle of 1 cm diameter pre-marked on a glass plate over which a second glass plate (75gm) was placed. A weight of 425g was allowed to rest on the upper glass plate for 5 min where no more spreading was expected[12,13]. The increase in the diameter due to spreading of the gels was noted. The spreadability was calculated by using the formula:

$$s = \frac{m \times 1}{t}$$

Where: S is spreadability, m is the weight of the upper plate and rested on it (g), l is the diameter of the spreading gel (cm) and t is the time taken (min).

Film formation

The films are formed in a Petri dish. Film-formation is evaluated and rated as complete and uniform, incomplete or non-uniform, with or without precipitation of the film-forming polymer. The cosmetic aspects of the film are as opaque, sticky or dry, peelable or non-peelable[14, 15].

Drug Content Determination

Take 1gm of gel and Mix it in suitable solvent. Filter it to obtain clear solution. Determine its absorbance using UV spectrophotometer. Same solvent is used for the preparation of standard plot of the drug. Concentration and drug content can be determined by using the same standard plot by utilizing the value of absorbance.

CHARACTERIZATION OF FILM FORMING SYSTEM

Film flexibility

Film flexibility is evaluated on the basis of cracking and skin fixation and this is determined by stretching the skin in 2-3 directions. The film is rated flexible if there is no cracking or skin fixation and non-flexible if there is cracking and skin fixation.

Drying time

For the evaluation of the drying time the formulation is applied to the inner sides of the forearm of a volunteer. After a fixed time period (5mins) a glass slide is placed on the film without pressure. If no liquid is visible on the glass slide after removal, the film is considered dry. If remains of the liquid are visible then the experiment is repeated with increased drying time[16].

Stickiness

The stickiness of the film formed is determined by pressing cotton wool on the dry film with low pressure. Depending on the quantity of cotton fibres that are retained by the film, the stickiness is rated high if there is dense accumulation of fibers on the film, medium if there are thin fiber layer and low if there are occasional or no adherence of fibers. This evaluation parameter is essential, as the formulation should be non-sticky to avoid adherence to the patients, clothes[17].

***In-vitro* diffusion study**

In-vitro diffusion studies were carried out using a modified Franz diffusion cell. Formulation equivalent to 100mg of Moxifloxacin HCl was weighed and placed on the dialysis membrane having the surface area of 2.5cm^2, which is placed between donor and receptor compartment of the diffusion cell. Phosphate buffer pH 6.8 was prepared and used as the diffusion media. The temperature of the cell was maintained at 37^{o}C. This whole setup was stirred using the Teflon coated magnetic stirrer at 50rpm. At specified time intervals 5ml of the sample solution was taken and analyzed spectrophotometrically at 289nm. The cumulative % drug release was determined[17,18].

RESULTS AND DISCUSSION

Characterization of Gel

Physical appearance

The formulated gels were examined for their color, homogeneity, consistency and phase separation after 24 hr of preparation. They were light yellowish, homogenous, transparent to opaque and from viscous gel preparations with a smooth homogeneous appearance and there was no significant phase separation observed in the formulations.

Measurement of pH

The pH of the gel formulations was in the range of 6.07 to 6.69, which lies in the normal pH range of

the skin and would not produce any skin irritation. The results are represented in Table No.2.

Spreadability

One of the essential criteria for an gel is that it should possess good spreadability and it is shown as index of ease of application. The spreadability of the formulation determines the delivery of the correct dose of the drug. The spreadability of Moxifloxacin HCl film forming gel formulation following the spreadability test was found to range from 8.5g.cm/sec to 10.6g.cm/sec for the formulations F1-F8 and the results are given in the Table No.3.

The Spreadability of formulations was found to decrease with increasing the concentration of gelling agent. The value of Spreadability for optimized gel was found out to be 8.5g.cm/sec indicating that the gel is easily spreadable by small amount of shear. The results indicated that the formulation can be applied easily without being runoff. This assures that the formulation maintain a good wet contact time when applied to the site of application.

Film Formation

Film was formed in the petri plate and was observed for the properties such as its completeness, its transparency, peelability and its flexible nature and reported in Table No.4.

Drug Content Determination

Drug content of the formulations were determined by using standard plot and the values were given in the Table No.5 and the values ranged from 94.21% to 98.94%.

CHARACTERIZATION OF FILM FORMING SYSTEM

Drying time

Drying time for all the formulations has been determined and is observed that the formulations containing guargum, HPMC and Sodium CMC dried within 5 mins but the formulations containing Sodium alginate took more than 5 mins for complete drying of the gel to form a film. Ideally, the dermal gel should dry to form a thin invisible film on the surface of skin at the application site within 5 minutes, so as to minimize discomfort to patient.

Stickiness

The stickiness of the film formed is determined as per the procedure and was observed that no or very little cotton fibers have remained on the film for all the formulations developed.

