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DEVELOPMENT AND EVALUATION OF ANTIFUNGAL GEL BY USING NATURAL POLYMER

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ABSTRACT

In the present study, an attempt has been made to formulate the topical drug delivery system of Oxiconazole Nitrate in the form of Hydrogel. Oxiconazole Nitrate is widely used antifungal agent for fungal disease. The sample Oxiconazole Nitrate was firstly characterized for its identification by using physical characterization like melting point, FTIR and DSC. Hydrogels were developed using gelling agent, carbopol 934, Aloe vera and Carageenan. All the formulation developed were evaluated for the post formulation studies like visual inspection, pH, viscosity, spreadability, drug content, *In-vitro* drug release and Antifungal studies. All the result observed was within official limit. Formulation developed using Aloe vera (F6) show acceptable value as compared to hydrogel developed using other polymers. No phase separation was observed in F6 formulation. Drug content was found to be 96.91%, Spreadability 7.5 g.cm/sec, Viscosity 1025 cps, *In-vitro* drug release 65.64 %, Antifungal activity for *A. Niger* with 20mm zone of inhibition for F6 formulation. It was found that pH of all the formulation is in the range of 6.7 to 6.8 that suits the skin pH indicating skin compatibility. From the above study we have concluded that the topical gel prepared from the Aloe vera having good spreadability, bioadhesive strength and soothening effect. So the topical gel prepared from Aloe vera will be greatly for making an ideal topical preparation with no extra addition of smoothening effect.

KEYWORDS: Aloe Vera, Antifungal Gel, Oxiconazole Nitrate, Hydrogel.

INTRODUCTION

An antifungal medication is a pharmaceutical fungicide used to treat mycoses such as athlete's foot ringworm, candidiasis. Antifungal works by exploiting differences between

mammalian and fungal cells to kill the fungal organism without dangerous effect on host. The oral use of azoles is not recommended as it has many side effects. The topical route is generally preferred due to the possible side effect of oral medication and usually formulated as creams, lotion, or gels. Antifungal topical gel formulation using natural polymer is made for better patient compliance and to avoid the side effects. The gel was formulated by changing the polymer ratio. Gel are semisolid system in which a liquid phase is constrained within a three dimensional polymeric matrix of natural or synthetic gums in which a high degree of physical or chemical cross linking has been established.[1]

Most topical gels are prepared with organic polymer, such as carbomers, that impart an aesthetically pleasing, clear, sparkling appearance to the product and are easily washed off from the skin with water. The type of base used in formulating a topical dermatological product greatly influences its effectiveness. Bases containing large amount of oleaginous substances provide an emollient effect to dry irritated skin. More importantly, bases made up of non-volatile oleaginous substances (e.g. hydrocarbon bases) can form an occlusive barrier on the skin that prevents escape of moisture from the skin into the environment.[2]

The need of herbal excipients are increasing rapidly due to their lack of side effects. Herbal constitute having a major part in all traditional systems of medicines. The side effects of azole antifungal drugs can be minimized by converting it into formulation by using natural polymer. Extra addition of smoothening agent is not necessary. Oxiconazole nitrate is a potent anti-fungal drug, used in the treatment of fungal infection. Oxiconazole is a cream or lotion applied to the skin in the treatment of *tinea corporis, tinea pedis and tinea cruris*. Oxiconazole nitrate is BCS-II drug. It has adverse effects include: Burning, itching, blistering, crusting, dryness or flaking of the skin, scaling, severe redness, soreness, swelling and pain in hairy areas with pus at the root of hair and side effects like pruritus, burning, irritation, erythema, stinging and allergic contact dermatitis and folliculitis, fissuring, maceration rash and nodules. In this research work attempt has been made to formulate the topical drug delivery system of Oxiconazole Nitrate in the form of Hydrogel using natural polymer. Gel is viscous semisolid preparation which sticks to skin for long time. So to treat fungal conditions for long time, gel is the suitable dosage form. The gel is also targeted towards the synergistic effect of natural polymer which has antibacterial and antifungal activities. The gel is also expected to give emollient activity due to presence of aloe.

Gels are only the drug delivery system that have vast range of the advantages over the other topical drug delivery system.[3,5]

MATERIALS AND METHODS

Materials: The raw materials like drugs, polymers, excipients and chemicals required for the present work were procured from different sources.

Table 1: List of Materials.

Sr.No.	Drugs /polymers/Excipients/Solvents	Manufacturer
1.	Oxiconazole Nitrate	Yerrow chem products.Mumbai
2.	Carbopol-934	Loba Chemie Pvt. Ltd., Mumbai.
3.	Aloe Vera	Yerrow chem products.Mumbai
4.	Carageenan	Yerrow chem products.Mumbai
5.	Sodium benzoate	Vishal Chem, Mumbai
6.	Propylene glycol	Vishal Chem, Mumbai
7.	Triethanolamine	Vishal Chem, Mumbai

CHARACTERIZATION OF PURE DRUG

Melting Point[5]

Melting point of Oxiconazole nitrate was determined by capillary method. The sample was inserted in capillary tube having one end closed. Then the capillary was inserted in Thiele's tube which was heated in controlled manner. The temperature at which drug sample started melting was noted as melting point temperature. Average of triplicate readings was noted and compared with the literature value.

