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FORMULATION AND EVALUATION OF MINOXIDIL EMULGEL FOR ANDROGENIC ALOPECIA

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Abstract:

Androgenic alopecia is the loss of hair, pertains on the scalp although on other body sites. Alopecia is characterized by round or oval patches of non scarring hair loss. Scalp hair loss can be partial or complete, but it progress to cause total body hair loss. Emulgel are emulsion gel which contains widely distributed oil droplets. Chemically, minoxidil is 2,4-pyrimidinediamine, 6-[1-piperidinyl]-,3-oxide. Minoxidil is antihypertensive drug; a powerful vasodialator which act by direct relaxation of arteriolar smooth muscle. An attempt was made to formulate minoxidil emulgel for the treatment of male pattern baldness with the use of different gelling agents i.e. carbopol 940, carbopol 934, xanthan gum, methyl cellulose. Infra red [IR] spectroscopy was performed to identify any physicochemical interaction between drug and carriers. The dissolution profile and various evaluation parameters viz. pH, spreadability, viscosity, drug content, etc. of emulgel formulation and marketed formulation were compared. Release kinetics by various models were studied and compared between final formulation and marketed formulation. Thus, results showed no interactions between drug and polymers. Thus, minoxidil emulgel was found to be feasible over other dosage form in the treatment of androgenic alopecia.

Keywords: *Androgenic alopecia, minoxidil, emulgel, FTIR, dissolution profiles.*

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INTRODUCTION:

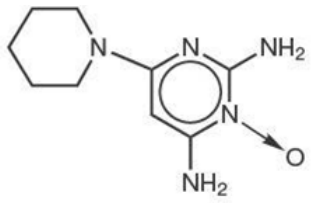
Androgenic alopecia is the loss of hair, pertains on the scalp although on other body sites. It is the common problem of the society which causes economical and physiological consequences. [16] alopecia is generally of two types i.e. alopecia areata and androgenic alopecia. Alopecia areata is characterized by round or oval patches of non scarring hair loss. Scalp hair loss can be partial [transiet or persistent] or complete [alopecia totalis], but it progress to cause total body hair loss [alopecia universalis]. [13]

Transdermal drug delivery system provides sustain drug release as well as reduce the intensity of action and side effects of oral therapy. It delivers the drug across the skin by the process of diffusion and have an effect on the tissue adjacent to the site of application [topical] or to have an effect after through the circulatory system [systemic]. It bypasses the gastrointestinal tract and obviates the GI irritation that would occur frequently. [2].

Emulgel are emulsion gel which contains widely distributed oil droplets. They are generally emulsions either of oil-in-water or water-in-oil type, which are gelled by mixing with gelling agent. Minoxidil emulgel was applied topically and was shown to improve blood flow in human balding skin.

Chemically, minoxidil is 2,4-pyrimidinediamine, 6-[1-piperidinyl]-,3-oxide. Minoxidil is antihypertensive drug; a powerful vasodialator which act by direct relaxation of arteriolar smooth muscle. [6] Tachycardia, palpitations, angina and edema are observed when doses of β-blockers and diuretics are inadequate. Headache, sweating, and hirsutism, which is particularly bothersome in women are relatively common. [8].

Chemical Structure of Minoxidil



[1]

Fig 1: Structure of Minoxidil

MATERIALS AND METHODS:

Minoxidil was kindly provided by ONS pharmaceuticals pvt ltd, Jaipur, carbopol 940 and sodium hydroxide from Lobi chem, mumbai; carbopol 934 and methyl cellulose from molychem, HPMC from Alembic pharmaceuticals ltd, vadodara, Xanthan gum from Vinubhai agencies pvt ltd, Potassium dihydrogen-ortho-phosphate and hydrochloric acid from Central drug House pvt ltd, New Delhi.. All chemical and reagents used were of analytical grade. De-ionized water was used for the complete study.

Preformulation Studies

Preformulation studies are required to ensure the development of a stable as well as therapeutically effective and safe dosage form. These studies focus on the physicochemical properties of the drug that could affect performance and development of an efficacious dosage form.

Description of drug

Organoleptic properties of drug i.e. color, odor, hygroscopicity, solubility was observed.

Drug Identification

UV spectrophotometric analysis of drug

UV absorption in the range 200 to 400 nm of a 2mg/ml solution in water was determined. [19].

Fourier Transform Infra Red analysis of drug

FTIR spectrum of the drug was taken and compared with the reference spectrum to identify the drug. Accurately weighed quantity of minoxidil was placed in vial and kept at 50ºC for 15 days. The sample was placed in ATR based Brukers Tensor 27 instrument.

Drug excipient compatibility study

Drug and different polymers alone and together were taken to study the interaction between them under certain experimental conditions. They were taken in ratio 1:1 ratio and were kept at 50ºC for 15 days. [17].

Solubility determination:-

For quantitative solubility studies, known amount of drug [10mg] was suspended in a series of different solvents i.e. water, ethanol, propylene glycol and chloroform and shaken for 24 hrs. using wrist action shaker [York India]. Solubility of minoxidil in different solvents is recorded. [11].

Melting point determination:-

Melting point determination of minoxidil is done by using Melting Point Apparatus. In that method the pre-sealed capillary is filled by the small amount of drug. Then capillary and thermometer were placed in Melting Point Apparatus. Then see capillary for melting the drug. The temperature were noted when the drug start to melt and the drug till complete melt. [18]

Analytical estimation of drug

Determination of absorption maxima

Stock solution of minoxidil was prepared by dissolving 50 mg of drug using water in 100 ml volumetric flask. This stock solution was further diluted in water to get standard solution of concentration 100 microgram per ml and was scanned between 200 – 400 nm using UV spectrophotometer [shimadzu 1700] [12]

Standard curve of minoxidil

Standard curve was prepared using phosphate buffer pH 7.4. 100mg of minoxidil was dissolved in 100 ml of PBS to give a solution of 1mg/ml i.e. 1000 µg/ml. thus served as first standard stock solution. From this stock solution 1 ml was taken and diluted to 100 ml using pH 7.4 phosphate buffers to get a solution of 10 µg/m concentration and this solution served as the second standard solution. Into a series of 10 ml volumetric flasks, aliquots of second standard solution [i.e.] 2 ml, 4 ml, 6 ml, 8ml, 10ml and 12 ml was added and the volume made up to 10 ml using pH 7.4 phosphate buffer. The absorbance of these solutions was measured against reagent blank at 286 nm using Shimadzu [UV-1700] UV spectrophotometer. Standard curve was plotted with concentration on x-axis and absorbance on y-axis. [9]

Formulation and Evaluation of Emulgel

Fabrication of minoxidil emulgel:

Dissimilar formulations were formulated using altering amount of gelling agents. the method only differed in the process of making gel in diverse formulations. The formulation of emulsion was same in all formulations. Total 20 formulations; four formulations with each polymer were formulated. Gel bases were prepared by dispersing carbopol 940, carbopol 934, HPMC, xanthan gum and methyl cellulose in the de-ionized water. These dispersions were kept overnight in refrigerator for complete swelling of the gelling agent. pH of all the gel formulations were adjusted to 6.0-6.5 using triethanolamine Oil phase and aqueous phases are prepared separately to formulate emulsion. Emulgels were prepared by equal mixing of gel and emulsion in ratio of 1:1 with gentle stirring.

Formulation and Evaluation of Emulgel

Sixteen formulations using four polymers i.e. Carbopol 940, Carbopol 934, Xanthan Gum, Methyl Cellulose of different concentration [1%, 1.5%, 2%, 2.5%] were formulated. HPMC was also the choice of polymer but due to poor viscosity it was not used for the study. Tables below show the formulae of different polymers with different ratio. F1 to F4 was formulated with carbopol 940, F5 to F8 was formulated with carbopol 934, F9 to F12 was formulated with xanthan gum, F13 to F16 was formulated with Methyl cellulose. F17 to F20 was formulation with HPMC but due to poor viscosity these four formulations were not carried for further study.

