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FORMULATION AND EVALUATION OF TOPICAL HYDROGEL OF ANTIFUNGAL DRUG OF TERBINAFINE HCL (RESEARCH PAPER)

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ABSTRACT
Topical Hydrogel preparations are intended for skin application or to certain mucosal surfaces for local action or transdermal penetration of medicament or for their emollient or protective action**.** Terbinafine HCl is an antifungal drug use to treatment of fungal infection. The oral rout of drug is not recommended due to the side effect. Topical Preparation avoid the side effect associated due to oral formulation and give the local effect. This study was conducted to formulate and evaluate Terbinafine hydrochloride topical hydrogel for treatment of fungal infection of skin. The hydrogel was formulated by using different gelling agents like HPMC, Carbapol 934, Guar Gum and CMC in different concentration. The prepared hydrogel formulations were evaluated for physico-chemical parameters like physical appearance, pH, drug release, drug content. The in vitro drug release from Hydrogels was evaluated using Franz diffusion cell containing cellophane membrane with phosphate buffer pH 7.4 as the receptor medium. Drug-excipients compatibility studies were performed by FT-IR analysis. All Hydrogel formulations showed acceptable physico-chemical and rheological properties and results were found to be within the limits. The drug release was found to decrease with increase in polymer concentration. Among all the Hydrogel formulations HPMC and Guar Gum showed superior drug release than followed by Carbapol 934, CMC. Drug-excipients compatibility studies showed that there is no interaction between the drug and selected excipients.

KEYWORD: Terbinafine Hydrochloride, HPMC, CMC, Guar Gum, Carbapol 934, Franz diffusion, FTIR, Topical Hydrogel.

1. INTRODUCTION[1-12]
The topical route of drug delivery has been utilized to produce local effect for treating skin diseases and produce systemic drug effects.[1] Hydrogels are prepared both in cosmetics and in pharmaceutical preparations.[2] Gels often provide better release of drug substance independent of the water solubility of the drug when compared to creams and ointments.[3] Local application of therapeutic compounds has many advantages over oral and parenteral drug delivery systems. The advantages include ease of application to skin, ability to deliver drugs selectively to a site of local action, elimination of hepatic first pass metabolism and better patient compliance.[4,5] Hydrogels are widely used in topical drug delivery systems due to their physical and chemical properties such as controllable and prolonged release of drug.[6,7] These formulations on contact with the skin forms a semi occlusive film over the skin and release the drug in controlled manner.[8] Lipophilic drug can cross the Stratum corneum, but rate of diffusion decreases as it enters the more aqueous lower regions of the epidermis[9] Fungal infections have been divided into superficial and systemic infections.[10]

Antifungal drugs are classified according to their chemical structure as azoles, polyenes, allylamines, echinocandins. Terbinafine hydrochloride is an antifungal medication used in the treatment of superficial skin infections such as jock itch, athlete's foot. it is mainly effective on the dermatophyte group of fungi. It is an allylamine antifungal drug and has a broad spectrum of antimycotic activity at low concentrations. It acts by inhibiting fungal sterol biosynthesis which leads to a deficiency in ergosterol and to an intracellular accumulation of squalene, which results in cell death of fungus. It has been reported that terbinafine does not influence the metabolism of hormones or other drugs.[11,12] The goal of our research to formulate and evaluate Terbinafine hydrochloride hydrogels and also evaluate the in-vitro antifungal activity for prepared formulations.[12]

2. METHODOLOGY

Sr. No.	Materials	Source
1	Terbinafine HCl	UNIJULES LIFE SCIENCES LTD.Kalmeshwar, Dist. Nagpur.
2	HPCM K4M	SD fine chemicals Ltd. Mumbai.
3	CMC	SD fine chemicals Ltd. Mumbai.
4	Carbapol- 934	SD fine chemicals Ltd. Mumbai.
5	Guar Gum	SD fine chemicals Ltd. Mumbai.
6	Methyl paraben	SD fine chemicals Ltd. Mumbai.
7	Propylene paraben	SD fine chemicals Ltd. Mumbai
8	Glycerine	SD fine chemicals Ltd. Mumbai
9	Concentrated Hydrochloric Acid.	SD fine chemicals Ltd. Mumbai.

Preparation of Gel

All the ingredients were collected according to the formula the given in table. Required number of gelling agents HPMC, Gaur Gum, CMC and Carbapol-934 were added in water with constant stirring at 500 rpm for about 2 hours. Drug was added to the above mixture. Glycerine, propylene glycol, methyl paraben and propyl paraben were added to it. Final weight was made with water. All the samples were allowed to equilibrate for 24Hr at room temperature prior to performing evaluation test. Conc. Hydrochloric acid used to maintain pH of sample.

Fourier Transfer Infrared spectrophotometer (FTIR)

The FTIR studies were carried for the drug and the drug-polymer physical mixture, mixed separately with IR grade KBr in the ratio of (1:1). Discs were prepared by applying 5.5 metric ton of pressure in a hydraulic press using FTIR Spectrophotometer (SHIMADZU). The disks were scanned over a wave number range (4000 - 400cm).[13]

Evaluation of Gels

The formulated gels were examined for their physical properties, rheological properties and antifungal activity. Skin irritation test was carried out only on all formulations.

Homogeneity

The gels were examined for their physical properties like color, clarity and phase separation by visual inspection. They are tested for the presence of any aggregates.[14]

Grittiness

Presence of any particulate matter in the formulations was observed microscopically.

pH measurement

The pH of gel formulations was determined by using digital pH meter. 1gram of gel was dissolved in 100 ml distilled water and stored for two hours. The measurement of pH of each formulation is done in triplicate and average values are calculated and reported.[15]

Spredability

Concentric circles of different radius were drawn on graph paper and a glass plate was fixed onto it. 5gms of gel was placed on the centre of the lower plate. Another glass plate of 100±5 gm was placed gently on the gel and the spread diameter was recorded after 1 minute of each addition.

