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Case Report

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FORMULATION AND EVALUATION OF ANTISEPTIC FILM FORMING LIQUID FOR SKIN INJURY

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ABSTRACT

Objective-The localized treatment of body tissues, skin diseases, injury and wounds requires that the particular pharmaceutical components be maintained at the site of treatment for an effective period of time but dermatological administration of creams, foams, gels and lotions are considered to reside for a relatively short period of time at the targeted site. To overcome this problem here the approach chosen for the new dosage form is a in-situ film forming polymeric formulations. On the skin surface this formulation solidifies into a film which is able to deliver the active moiety to the skin. **Materials-**Materials used for this dosage form are Eudragit L-100, Polyethylene glycol, Isopropyl alcohol, 6.8 phosphate buffer and Povidone-iodine (API). **Methods-** Methods used are Solvent casting method and Spray method. **Conclusion-**The formed film was sufficiently substantial to provide a sustained drug release to the skin and prevent the deposition of dust particles which reduces the chances of further infection. **Result-**Prepared films were evaluated by evaluation parameters appearance, thickness of film, drying time, moisture absorption, water vapor transmission, folding endurance, weight variation, in vitro drug diffusion study.

KEYWORDS: In-situ film, Drug diffusion, Solvent Casting, Skin, Sustained release.

I. INTRODUCTION

The approach chosen for the new dosage form is an in-situ film forming polymeric formulations. On the skin surface the solution solidifies into a film which is able to deliver the active moiety to the skin. In-situ Film forming preparations or formulations are defined as non-solid dosage forms that produce a substantial film in situ after application on the skin or any other body surface. Such compositions can either be liquids or semisolids with a film forming polymer as basic material for the matrix.[1] Film forming preparations have been known predominantly from the field of surgery or wound care. Film forming solutions or gels has been used for example as tissue glues for the sealing of operative wounds. A wide variety of other ingredients such as fragrances, glycerol, petroleum jelly, dyes, preservatives, proteins and stabilizing agents are commonly added to polymeric formulations and can be used for the delivery of medication such as Antibiotics, Antiseptics, Antifungal, Anti-acne agents, Corticosteroids, Moisturizing or Protective agents (such as calamine) related to skin disorders and/or injury.[2&3]

Advantages of in-situ film forming pharmaceutical preparations

1. Many agents are applied to the skin deliberately with beneficial outcomes. Conventional formulations intended for topical and dermatological administration of drugs such as creams, foams, gels and lotions are considered to reside for a relatively short period of time at the targeted site. The localized treatment of body tissues, diseases and wounds requires that the particular pharmaceutical component be maintained at the site of treatment for an effective period of time. In-situ Film forming formulations are potential drug delivery systems for topical application to the skin. Topical film forming formulations are intended for skin application or to certain mucosal surfaces for local action or percutaneous penetration of medicament or for their emollient or protective actions. These compositions adhere to the body tissue, forming a thin transparent film and provide a localized delivery of the pharmaceuticals to the body tissue.

2. Topical drug delivery is an attractive route for local and systemic treatment. The delivery of drugs onto the skin is recognized as an effective means of therapy for local dermatological diseases. It can penetrate deeper into skin and hence give better absorption. Majority of the skin diseases may be treated topically with treatment delivered directly to the desired site of action, thereby avoiding or at least attenuate the potential systemic side effects. The skin became popular as a potential site for drug delivery because of the characteristics such as: (a) Avoid the problems of stomach emptying, pH effects, and enzyme deactivation associated with gastrointestinal passage (b) To avoid hepatic first-pass metabolism and

to enable control of input, as exemplified by termination of delivery through removal of the device.