Purity of Drug

Differential Scanning Calorimetry (DSC)[5,14]

DSC was performed in order to assess the thermotropic properties and thermal behavior of the drug. It measures the heat flow in and out of both sample and reference during a controlled temperature program. The crystalline nature of the pure drug and its thermal behavior was studied by differential scanning calorimetry (DSC). About 5 mg of the sample was sealed in the aluminum pan and heated at the rate of 100˚C /min, covering a temperature range of 30˚C to 300˚C under nitrogen atmosphere of flow rate 20 ml/min and DSC thermogram (PerkinElmer 4000) for pure drug was obtained.

FTIR Spectroscopy[5,14]

IR study was carried out to check purity of drug. It was determined by Fourier Transform Infrared spectrophotometer (FTIR-Shimadzu). The sample was scanned over wavelength

region of 4000 to 400 cm-1 at resolution of 4 cm-1 by dispersing sample in KBr and compressing into disc by applying pressure of 5 tons for 5 minutes in hydraulic press. The pellet was placed in light path and the spectrum was obtained.

Drug Excipient Interaction Study[5,14]

Drug-excipient interaction study was performed by FTIR and DSC studies. IR study was carried out to check purity of drug. It was determined by Fourier Transform Infrared spectrophotometer (FTIR-Shimadzu). The spectra were scanned over wavelength region of 4000 to 400 cm-1 at resolution of 4 cm-1. The procedure consisted of dispersing sample in KBr and compressing into disc by applying pressure of 5 tons for 5 min in hydraulic press. The pellet was placed in light path and the spectrum was obtained.

DSC provides information about the physical properties of the sample as crystalline or amorphous nature and demonstrates a possible interaction between drug and other compounds. Thermal analysis using DSC (PerkinElmer 4000) study was carried out on drug Oxiconazole nitrate, physical mixture of drug and Carbopol 934, Aloe vera, Carageenan. Indium was used as a standard to calibrate the DSC temperature and enthalpy scale. Accurately weighed samples were used for the DSC study. Heating was done at a rate of 10°C/min.

Preparation of Oxiconazole Nitrate Antifungal gel[3,5]

Accurately weighed amount of carbopol 934 and natural polymers was taken and dissolved in water using propeller. Oxiconazole nitrate was added to the above solution with constant stirring. This final solution was neutralized slowly adding triethanolamine with constant stirring until the gel is formed. The formulation components for Antifungal gel are given in Table 2.

Table 2: Formulation of Oxiconazole Nitrate Antifungal Gel.

Ingredients	Formulation								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Oxiconazole Nitratre(mg)	100	100	100	100	100	100	100	100	100
Carbapol 934(mg)	500	750	1000	250	250	250	250	250	250
Aloe Vera powder (mg)	---	---	---	750	1250	1750	---	---	---
Carageenan (mg)	---	---	---	---	---	---	750	1250	1750
Sodium benzoate (mg)	50	50	50	50	50	50	50	50	50
Propylene glycol (ml)	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75
Triethanolamine (ml)	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Water q.s to (gm)	10	10	10	10	10	10	10	10	10

Evaluation of Oxiconazole nitrate Gel

Visual Inspection[15]

The prepared gel formulations of Oxiconazole nitrate were inspected visually for their color, texture and appearance.

pH Measurement[7,12,16]

The pH of gel formulation was determined by using digital pH meter. One gram of gel was dissolved in 100 ml distilled water and stored for two hours.The measurement of pH of formulation was done.

Spreadability Studies[10,15,17]

One of the criteria for a gel to meet the ideal qualities is that it should possess good spreadability. It is the term expressed to denote the extent of area to which gel readily spreads on application to skin or affected part. The therapeutic efficacy of a formulation also depends upon its spreading value. Spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel placed in between the slides under the direction of certain load. Lesser the time taken for separation of two slides, better the spreadability.

Spreadability was determined by glass slides and a wooden block, which was provided by a pulley at one end. By this method, spreadability was measured on the basis of Slip and Drag characteristics of gels. A ground glass slide was fixed on this block. An excess of gel (about 1gm) of different formulations were placed on the ground slide. The gel was then sandwiched between this slide and another glass slide having the dimension of fixed ground slide. Excess of the gel was scrapped off from the edges. The top plate was then subjected to pull of 20gms, lesser the time taken for separation of two slides better the spreadability.

