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Original Research Article

DEVELOPMENT AND EVALUATION OF ECONAZOLE ORGANOGEL

Dr. Dilip Agrawal[1]*, Dr. Rakesh Goyal[2], Dr. Mukesh Bansal[2], Mr. Ashok Kumar Sharma[2], Mr. Mohit Khandelwal[2], Ms. Shaneza Aman[2]

[1]Professor, Mahatma Gandhi College of Pharmaceutical Sciences, Jaipur, Rajasthan
[2] Asso. Professor, Mahatma Gandhi College of Pharmaceutical Sciences, Jaipur, Rajasthan

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Corresponding author: Dr. Dilip Agrawal
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Abstract

The main purpose of this study was to develop a topical drug delivery (Organogel) of Econazole to reduce the dose of the drug, to improve patient compliance, to avoid the side effects and increase local onset absorption. Econazole is an imidazole derivative antifungal to treat fungal and protozoal infections. **Methods:** Topical Organogel formulations of Econazole were prepared using span-60 with different penetration enhancer with their different concentrations. Six different formulations of econazole were prepared and evaluated with respect to their colour, 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 designed formulations of Econazole show acceptable standard physical properties. The drug content and percentage yield were higher for F2 formulation among all formulation F2 shows better drug release. Stability study of the best formulation F2 (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 F2 formulation (Coconut oil) may be more encouraging topical substitute for the healing of fungal infections in the skin.

Keywords: Econazole, Organogel, 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. Econazole acts as interacts with 14-α demethylase, a cytochrome P-450 enzyme necessary to convert lanosterol to ergosterol which is essential process for fungi cell growth. As ergosterol is an essential component of the fungal cell membrane, inhibition of its synthesis results in the increased cellular

permeability causing leakage of cellular contents responsible for cell death.

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 are classified into Inorganic (two-phase system) kind of force that is 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. Example-plastibase (low molecular wt. polyethylene dissolved in oil) Olag (aerosol) gel and dispersion of metallic stearate in oils.

Organogel

An organogel, is a semisolid formulation of gel dosage forms, which has an immobilized external apolar phase. The apolar phase is immobilized within spaces of the 3D network structure formed due to the physical interactions amongst all polymers the self-assembling structures of compounds regarded as gelators.

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 swell 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 behaviour. 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 temperature. However, few of polymers such-Synthetic and Natural need special treatment before processing. Gels are also prepared by following methods.

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

MATERIALS AND METHODS

Econazole was received gift sample from Nicholas Piramal India Ltd, Mumbai, India. All Other Chemicals used in the formulation development were of the standard analytical grade. Econazole formulations organogel were prepared by using penetration enhancer (Coconut Oil and Almond Oil) are dispersed in distilled water with constant stirring by magnetic stirrer at a medium pace maintaining the temperature at 300C. Gels are packed in a wide mouthed glass jar, and it is covered with screw copped plastic lid after covering with aluminium foil [5,6]. Various preparations of Econazole topical gel are shown in Table 1. They were kept in the dark and cool place. Evaluation of physicochemical parameters of prepared Econazole gel Drug-excipients compatibility studies Fourier transfer infrared spectrophotometer (FTIR). The drug, polymer, and excipients 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 carried 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 Econazole 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 Econazole and Econazole gel formulations that used 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 physical properties and color of the developed formulation. The preparations must be logical and translucent. Eventually, the formulated gel shows better homogeneity without any lumps and aggregation.

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.

Spread ability

The study has a few major elements that show the gel character that emerges out from the tube. Spread ability test is carried for all the formulations. Spread ability 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 Econazole was in the range of 95.51–97.54%. This was identified that the percentage yield of F2 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 Econazole topical gel formulations was accomplished by diffusion cell. As an outcome of the *in vitro* release studies of all formulations are given in Table 3, and the statistically represented is shown in Figure