3. Topical application has many advantages over the conventional dosage forms. They are deemed more effective less toxic than conventional formulations due to bilayer composition and structure. In the formulation of topical dosage forms efforts are being made to utilize drug carriers that ensure adequate localization or penetration of the drug within or through the skin in order to enhance the local action and minimize the systemic effects or to ensure adequate percutaneous absorption**.**

The aim of the drug administration via the skin can be either the local therapy of dermatological diseases or the transdermal delivery of drugs to the underlying tissues or the systemic circulation. Due to the considerable advantages of the transdermal application route for some drugs different dosage forms have been developed for the drug delivery through the skin: polymeric patches and semisolids. Although the number of transdermally applied drugs is limited the existing dosage forms are quite successfully marketed for various indications. However, each of the dosage forms is associated with certain drawbacks that can negatively influence the patient compliance or limit the usage of the dosage form. Hence the search for alternatives to the conventional transdermal dosage forms is reasonable to further improve the transdermal drug application for the patient.[4]

METHODS OF IN-SITU FILM FORMATION

1) Spray method

Topical spray is dosage form in which polymeric solution of drug is sprayed over the intact skin so as to get a sustained release of drug from the polymeric matrix. The drug is present in saturated form in the polymer matrix. As the organic solvent evaporates slowly the drug diffuses through the polymer matrix and passes from the skin barrier.[5]

2) Solvent casting method

In this method water soluble polymer and plasticizer are dissolved in the distilled water. The solution was stirred up for 2 hrs on the magnetic stirrer and kept aside to remove all the air bubbles entrapped. Mean while, the excipients and API are dissolved and stirred well for 30 min, after the completion of stirring both the solutions are mixed together. Finally the solution was casted on a suitable flat surface to form a film. The film was dried and carefully removed.[6&7]

II. MATERIALS AND METHOD

Povidone iodine powder was prepared at laboratory (GNCP) by using following procedure and evaluated the same prepared powder.

Procedure- Weighed 5g of PVP-K 30 and transfer into the beaker containing 100 ml of heptane, the resultant slurry was stirred for 1/2 hour at ambient temperature and then 0.25 g of water was added drop wise with stirring for 1/2 hour. Then 1g of iodine was added as a fine powder over a period of 3 to 4 hours. After the addition was completed mixture was heated at 70^0c upto 1 hour and held at 70^0c for 3 hours. The powder then cooled, filter, rinse and dried.[8]

Figure 1: Synthesized Povidone-Iodine Powder.

The above synthesized Povidone-iodine powder was used as antiseptic agent in given In-situ film forming solution.

Evaluation Parameters of prepared Povidone-iodine powder

- Assay
- Identification
- Colour
- Determination of "Free" Iodine in Povidone-iodine powder
- Stability determination of Povidone iodine powder
- Antiseptic activity
- Fourier Transform Infrared (FTIR)

Following optimization method was used for the selection of polymers, plasticizers and solvents.

Table 1: Optimization of formula.

Formula	Eudragit L-100 (%)	PEG-400 (%)	Povidone-Iodine powder (%)	IPA (ml)	6.8 phosphate buffer (ml)
F1	1	2	5	75	25
F2	1.5	2.5	5	75	25
F3	2	3	5	75	25
F4	2.5	3.5	5	75	25
F5	3	4	5	75	25
F6	3.5	4.5	5	75	25

Based on the evaluation of **table no 1** following formulas was selected.

Table 2: Selected formula.

Formula	Eudragit L-100 (%)	PEG-400 (%)	Povidone-Iodine powder (%)	IPA (ml)	6.8 phosphate buffer (ml)
F5	3	4	5	75	25

Weighed given quantity of Eudragit L-100 and transfer into the beaker containing IPA and 6.8 Phosphate buffer and dissolved the polymer. Then added prepared Povidone-iodine powder and also dissolved them into the polymeric solution then add plasticizer.

Evaluation Parameters of In-situ film forming polymeric solution

1) Density
2) Viscosity
3) Iodine content
4) Spreadability
5) Antiseptic activity

Solvent Casting method

Film was produced by solvent evaporation on a glass slide. On glass slide pour 15 ml of the polymeric solution and left to dry at room temperature for 24 hours.

Evaluation parameters of film

1. *Appearance*

All prepared films were evaluated for their appearances i.e. if they are transparent or opaque.

2. *Thickness of film*

The thickness of film was measured by vernier caliper. The thickness uniformity was measured at five different sites of film and average of five reading was taken with standard deviation.