Table 1: Formulation batches of minoxidil emulgel

Formulation code/ Ingredient	F 1	F 2	F 3	F 4	F 5	F 6	F 7	F 8	F 9	F 10	F 11	F 12	F 13	F 14	F 15	F 16
Minoxidil	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Polymer	1	1.5	2	2.5	1	1.5	2	2.5	1	1.5	2	2.5	1	1.5	2	2.5
Propylene glycol	15	15	15	15	15	15	15	15	15	15	15	15	15	15	15	15
Triethanol amine	0.6	0.7	0.8	0.9	0.6	0.7	0.8	0.9	0.6	0.7	0.8	0.9	0.6	0.7	0.8	0.9
Ethanol	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Propyl paraben	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Span 80	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Liquid paraffin	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25
Distilled water	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	Qs

Selection of emulgel formulation
On the basis of various evaluation parameter viz. viscosity, spreadability and in vitro drug release study two formulations i.e. F3 and F5 were found to be optimum for the further study. These two formulations were analyzed again and were evaluated and one best formulation was selected i.e. F5. This final formulation was then reformulated and evaluated; and was compared with the available marketed preparation i.e. Tugain gel 5% by cipla for all evaluation parameters.

Evaluation of emulgel:
Following parameters were used for the evaluation of emulgel

Physicochemical characters

Homogeneity
All the formulations were inspected visually for the physical appearance and for the presence of aggregates.

pH
pH of all formulations was determined by using digital pH meter. One gram of the emulgel formulations was dissolved in 100 ml of distilled water for pH measurement in triplicate and average was taken.

Drug content study
All the formulations were dissolved in 50 ml of phosphate buffer pH7.4. The volumetric flasks were kept for 2 hr and shaken well in shaker to mix it properly. The solution was passed through the whatman filter paper and filtrates were analyzed for drug content spectrophotometrically at 286nm against corresponding gel concentration as blank

Viscosity
Viscosity of all the formulations were measured using Brookfield viscometer using spindle no 61, 63, 64.

Spreadability
The spreadability was determined by parallel plate method which is widely used for determined and quantifying the spreadability of semisolid preparations. Formulations [1gm] were passed between two 20*20 cm horizontal plates, the upper of which weighed 125 gm. The spread diameter was measured after 1 min.

In Vitro Drug Release Study
The in vitro drug release studies were carried out using Franz Diffusion Cell. Weighed quantity of emulgel formulation was sandwiched between egg membranes of donor compartment and receptor compartment of FD cell using phosphate buffer of pH 7.4 as dissolution media. Temperature of the cell was maintained at 37°C and was placed on magnetic stirrer. 1 ml of the sample was withdrawn at suitable time interval and sink conditions were maintained. Samples were analyzed spectrophotometrically at 286nm. [8,14]

Stability study
The stability study was carried out for the most satisfactory formulation. The most satisfactory formulation i.e. final formulation was packed in a collapsible tube was submitted to accelerated stability tests Doaa A. Helal, 2012]. The emulgel formulation was kept at 4° C and 40° C for 30 days for evaluation of color, odor, pH, viscosity, etc. [21].

Drug Release Kinetic
Statistical Method
ANOVA
Analysis of variance is the method based on repeated measures design where time is the repeated factor and percent dissolved is dependent variable. ANOVA for varying concentration for different polymer and all together are measured. ANOVA studies are done through Graph Pad Prism version 7.02. [5]

Model Independent Methods
A simple model independent approach uses a difference factor [f1] and a similarity factor [f2] to compare dissolution profiles. [3]

Difference Factor [f1]

It calculates the percent difference between the two curves at each time point. It is a measure of the relative error between the two curves. Formulae for calculating f1is mentioned below:

$$f1 = \sum[\text{Rt-Tt}] / \sum Rt \times 100$$

Similarity Factor [f2]
The similarity factor is a logarithmic reciprocal square root transformation of the sum of squared error and is a measurement of the similarity in the percent dissolution between the two curves i.e. test and reference. It represents closeness of two comparative formulations. It is calculated by:

$$f_2 = 50 \times \log\left\{\left[1 + \frac{1}{n}\sum_{t=1}^{n}(R_1 - T_1)^2\right]^{-5} \times 100\right\}$$

[3, 15]

Table 2: comparison of dissolution profiles [3]

f1	f2	Inference
0	100	Dissolution profiles are identical
≤15	≥ 50	Similarity or equivalence of two profiles

Model dependent methods

Data obtained from in vitro release studies of minoxidil emulgel was fitted to various kinetic equation to know about the release mechanism of drug from the formulation compared to commercial products Model dependent approach includes zero order, first order, Higuchi, Korsmeyer – Peppas Model, etc. Quantitative as well as the qualitative changes in a formulation alter drug release and in vivo performances that facilitate the product development. In case of zero order, it follows $Q_t = Q_o + K_o t$ equation, the graph was plotted in log cumulative percent of drug released versus time. In case of first order, it follows log C = log C_o – Kt/2.303 equation, the graph was plotted in log cumulative percent of drug remaining versus time. In case of higuchi model, it follows $Q = K_H \times t^{½}$ equation, the graph was plotted between %cumulative drug release versus square root of time. In case of Korsmeyer peppas model, it follows $Q/ Q_o = Kt^n$ equation, the graph was plotted between cumulative percent drug release versus log time. [4,5, 20]

RESULTS AND DISCUSSION:

Description of Drug

Various properties of drug related with color, odor are given in table

Table 2: Description of Drug

S. No.	Properties	Inference
1.	Colour	White
2.	Odour	Odourless

Identification of drug

By UV spectrophotometric analysis of drug:

The wavelength at which maximum absorbance obtained was considered as maximum wavelength [λ_{max}] i.e. 286 nm for the drug. [12]

By FTIR spectrum method:

The IR spectra indicates absorption peaks of minoxidil at 3451 cm^{-1} due to N-H, 3282 cm-1 due to H-bonded N-H, 2926 cm^{-1} due to C-H stretch [aromatic and aliphatic], 1723 cm^{-1} show the peak of C=N, 1543 cm^{-1} shows the presence of aromatic C=C stretching and N-O stretching is observed at 1223 cm^{-1}. Peaks obtained in spectrum of pure drug [immediate and after 15 days] were similar to the given in standard.

