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FORMULATION AND EVALUATION OF TOPICAL EMULGEL OF ANTIACNE AGENT

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ABSTRACT

The aim of present work was to develop a topical emulgel of antiacne agent, which would effectively deliver the drug without pain or irritation. The major objectives behind the formulation is enhancing the topical delivery of hydrophobic drug (Adapalene), and increases the Absorption of adapalene through human skin by formulating Adapalene Emulgel using Carbopol 934, Hydroxypropyl methylcellulose (HPMCK100M), and combination of both polymers. Isopropyl myristate (IPM) is used as permeation enhancer. The prepared emulgel were evaluated for their physical appearance, pH determination, viscosity, spreadability, extrudability, in vitro drug release, skin irritation test, and stability. All the prepared Emulgel formulation showed acceptable pH, Drug contents, Spreadability, Extrudability, Viscosity. Formulation with combination of both polymers 0.5 % (Carbopol 934 + HPMC K100M) and high amount of emulsifiers (4%) was found to give higher release profile 83.73 %. In-vitro diffusion profile of Adapalene emulgel (optimized batch F10) indicate that 83.73% drug release within 24 hrs, while 77.56% of marketed formulation. Accelerated stability studies were conducted as per ICH guidelines at 40°C± 2°C temperature and 75%RH± 5%RH for 1 Month and indicated that optimized formulation F10 were stable. Skin irritation studies of optimized formulation F10 was performed using rabbit as an animal model for 24 hrs and no erythema and edema were recorded after 24 hrs. The result obtained shows that Topical Emulgel of Adapalene can be used as effective topical system for treatment of Acne.

Key Words: Topical Emulgel, Adapalene, Carbopol 93, HPMC K100M, Permeation enhancer.

INTRODUCTION

In the past, the most commonly applied systems were topically applied lotions, creams, and ointments for dermatological disorders. The occurrence of systemic sideeffects with some of these formulations is indicative of absorption of the drugs through the skin, which leads to the idea of topical drug delivery system. Topical drug delivery system established itself as an Integral part of novel drug delivery systems.

Advantages of topical dosage forms [1, 2, 3] **1**. They can avoid gastrointestinal drug absorption difficulties caused by gastrointestinal pH and enzymatic activity and drug interaction with food and drinks. **2.** They can substitute for oral administration of medication when that route is unsuitable. **3.** To avoid the first pass effect, that is, the initial pass of drug substance through the systemic and portal circulation following gastrointestinal absorption, possibly avoiding the deactivation by digestive and liver enzyme. **4.** They are non-invasive and have patient

compliance. **5.** They are less greasy and can be easily removed from the skin. **6.** They reduce doses as compare to oral dosage forms. **7.** Their effect is localized with minimum side effects.

Acne Vulgaris [4, 5, 6]

Acne Vulgaris may be defined as any disorder of the skin whose initial pathology is the Microscopic microcomedo. Acne vulgaris is an extremely common disorder of skin (pilocebaceous u nit) that affects virtually all individuals at least once during life. The incidence of acne peaks at teenage, but substantial numbers of men and women between 20-30 years of age are also affected by the disorder. Acne may be classified as comedonal, papular , pustular, cystic, and nodular.

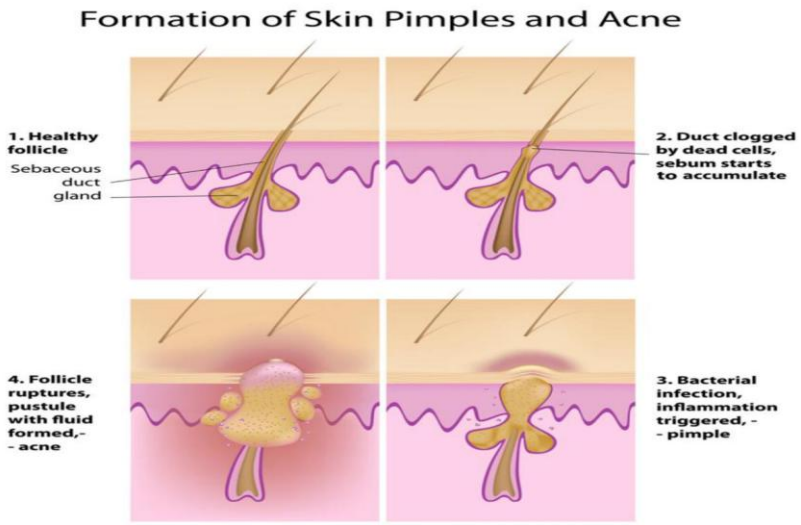


Figure 1: Formation of skin pimples and Acne

Emulgel as drug delivery system [8, 9, 10, 11, 12]

When gel and emulsion are used in combined form, the obtained dosage form is referred as emulgel. Emulgels are preparation widely used for delivery of drug through skin. Its application in dermatology is realized mainly due to the advantages it offers such as easy incorporation of hydrophobic drugs, thixotropy, greaseless, spreadability, easy removability, emollient, non-staining, water-solubility, biocompatibility and transparency with longer shelf life and pleasing appearance. Moreover, feasible and low cost of production are added advantages.