Spreadability was then calculated using the following formula:

$S = M \times L / T$ ….Eqn (1)

Where, S = is the spreadability, M = is the weight in the pan (tied to the upper slide), L = is the length moved by the glass slide T = represents the time taken to separate the slide completely from each other.

Fig.1: Spreadability Measurement Instrument.

Viscosity Measurement[8,17,19]

The viscosity of the different gel formulations was determined using a Brookfield viscometer with spindle no. 64 at 100 rpm at temperature 25˚C. The viscosity of the optimized formulation was determined as such without dilution using Brookfield Viscometer (Model - LVDV-E). Brookfield Viscometer consists of a cup, which is stationary and a spindle which is rotating. Different sized rotating spindles are used and immersed in test material. For liquids with low viscosity, large size spindles (large diameter and surface area) are used while for higher viscosity liquids small spindles (small diameter and surface area) are used. Rotate the spindle in the Antifungal gel till we get a constant dial reading on the display of the viscometer. This procedure is repeated three times for reproducible results.

Drug content[10,17]

1gm of Oxiconazole nitrate antifungal gel was accurately weighed dissolved using methanol, sonicated for a period of 10- 15 mins and made up to the mark in 100 ml volumetric flask with methanol. From this 10 ml was pipetted out and diluted to 100 ml with methanol and the final dilution was made using distilled water to get a concentration within Beer's range. The absorbance was measured by UVspectrophotometer (Dynamica, Halo DB-20) at 260 nm against blank gel treated in the same manner as sample.

Motic Digital Microscopy[18]

For morphology and surface topography, prepared Antifungal gel can be placed on glass slide at room temperature and then the surface morphology of the gel can be studied by Motic Digital Microscopy (B1 advanced series). Motic Digital Microscopy of a gel can also be taken to illustrate its ultra structure.

The morphology of Oxiconazole nitrate Antifungal gel was examined with a Motic Digital Microscopy. The samples were mounted on a glass slide and observed under 10X object.

***In-vitro* Diffusion Study**[14,17]

In-vitro studies of the gel were carried out across the egg membrane extracted by using the concentrated HCl. The receptor compartments were filled with phosphate buffered saline (PBS) pH 7.4, Study was carried out using excised egg membrane. Franz diffusion cell with 30ml receptor compartment and effective area 4.52cm² was placed on a thermostatic magnetic stirrer and the temperature was maintained at 37˚C throughout the study. All batches of Antifungal gel were used for the diffusion study using diffusion cell. Aliquots, each of 1 ml volume were withdrawn at specific intervals and replaced by an equal volume of the receptor medium. The aliquots were suitably diluted with the receptor medium. Release studies were carried out over a period of 8 hrs at regular intervals. Samples were withdrawn and analyzed by UV spectrophotometer (Dynamica, Halo DB-20) at 261 nm. Calculations were done by following formulae:

1. Determination of concentration of diffused drug (µg/ml)

Slope and intercept were determined by using graph of absorbance versus concentration.

Y = mX + c …. Eqn (2)

Where, Y = Absorbance, m = Slope, X = Concentration and c = Intercept.

2. Cumulative amount of drug diffused (CADD)

[Concentration (µg/ml)* Volume of diffusion medium* Dilution factor] / 1000

3. Surface area (A) of egg membrane (cm2)

A = πr2 ….Eqn (3)

4. Cumulative amount of drug diffused per unit area (CADD/cm2)

CADD/cm2 = CADD/ Area of membrane ….Eqn (4)

5. Flux (Jss): Slope of linear portion of amount of drug diffused per unit area versus time.

6. Permeability Coefficient (Kp): Jss/Cv ….Eqn (5)

Determination of Antifungal activity[8,20]

Test Microorganism:

Fungi: *A. Niger*,

Preparation of Inoculums

For evaluation of antifungal activity, 24 hours fresh culture of fungi was suspended in sterile water to obtain a uniform suspension of microorganism.

Determination of zone of inhibition

Antifungal activity was checked by agar well diffusion method. In this method a previously liquefied medium was inoculated with 0.2 ml of fungal suspension having a uniform turbidity at temperature of 40^0C. 20 ml of culture medium was poured into the sterile petri dish having a internal diameter of 8.5 cm. Care was taken for the uniform thickness of the layer of medium in different plates. After complete solidification of liquefied inoculated medium, the wells were made aseptically with cork borer having 6mm diameter. In each of these plate gel solution was placed carefully. Plates were kept for pre diffusion for 30 mins. After it normalized to room temperature; the plates were incubated at 27ºc for 48 hrs in case of fungi. After incubation period was over, the zone of inhibition was measured with the help of Hi-antibiotic zone scale.

RESULTS AND DISCUSSION

Characterization of Pure Drug

Melting Point

Melting point of oxiconazole nitrate was found to be in the range of 137-138˚C, while as per literature standard it is reported to be 137-138°C. As experimental values were in good agreement with official values, it could be concluded that oxiconazole nitrate procured was in pure state.