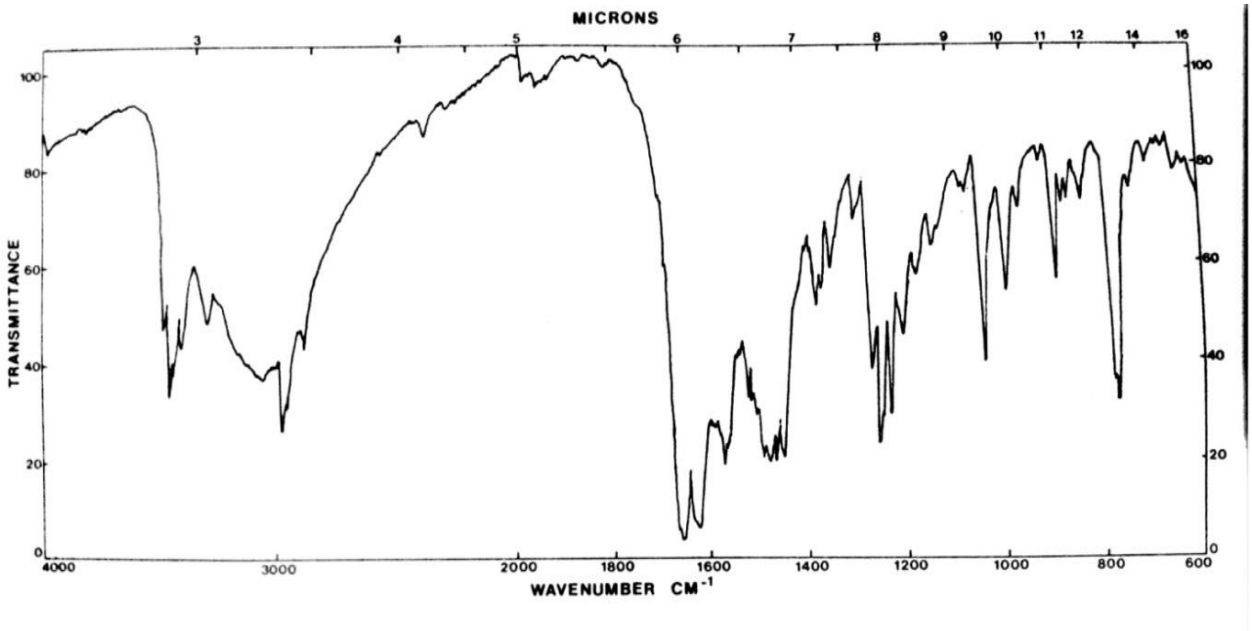


Fig 2: Reference FTIR Spectrum of Minoxidil

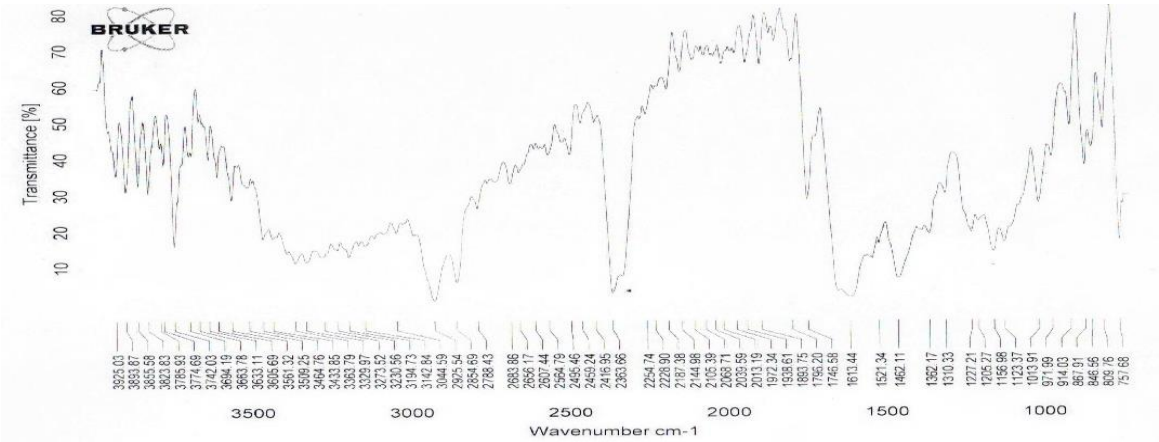


Fig 3: FTIR spectrum of minoxidil [immediate]

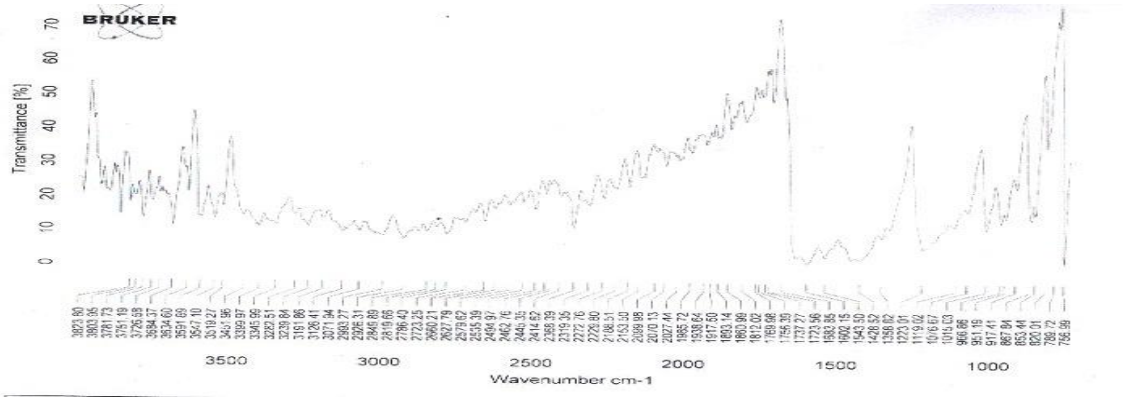


Fig 4: FTIR spectrum of minoxidil [after 15 days]

Drug excipient compatibility study

The possible interaction between drug and excipient were studied by IR spectroscopy. The peaks of drug and polymer immediate and after 15 days at 50°C were compared to standard drug sample that occurs between drug and polymers.

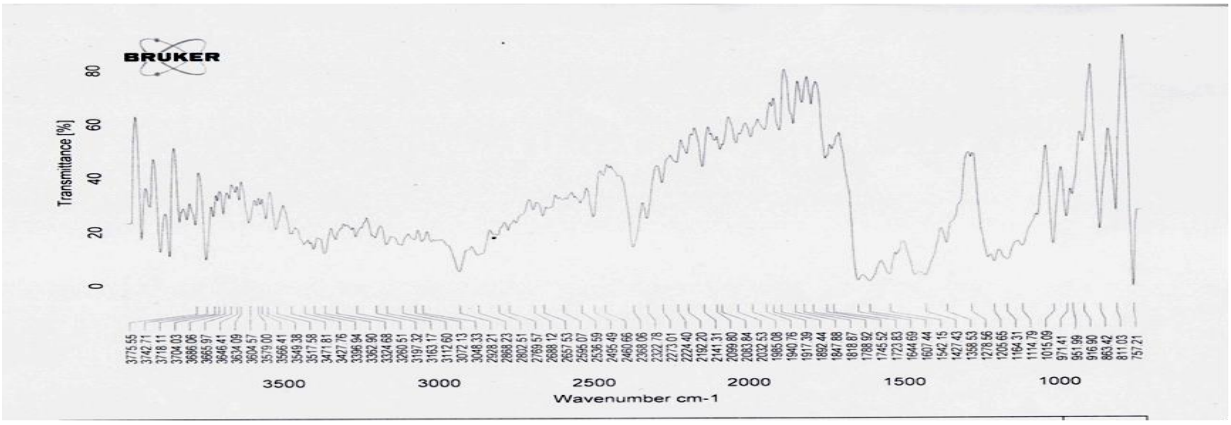


Fig 5: FTIR spectrum of drug + carbopol 940 [immediate]

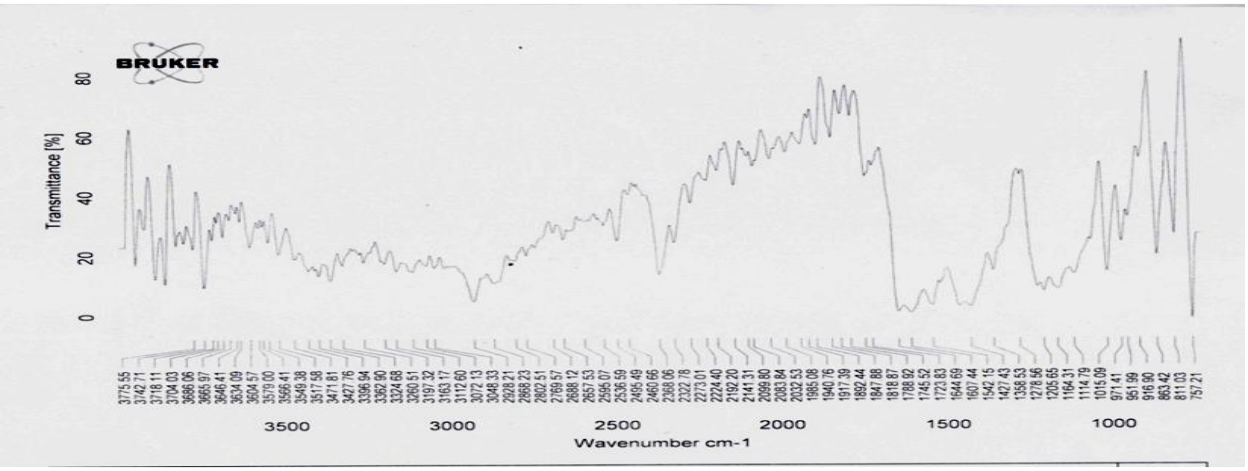


Fig 6: FTIR spectrum of drug + carbopol 940 [after 15 days]