Extrudability

The gel formulations were filled in collapsible tubes. After being set in the containers, the extrudability of gel formulations was determined in terms of weight required in grams to extrude 0.5 cm. ribbon of gel in 10 sec.[16]

Drug content

1 g gel was dissolved in 100 ml of phosphate buffer pH7.4. Suitable dilutions were made using phosphate buffer pH7.4. Absorbance was measured at 283 λmax nm using UV spectrophotometer.[17]

In-vitro drug diffusion study

In-vitro drug release studies were carried out using Franz diffusion cell. 0.5 g of gel was applied on cellophane membrane as donor compartment. Phosphate buffer pH 7.4 was placed in the receptor compartment as the dissolution medium. The whole assembly was place on magnetic stirrer with thermostat maintained at 37o c. samples were collected regular time interval and sink conditions were maintained by replacing with new buffer solution. Collected samples are analyzed at 283 λmax nm using UV spectrophotometer.[18]

Skin irritation test

Skin irritation test was conducted on ten healthy male and female volunteers. 100 mg of gel was applied on area of 2 cm and observed for any lesions or irritation/redness.

3. RESULTS AND DISCUSION

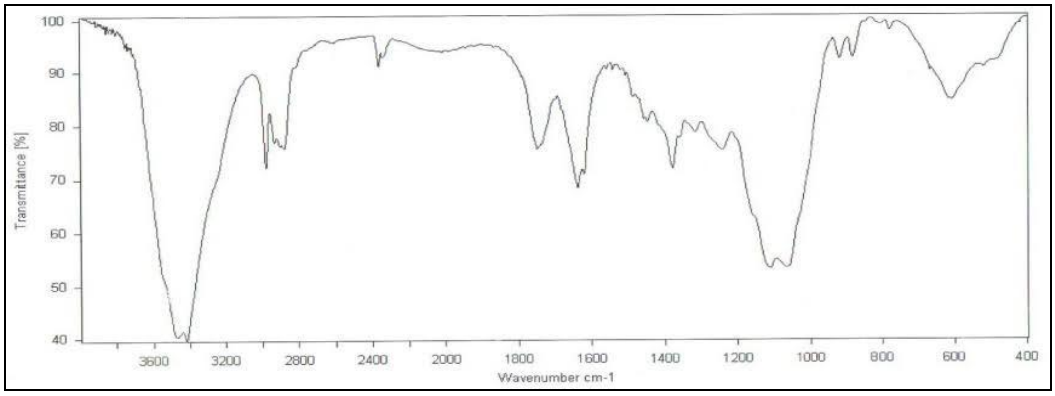
3.1. Preformulation Study

Physical Characterization of Terbinafine Hcl

a. Colour: White
b. Odour: odourless
c. Nature: crystalline powder
d. Taste: slight bitter and sour
e. Melting point: 195-205°C
f. Molecular weight: 291.4 g/mol

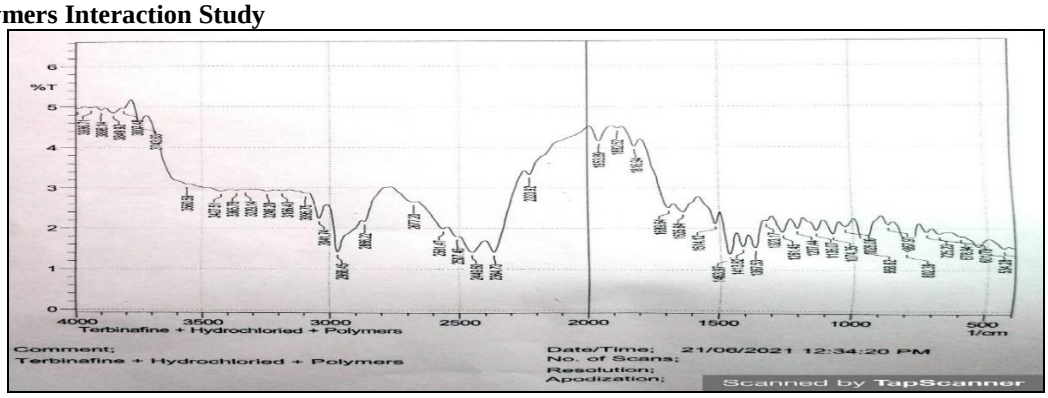
3.2 FTIR Spectroscopy

Drug characterization study by FTIR was carried out as per standard procedure. FTIR spectra of Terbinafine HCl are shown in graph 1. It was observed that principal peak of Drug was found in FTIR spectra of a drug. It was suggested that there was no physical and chemical change of pure drug. The results are shown in Graph No. 1.



Graph No.- 1 FTIR Spectrum of Terbinafine HCl.

Drug Polymers Interaction Study



Graph No- 2 FTIR Spectrum of Terbinafine HCl and polymers.

Drug characterization study by FTIR was carried out as per standard procedure. FTIR spectra of Terbinafine HCl and polymer mixture are shown in graph 2. It was observed that principle peak of Drug was found in FTIR spectra of a drug. It was suggested that there was no physical and chemical interaction is observed. The results are shown in Graph No.2.

Table No. 12 Standard Calibration Curve of Terbinafine HCl in Phosphate Buffer pH 7.4 at 283.

Sr.No.	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.069 ±0.0012
3	4	0.145±0.0008
4	6	0.201±0.0027
5	8	0.260±0.0014
6	10	0.343±0.0015
7	12	0.365±0.0030

n=3

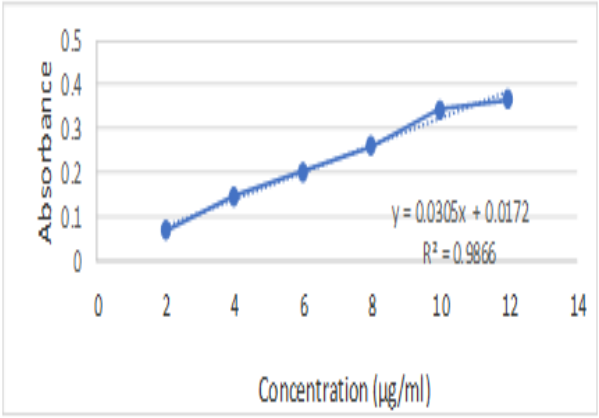


Fig.No.3 Standard Clibration Curve of Terbinafine HCl.

