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FORMULATION AND *INVITRO* EVALUATION OF ECONAZOLE NITRATE TOPICAL GEL

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Abstarct:
In the present work an attempt was being made to formulate and evaluate Topical gel containing anti inflammatory drug Econazole nitrate. Carbopol 971, Guar gum and carbopol 934 were selected as polymers.The drug and excipient compatability was studied by using FTIR Nine formulations of gels were prepared by taking different quantities of polymers. The prepared gel was subjected to various evaluation tests like pH, spreadability, viscosity, content uniformity and diffusion studies conducted upto 12hrs.All the results were with in the limits , by diffusion studies it was observed that formulation F7 shown maximum drug release of 95.49% which was considered as optimized formulation.

Key words: *Econazole nitrate, Topical , Carbopol 971, Guar gum and carbopol 934*

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INTRODUCTION:

Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. Skin is one of the most readily accessible organs on human body for topical administration and is main route of topical drug delivery system. Topical drug delivery systems have been used for centuries for the treatment of local skin disorders, one side the topical applications of the drug offer the potential advantages of delivering the drug directly to the site of action and delivering the drug for extended period of time at the affected site that mainly acts at the related regions. When applied to diseased skin, topical drug products induce one or more therapeutic responses. For the most part topical preparations are used for the localized effects at the site of their application by virtue of drug penetration into the underlying layers of skin or mucous membrane. Although some unintended drug absorption may occur, it is sub therapeutics quantities and generally of minor concern. The delivery of drug onto the skin is recognized as an effective means of therapy for local dermatological diseases. Econazole nitrate is an antifungal agent which belongs to imidazole derivate/ ring structure. The spectrum of activity includes dermatophytes, Candida, yeasts, dimorphic fungi and Gram-positive bacteria. Its mechanism of action may involve inhibition of membrane enzymes, including cytochrome P450, and lipid biosynthesis. The bactericidal and inhibitory effects of several azole antifungal compounds, including econazole nitrate against Mycobacterium segmatis has been investigated. No significant side-effects or adverse effects have been recorded with this compound either during drug safety trials or during clinical use, among pregnant and non-pregnant patients. Econazole nitrate is available commercially as tablets and injections, in spite of its well known adverse effects including nausea, vomiting, bloating, and abdominal discomfort. Oral econazole cannot be taken in conjunction with a number of medications. In order to bypass these disadvantages, the topical gel formulation have been proposed. The aim of the present research work is to formulate and evaluate antifungal gel containing econazole nitrate for topical drug delivery. To treat the disease caused by *Candida species* by using different types of smart polymers (synthetic and natural polymers).

MATERIALS AND METHODS:

Carbopol 971, Carbopol 934, Guar gum, Methanol, Water, Triethanolamine, Polyethylene glycol, Methyl parabben, all the chemicals used were lab grade.

Preparation of Econazole Nitrate Topical Gel

Table-1 Composition of different emulgel formulations

Formulation (F)	Drug (mg)	Carbopol 971 (mg)	Guar gum	Carbopol 934 (mg)	Methanol (ml)	Triethanolamine(ml)	Polyethylene glycol (mg)	Methyl parabben (mg)	Water
F_1	50	50	-	-	10	5	2	2	Q.s
F_2	50	100	-	-	10	5	2	2	Q.s
F_3	50	150	-	-	10	5	2	2	Q.s
F_4	50	-	50	-	10	5	2	2	Q.s
F_5	50	-	100	-	10	5	2	2	Q.s
F_6	50	-	150	-	10	5	2	2	Q.s
F_7	50	-		50	10	5	2	2	Q.s
F_8	50	-		100	10	5	2	2	Q.s
F_9	50	-		150	10	5	2	2	Q.s

Preparation of Econazole nitrate gel

Above mentioned quantity of carbopol 934, Carbopol 971, Guar gum was soaked in water for a period of 2 hours. Carbopol was then neutralized with triethanolamine (TEA) with stirring. Then specified amount of drug was dissolved in appropriate and preweighted amounts of propylene glycol and methanol. Solvent blend was transferred to carbopol container and agitated for additional 20 min. The dispersion was then allowed to hydrate and swell for 60 min, finally adjusted the pH with 98% TEA until the desired pH value was approximately reached (6.8-7). During pH adjustment, the mixture was stirred gently with a spatula until homogeneous gel was formed. All the samples were allowed to equilibrate for at least 24 hours at room temperature prior to performing rheological measurements.