3. *Drying time*

For the assessment of the drying time the formulation was applied to the inner sides of the forearm after 2 minutes a glass slide was placed on the film without pressure. If no remains of liquid were visible on the glass slide after removal, the film was considered dry. If remains of liquid were visible on the glass slide the experiment was repeated until the film was found to be completely dry.

4. *Moisture absorption studies*

The moisture absorption study was carried out at 75% RH at 25 ± 1°C using saturated solution of sodium chloride. The pre-weighed samples of film were kept under the humidity condition as mention above and weighed the film after 24 hours. The increase in the weight indicates the moisture absorption by samples which can be calculate by using the following formula,

$$\% \text{ moisture absorption} = \frac{W2-W1}{W1} \times 100 \qquad (1)$$

Where,

W1 = initial weight of film.

W2 = weight of film after 24 hours placed in desiccators.

5. *Water vapor transmission rate (WVTR)*

The WVTR study was carried out in desiccators maintained at 43% and 75% RH at 25 ± 1°C using saturated solution of potassium carbonate and sodium chloride respectively. Film were placed on the mouth of glass vials containing fused calcium chloride and sealed using silicon wax. These vials were accurately weighed and placed in desiccators at 43% and 75% RH. The weight of the vials was recorded after 24 hours. The water vapor transmission rate was calculated by using the following formula,

$$\text{WVTR} = \frac{W2-W1}{W1} \times /100 \qquad (2)$$

Where,

W1 = initial weight of vials sealed with film.

W2 = weight of vials after 24 hours placed in desiccators

6. Folding endurance of film

The folding endurance was measured manually for the prepared film. A strip of film (4✕3 cm) was cut evenly and repeatedly folded at the same place till it broke. The number of times the film could be folded at the same place without breaking gave the exact value of folding endurance.

7. *Weight variation test of film*

The three disks of 2✕2 cm^2 of film was cut and weighed on electronic weigh balance for weight variation test. The test was done to check the uniformity of weight and thus check the batch-to-batch variation.

8. *In-vitro drug diffusion study of film*

The drug diffusion study through film were conducted by using vertical type diffusion cell (Franz type) having receptor compartment 15ml volume with 2cm^2 area. The receptor compartment was filled 15ml of phosphate buffer pH 7.4; the activated dialysis membrane was mounted on the flange of the diffusion cell receptor compartment. The prepared film placed on center of membrane with sufficient quantity of drug, the donor compartment was then placed in position and the two valves of the cell clamped together. The whole assembly was kept on a magnetic stirrer and solution in the receptor compartment was constantly stirred using a magnetic bead at 32°C maintained.

III. RESULT AND DISCUSSION

Table 3: Result of Selection of In situ-film forming polymers.

Sr. no.	Polymers	pH	Density g/cm^3	Melting point	Solubility
1.	Hydroxy propyl cellulose	5.0-8.5	0.5	120-130^0	Ethanol and methanol
2.	Hydroxy propyl methyl cellulose-	5.5-8.0	1.39	190-200^0	cold water
3.	Polyvinyl alcohol-	5.0-6.5	1.19-1.31	228-230^0	water and in organic solvents
4.	PVP-K-30	3.0-7.0	1.2	150-180^0	Water
5.	Sodium alginate	6-8	1.601	300^0	Water
6.	Eudragit L-100	6.0-6.5	1.062	216-220^0	IPA, ethanol

From the above study of polymers Eudragit L-100 was selected because of its solubility in volatile solvents like IPA and ethanol. For rapid film drying purpose its necessary to soluble in volatile solvents also pH of this polymer are compatible with skin pH.

Table 4: Result of Optimization of polymer and plasticizer concentration.