***In-vitro* drug release study**

The *in-vitro* release profiles of Moxifloxacin HCl from its various film forming gel formulations are represented in Table No.6. The better release of the drug from all gel formulation can be observed and the gel formulation can be ranked in the order of F4 > F1 > F3 > F2 > F5 > F7 > F6 > F8. Of the developed formulations F4 containing guargum has shown the good drug release of 98.14% at the end of 120mins.

Table No.1: Formulation of Moxifloxacin hydrochloride film forming gels

S.No	Ingredients	Formulation codes							
		F1	F2	F3	F4	F5	F6	F7	F8
1	Moxifloxacin HCl	1%	1%	1%	1%	1%	1%	1%	1%
2	HPMC K100M (%)	0.5	1	-	-	-	-	-	-
3	Guar Gum (%)	-	-	0.5	1	-	-	-	-
4	Sodium CMC (%)	-	-	-	-	0.5	1	-	-
5	Sodium Alginate (%)	-	-	-	-	-	-	0.5	1
6	HPMC K4M (%)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
7	Polyethylene glycol (%)	1	1	1	1	1	1	1	1
8	Methyl Paraben (%)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
9	Tween 80	1%	1%	1%	1%	1%	1%	1%	1%
10	Water	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

Table No.2: pH of the prepared gels

S.No	Formulation Code	pH
1	F1	6.51
2	F2	6.64
3	F3	6.43
4	F4	6.20
5	F5	6.61
6	F6	6.69
7	F7	6.58
8	F8	6.63

Table No.3: Spreadability of the prepared gels

S.No	Formulation code	Spreadability (g.cm/sec)
1	F1	9.6
2	F2	9.5
3	F3	8.6
4	F4	8.5
5	F5	10.6
6	F6	10.3
7	F7	10.3
8	F8	10

Table No.4: Film properties of moxifloxacin HCl film forming gel formulations

S.No	Formulation Code	Integrity	Film Formation	Observation
1	F1	Complete	Transparent and peelable	Flexible
2	F2	Complete	Transparent and peelable	Flexible
3	F3	Complete	Transparent and peelable	Flexible
4	F4	Complete	Transparent and peelable	Flexible
5	F5	Complete	Transparent and slightly peelable	Flexible
6	F6	Partial	Transparent and non peelable	Brittle
7	F7	Complete	Transparent and peelable	Flexible
8	F8	Partial	Transparent and non peelable	Brittle

Table No.5: Drug content of moxifloxacin Hydrochloride Film Forming Gels

S.No	Formulation Code	Drug Content
1	F1	98.86
2	F2	98.94
3	F3	97.27
4	F4	98.37
5	F5	96.64
6	F6	95.47
7	F7	94.21
8	F8	94.52

Table No.6: *In-vitro* drug release studies of Moxifloxacin film forming gel

S.No	Time (mins)	Cumulative % drug release (n=3)							
		F1	F2	F3	F4	F5	F6	F7	F8
1	15	18.42 ± 1.85	21.44 ± 2.01	12.14 ± 1.25	15.65 ± 1.08	25.87± 0.86	10.96± 1.47	16.43 ± 1.54	18.65± 0.97
2	30	33.08 ± 2.17	38.86 ± 1.06	23.08 ± 2.05	31.32 ± 1.64	35.14± 0.78	25.41± 2.17	31.78 ± 0.95	29.41± 1.17
3	45	50.28 ± 1.67	58.45 ± 1.47	41.55 ± 1.81	57.43 ± 1.31	56.87± 1.16	57.65± 1.67	52.81 ± 1.40	48.36± 1.04
4	60	73.28 ± 1.97	78.34 ± 1.09	63.41 ± 1.74	71.32 ± 1.55	62.87± 1.96	64.84± 2.21	70.30 ± 1.55	57.65± 1.67
5	90	84.36 ± 2.17	85.34 ± 1.14	88.75 ± 1.34	82.14 ± 2.43	78.23± 0.39	72.11± 1.33	78.64 ± 1.07	78.31± 0.33
6	120	96.34 ± 2.08	90.91 ± 2.07	94.12 ± 2.08	98.14 ± 2.11	88.49± 1.64	80.55± 1.41	85.48 ± 2.17	88.55± 1.41

CONCLUSION

The present study was carried out with the aim to prepare film forming gel formulations for Moxifloxacin Hydrochloride. Formulations (F1 to F8) were developed using various polymers as gelling agents and HPMC K4M as the film forming agent. Almost all the formulations F1-F8 have passed all the evaluations with a good values. The formulations were found to be stable and homogenous in nature, pH of the formulations suggest was within the limits of the skin pH. There was no stickiness of the film after its formation over the surface of skin. F_4 (Guargum- 1%) formulation has shown best spreadability among all and can be used for good quick pharmacological action. Gels also shows good spreadability, better loading capacity ease of application and a good patient compliance. The *in-vitro* release study has shown that formulation with Guargum in 1% concentration has shown a good release when compared with the other. Among the various formulations developed F_4 formulation was found to better and is thus optimized.

Considering the various dermatological topical preparation with various advantages and disadvantages, film forming gels serve as the better alternative of the present available marketed topical formulation for delivery of drugs topically.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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