Evaluation Of Prepared Gel Formulations

The prepared gels were evaluated for various evaluation parametrers like Percentage yield, pH measurement, spreadability, viscosity measurement, in-vitro diffusion study of the topical gel.

RESULTS AND DISCUSSION:

Analytical Study

Scanning of drug

Econazole nitrate pure drug was scanned in methanol between 200 nm and 400 nm using ultraviolet spectrophotometer. Econazole nitrate was identified by its light absorption pattern which follows the absorption of light in the range 220 to 400 nm and a maximum absorbance at about 234 nm. A broad shoulder at about 234 nm was observed which confirm the presence of Econazole nitrate .Econazole nitrate gave highest peak at 234 nm and the same was selected for further evaluations.

Calibration curve in water (make up with ph 6.8 phosphate buffer)

Standard solutions of different concentrations were prepared and their absorbance was measured at 234 nm (Table 13). Calibration curve was plotted against drug concentrations versus absorbance as given in the (Figure.7).

Table 2 Determination of λ_{max} of Econazole nitrate in methanol-- λ_{max} = 234 nm

Concentration (µg /ml)	Absorbance
0	0
2	0.139
4	0.258
6	0.391
8	0.501
10	0.616
12	0.734

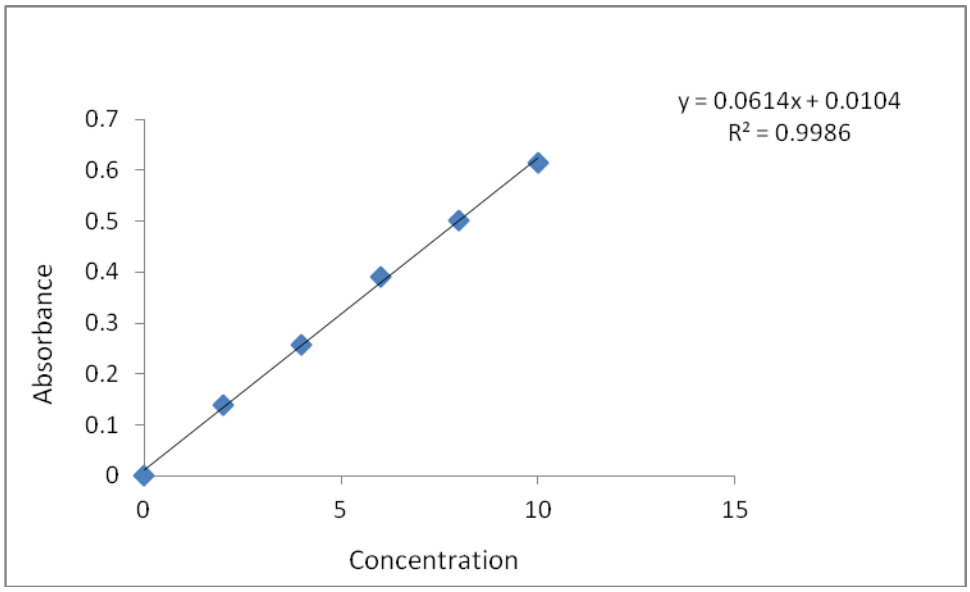

Figure 1: Standard graph of Econazole nitrate

Since the physical characterization is meant for physical integrity of the dosage form, the results were pooled at one place. Discussion on the results, described for gel formulation under the same heading.