From the standard curve, it was observed that the drug obeys Beer's law inconcentration range of 2.0-1.5 µg/ml in phosphate buffer pH 7.4. Drug shown goodlinearity with regression of coefficient (**r^2 = 0.9866**) and equation for this line obtainedwas found to be **y = 0.0305±0.0015**which is used for the calculation of amount of drug anddissolution study.

3.3 Evaluation of Prepared Hydrogel

Physical Appearance

A prepared Terbinafine HCl Hydrogel was inspected visually for colour, Homogenecity, consistency. All formulations showed yellowish color, white buff, gray appearance therefore showed suitable Homogenecity and consistency. And theobservations are mentioned in Table No. 13.

Table No. 13: Physical Evaluation of Formulations.

Formulation Code	colour	Feel on Application	Spreadability gm.cm/sec. with S.D
H1	White	Smooth	15.7±0.07
H2	White	Smooth	13±0.45
H3	White	Smooth	14±0.35
H4	White	Smooth	14.5±0.45
H5	White	Smooth	13.86±0.8
CM1	White	Smooth	15±0.45
CM2	White	Smooth	14±0.42
CM3	White	Smooth	12±0.49
CM4	White	Smooth	11±0.62
CM5	White	Smooth	9±0.65
CA1	White buff	Smooth	14±0.38
CA2	White buff	Smooth	13±0.40
CA3	White buff	Smooth	11±0.42
CA4	White buff	Smooth	10±0.50
CA5	White buff	Smooth	8±0.68
GG1	Yellowish	Smooth	14±0.42
GG2	Yellowish	Smooth	14±0.45
GG3	Yellowish	Smooth	13±0.53
GG4	Yellowish	Smooth	11±0.58
GG5	Yellowish	Smooth	10±0.62

N=3

Spreadability Studies

All the formulations developed were checked for the Spredability. All theformulations show the Spreadability between 8-15. The highest Spreadability showsH1and CM1 formulations and lowest Spredability showed by CM5 and CA5. Resultsof various formulations are in the Table No. 13**.**

Measurement of pH

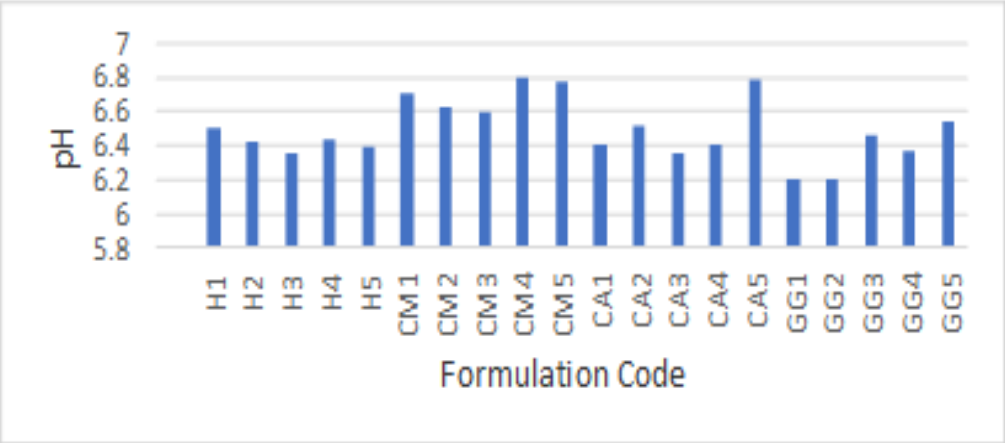
The pH of Hydrogel formulations was in the range of 6.2 to 6.8which consideredacceptable to avoid the risk of skin irritation upon application to skin. The highest pHshowed by CM4 and lowest pH showed by GG1 results are shown in Table No. 14.

Table No. 14: pH, Viscosity and Drug Content.

Formulation Code	pH	Viscosity (cp)	Drug Content (%)
H1	6.50 ± 0.085	1130±6.2	96.65±0.30
H2	6.42±0.075	2350±6.23	97.32±0.412
H3	6.35±0.068	5450±7.2	97.06±0..86
H4	6.44±0.085	8500±8.60	96.71±0.280
H5	6.40±0.082	9410±10.12	98.11±0.25
CM1	6.70±0.068	1270±6.8	97.68±0.34
CM2	6.62±0.080	2170±7.4	96.45±0.356
CM3	6.60±±0.075	6110±7.8	98.60±0.420
CM4	6.80±0.086	7830±8.4	96.54±0.36
CM5	6.78±0.087	8840±9.235	96.80±0.28
CA1	6.41±0.092	1310±5.56	96.90±0.325
CA2	6.52±0.098	2460±6.842	96.13±0.386
CA3	6.35±0.076	6030±6.20	98.23±0.294
CA4	6.41±0.072	8150±8.446	96.57±0.30
CA5	6.79±0.088	9560±11.25	95.88±0.52
GG1	6.2±0.076	1540±6.2450	96.70±0.42

GG2	6.21±0.068	2220±7.860	97.30±0.355
GG3	6.46±0.084	5740±9.230	96.45±0.268
GG4	6.37±0.086	7990±9.84	96.38±0.396
GG5	6.54±0.080	9870±10.85	97.56±0.322

n=3

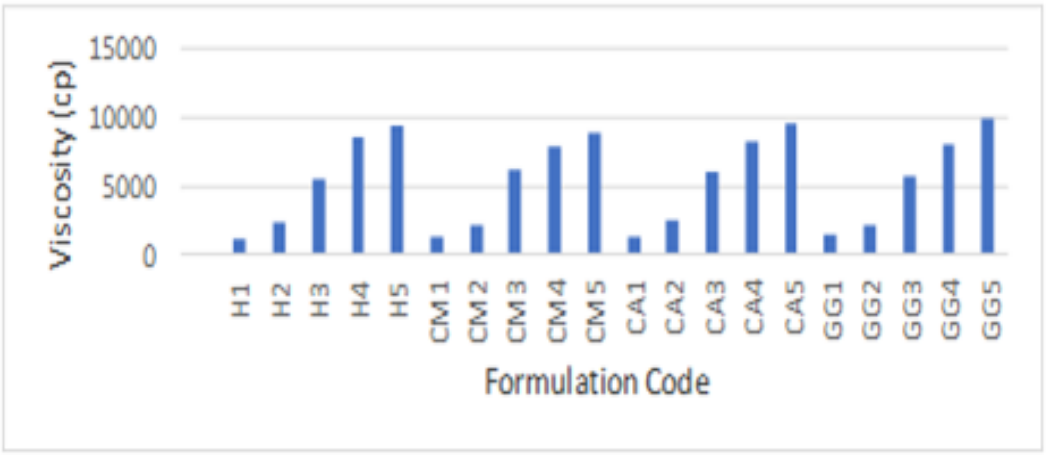


Graph No.4 pH Topical Hydrogel Formulation.