Important Constituents of Emulgel Preparation

1. Aqueous Material: This forms the aqueous phase of the emulsion. Sometimes instead of water as vehicle, alcohols can also been used.

2. Oils: This constitutes the oil phase of the emulsion. They may also act as permeation enhancers (e.g. Linseed oil, Oleic oil). Commonly used oils are Liquid Paraffin, Oleic Acid, Isopropyl Myristate, and jojoba oil.

3. **Emulsifiers:** Emulsifying agents are used both to promote emulsification at the time of manufacture and to control stability during a shelf life; that can vary from days for extemporaneously prepared emulsions to months or years for commercial preparations. e.g.

Stearic acid, Sorbitan monooleate (Span 80), Polyoxyethylene sorbitan monooleate (Tween 80).

4. **Gelling Agent**: These are the agents used to increase the consistency of any dosage form can also be used as thickening agent. e.g. Carbopol, HPMC.

5. **Permeation Enhancers:** These are agents that partition into, and interact with skin constituents to induce a temporary and reversible increase in skin permeability.

e.g. Menthol, clove oil, isopropyl myristate.

6. **Co-surfactants:** In most cases, single-chain surfactants alone are unable to reduce the o/w interfacial tension sufficiently. Therefore, to enable an emulsification co-surfactant is used for g. Propylene Glycol (PG), Cetostearyl alcohol.

7. **Preservative:**may be a part of tablet formulation in order to prevent the growth of microorganisms in tablet formulation. Parabens like methyl, propyl, benzyl and butyl and p-hydroxy benzoate are used as preservatives.

MATERIALS

Adapalene (Videv intermediates, surat), Span 80,Tween 80, HPMC K100M, Carbopol 934,Isopropyl alcohol, propylene glycol, Triethanolamine & Methyl paraben were purchased from Astron chemicals Ahmadabad, India.

METHOD

Screening of Excipients

To find out suitable excipient, the solubility of Adapalene was measured in various oils, surfactants, solvents, co-solvents.

Solubility study [13,14]

50 mg Adapalene was taken in capped vile containing 2 ml of each of the screened vehicle. After sealing, the mixture was heated in water bath at 40ºC for 30 minutes to facilitate solubilisation of drug. The mixing of system was prepared using magnetic stirrer at room temperature for 48hr. mixing of the systems was performed at 50 RPM. These systems were centrifuged at 5000 rpm for 15 min and then analyzed for Adapalene by UV-VIS Spectroscopy.

Calculation of Required HLB Value for O/W Emulsion [15,16]

RHLB value means the HLB value required to prepare stable emulsion using combination of emulsifiers. The combination includes two emulsifiers of diverse HLB values, one with low and other with high HLB.

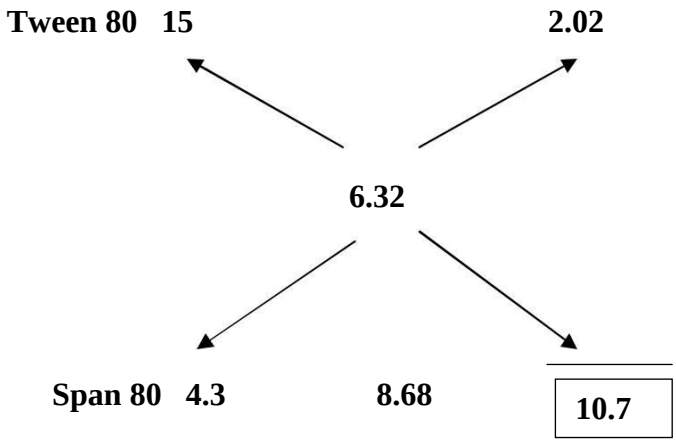
RHLB value of oil and co-surfactant is given in table 5.3
Total amount of Oil: - 40% & Water: - 60%

Table 1: Calculation of RHLB

Components	HLB value	% w/w	%w/w
Jojoba-oil	6.6	30 %	6.5*30/40 = 8.5
Propylene glycol	11.6	5%	11.6*5/40 = 1.45

RHLB value = 4.87 + 1.45 = 6.32

To achieve the RHLB value of 6.32, amount of emulsifiers required can be calculated by **Alligation method**.



