ejpmr, 2021,8(3), 429-433

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

FORMULATION, DEVELOPMENT AND EVALUATION OF MICONAZOLE OLEOGEL USING COCONUT OIL AS PENETRATION ENHANCER

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Article Received on 05/01/2021 **Article Revised on 26/01/2021** **Article Accepted on 16/02/2021**

ABSTRACT

The main purpose of this study was to develop a topical drug delivery (Oleogel) of Miconazole to reduce the dose of the drug, to improve patient compliance, to avoid the side effects and increase local onset absorption. Miconazole is a triazole derivative to treat antifungal and antiprotozoal infections. **Methods:** Topical oleogel formulations of Miconazole were prepared using Carbopol 940 as a gelling agent with different penetration enhancer with their different concentrations. Nine different formulations were prepared and evaluated with respect to their color, spreadability, viscosity parameter, determination of pH, formulation drug content, in vitro drug release studies, zeta potential studies, and stability studies. The Compatibility study was carried out by Fourier-transform infrared (FT-IR) spectral analysis. **Results:** FT-IR study revealed that there were no any significant interaction between the drug, excipients and polymers. All the prepared formulations of miconazole show acceptable physical properties. The drug content and percentage yield were higher for F5 formulation among all formulation F5 shows better drug release. Stability study of the best formulation F5 (Coconut oil) shows that there was no difference in drug content and in vitro drug release studies. **Conclusion:** From the above observation results that this F5 formulation (Coconut oil) may be more encouraging topical substitute for the healing of fungal infections in the skin.

KEYWORDS: Miconazole, Carbopol 940, oleogel, Zeta potential, Stability study.

INTRODUCTION

A gel may be a two-component, cross linked three-dimensional network consisting of structural materials interspersed by an adequate but proportionally large amount of liquid to make an infinite rigid network structure which immobilizes the liquid continuous phase within. The structural materials that form the gel network are often composed of inorganic particles or organic macromolecules, primarily polymers. Cross links are often formed via chemical or physical interactions. This results in gel classification into chemical and physical gel systems, respectively.

CLASSIFICATION OF GELS

Gels may be classified supported colloidal phases, nature of solvent used, physical nature and rheological properties.

1. Based on colloidal phases: They're classified into Inorganic (two phase system) kind of force that's accountable for the linkages determine the structure of the network and therefore the properties of the gel.

Single-phase system these contain large organic molecules existing on the twisted strands dissolved during a continuous phase.

2. Based on nature of solvent

Hydro gels (water based)

Here they contain water as their continuous liquid phase E.g. bentonite, derivatives of cellulose, carpooler, and synthetic poloxamer gel. E.g. plastibase (low molecular wt. polyethylene dissolved in oil & short Cooled) Olag (aerosol) gel and dispersion of metallic stearate in oils.

Xerogels

Solid gels with low solvent concentration are called xerogels. These are produced by evaporation of solvent or freeze drying, leaving the gel framework behind on contact with fresh fluid, they swells and may be reconstituted. E.g. Tragacanth ribbons, acacia tear β1-cyclodextrin, dry cellulose and polystyrene.

3. Based on rheological properties

Usually the gels show non-Newtonian flow properties. They're classified into, a) Plastic gels b)

Pseudo plastic gels c) Thixotropic gels. (a) Plastic gels E.g. - Bingham bodies, flocculated suspensions of aluminium hydroxide exhibit a plastic flow and also the plot of rheogram gives the yield value of the gels above which the elastic gel distorts and begins to flow. (b) Pseudo-plastic gels E.g. - Liquid tragacanth dispersion, sodium alginate, Na Carboxy methyl cellulose etc. exhibits pseudo-plastic flow. The viscosity of those gels decreases with increasing rate of shear, with no yield value. The rheology results from a shearing action on the long chain molecules of the linear polymers. because the shearing stress is increased the disarranged molecules begin to align their long axis within the direction of flow with release of solvent from gel matrix. (c) Thixotropic gels The bonds between particles in these gels are very weak and may be broken down by shaking. E.g.: Kaolin, bentonite and agar.