DISCUSSION

The pH of topical Hydrogel formulations (H1 to GG5) was found to be range **6.5** to **6.54±0.086**. It was observed that pH of Hydrogel depends onconcentration of preservati. Here, as concentration of methyl paraben and propylene paraben increases pH of formulation also increases.

6.4.4 Viscosity: All the formulations were checked for viscosity. All formulationsshows satisfactory viscosity, the highest viscosity observed in formulation H5, CA5 and CG5, while lowest viscosities were observed in H1 and CM1. The results are in the Table No. 14.



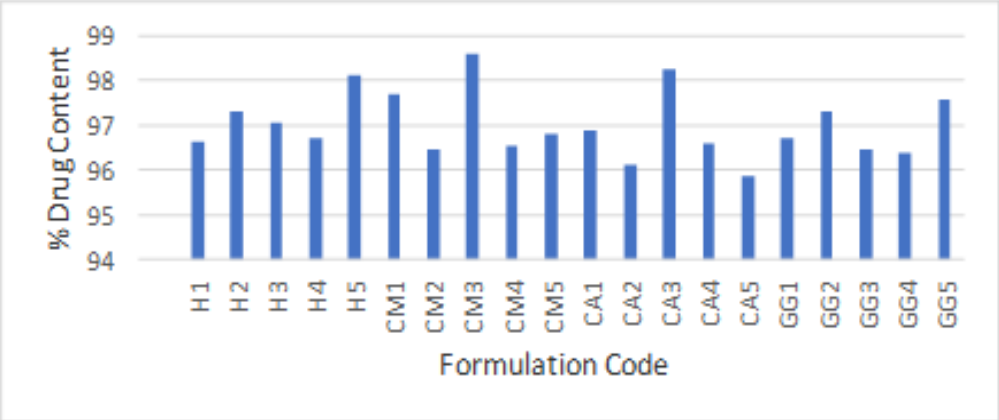
Graph. No. 5 Viscosity of Hydrogel formulation.

DISCUSSION

The Viscosity of topical Hydrogel formulations (H1 to GG5) was found to be range**1130 ±6.2** to **9870±10.85cp**. It was observed that viscosity of Hydrogel depends onconcentration of polymers used for preparation of Hydrogel. Here, as concentration ofpolymers increases viscosity of formulation also increases.

Drug Content

The drug content of different Hydrogels was estimated and results were in officiallimit in the range of **96-98** % which indicates uniform distribution of drug. The resultof drug content is shown in Table No.14.



Graph No.6 Comparison of Drug Content of Batches.

DISCUSSION

The % Drug content of topical Hydrogel formulations (H1 to GG5) was found to berange 96.5±0.52 % to 98.50±0.420 %. It was observed that % Drug content ofHydrogel depends on practical skill. Here, as the optimum % drug content can beachieved by result reproducibility.

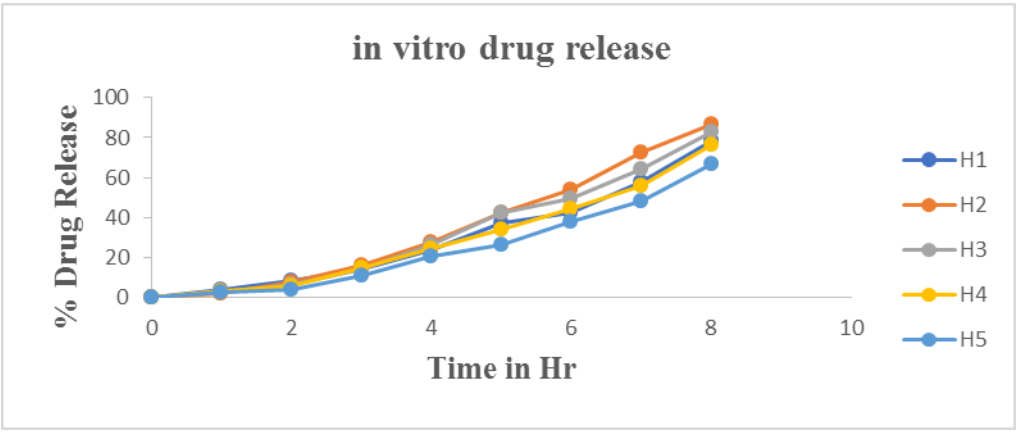
6.5 In *Vitro* Drug Release

The in vitro release of Terbinafine HCl from different hydrogel formulation was carried out in phosphate buffer pH 7.4 for 10 hour at 37 ±o.5^{0}C was investigated and resultsare represented in Table No. 15-18 resp. The plot of % drug release verses time wereplotted % drug release from batches H1 to H5. The plot % drug release verses times were plotted % drug release from batches CM1-CM5. The plot of % drug release verses time were plotted % drug release from batches. It was noticed that the release ofTerbinafine HCl from its Hydrogel can be ranked in the following descending order.

Table No. 15 In-Vitro Drug Release of Batch H1 – F5.

Time (Hr)	H1	H2	H3	H4	H5
0	00	00	00	00	00
1	3.767±0.036	1.912±0.034	2.722±0.042	2.825±0.034	2.210±0.032
2	8.579±0.086	7.468±0.092	6.517±0.078	5.415±0.082	4.068±0.076
3	14.182±0.164	15.576±0.168	14.352±0.122	14.474±0.126	10.965±0.146
4	23.703±0.242	27.667±0.262	26.377±0.178	24.117±0.192	20.394±0.202
5	36.953±0.322	42.339±0.312	42.669±0.288	34.099±0.276	26.518±0.304
6	42.56±0.42	54.22±0.40	49.73±0.338	44.56±0.384	38.00±0.394
7	57.88±0.562	72.8±0.546	64.42±0.400	56.12±0.46	47.84±0.483
8	78.23±0.66	86.5±0.644	82.95±0.48	76.63±0.52	66.74±0.56

n=3



Graph No. 7: Comparison of % Drug Release of Batches H1 to H5.