DISCUSSION

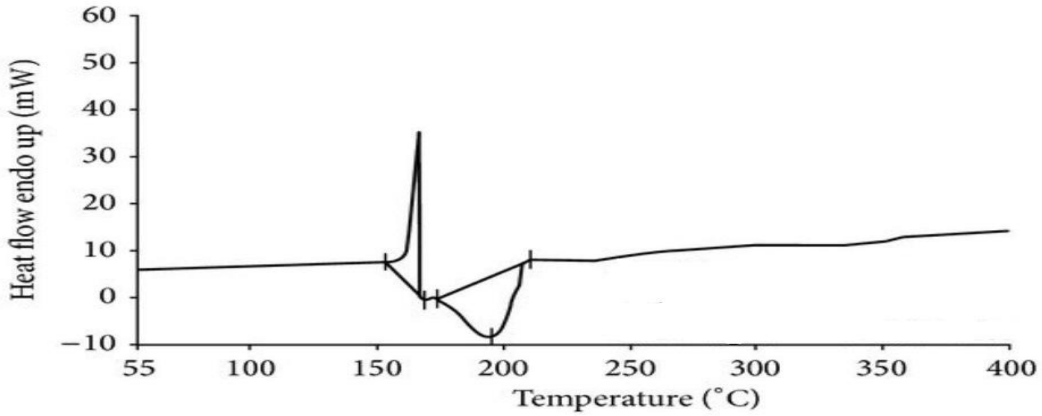
The imidazole derivative of Econazole is one of the best drugs used for the treatment of fungal infections. In this study, the topical gel preparation of Econazole was formulated for efficient that absorption of the drug across the skin. UV spectrophotometer studies of prepared Econazole gel show the absorption at the wavelength of 230 nm. Advanced formulations of Econazole were analyzed for physiochemical parameters such as viscosity, spread ability, drug content, and *in vitro* drug release studies.

CONCLUSION

By analysing the above results, concluded that our drug Econazole was incorporated with success into the topical gel development among all the designed formulation, the formulation F2 shows better Spread ability, drug content, viscosity, and drug release studies. Therefore, this was concluded that our formulation would be very effective and safe topical alternative for the treatment of skin fungal infections.

Table 1: Econazole Formulation

Ingredients (Gm)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Econazole	1	1	1	1	1	1
DMSO	5	5	5	5	5	5
Span-60	10	10	10	10	10	10
Coconut Oil	81	81	81	-	-	-
Almond Oil	-	-	-	81	81	81
Propyll Galate	1	1	1	1	1	1
Methyl Paraben	2	2	2	2	2	2
Propyl Paraben	0.5	0.5	0.5	0.5	0.5	0.5
Total	**≈100**	**≈100**	**≈100**	**≈100**	**≈100**	**≈100**