Percentage yield

Sl.no	Formulation	Percentage yield
1	F1	90.54
2	F2	95.67
3	F3	93.48
4	F4	92.33
5	F5	93.75
6	F6	94.28
7	F7	91.22
8	F8	95.89
9	F9	91.33

Table 3: Percentage yield of gel formulations

Drug content

Sl.no	Formulation	Drug content
1	F1	92
2	F2	96
3	F3	91
4	F4	95
5	F5	94
6	F6	93
7	F7	92
8	F8	97
9	F9	94

Table 4: Drug content of gel formulations

Viscosity

Sl.no	Formulation	Viscosity (cps)
1	F1	63,540.06
2	F2	91,669.03
3	F3	92362.37
4	F4	1,19,000.01
5	F5	1,35,677.30
6	F6	61,552.01
7	F7	99,882.04
8	F8	1,27,023.07
9	F9	97,489.04

Table 5: Viscosity of gel formulations

pH measurement

Sl.no	Formulation	pH
1	F1	6.8
2	F2	7
3	F3	6.4
4	F4	6.2
5	F5	6.8
6	F6	7.1
7	F7	6.8
8	F8	6.4
9	F9	6.9

Table 6: pH of gel formulations

Spreadability studies

Sl.no	Formulation	Spreadability $gm.cm^2$
1	F1	11.06
2	F2	11.96
3	F3	10.72
4	F4	11.88
5	F5	10.57
6	F6	11.10
7	F7	10.84
8	F8	11.65
9	F9	11.09

Table 7: Spreadability values of gel formulations

***In-Vitro* Drug Permeation Studies**

In-vitro skin permeation study or in-vitro diffusion study has been extensively studied, developed and used as an indirect measurement of drug solubility, especially in preliminary assessment of formulation factors and manufacturing methods that are likely to influence bioavailability. The objectives in the development of in-vitro diffusion tests are to show the release rate and extent of drug from the dosage form. The in-vitro drug permeation study of Econazole nitrate from gel formulation was studied using Franz diffusion cell and the method described in methodology chapter. The release data was obtained for all the gel formulations. Spectrometric

results were obtained and given consideration to sampling loss, to calculate actual cumulative drug diffused was calculated since the volume of receptor cell was only 20 ml (table-8). The obtained diffused amount of drug was extrapolated to diffusion by unit surface area of semi permeable membrane.

***In-Vitro* Release Studies**

Table 8 In-vitro cumulative % drug release profile for Econazole nitrate

Time	Cumulative % drug release								
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
0	0	0	0	0	0	0	0	0	**0**
30min	13.56	18.5	11.09	18.09	12.39	12.01	10.21	3.11	**5.54**
1hr	24.55	33.52	19.26	32.51	22.21	17.09	20.62	7.15	**12.17**
2hr	31.86	35.3	25.21	37.42	26.22	25.31	30.72	14.21	**24.58**
3hr	34.22	40.52	31.71	46.42	32.09	29.69	33.32	27.54	**33.19**
4hr	39.26	45.81	35.21	50.31	35.21	31.03	37.29	35.45	**39.79**
5hr	41.62	55.32	39.05	56.51	38.02	33.61	40.25	45.21	**48.69**
6hr	44.72	59.5	45.02	59.41	43.3	35.3	44.91	53.77	**52.75**
7hr	49.25	62.32	49.05	61.21	47.31	41.65	52.41	59.34	**61.38**
8hr	53.45	66.92	55.51	65.72	49.85	43.32	57.86	66.73	**67.54**
9hr	60.53	70.07	59.37	72.46	55.31	47.32	59.92	77.69	**75.28**
10hr	67.02	75.41	68.42	78.32	65.21	51.09	62.59	85.54	**79.19**
11hr	73.52	79.2	71.31	85.31	69.71	56.31	65.43	91.15	**81.14**
12hr	**76.89**	**82.41**	**74.62**	**87.42**	**73.09**	**65.21**	**67.19**	**95.49**	**86.68**