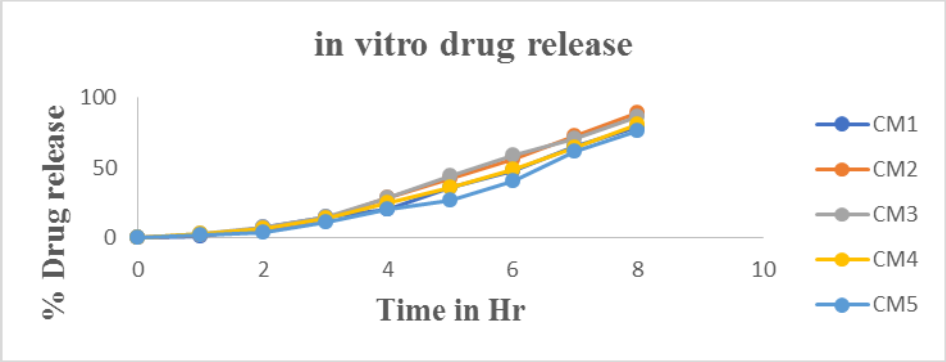
DISCUSSION

Cumulative % Drug Release of topical Hydrogel (CM1 to CM5) was found to be range **74.36±0.54** (8hours) to **86.48±0.50** (8 hours). It was observed that Cumulative % Drug Release of Hydrogel depends on concentration of CMC. Here, as concentration of CMC increases % Drug release time of formulation also decreases. Maximum Cumulative % Drug Release i.e., **86.48±0.50** (8 hours) was found to be forCM2, and prolong Cumulative % Drug Release was **74.36±0.54** (8hours) Found to before CM5. Here, CMC show concentration dependence release behaviour for these formulations.

Table No.17: In-Vitro Drug Release of Batch CM1 –CM5.

Time (Hr)	CM1	CM2	CM3	CM4	CM5
0	00	00	00	00	00
1	1.780±0.036	2.364±0.028	3.522±0.025	2.835±0.033	2.210±0.034
2	7.826±0.056	5.735±0.044	7.430±0.040	6.592±0.056	4.068±0.76
3	14.549±0.12	14.427±0.102	15.453±0.094	14.154±0.093	10.965±0.128
4	20.030±0.26	28.760±0.235	28.609±0.164	25.275±0.192	20.394±0.214
5	36.284±0.32	42.744±0.28	44.373±0.31	35.888±0.320	26.518±0.334
6	48.02±0.386	56.44±0.38	58.34±0.362	48.62±0.40	40.28±0.392
7	64.80±0.442	72.08±0.423	70.64±0.406	64.54±0.448	61.62±0.45
8	78.66±0.521	88.92±0.48	86.24±0.486	80.72±0.512	76.34±0.516

n = 3



Graph No. 8: Comparison of % Drug Release of Batches CM1 to CM5.

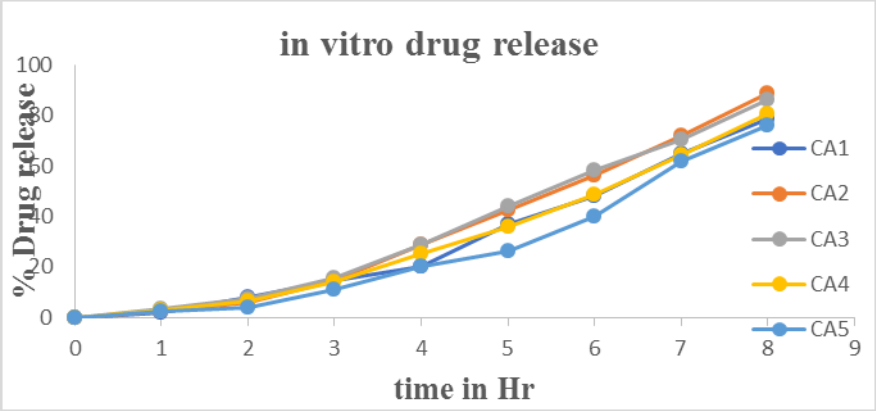
DISCUSSION

Cumulative % Drug Release of topical Hydrogel (CM1 to CM5) was found to berange 74.36±0.54 (8hours) to 86.48±0.50 (8 hours). It was observed that Cumulative% Drug Release of Hydrogel depends on concentration of CMC. Here, asconcentration of CMC increases % Drug release time of formulation also decreases.Maximum Cumulative % Drug Release i.e, 86.48±0.50 (8 hours) was found to be forCM2, and prolong Cumulative % Drug Release was 74.36±0.54 (8hours) Found to befor CM5. Here, CMC show concentration dependence release behavior for theseformulations.

Table No.17: In-Vitro Drug Release of Batch CA1 – CA5.

Time (Hr)	CA1	CA2	CA3	CA4	CA5
0	00	00	00	00	00
1	1.780±0.036	2.364±0.028	3.522±0.025	2.835±0.033	2.210±0.034
2	7.826±0.056	5.735±0.044	7.430±0.040	6.592±0.056	4.068±0.76
3	14.549±0.12	14.427±0.102	15.453±0.094	14.154±0.093	10.965±0.128
4	20.030±0.26	28.760±0.235	28.609±0.164	25.275±0.192	20.394±0.214
5	36.284±0.32	42.744±0.28	44.373±0.31	35.888±0.320	26.518±0.334
6	48.02±0.386	56.44±0.38	58.34±0.362	48.62±0.40	40.28±0.392
7	64.80±0.442	72.08±0.423	70.64±0.406	64.54±0.448	61.62±0.45
8	78.66±0.521	88.92±0.48	86.24±0.486	80.72±0.512	76.34±0.516

n=3



Graph No. 9 Comparison of % Drug Release of Batches CA1 to CA5.