Purity of Drug

Differential Scanning Calorimetry (DSC)

According to the thermogram, a sharp endothermic peak was observed at 133.74˚C corresponding to the melting point of drug in the crystalline form. Thus the thermogram confirmed the purity of drug shown in Fig. 2.

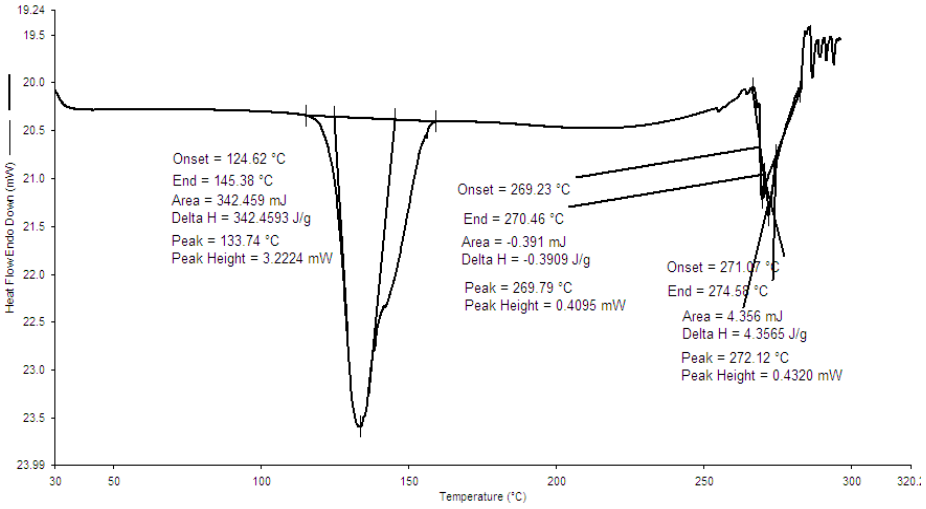

Fig. 2: DSC OF Oxiconazole Nitrate.

FTIR Spectroscopy

The infrared spectrum of Oxiconazole Nitrate was recorded and spectral analysis was done using FTIR spectroscopy which is shown in Fig. 3.

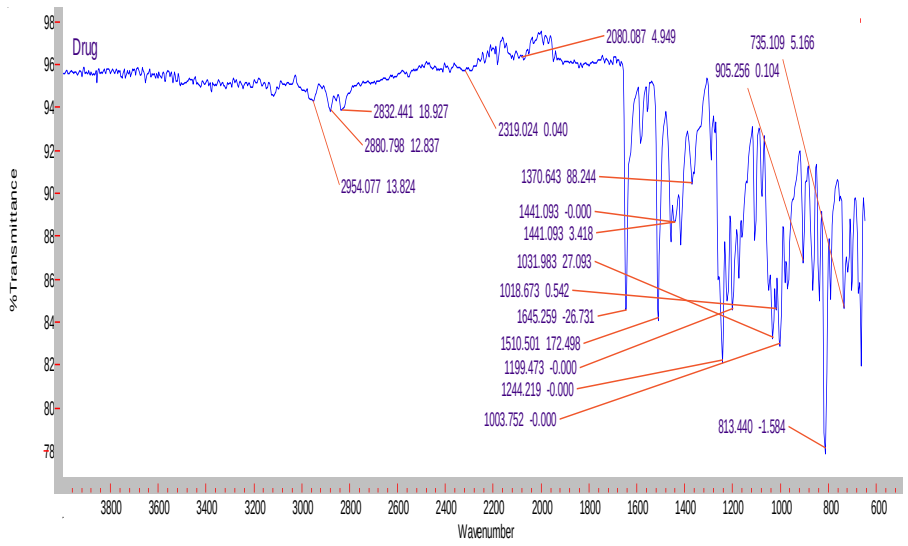

Fig. 3: FTIR spectrum of Oxiconazole Nitrate.

Table 3: Characteristic peaks of FTIR spectrum of Oxiconazole Nitrate.

Sr. No.	Wave number(cm-1)	Standard Ranges	Functional groups Associated
1.	1510.501	1600-1475	C=C stretching (Aromatic)
2.	735.109	785-540	C-Cl stretching
3.	2945.077	2900-2800	C-H (Methylene) stretching
4.	1441.093	1475-1455	C=N stretching
5.	1370.643	1330-1384	N-O stretching

The IR spectrum of drug exhibited distinctive peaks at 1441.093 (cm-1) due to C=N stretching. The peaks at 1510.501 (cm-1) is due to the C=C stretching and at 735.109 (cm-1) is due to the C-Cl stretching. The peak at 2945.077 (cm-1) is due to the C-H (methylene) stretching. The peak at 1370.643 (cm-1) is due to N-O stretching.