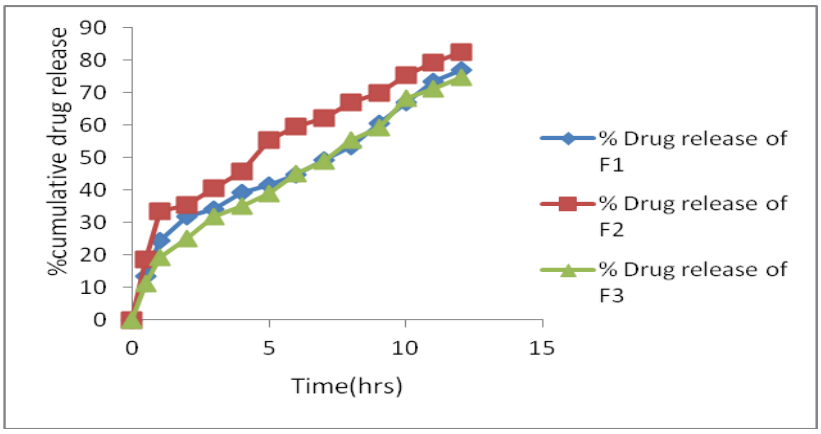

Figure :2. Dissolution graphs for the formulations F1,F2,F3

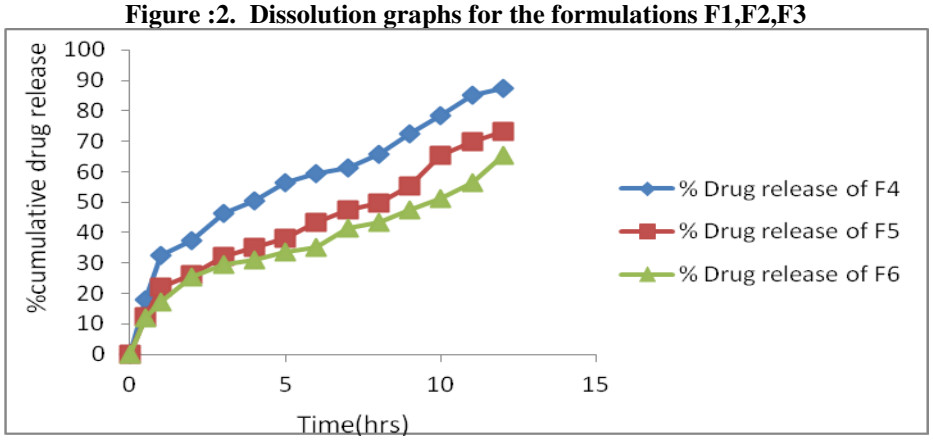

Figure :3 Dissolution graphs for the formulations F4,F5,F6

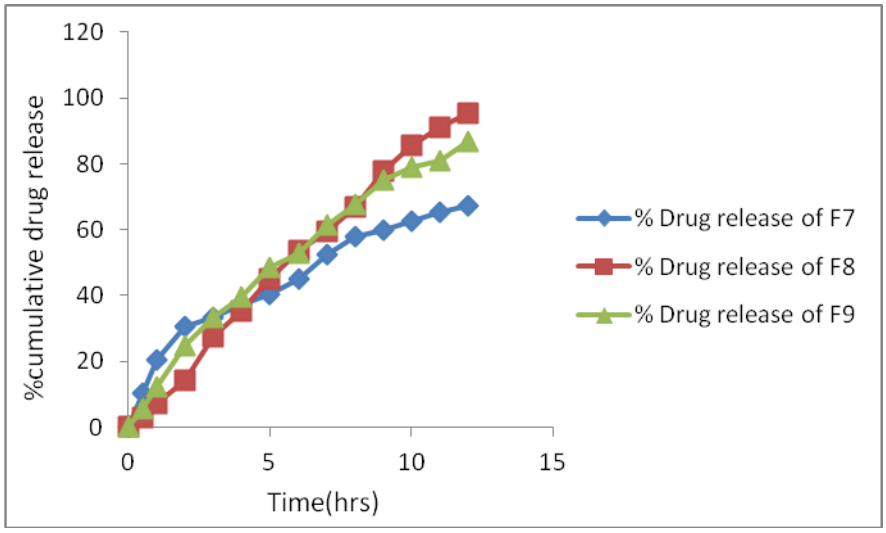

Figure :4 Dissolution graphs for the formulations F7,F8,F9

Table :9 Release kinetics

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN
0	0	0			2.000
3.11	0.5	0.707	0.493	-0.301	1.986
7.15	1	1.000	0.854	0.000	1.968
14.21	2	1.414	1.153	0.301	1.933
27.54	3	1.732	1.440	0.477	1.860
35.45	4	2.000	1.550	0.602	1.810
45.21	5	2.236	1.655	0.699	1.739
53.77	6	2.449	1.731	0.778	1.665
59.34	7	2.646	1.773	0.845	1.609
66.73	8	2.828	1.824	0.903	1.522
77.69	9	3.000	1.890	0.954	1.348
85.54	10	3.162	1.932	1.000	1.160
91.15	11	3.317	1.960	1.041	0.947
95.49	12	3.464	1.980	1.079	0.654