Sr. no	Polymers	(gm)	Plasticizers	(gm)	Solvent	(ml)	Result
1	HPC	0.5	Triethyl citrate	0.2	Ethanol	20	Film not formed
2	Eudragit l-100	2	Triethyl citrate	0.5	IPA	20	Thick film formed
3	PVP-K 30	2	Dibutyl phthalate	0.8	Ethanol	20	Film not formed
4	Eudragit L-100	1.5	Glycerol	1.5	Ethanol	20	Film not formed
5	Eudragit L-100	2	Propylene glycol	1	IPA	20	More plastic film formed
6	Eudragit L-100	2	PEG- 400	0.75	IPA	20	Good film formed
7	Sodium alginate	2	Propylene glycol	0.5	Ehanol	20	Film not formed
8	PVA	2	Triethyl citrate	0.5	Ethanol	20	Good film formed

The above **table 4** shows film forming property of various polymers using different plasticizer concentrations and solvents. From the above study PEG-400 was selected as plasticizer.

Table 5: Result of evaluation of Povidone-iodine powder.

Parameters	Assay	Identification	Colour	Determination of "Free" Iodine in Povidone-iodine	Stability determination of Povidone-iodine	Antiseptic activity
Result	Practical yield 5% = available iodine 0.833%	A- A deep blue colour. B-A brown, dry, non-smearing film is formed which dissolves readily in water	Brown colour	K=121	Iodine loss = 28%	Area of inhibition=2.8cm

Table 6: Details of FT-IR of Povidone-iodine powder.

Sr. no	Frequency (cm^{-1})-1)	As Assignment g
1	2949	Aliphatic –CH- stretching mode
2	2884	Aliphatic –CH- stretching mode
3	1678	Carbonyl stretching mode
4	1453	Hetrocyclic ring mode
5	1420	-CH2 scissors deformation mode
6	1337	-CH2 and –CH wagging mode
7	1283	-CH2 bending mode

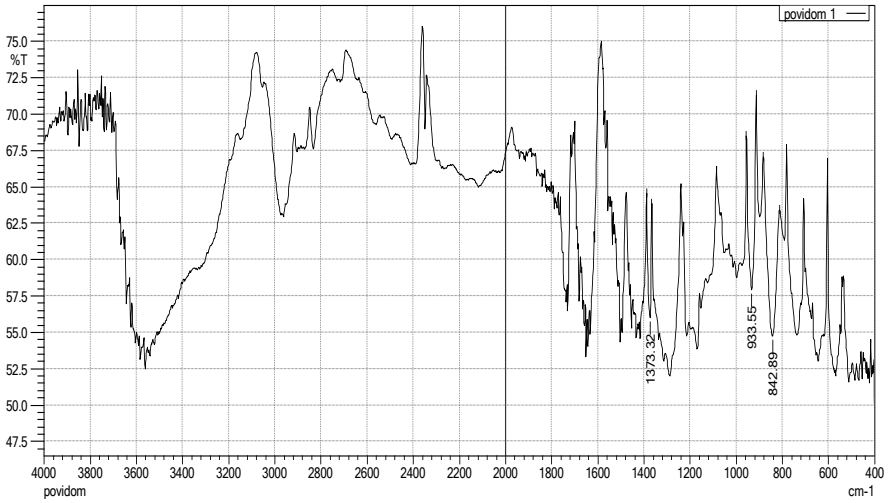

Figure 2: Fourier Transform Infrared (FTIR).
Spectral graph of Povidone-iodine powder

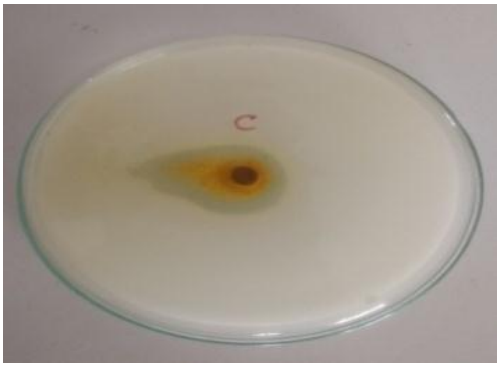

Figure 3: Sample plate shows antiseptic activity
(Povidone-iodine powder)

Above table, sample plate of antiseptic activity and details of FTIR shows that synthesized Povidone-iodine powder was evaluated and shows the appropriate result. Hence this synthesized powder used as antiseptic agent in In-situ film forming polymeric solution.