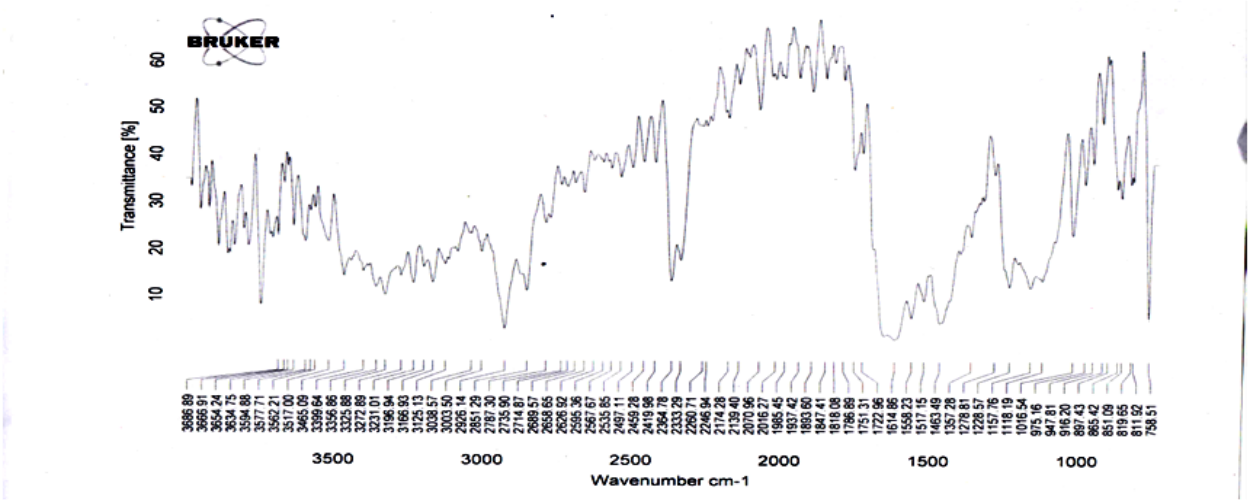


Fig 7: FTIR spectrum of drug + carbopol 934 [immediate]

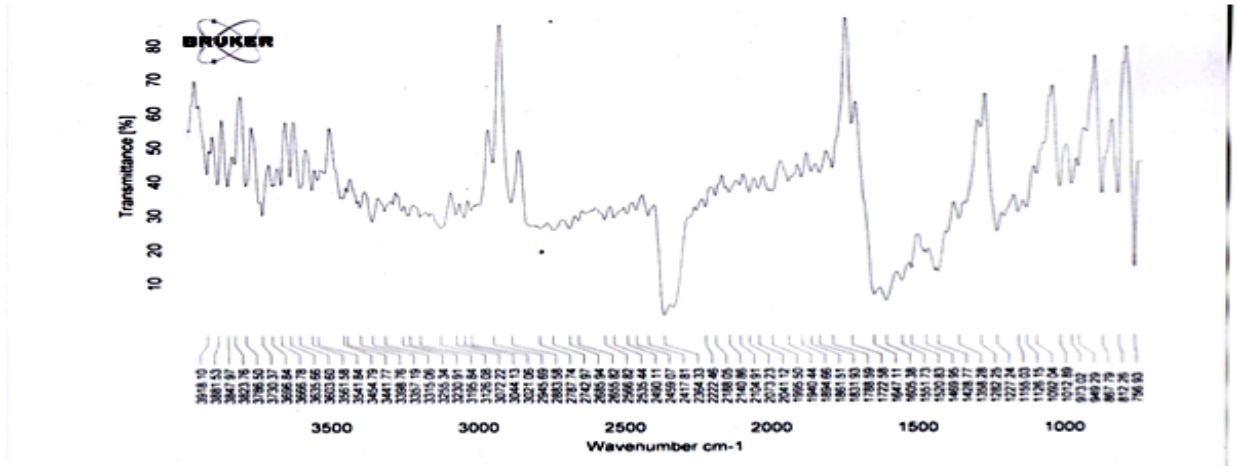


Fig 8: FTIR spectrum of drug + carbopol 934 [after 15 day]

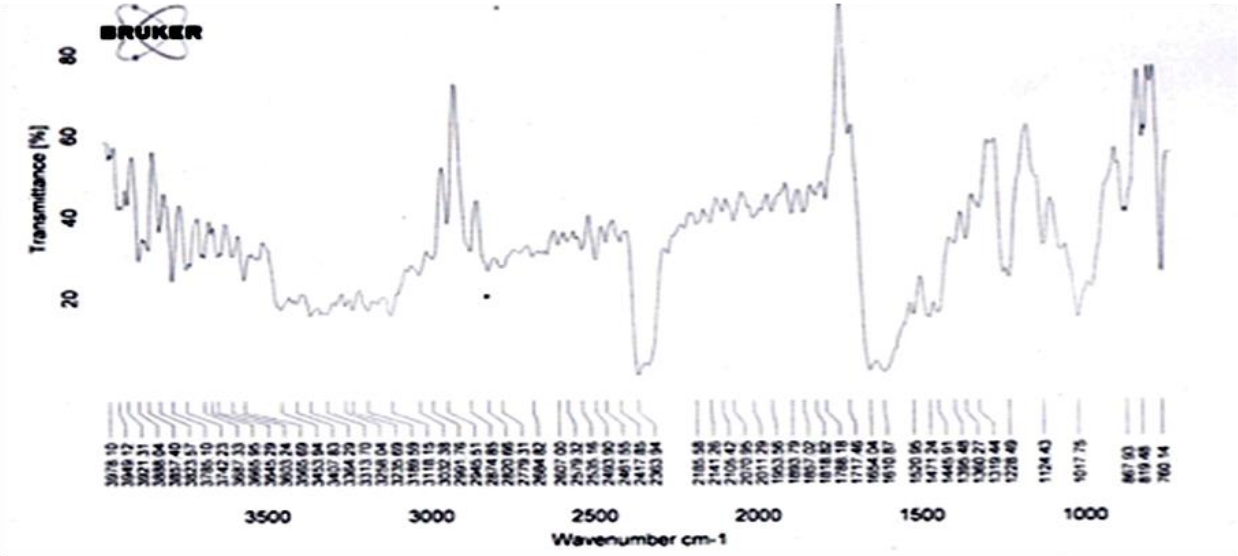


Fig 9: FTIR spectrum of drug + xanthan gum [immediate]

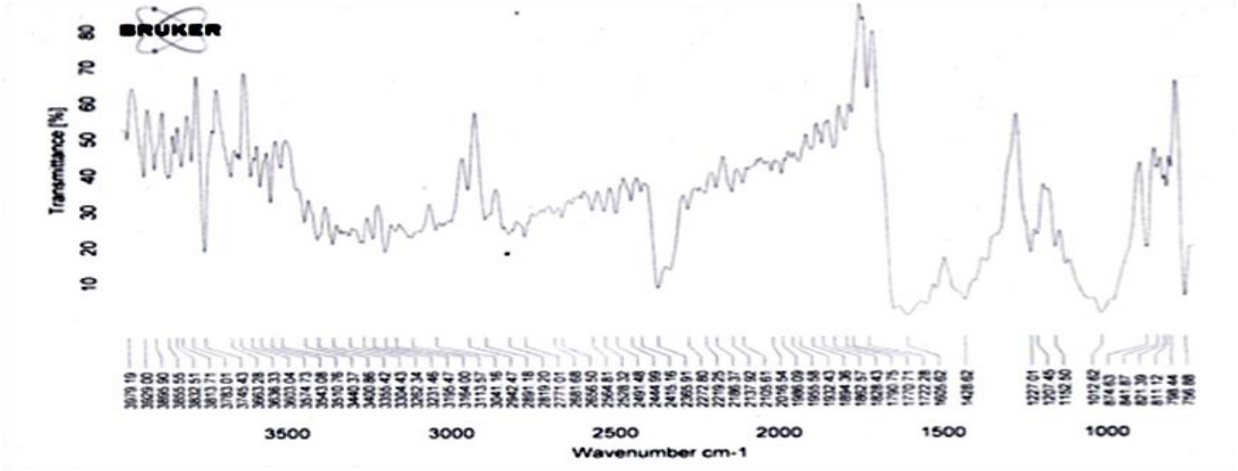


Fig 10: FTIR spectrum of drug + xanthan gum [after 15 days]