The infrared spectral analysis of the procured oxiconazole nitrate was compared with the standard IR values of oxiconazole nitrate. In the course of IR study, it was found that all the important characteristic peaks were present, which confirmed the purity of drug sample.

Drug Excipient Interaction Study

Compatibility study was carried out to check for any possible interaction between the drug and the excipients used. Drug - excipient interaction study was performed by FTIR and DSC study.

Drug-Excipient Interaction Study by FTIR Spectrum:

The FTIR spectra of drug, physical mixture of drug and Carbopol-934, Aloe vera and Carageenan and Optimized formulation (F6) respectively.

FTIR spectroscopic study revealed that there was no appearance of any new peak and disappearance of existing peaks, which indicated that there was no chemical interaction between the drug and polymer used. The IR spectrum exhibited distinctive peaks at 1406.022 (cm-1) due to C=N stretching. The peaks at 1637.188 (cm-1) is due to the C=C stretching and at 752.28 (cm-1) is due to the C-Cl stretching. The peak at 3267.991is due to the C-H methylene stretching. The peak at 1384.89 is due to N-O stretching.

All the characteristic peaks of Oxiconazole nitrate were observed in the IR spectra of physical mixture and optimized formulation during the investigation of compatibility study. Hence IR spectroscopy results showed that the drug was compatible with selected polymer and was stable in all gel formulations.

Table 4: Characteristic peaks of FTIR spectrum of Optimized Formulation.

Sr. No.	Observed value	Standard Ranges	Functional groups Associated
1.	1637.188	1600 -1475	C=C stretching (Aromatic)
2.	752.28	785-540	C-Cl stretching
3.	3267.991	2900-2800	C-H (Methylene) stretching
4.	1406.022	1475-1455	C=N stretching
5.	1384.89	1330-1384	N-O stretching

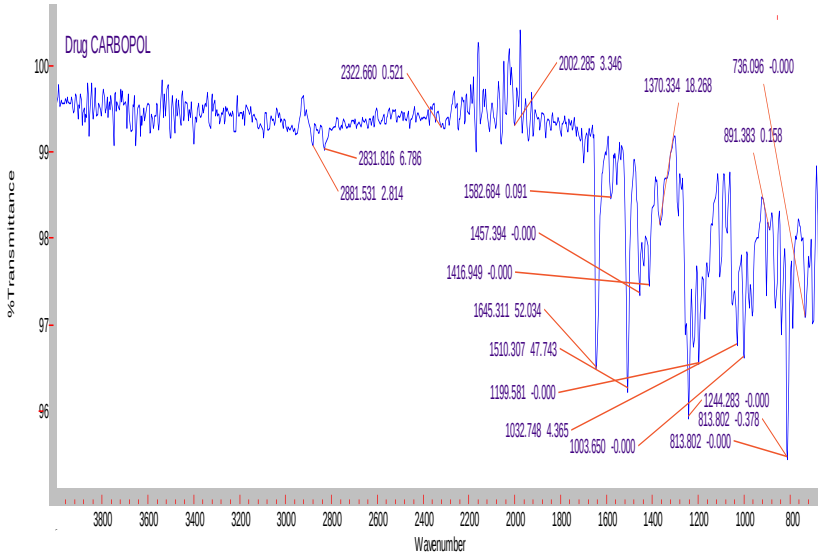

Fig. 4: FTIR Spectrum of Physical mixture(Drug & Carbapol-934).

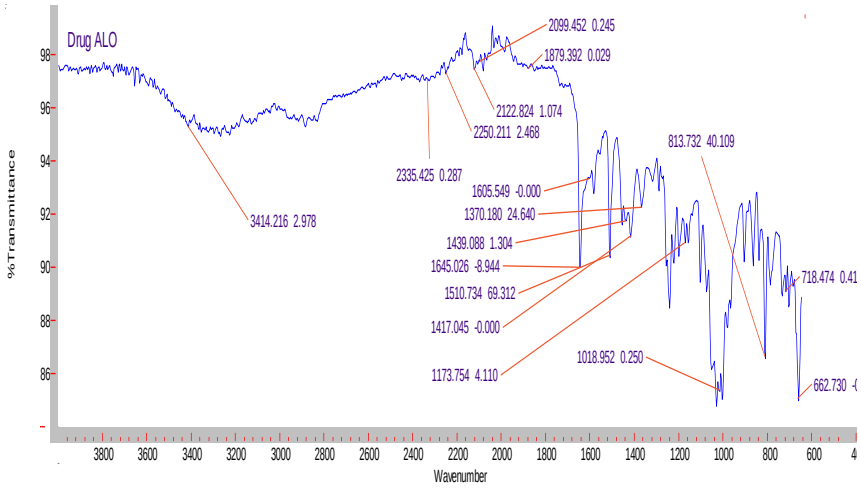

Fig. 5: FTIR Spectrum of Physical mixture(Drug&Aloe vera).