4. Based on physical nature (a) Elastic gels Gels of agar, pectin, guar gum and alginates exhibit an elastic behavior. The fibrous molecules being linked at the purpose of junction by relatively weak bonds like hydrogen bonds and dipole attraction. E.g.: Alginate and Carbapol. (b) Rigid gels this may be formed from macromolecule within which the framework linked by primary valance bond. E.g.: In colloid, silic acid molecules are held by Si-O-Si-O bond to provide a polymer structure possessing a network of pores.

PREPARATION OF GELS

Gels are generally prepared at the industrial scale under room/ Standard temperature. However few of polymers need special treatment before processing. Gels are also prepared by following methods.

1. Thermal changes
2. Flocculation
3. Chemical process/ reaction

MATERIALS AND METHODS

Miconazole was acquired from Cipla Limited, Chennai, India. Carbopol was obtained from Sigma-Aldrich, Chennai, India. All Other Chemicals used were of the standard analytical grade. Method of preparation of topical gel containing Miconazole Topical gel formulations were prepared using various concentration of polymer Carbopol 940 with penetration enhancer is dispersed in cozy water with constant stirring by magnetic stirrer at a medium pace. Gels are packed in a widemouthed glass jar, and it is covered with screw copped plastic lid after covering with aluminum foil.[5,6] Various preparations of Miconazole topical gel are shown in Table 1. They were kept in the dark and cool place. Evaluation of physicochemical parameters of prepared Miconazole gel Drug-excipients compatibility studies Fourier transfer infrared spectrophotometer (FTIR) The drug, polymer, and excipient interactions are studied using the FTIR method. In general, drug and excipients must be coinciding with each other which produce a stable, safe, and efficacious product. IR spectral analysis of pure drug and polymers was transported out.[7] Pure drug that gives peak and patterns were compared with the peaks and patterns with the combination of polymer and drug.

RESULTS AND DISCUSSION

Drug-excipients compatibility studies

The IR studies of clear Miconazole formulation comprises greater proportion of the polymers that are conducted to know about the bond between the used polymers and the drug.

The IR spectrum of pure Miconazole and Miconazole gel formulations that posses greater proportion of polymer that gives comparable basic patterns and peaks. Outcome status that no notable drug and polymer interactions.

Visual inspection

Visual determination is done to examine the syneresis and color of the developed formulation. The preparations must be logical and translucent. Eventually, the formulated gel shows better homogeneity without any lumps and syneresis.

Determination of pH

The pH value of all developed gel was in the range of 6.6–7.1. This is sufficient for appealing to skin and avoid the chances of irritation.

Spreadability

The study has a few major elements that show the gel character that emerges out from the tube. Spreadability test is carried for all the formulations. Spreadability of the gel formulation drops with respect to increase in the polymer concentration.

Determination of drug content

The drug content of the formulated gel was estimated. The drug content manifests that the drug was distributed equally throughout the gel.

Percentage yield and viscosity

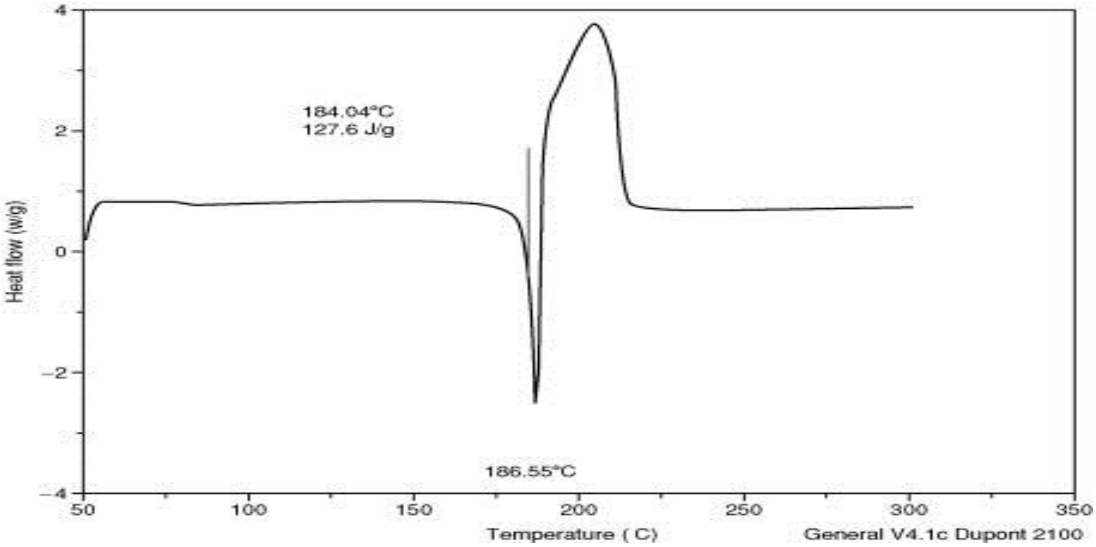
Percentage yield of a topical gel consisting of Miconazole was in the range of 96.09–99.03%. This was identified that the percentage yield of F5 formulation showed an increase in percentage yield than the other preparation due to use of coconut oil as penetration enhancer. In general, consistency of formulation depends on the ratio of the solid fraction to liquid fraction which produces gel structure.