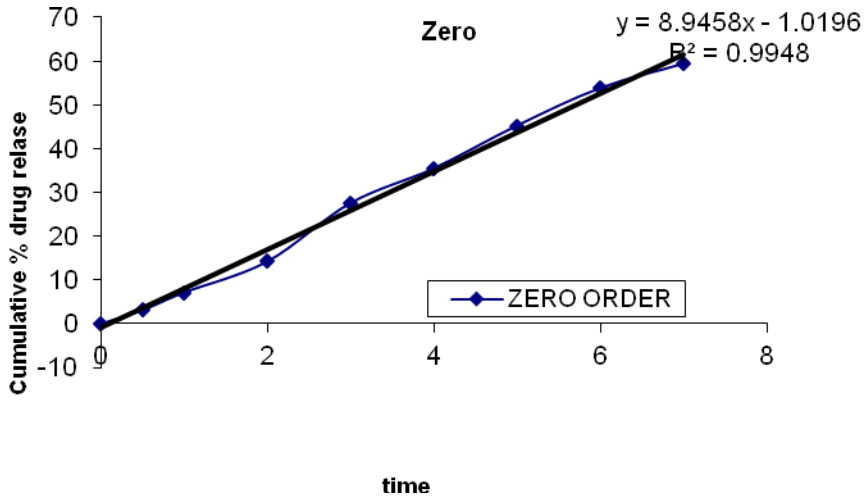

Figure: 5 kinetic model Zero order

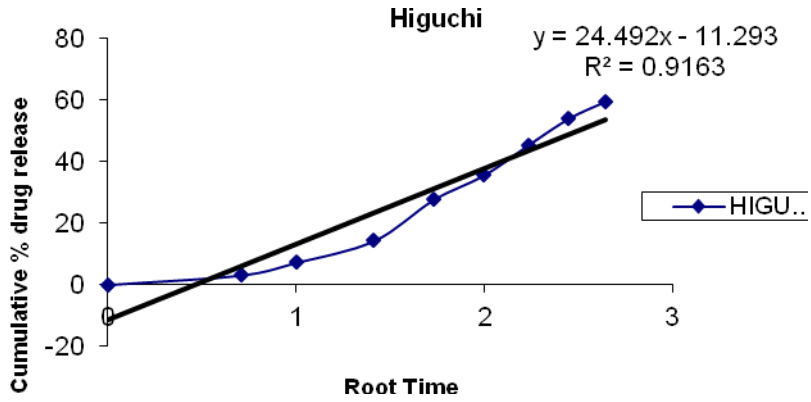

Figure :6 kinetic model-higuchi

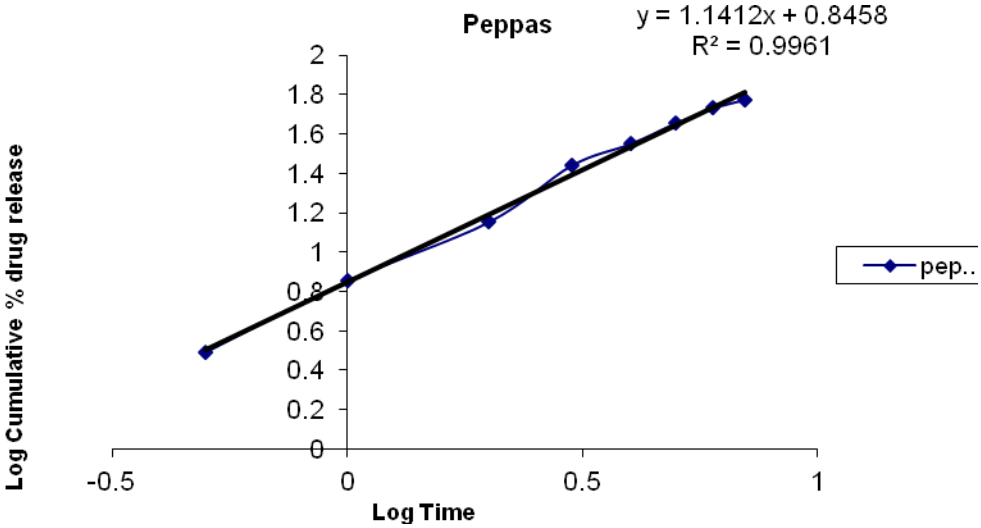

Figure : 7 kinetic model-peppas

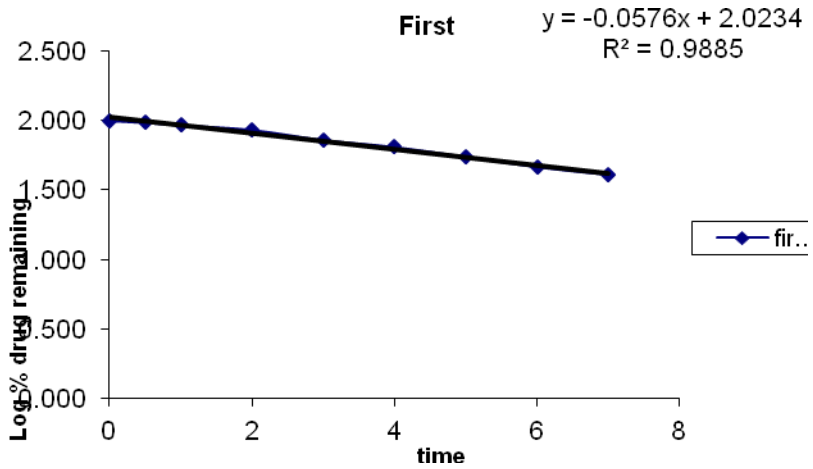

Figure: 8 kinetic model First order

CONCLUSION:

In the present work an attempt was being made to formulate and evaluate topical gel containing anti inflammatory drug Econazole nitrate. Carbopol 971, Guar gum and carbopol 934 were selected as polymers. The drug and excipient compatability was studied by using FTIR Nine formulations of gels were prepared by taking different quantities of polymers .The prepared gel was subjected to various evaluation tests like pH, spreadability, viscosity, content uniformity and diffusion studies conducted upto 12hrs. All the results were with in the limits , by diffusion studies it was observed that formulation F7 shown maximum drug release of 95.49% which was considered as optimized formulation.

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