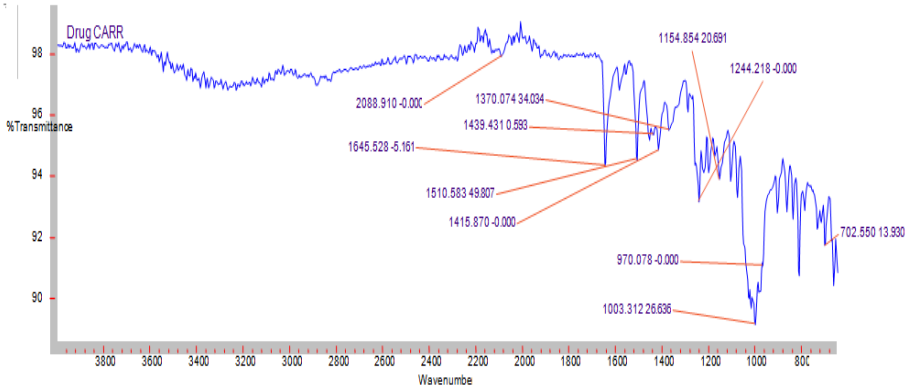

Fig. 6: FTIR Spectrum of Physical mixture(Drug & Carageenan).

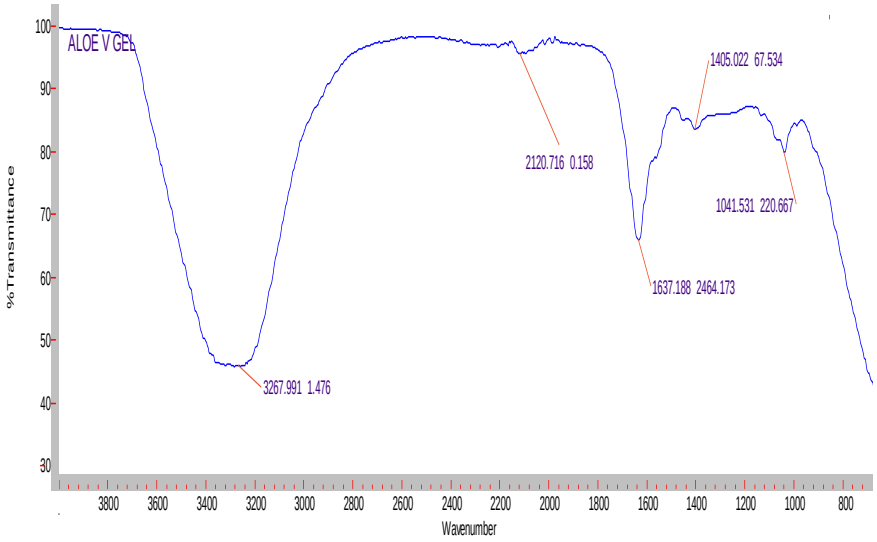

Fig. 7: FTIR spectrum of Optimized formulation.

Drug-Excipient Interaction Study by DSC Thermogram

In DSC studies, dispersed in polymer showed the same thermal behavior as pure compound. In the thermogram the endothermic peak was observed at 106.31°C which does not corresponds to the melting point of the pure drug (Fig.No.8). During formulation of Antifungal gel, the drug was entrapped inside it and was not available for showing any exothermic peak. Hence, no endothermic peak near to melting point of drug was observed confirming the entrapment of drug in natural polymer used in Antifungal gel. This indicates that the physical properties of Oxiconazole nitrate are altered during gel formulation.

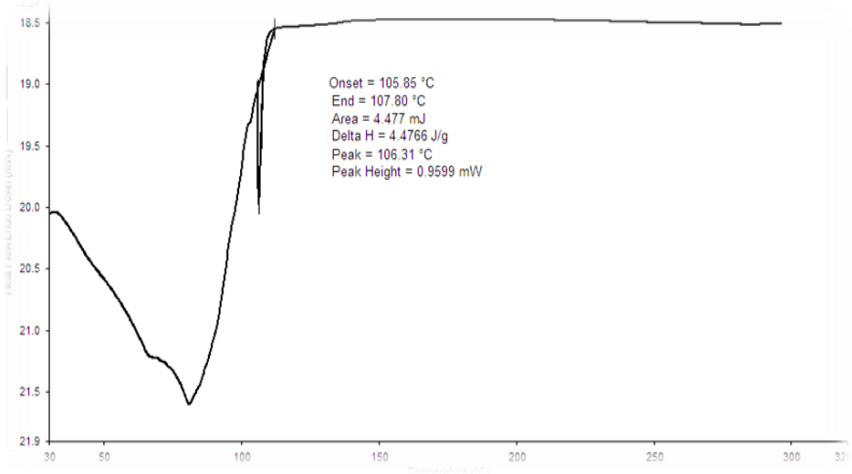

Fig. 8: DSC OF Optimized formulation.