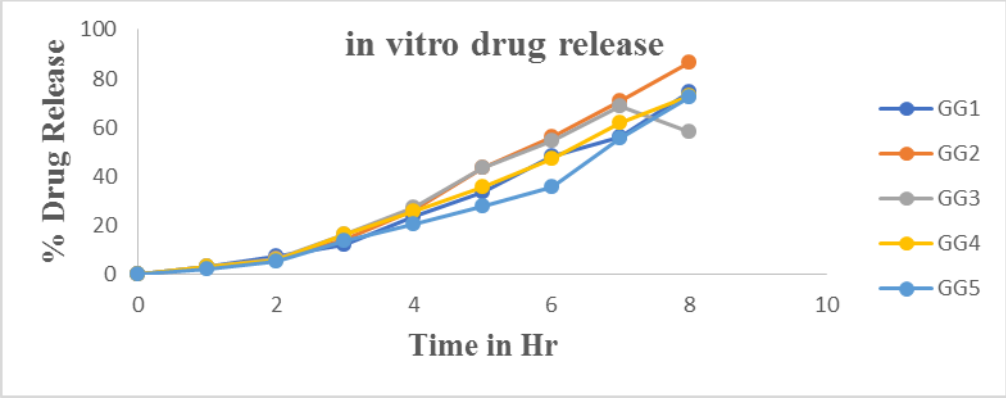
DISCUSSION

Cumulative % Drug Release of topical Hydrogel (CA1 to CA5) was found to be range **76.34±0.516** (8hours) to **88.92±0.48** (8 hours). It was observed that Cumulative % Drug Release of Hydrogel depends on concentration of Carbopol. Here, as concentration of Carbopol increases % Drug release time of formulation also decreases. Maximum Cumulative % Drug Release i.e., **88.92±0.48** (8 hours) was found to be for CA2, and prolong Cumulative % Drug Release was **76.34±0.516** (8hours) Found to be for CA5. Here, Carbopol show concentration dependence release behaviour for these formulations.

Table No. 18 In-Vitro Drug Release of Batch GG1 –GG5.

Time (Hr)	GG1	GG2	GG3	GG4	GG5
0	00	00	00	00	00
1	2.872±0.045	2.411±0.038	2.929±0.024	2.985±0.032	2.113±0.032
2	7.289±0.0145	6.470±0.128	6.422±0.064	5.820±0.078	5.007±0.086
3	11.837±0.18	14.380±0.18	15.199±0.142	16.47±0.161	13.605±0.18
4	23.364±0.246	25.963±0.2	27.300±0.264	25.888±0.28	20.539±0.28
5	33.628±0.30	43.799±0.40	43.695±0.42	35.757±0.32	27.642±0.28
6	48.02±0.386	56.00±0.454	54.34±0.462	47.36±0.386	35.46±0.36
7	56.24±0.421	70.64±0.512	68.58±0.516	62.16±0.442	55.36±0.428
8	74.6±0.502	86.82±0.526	85.20±0.54	73.08±0.496	72.48±0.46

n=3



Graph No. 10 Comparison of % Drug Release of Batches GG1 to GG5.

DISCUSSION

Cumulative % Drug Release of topical Hydrogel (GG1 to GG5) was found to be range **72.48±0.46** (8hours) to **86.82±0.526** (8 hours). It was observed that Cumulative % Drug Release of Hydrogel depends on concentration of Guar Gum. Here, as concentration of Guar Gum increases % Drug release time of formulation also decreases. Maximum Cumulative % Drug Release i.e**, 88.92±0.48** (8 hours) was found to be for GG2, and prolong Cumulative % Drug Release was **76.34±0.516** (8hours) Found to be for GG5. Here, Guar Gum shows concentration dependence release behavior for these formulations**.**

6.6 Evaluation of Factorial Batches

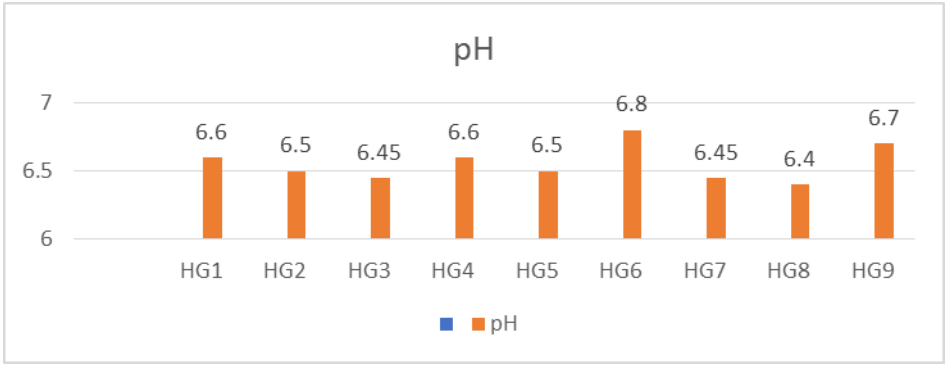
Formulation code	colour	Feel on Application	Spreadability gm.cm/sec. With S.D
HG1	White-off	Smooth	13±0.47
HG2	White-off	Smooth	11±0.42
HG3	White-off	Smooth	11±0.45
HG4	White-off	Smooth	13±0.48
HG5	Yellowish	Smooth	13±0.56
HG6	Yellowish	Smooth	14±0.42
HG7	Yellowish	Smooth	11±0.50
HG8	Yellowish	Smooth	10±0.42
HG9	Yellowish	Smooth	8±0.58

n=3

Table No.20 pH, Viscosity and Drug Content.