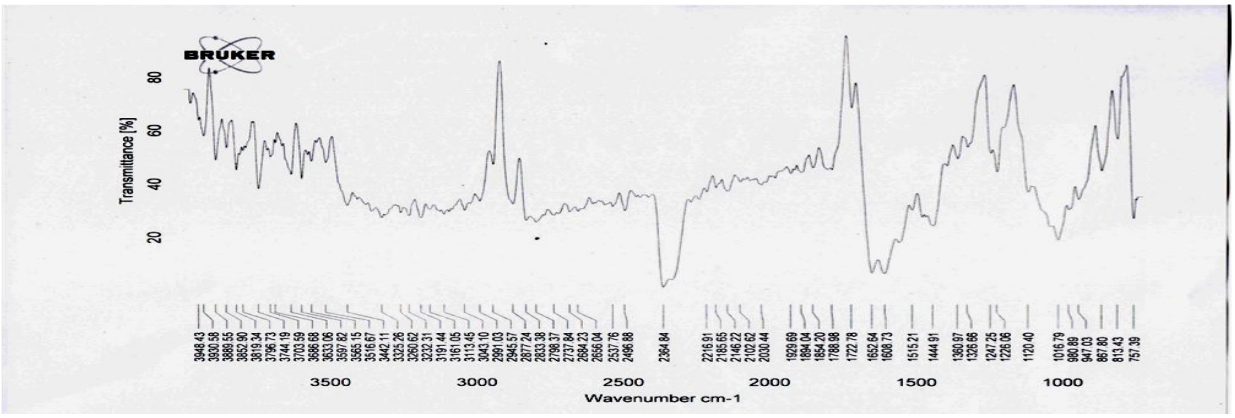


Fig 11: FTIR spectrum of drug + HPMC [immediate].

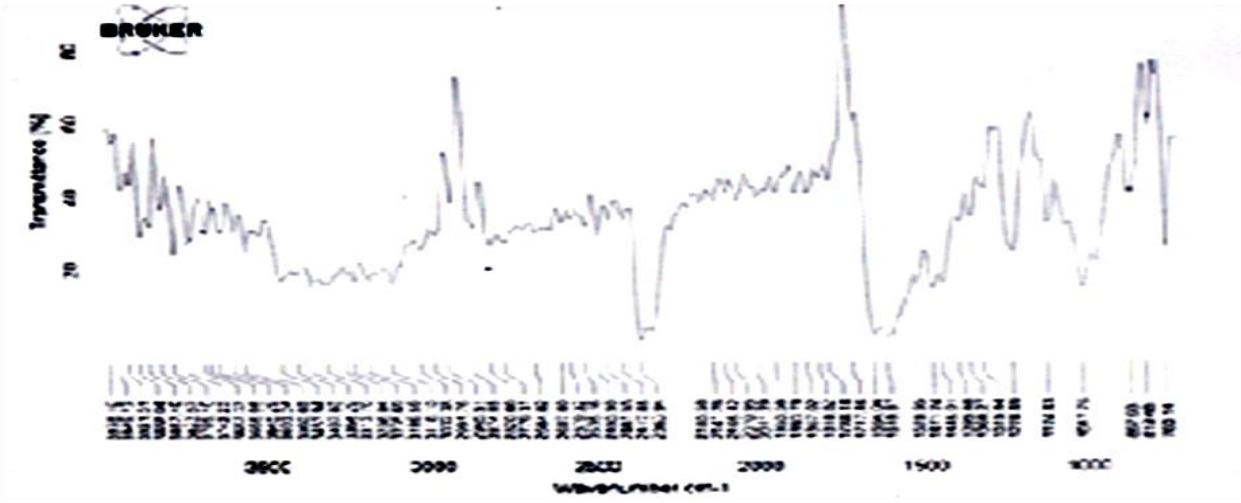


Fig 12: FTIR spectrum of drug +HPMC [after 15 days].

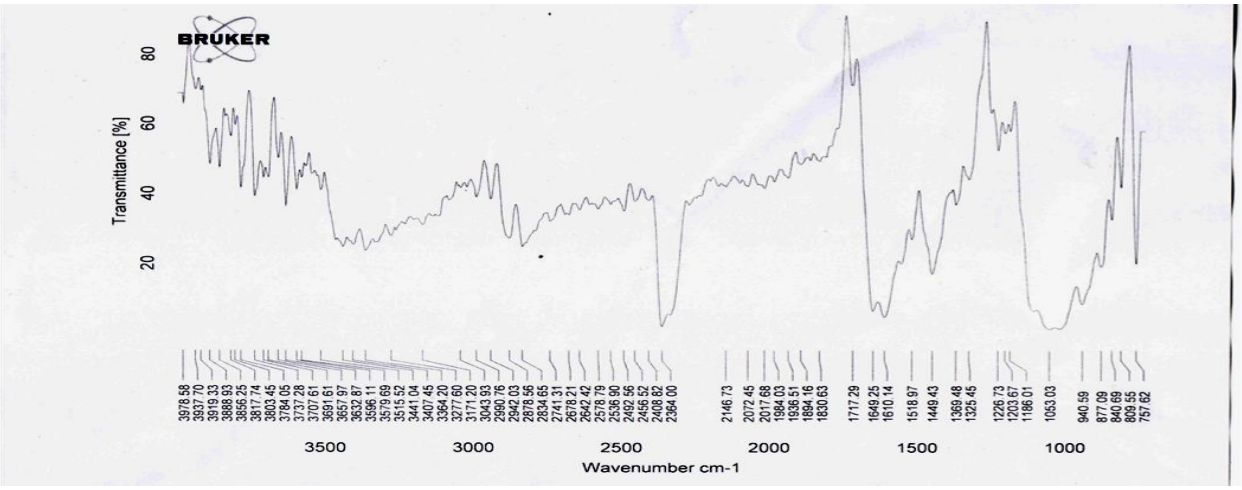


Fig 13: FTIR Spectrum of drug + Methyl Cellulose [immediate].

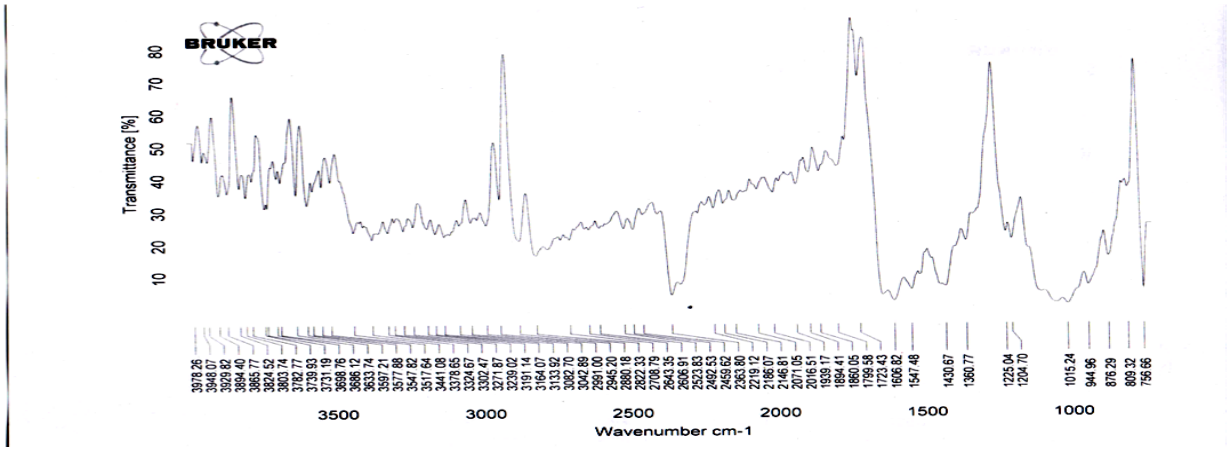


Fig 14: FTIR spectrum of drug + Methyl cellulose [after 15 days]

Table 3: Quantity used for Drug and Polymer identification

S. No.	API and Excipients	Quantity per vial [mg]	No. of Vials		Results [complies or not]
			Initial	50^0C After 15 Days	
1	Minoxidil	10	1	1	Complies
2	Minoxidil and Carbopol 940	10	1	1	Complies
3	Minoxidil and Carbopol 934	10	1	1	Complies
4	Minoxidil and Methyl Cellulose	10	1	1	Complies
5	Minoxidil and Xanthan Gum	10	1	1	Complies
6	HPMC	10	1	1	Complies

Analytical methods of estimation

Analytical methods were developed for the analysis of minoxidil using UV Spectroscopy. This method obeyed Beer's law.