DSC Thermogram of Econazole

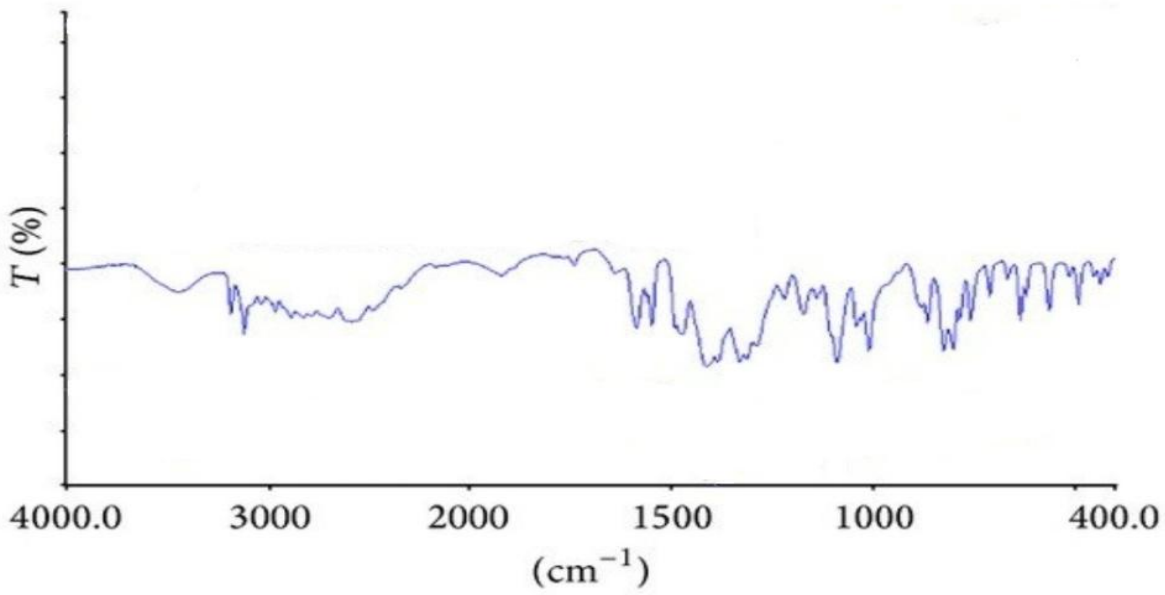


Figure: IR Spectra of Econazole

Table 2: Characterization of formulation of Econazole Gel

Characterization	Formulation code					
	F1	F2	F3	F4	F5	F6
pH	7.2	7.1	7.3	7.1	7.1	6.9
Viscosity	70	96	132	157	173	169
Gelling capacity	++++	++++	++++	+++	++	++
Content uniformity	96.09 ±0.38	97.54 ±0.70	96.17 ±0.81	95.51 ±0.34	96.03 ±0.21	95.97 ±0.54

Table 3: In-vitro release data of Econazole gel

Time (Hrs)	% Cumulative drug release from various batches					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0.00
1	16.50	17.40	21.40	12.24	21.32	18.40
2	25.30	24.20	20.42	12.46	22.31	28.17
3	44.25	46.13	43.16	26.21	33.45	30.46
4	64.23	60.41	62.12	38.29	46.56	49.81
5	72.27	77.46	76.33	40.09	60.01	61.21
6	87.42	85.03	83.14	53.46	69.21	70.15
7	92.02	92.46	93.33	75.63	74.91	74.96
8	97.98	98.72	98.04	89.32	84.12	83.28

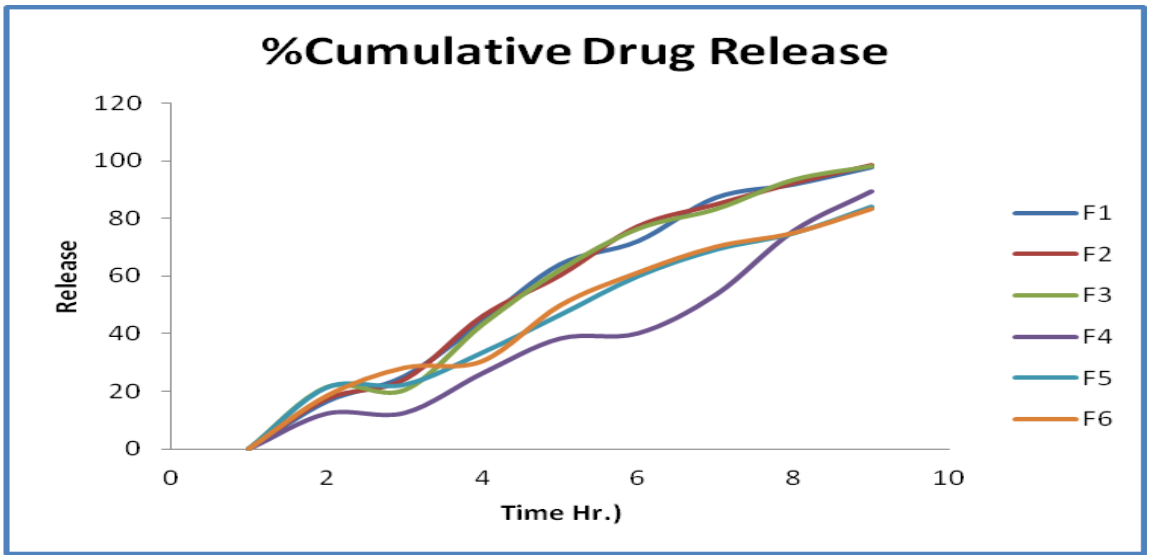


Figure: In vitro release curve of Econazole

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