In vitro drug release

The drug release profile of Miconazole topical gel formulations was accomplished by diffusion cell. As an outcome of the *in vitro* release studies of all formulations are given in Table 5, and the statistically represented is shown in Figure.

Miconazole Formulation Table

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Miconazole	2	2	2	2	2	2	2	2	2
Carbopol	2	2	2	2	2	2	2	2	2
Tween-80	2	4	6	-	-	-	-	-	-
Coconut Oil	-	-	-	2	4	6	-	-	-
Lemmon Oil	-	-	-	-	-	-	2	4	6
Propyll Galate	1	1	1	1	1	1	1	1	1
Methyl Paraben	2	2	2	2	2	2	2	2	2
Propyl Paraben	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Water	90	88	84	90	88	84	90	88	84



DSC Thermogram of Miconazole

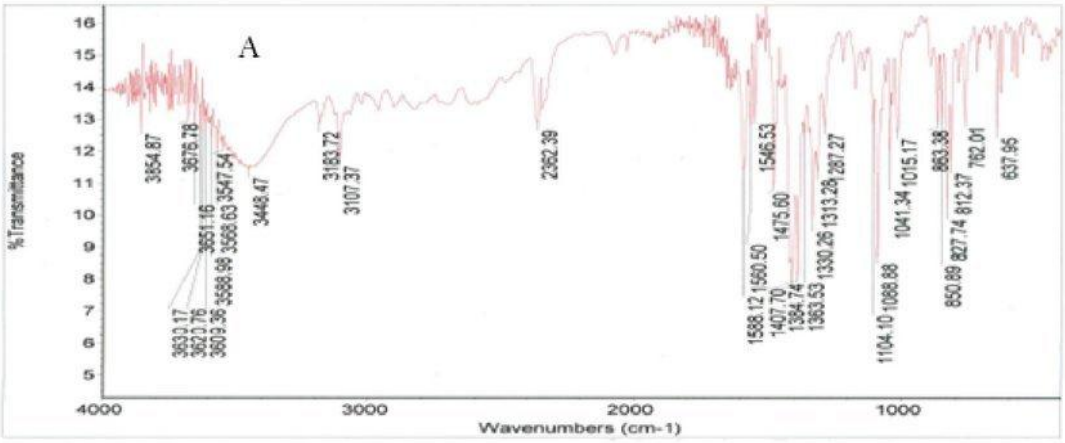


Figure: IR Spectra of Miconazole.

Table: Characterization of formulation of Miconazole Gel.

Characterization	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
pH	7.2	7.1	7.3	7.1	7.1	6.9	7.0	7.3	7.1
Viscosity	70	96	132	157	173	169	196	232	266
Gelling capacity	++	++	++	++++	++++	++++	+++	++++	++++
Content uniformity	96.09 ±0.38	97.54 ±0.70	96.17 ±0.81	98.51 ±0.34	99.03 ±0.21	98.97 ±0.54	96.63 ±0.87	98.68 ±0.21	97.74 ±0.18

Table: In-vitro release data of Miconazole gel.