Determination of absorption maxima [λ max]/wavelength maxima:

Absorption maxima of minoxidil found to be 286 nm.

Standard curve of minoxidil in phosphate buffer solution [pH 7.4]

Calibration curve of minoxidil was obtained with phosphate buffer pH7.4. Calibration curve was drawn using different values of absorbance at their respective concentration mentioned below in a table 4.

Table 4: Standard calibration curve in phosphate buffer pH 7.4 at λmax 286 nm

Concentration [mcg/ml]	Absorbance 1 [nm]	Absorbance 2 [nm]	Absorbance 3 [nm]	Average
4	0.149	0.103	0.195	0.149
8	0.320	0.217	0.423	0.320
12	0.502	0.392	0.612	0.502
16	0.624	0.507	0.714	0.624
20	0.820	0.731	0.909	0.820
24	1.016	0.934	1.098	1.016

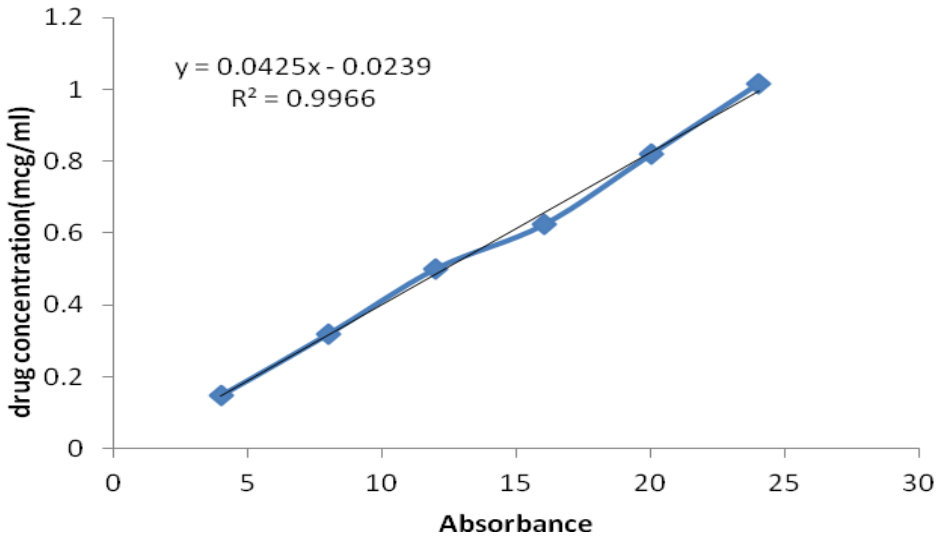


Fig 15: Calibration curve of minoxidil in PBS pH 7.4 at 286 nm

Solubility determination

Solubility of minoxidil was studied in different solvents. Minoxidil was soluble in water, readily soluble in ethanol or propylene glycol and insoluble in chloroform.

Table 5: Solubility studies of Minoxidil

S.No.	Solvent	Solubility Standard [mg.ml]	Solubility observed [mg/ml]
1	Water	2.0 - 2.5	2.04
2	Alcohol	29	23
3	Chloroform	0.5	0.3
4	Propylene Glycol	75	72.38

Melting Point Determination

Melting point of minoxidil was estimated using melting point apparatus and was found to be in the range of 223-225°C.

Evaluation

Physicochemical properties

The physicochemical properties viz. homogeneity, pH, viscosity, color were studied and are mentioned in table 6.

Table 6: Physicochemical properties of all formulation

Formulation code	Homogeneity	pH	Viscosity [cps]	Color
F1	Homogeneous	6.4	1970	White
F2	Homogeneous	6.3	4310	Off white
F3	Homogeneous	6.7	10570	White
F4	Homogeneous		10930	White
F5	Non homogeneous	6.2	79	White
F6	Homogeneous	6.5	142	White
F7	Homogeneous	6.5	427	White
F8	Homogeneous	6.6	924	Off white
F9	Homogeneous	6.3	1370	White
F10	Homogeneous	6.4	1458	White
F11	Homogeneous	6.7	1689	White
F12	Homogeneous	6.5	1783	White
F13	Homogeneous	6.4	34	White
F14	Homogeneous	6.5	72	White
F15	Homogeneous	6.5	221	White
F16	Homogeneous	6.4	294	White

In vitro drug release

In vitro drug release studies were carried out using Franz diffusion cell using phosphate buffer solution pH 7.4. The rate release profile was plotted as the percentage versus time thus showing drug release increases with increase in time. The dissolution profile is presented in table 7.

Table 7: In vitro dissolution profiles of all formulations

Formulation code	5 [min]	10 [min]	15 [min]	30 [min]	45 [min]	60 [min]
F1	40.2	45.8	52.24	74.08	77.4	89.2
F2	82.2	83.8	94.4	138.4	148.6	167.8
F3	25.6	28.8	37	60.6	77.6	91.4
F4	24	26.4	34.6	51.4	63.6	78.2
F5	29.2	35.8	43.4	55	73	90.4
F6	15.4	14.8	20.8	28.4	37.4	43
F7	10	11.6	14.6	18.8	24.8	33.2
F8	25.2	31.8	37.6	51.8	62.4	68.6
F9	33.2	37.6	41.2	54.6	67.6	75.2
F10	25.8	32.2	37.4	53.2	64.6	75.2
F11	24.6	30.4	36.6	45	58.2	67
F12	25.2	31.8	37.6	51.8	62.4	68.6
F13	36	46.8	55.2	75.8	87.6	91.8
F14	30	40.6	47	62.4	72.2	81.4
F15	29.4	35.4	43.6	57.2	68	76.2
F16	30.4	36.2	42.8	57.4	68	72

It was observed that the formulations F3 and F5showed high release of drug.

Physicochemical properties of selected formulation
Physicochemical properties of two selected formulations with code F3 and F5 were studied and results are shown in table 8.

In vitro drug release of selected formulation
Percentage release of F3 was found to be 88.1% and that of F5 was 89.9%. Drug release profiles of both formulations are shown in table 9.

Physicochemical properties of final formulation and marketed formulation
F5 was found to be the better choice of formulation on the basis of various evaluation parameters viz. pH, viscosity, in vitro drug release profile, etc. Physicochemical properties of final formulation and marketed formulation are enlisted in table 10.

Drug content
Drug content of the final formulation was found to be 99.04 and that of the marketed formulation 99.62.

In vitro drug release study
Release profiles of both i.e. final and marketed formulation were carried out using franz diffusion cell with phosphate buffer pH 7.4. Results are mentioned in table 11.

Table 8: Physicochemical properties of selected formulations

Formulation code	Homogeneity	pH	Viscosity [cps]	Color
F3	Homogeneous	6.4	84	White
F5	Homogeneous	6.7	11236	White

Table 9: In Vitro dissolution profile of selected formulations

Formulation code	5 [min]	10 [min]	15 [min]	30 [min]	45 [min]	60 [min]
F3	25.4	32.6	38.3	59.7	73.4	88.1
F5	30.1	36.5	47.3	62.4	77.6	89.9

Table10: Physicochemical properties of final formulation and marketed formulation

Formulation code	Homogeneity	pH	Viscosity [cps]	Color	Spreadability [gm*cm/sec]
Final formulation	Good	6.74	10513	White	208.55
Marketed formulation	Good	6.85	931	Pale yellow	190.14

Table 11: Dissolution profiles of final formulation and commercial formulation

Formulation code	5 [min]	10 [min]	15 [min]	30 [min]	45 [min]	60 [min]
Final formulation	26.4	29.4	38.2	58.4	84	90.6
Marketed formulation	36.54	40.14	41.68	77.36	86.9	102.06

Drug release profiles of final and marketed formulation
[red line indicates drug release profile of marketed formulation and blue line indicates drug release profile of final formulation]

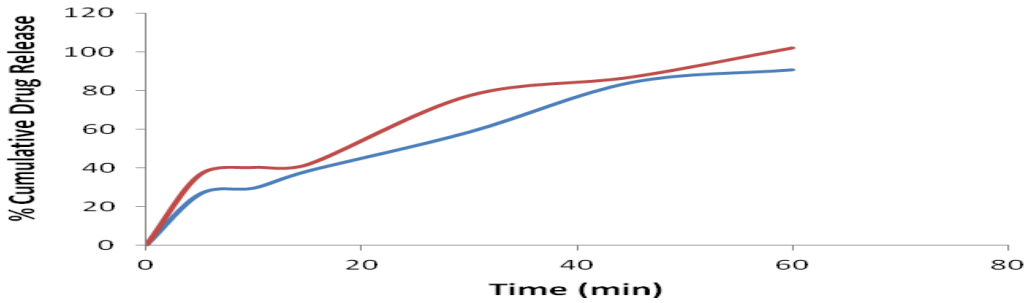


Fig 16: Drug release of marketed formulation

Stability study of Final formulation

Stability study for the final emulgel formulation was carried out at 4°C and 40°C for one month and no significant changes were observed. Thus results are enlisted in table mentioned below.