Formulation Code	pH	Viscosity(cp)	Drug Content (%)
HG1	6.6 ± 0.085	2450±6.2	96.88±0.28
HG2	6.5 ±0.075	5640±7.2	96.56±0.65
HG3	6.45±0.068	9020±8.5	97.24±0.84
HG4	6.6±0.085	3700±5.6	97.50±0.67
HG5	6.50±0.082	6200±8.4	98.80±0.64
HG6	6.8±0.068	9360±9.66	96.78±0.78
HG7	6.45±0.080	8530±9.34	97.30±0.820
HG8	6.4±0.075	9840±9.8	97.80±0.46
HG9	6.7±0.086	10950±10.12	97.33±0.66

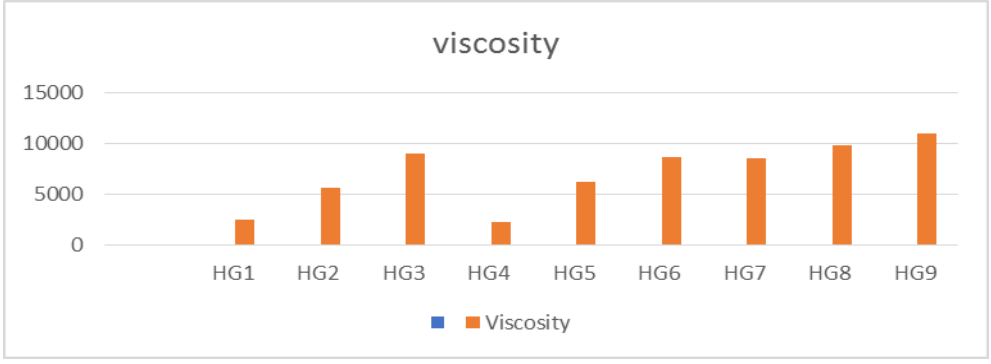
n=3



Graph No. 11 Comparison of pH of Factorial Batches.

DISCUSSION

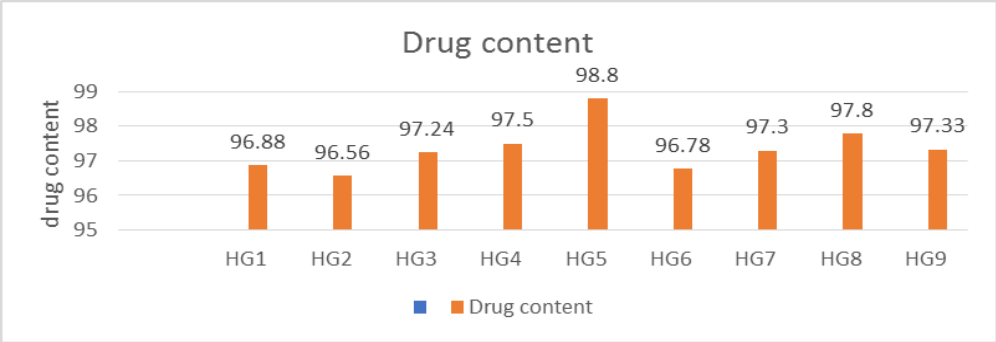
The pH of topical Hydrogel formulations (HG1 to HG9) was found to be range **6.4±0.075 to 6.8±0.068**. It was observed that pH of Hydrogel depends on concentration of preservative and conc. HCl. Here, as concentration of methyl paraben and propyl paraben increases pH of formulation also increases.



Graph No. 12 Comparison of Viscosity of Factorial Batches.

DISCUSSION

The Viscosity of topical Hydrogel Factorial formulations (**HG1** to **HG9**) was found to be range **2450±6.2** to **10950±10.12cp**. It was observed that viscosity of Hydrogel depends on concentration of polymer used for preparation of Hydrogel. Here, as concentration of polymers increases viscosity of formulation also increases.



Graph No. 13 Comparison of Drug content of Factorial Batches.

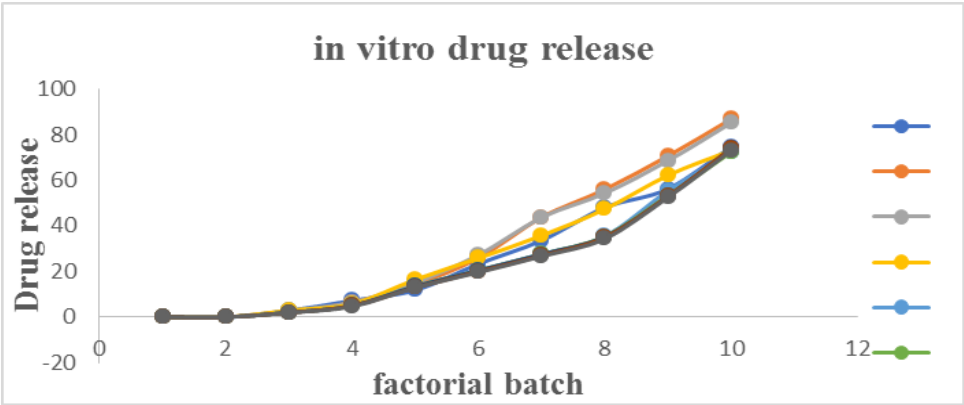
DISCUSSION

The % Drug content of topical Hydrogel Factorial formulations (**HG1** to **HG9**) was found to be range **96.56±0.65%** to **98.80±0.64%.** It was observed that % Drug content of Hydrogel depends on practical skill. Here, as the optimum % drug content can be achieved by result reproducibility.

Table No. 21: In-Vitro Drug Release of Factorial Batches HG1- HG9.

Time (Hr)	HG1	HG2	HG3	HG4	HG5	HG6	HG7	HG8	HG9
0	00	00	00	00	00	00	00	00	00
1	5.220 ±0.03	3.211 ±0.03	2.315 ±0.02	1.295 ±0.03	1.279 ±0.03	1.15± 0.04	1.10± 0.03	1.08± 0.03	1.06 0.02
2	7.999±0. 14	7.470±0. 12	7.25±0.0 64	6.200±0. 07	6.117±0. 08	6.05±0.1 4	5.67±0.1 6	4.73±0.1 5	4.68±0.1 4
3	18.17 ±0.18	17.90 0±0.1	17.79 ±0.14	17.70 ±0.16	16.880 ±0.18	16.69 0.15	15.70 0.14	11.65 0.12	9.22± 0.14
4	29.69 ±0.24	29.53 ±0.20	29.00 ±0.26	28.64 ±0.28	28.29 ±0.28	27.19 0.28	26.35 0.26	25.25 0.28	23.88 0.26
5	39.60 ±0.30	36.90 ±0.40	34.95 ±0.42	34.86 ±0.32	33.97 ±0.28	33.22 0.34	32.57 0.38	32.30 0.40	31.18 0.38
6	49.62 ±0.38	49.20 ±0.45	48.33 ±0.46	48.00 ±0.38	47.46 ±0.36	47.01 0.42	46.26 0.40	43.08 0.412	39.51 0.38
7	55.24 ±0.42	69.44 ±0.51	67.38 ±0.51	66.52 ±0.44	57.36 ±0.42	58.45 0.54	60.23 0.58	56.66 0.524	52.36 0.496
8	89.40 ±0.50	87.82 ±0.52	86.20 ±0.54	85.13 ±0.49	84.48 ±0.46	84.36 0.50	83.50 0.52	82.95 0.48	80.74 0.46

n =3



Graph No.14: Comparison of % Drug Release of Factorial Batches HG1 to HG9.