Table 7: Result of Evaluation of In-situ film forming polymeric solution.

Parameters	Batch1	Batch2	Batch3	Batch4	Batch5	Batch6	Mean± SD
Density g/cm^3	0.836	0.7170	0.948	0.883	0.934	0.901	0.86±0.084
Viscosity cps	40.32	33.42	29.51	37.90	39.15	34.45	35.79±4.077
Iodine content %	0.801	0.790	0.731	0.811	0.781	0.776	0.78 ±0.02
Spredability (gm cm / sec)	12.2	12.6	13.1	14	13.5	14.3	13.28±0.808
Antiseptic activity (zone of inhibition cm)	2.3	2.6	3.1	3	2.8	3.5	2.88 ±0.41

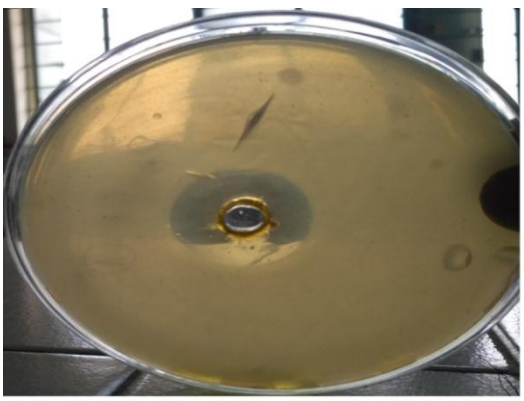

Figure 4: sample plate (antiseptic in-situ film forming polymeric solution)
(Zone of inhibition = 2.3 cm)

Table 8: Results of evaluation of film which was prepared by solvent casting method.

Parameter	F1	F2	F3	F4	F5	F6	Mean ±SD
Appearance	Transparent	Transparent	Transparent	Transparent	Transparent	Transparent	
Thickness	1mm	1mm	1mm	1mm	1mm	1mm	
Drying time in min.	5.43	3.45	5.23	5.55	4.45	6.35	5.07±1.00
Moisture absorption	2.20	4.33	3.16	3.78	4.41	4.90	3.79±0.98
Water vapor transmission rate(WVTR)	3.83	3.91	2.10	3.45	2.9	4.3	3.41±0.79
Folding endurance	37	27	33	38	21	40	32.66±7.33
Weight variation(avg.) in gm	0.292	0.286	0.285	0.290	0.285	0.275	0.285±0.005
% drug release	68.34	72.39	69.12	76.90	74.27	71.85	72.14±3.19

Table no 9: Results of evaluation of film which was prepared by spray method.

Parameter	F1	F2	F3	F4	F5	F6	Mean ±SD
Appearance	**Transparent**	**Transparent**	**Transparent**	**Transparent**	**Transparent**	**Transparent**	
Thickness	1mm	1mm	1mm	1mm	1mm	1mm	1mm ±0.031
Drying time in min.	6.34	6.54	6.12	6.00	6.43	6.45	6.33±0.67
Moisture absorption	2.45	2.14	2.25	2.55	2.90	2.56	2.64±0.89
Water vapor transmission rate(WVTR)	4.45	4.78	4.89	4.45	4.47	4.19	4.70±0.56
Folding endurance	33	32	33	35	36	37	34.16±4.66
Weight variation(avg.) in gm	0.281	0.286	0.285	0.290	0.280	0.275	0.282± 0.005
% drug release	71.34	72.39	73.45	71.56	72.23	73.85	72.88±2.77

A spray can be applied directly to the wound/injury and dry in short time, so there is no need to use cotton or gauze to spread or cover the wound. A spray preparation of PVP-I can be more effective if excipients such as a humectants and a film forming agent are added to enhance the bactericidal effects with the convenience of direct application to the skin.

IV. CONCLUSION

From the above studies it could be concluded that in-situ film was successfully prepared for topical release of a drug for local action on skin like skin injury. Also it can cover the skin injury and protect it from deposition of dust particles and prevent further infection and improved patient compliance.

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