Table 12: Stability study

Parameters	Initial	At 4°C		At 40°C	
		After 15 days	After 30 days	After 15 days	After 30 days
Color	White	White	White	White	White
pH	6.74	6.71	6.9	6.6	6.4
Viscosity [cps]	10513	10761	10106	10839	11041
Spreadability [gm*cm/sec]	208.55	207.91	206.85	207.63	206.01
% Drug release	90.6	90.1	89.3	89.8	89.1

Kinetic Modelling, Statistical Methods

ANOVA

The results found to be significant except for Carbopol 934 and are concluded in the table 13 and graph of all polymers together is shown in fig 17.

Table 13: p Values of all polymers

Polymer	p value	Result
Carbopol 940	0.0001	Significant
Xanthan gum	0.0003	Significant
Carbopol 934	0.0659	Not significant
Methyl Cellulose	0.0005	Significant
All polymers together	0.0010	Significant

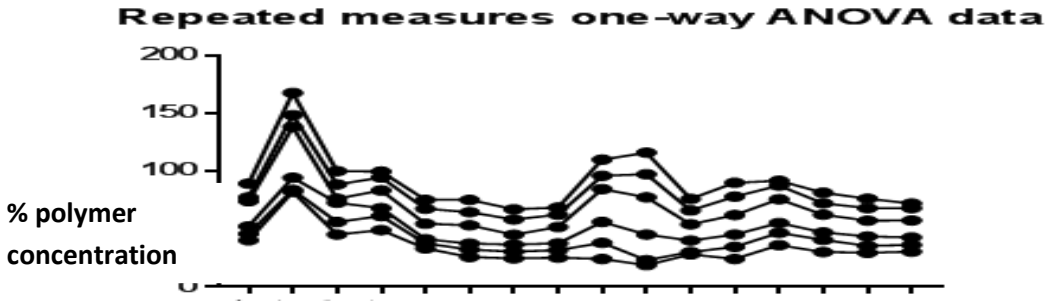


Fig 17: ANOVA Graph for all polymers together

Table 14: Calculation of similarity factor and difference factor

S.No.	Time [min]	Test	Reference	Reference - Test	$\sum[R_t-T_t]2$	f2 Difference Factor	f1 Similarity Factor
1	5	26.4	36.54	10.14	102.81	51.01	14.99
2	10	29.4	40.14	10.74	115.34		
3	15	38.2	41.68	3.48	12.11		
4	30	58.4	77.36	18.96	359.48		
5	45	84	86.9	2.9	8.41		
6	60	90.6	102.06	11.46	131.331		

Model Independent Methods

A simple model independent approach uses a difference factor [f1] and a similarity factor [f2] to compare dissolution profiles.

Difference Factor [f1] and Similarity factor [f2]

The similarity and difference factor obtained for minoxidil emulgel was found o be within the standard. f1 should be less than 15 and the results were found to be 14.99. There was no significant variation in the in vitro drug release profile of commercial product and final preparation. f2 should be more than 50. The result was found to be 51.01 thus indicates the similarity between dissolution profiles of both.

Model dependent Methods

The release of formulation F5 was indicated by highest r^2 values in zero order model which is similar to that of the commercial product i.e. highest r^2 value was seen in zero order model thus showed the release mechanism as Non –Fickian. Table 15 summarized the correlation coefficients for different release kinetics model of minoxidil emulgel and commercial formulation.

Table 15: R^2 values of different models for final formulation and marketed formulation

Formulation	Model	R^2 value
Final	Zero order	0.977
	First order	0.958
	Higuchi equation	0.972
	Korsmeyer Peppas	0.96
Marketed	Zero order	0.959
	First order	0.930
	Higuchi equation	0.957
	Korsmeyer	0.767