Evaluation of Oxiconazole nitrate Antifungal Gel

Visual Inspection

The prepared gel formulations of Oxiconazole nitrate were inspected visually for their color, texture and appearance. All prepared formulations were pearl white, viscous preparations with a smooth texture and showed good homogeneity with absence of any lumps and syneresis.

pH Measurement

The pH values of all prepared Antifungal gel formulations were found to be in the range of 6.7 to 6.8, which were considered to be acceptable to avoid the risk of irritation upon application to the skin are shown in Table 5.

Spreadability Study

The values of spreadability indicated that the gel was easily spreadable by small amount of shear. Spreadability of Antifungal gel was found to be 7.5g.cm/sec; indicating that spreadability of drug loaded Antifungal gel was good is shown in Table 5.

Viscosity Studies

The viscosity studies for Antifungal gel formulations were carried out. The viscosities of all formulations are shown in Table 5.

Drug content Studies

Drug content studies for Antifungal gel formulations were carried out. Drug content of all formulations are shown in Table 5.

Table 5: Evaluation of Antifungal gel formulation (Mean ± SD; n=3).

Formulation	P^H	Spreadability (g.cm/sec)	Viscosity (cps)	Drug content (%)
F1	6.8±0.06	5.5±0.33	1000±2	77.80±0.03
F2	6.7±0.06	5.0±0.25	1010±2	75.24±0.01
F3	6.8±0.06	6.0±0.17	1025±0.58	79.14±0.03
F4	6.7±0.06	5.0±0.25	1010±2	76.53±0.01
F5	6.8±0.06	6.0±0.17	1022±2	87.59±0.03
F6	6.8±0.06	7.5±0.33	1025±0.58	96.91±0.01
F7	6.7±0.06	5.0±0.25	1015±2	80.26±0.03
F8	6.7±0.06	6.0±0.17	1020±0.58	81.25±0.01
F9	6.8±0.06	6.0±0.17	1025±0.58	84.25±0.03

Motic Digital Microscopy

The morphology of the Antifungal gel prepared by Solid dispersion method and entrapment method was investigated by Motic Digital microscope (B1 Advanced series). The representative motic microscopic images of Antifungal gel are shown in Fig.13. Antifungal gel image by Motic Digital microscope (B1 Advanced series) showed that three dimensional cross-linked network within the liquid.

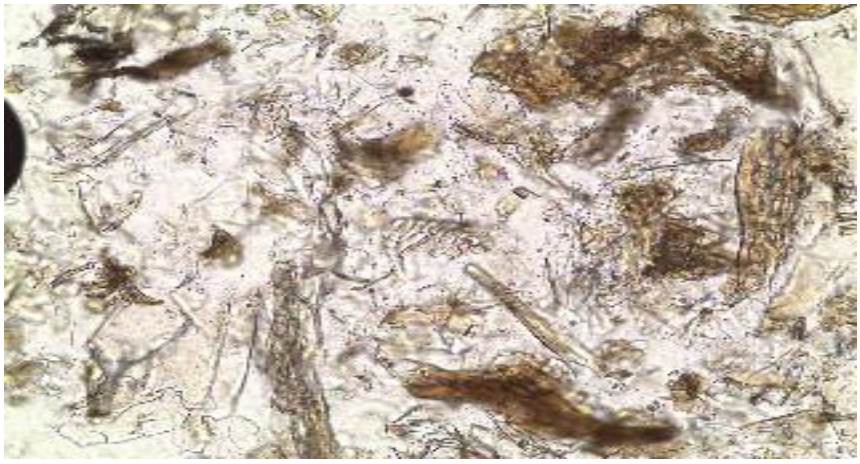

Fig. 9: Image of Antifungal gel.

***In-vitro* Diffusion Study**

The *in-vitro* diffusion studies were carried out for all formulations using PBS (pH 7.4). *In-vitro* diffusion of all formulation is shown in Table 6.

Table 6: %CADD per unit area of Antifungal gel formulations F1- F9.

Time (mins)	Formulations (%CADD/ cm^2)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
60	1.32	0.95	10.41	3.45	2.84	1.85	4.44	1.85	1.76
120	6.18	5.73	15.64	8.22	9.79	9.44	12.71	7.40	4.22
180	14.04	11.42	19.30	15.63	10.80	18.50	20.55	15.26	13.15
240	19.95	21.06	28.82	28.09	15.36	19.80	26.64	18.50	17.70
300	32.05	30.42	37.92	45.72	28.77	25.44	37.56	23.74	29.16
360	41.50	39.65	46.74	68.81	40.15	37.65	43.57	36.19	36.53
420	57.55	48.99	56.31	78.53	53.31	54.76	62.81	58.23	48.72
480	67.71	67.99	66.83	80.24	75.65	65.64	85.77	70.66	67.68