Time (Hrs)	% cumulative drug release from various batches				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	16.50	17.40	21.40	12.24	21.32
2	25.30	24.20	20.42	12.46	22.31
3	44.25	46.13	43.16	26.21	33.45
4	64.23	60.41	62.12	38.29	46.56
5	72.27	77.46	76.33	40.09	60.01
6	87.42	85.03	83.14	53.46	69.21
7	92.02	92.46	93.33	75.63	74.91
8	97.98	98.72	98.04	89.32	84.12
9	16.50	17.40	21.40	12.24	21.32
10	25.30	24.20	20.42	12.46	22.31
11	44.25	46.13	43.16	26.21	33.45
12	64.23	60.41	62.12	38.29	46.56

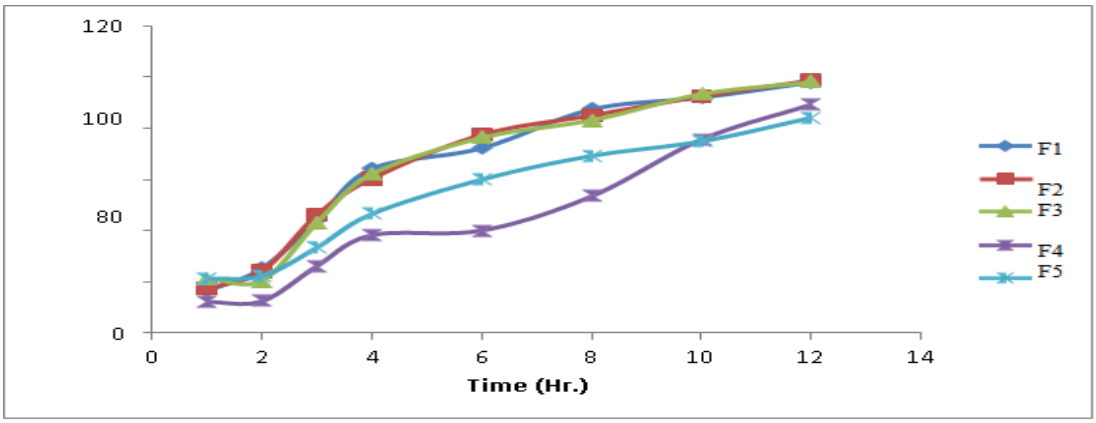


Figure: In vitro release curve of Miconazole.

Table: In-vitro release data of Miconazole gel.

Time (Hrs.)	% cumulative drug release from various batches			
	F6	F7	F8	F9
0	0.00	0.00	0.00	0.00
1	18.40	28.42	22.37	25.13
2	28.17	37.72	27.08	32.26
3	30.46	43.27	42.36	35.52
4	49.81	49.60	51.18	49.09
6	61.21	57.12	55.19	56.72
8	70.15	66.61	61.68	58.40
10	74.96	63.32	72.84	63.61
12	83.28	79.10	77.37	74.12

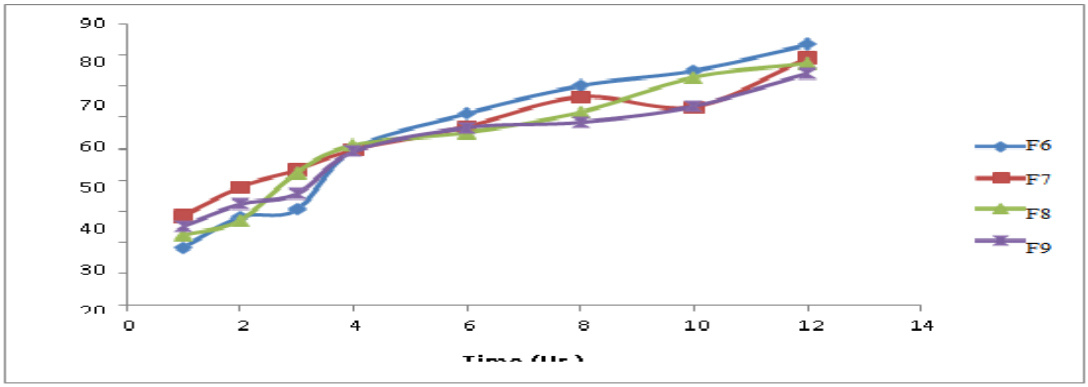


Figure: In Vitro release curve of Miconazole.

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