A. **Final Formulation**

- **Zero order equation**

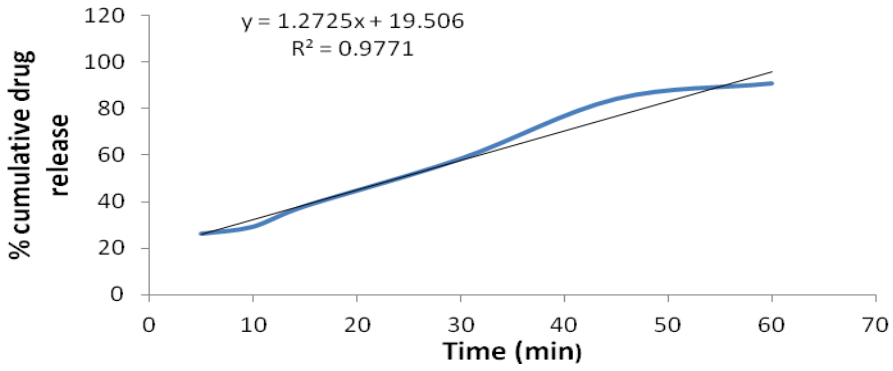


Fig 18: Zero order equation of Final Formulation

- **First order equation**

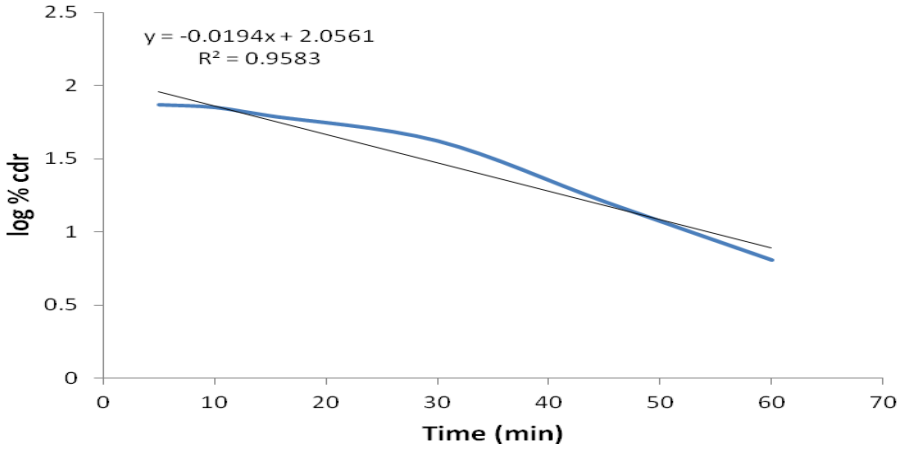


Fig 19: First order equation of Final Formulation

- **Higuchi equation**

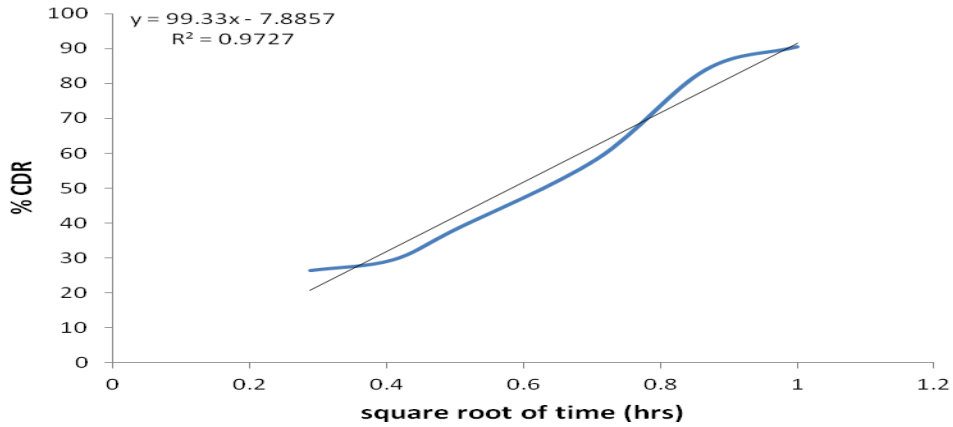


Fig 20: Higuchi equation of Final Formulation

- **Korsmeyer peppas equation**

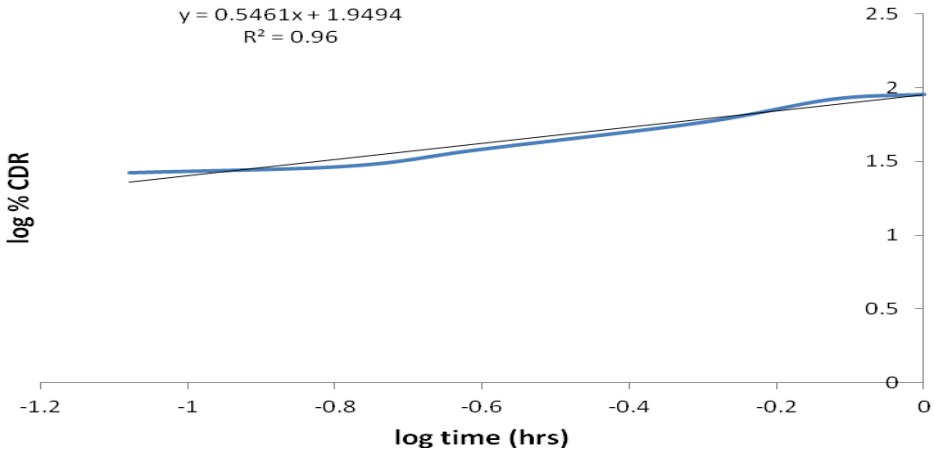


Fig 21: Korsmeyer peppas equation of Final Formulation

1. **Marketed formulation**
   - **Zero order equation**

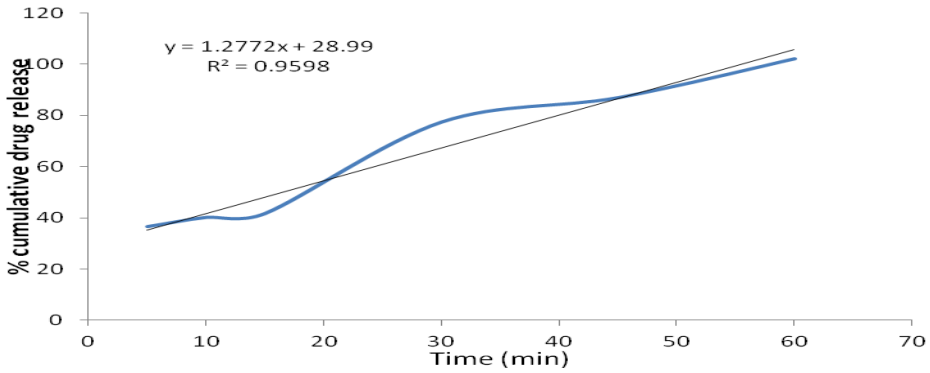


Fig 22: Zero order equation of Marketed Formulation

   - **First order equation**

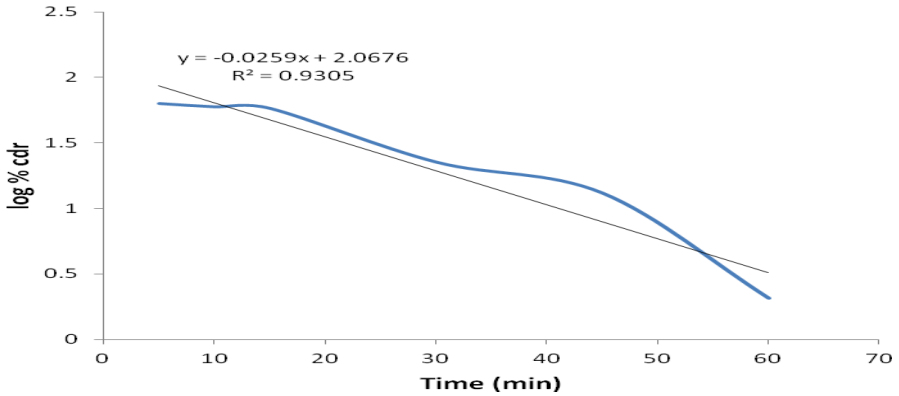


Fig 23: First order equation of Marketed Formulation

   - **Higuchi equation**

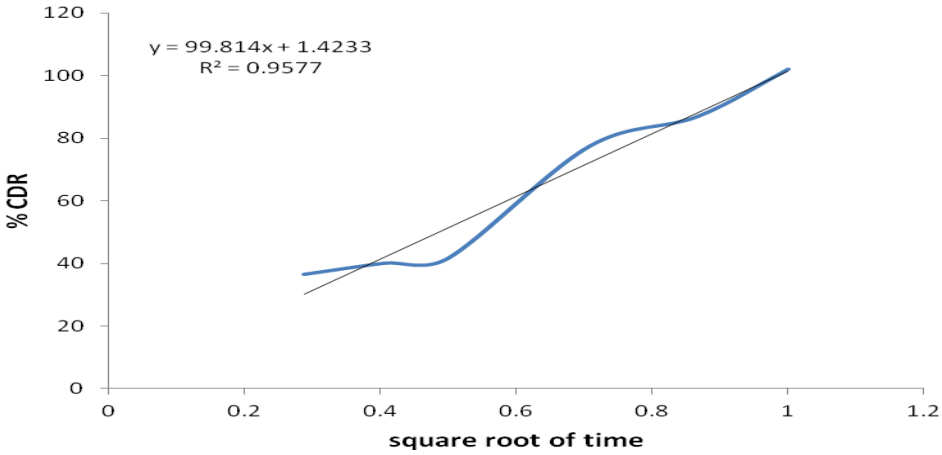


Fig 24: Higuchi equation of Marketed Formulation

- **Korsmeyer peppas equation**

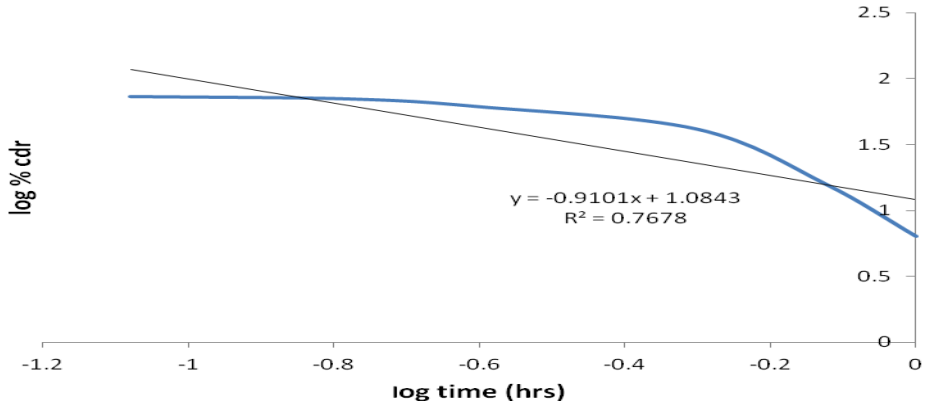


Fig 25: Korsmeyer Peppas equation of Marketed Formulation

CONCLUSION:

This research was carried out to develop minoxidil emulgel with aim to deliver the drug to systemic circulation through skin thus avoid first pass metabolism, improves stability and enhance residence time. Sixteen formulations were formulated and F5 was the one best out of all. Comparative study was done with the available minoxidil topical commercial preparation i.e. Tugain gel 5%. Thus minoxidil were found to be feasible over minoxidil gel as application of marketed formulation produces burning sensation [due to presence of high content of alcohol] but the emulgel formulation does not produce any burning sensation along with good spreadability Hence minoxidil emulgels were found to be effective for treating androgenic alopecia.

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Conflict of Interest:

No conflict of interest

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