The drug release was found to be decreased in the range of 85.77 % to 65.64 % for F1 to F9 as the drug: polymer ratio was changed. The drug release was found to be decreased in the range of 67.99 to 66.83% for Carbopol -934, 85.77 to 65.64% for Aloe vera and 85.24 % to 67.68% for Carageenan as the drug: polymer ratio was changed. The reason behind is as drug: polymer ratio was increased, longer diffusion path and ultimately to decreased drug release. The drug release i.e. 65.64 % was found for the formulation F6. It has been reported that with increasing amount of polymer from batches F1-F9, the drug release went on decreasing. It might be due to fact that the polymer matrix releases drug after complete swelling and time required for swelling of polymer is directly proportional to polymer concentration. Graphical presentation of all batches (F1–F9) is shown in Figure below respectively.

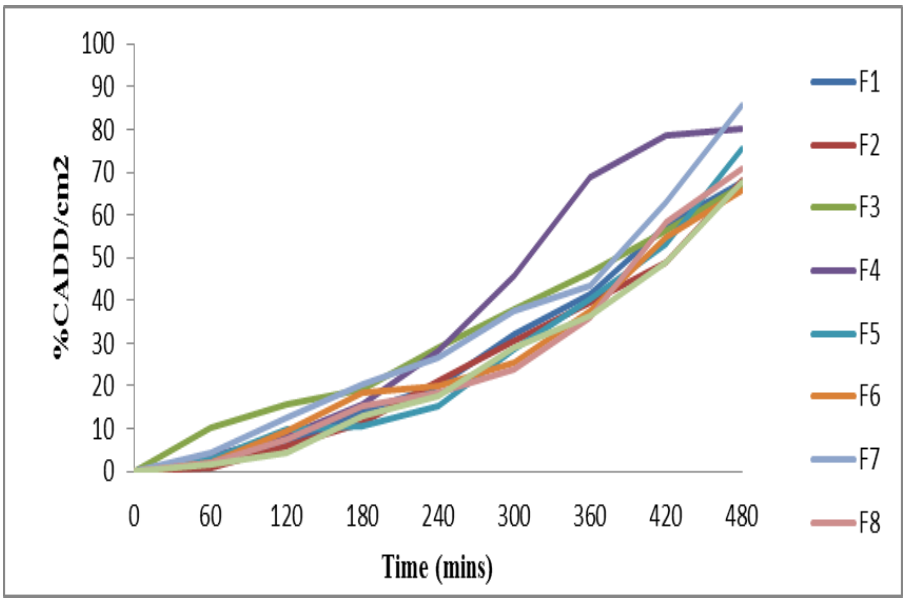

Fig. 10: Comparative drug release profile of F1- F9.

Determination of Antifungal activity

Fig. 11: Image of zone of Inhibition of Optimized Antifungal gel formulation.

Table 7: Zone of Inhibition of Optimized Antifungal gel formulation.

Strain	Conc^{n} in mg	Zone of inhibition
A. niger	10	20mm

CONCLUSION

In the present study, an attempt has been made to formulate the topical drug delivery system of Oxiconazole Nitrate in the form of Hydrogel. Oxiconazole Nitrate is widely used antifungal agent mostly used for fungal disease. The sample Oxiconazole Nitrate was firstly characterized for its identification by using physical characterization test like melting point, FTIR and DSC. Hydrogels were developed using gelling agent, carbopol 934, Aloe vera and Carageenan. Sodium Benzoate as a preservative and Oxiconazole Nitrate as hydrophobic drug in water soluble gel bases. All the formulation developed were evaluated for the post formulation studies like color, pH, viscosity, spreadability, drug content, *In-vitro* drug release and Antifungal studies. All the result observed was within official limit. Formulation developed using Aloe vera (F6) show acceptable value as compared to hydrogels developed using other polymers. No phase separation was observed in F6 formulation. Drug content was found to be 96.91%, Spreadability 7.5 g.cm/sec, Viscosity 1025 cps, *In-vitro* drug release is 65.64 %, Antifungal activity for *A. Niger* with 20mm zone of inhibition for F6 formulation. It was found that pH of all the formulation is in the range of 6.7 to 6.8 that suits the skin pH indicating skin compatibility. This is the primary requirement for a good topical formulation.

From the above study we have concluded that the topical gel prepared from the Aloe vera having good spreadability, bioadhesive strength and soothening effect. So the topical gel prepared from Aloe vera will be greatly for making an ideal topical preparation with on extra addition of smoothening effect and has the greater drug content properties in comparison of others it means topical gel prepared from other polymer. From the *In – vitro* drug diffusion study we have concluded that the gel prepared from Aloe vera, controls the release of drug for longer period of time which will be helpful to avoid the more fluctuation and also reduces the cost of therapy.

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