DISCUSSION

Cumulative % Drug Release of topical Hydrogel of Factorial Batches (**HG1 to HG9)** was found to be range **70.74±0.46** (8hours) to **88.40±0.50** (8 hours). It was observed that Cumulative % Drug Release of Hydrogels depends on concentration of HPMC and Guar Gum. Here, as concentration of HPMC and Guar Gum increases % Drug release time of formulation also decreases. Maximum Cumulative % Drug Release i.e, **88.40±0.50 (**8 hours) was found to be for **HG1**, and prolong Cumulative % Drug Release was **70.74±0.46** (8hours) Found to be for **HG9**. Here, HPMC and Guar Gum shows concentration dependence release behavior for these formulations.

Table No. 22 Kinetic Model Studies of Factorial Batches.

Kinetic Models	HG1	HG2	HG3	HG4	HG1	HG5	HG6	HG7	HG8
	R	R	R	R	R	R	R	R	R
Zero order									
1st order	0.9985	0.9918	0.9923	0.976	0.984	0.991	0.999	0.987	0.980
Matrix	0.9962	0.9887	0.9783	0.990	0.992	0.995	0.987	0.998	0.991
Peppas	0.9982	0.9966	0.9910	0.976	0.991	0.996	0.997	0.976	0.991
Hix.crow	0.9945	0.9926	0.9649	0.956	0.955	0.951	0.986	0.961	0.970
Best FittedTo	1stOrder	1stOrder	1stOrder	Matrix	Matrix	Peppas	1stOrder	Matrix	Matrix

n =3

DISCUSSION

It was observed that the Topical Hydrogels (HG1, HG2, HG3, HG7) have best fitted to the First order model. The Topical Hydrogel HG1 has r^2 value 0.9992. Also, it was observed that Topical Hydrogels (HG3, HG4, HG8 and HG9) formulations have best fitted to Matrix model. The Hydrogel HG8 with r^2 value 0.9985.Hence, from above it was concluded that Topical Hydrogel formulation HG1 containsHPMC and Guar Gum 1% each and methyl parben0.1% and propyl paraben 0.05% which could bemost promisingTopical Hydrogel formulation for Terbinafine HCl.

Table No 23: Stability Study for Factorial Batch HG 1 at Temp.2-8 ºC.

Duration Time	Humidity (%)	Temp.(ºC)	Drug Content (%)	% Drug Release	pH of Formulations
0 Days	60±05	2 -8ºC	96.78±0.6	86.60±.35	6.8±0.038
15 days	60±05	2 -8ºC	96.55±0.52	86.40±0.36	6.6±0.08
30 days	60±05	2 -8ºC	96.40±0.42	85.72±0.54	6.4±0.035
45 days	60±05	2 -8ºC	96.29±0.56	85.30±0.50	6.2±0.028

n=3

Table No 23: Stability Study for Factorial Batch HG1 at Temp. 25 ºC.

Duration Time	Humidity (%)	Temp.(ºC)	Drug Content (%)	% Drug Release	pH of Formulations
0 Day	64±05	25 ºC±2ºC	96.78±0.6	86.60±0.42	6.6±0.038
15 days	64±05	25 ºC±2ºC	96.69±0.52	86.40±0.56	6.6±0.08
30 days	64±05	25 ºC±2ºC	96.40±0.42	85.72±0.54	6.6±0.035
45 days	64±05	25 ºC±2ºC	96.29±0.56	85.30±0.50	6.6±0.028

n= 3

Table No 23: Stability Study for Factorial Batch HG1 at Temp 40 ºC.

Duration Time	Humidity (%)	Temp. (ºC)	Drug Content (%)	% Drug Release	pH of Formulations
0 Day	54±05	40 ºC	95.45±0.6	86.60±0.42	6.0±0.038
15 days	54±05	40 ºC	94.39±0.42	86.40±0.56	5.9±0.08
30 days	54±05	40 ºC	92.25±0.32	85.72±0.54	5.7±0.035
45 days	54±05	40 ºC	89.99±0.66	85.30±0.50	5.6±0.028

n=3

DISCUSSION

The stability study of optimum batch (HG1) revealed that there is silightly reduction in drug content was observed over period of 45 days. No significant change was obseve in % drug content. The release condition depends upon the temp.and duration of period. Drug release (after 8 Hrs) at various storing condition 2-8 ºC,25 ºC and 40ºC Hence formulation was found to be stable for 45 days.

CONCLUSION

From the above result it was concluded that Terbinafine HCl hydrogel formulation prepared by using different gelling agent HPMC, Carbopol-934, Gaur gum and CMC possesses and edge in terms of Spredability pH, viscosity, drug content, drug release shows acceptable physical properties. Formulated Hydrogel can be used extensively to impart better patient compliance and loading for hydrophilic and hydrophobic drug in a water-soluble Hydrogel bases more over this formulation can be used to overcome the problem associated with Hydrogel or oil-based ointment and cream. Hydrogel are the current trend in delivery of hydrophobic and hydrophilic drug topically. Despite of various advantages Hydrogel face problem of bubble formation during its formulation and stratum corneum is permeable to small molecule so concerning these facts, we can incorporate micro sponge that are highly porous micro sized particles with unique ability to entrap pharmaceutical ingredients into a Hydrogel base. Characterization such as better loading capacity than other vesicular system, less sticky nature and Spredability of Hydrogel formulation promise them as a better available option for dermatological use. Various herbal oil with medicinal properties can also be incorporated into the Hydrogel formulation that may act as synergistic approach for treating a disease. The side effect associated with oral therapy of terbinafine HCl tablets can be avoided by using the topical drug.

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