Total 10.7% w/w emulsifiers were required: 2.02 % w/w Tween-80 and 8.68 % w/w Span-80

For 4 % w/w total emulsifiers Tween-80 required will be			
10.7 %	2.02		
4 %	4 * 2.02/10.7 = 0.75 % w/w		
As per above calculation Span 80 required for 4 % total emulsifier = 3.24 % w/w			
Above 4 % they cross IIG limit (Inactive Ingredient Guideline)			

Preparation of Adapalene Emulgel formulation:

Gel: The Carbopol gel was prepared by dispersing carbopol 934 in purified water with constant stirring at a moderate speed and soaked overnight. The gel was obtained by neutralizing the dispersion with triethannolamine and adjusting pH to 6.5. In case of HPMC K100M, gel was prepared by dispersing HPMC K100M in hot purified water (80º C), and the dispersion was cooled, soaked overnight.

Emulsion: The oil phase was prepared by dissolving span 80, isopropyle myristate in jojoba-oil and drug in IPA. Both solutions were mixed. The aqueous phase was prepared by methyl paraben dissolved in propylene glycol and this solution was mixed with tween 80. Both oil and aqueous phases were heated separately to 70ºC and then oily phase was mixed with aqueous phase with continuous stirring (up to 2 hours)

Emulgel: The obtained emulsion was mixed with the gel in 1:1 ratio according to the formula given in table 5.4 to get an emulgel.

Table 2: Formulation of topical Adapalene Emulgel (%w/w)

Batch Code	Polymer used	Polymer concentration	Drug (%)	Jojoba oil (%)	Propylene glycol (%)	Span 80 (%)	Tween 80 (%)	IPM (%)	Propyl paraben (%)
F1	Carbopol 934	0.5 %	0.1	20	5	0.4	1.6	5	0.03
F2			0.1	20	5	0.75	3.2	5	0.03
F3		1 %	0.1	20	5	0.4	1.6	5	0.03
F4			0.1	20	5	0.75	3.2	5	0.03
F5	HPMC K 100 M	0.5 %	0.1	20	5	0.4	1.6	5	0.03
F6			0.1	20	5	0.75	3.2	5	0.03
F7		1 %	0.1	20	5	0.4	1.6	5	0.03
F8			0.1	20	5	0.75	3.2	5	0.03
F9	Carbopol 934 + HPMC K 100 M	0.5 %	0.1	20	5	0.4	1.6	5	0.03
F10			0.1	20	5	0.75	3.2	5	0.03
F11		1 %	0.1	20	5	0.4	1.6	5	0.03
F12			0.1	20	5	0.75	3.2	5	0.03

EVALUATION OF FORMULATION

Appearance

Appearance of Emulgel was evaluated on the bases of visual inspection.

pH [17]

The pH of prepared emulgel was measured using digital pH meter by dipping the glass electrode into an emulgel for a minute and the pH was noted. The measurement of pH of each formulation was done in triplicate and mean values were calculated.

Drug content studies [17]

1 gm emulgel was taken in 10 ml volumetric flask containing 5 ml IPA and diluted upto 5ml with the same solvent. From the above solution, 1 ml was further diluted with 10 ml IPA. The resultant solution was filtered through Whatman filter paper and absorbance of the solution was measured at 320 nm using UV spectrophotometer.

Spreadability Test [17]

Spreadability is determined by apparatus suggested by Lalit kumar et al which is suitably modified in the laboratory and used for the study. It consists of a wooden block, which is provided by a pulley at one end. By this method, spreadability is measured on the basis of 'Slip' and 'Drag' characteristics of emulgels. A ground glass slide is fixed on this block. An excess of emulgel (about 2 gm) under study is placed on this ground slide. The emulgel is then sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided with the hook. A 500 mg weight is placed on the top of the two slides for 5 minutes to expel air and to provide a uniform film of the emulgel between the slides. Excess of the emulgel

is scrapped off from the edges. Measured quantity of weight was placed in the pan attached to the pulley with the help of string attached to the hook and the time (in seconds) taken by two slides to slip off from emulgel. A shorter interval indicates better spreadability is calculated by using the formula:

S = M*L / T

Where M = weight tied to upper slide, L = length of glass slides, T = time taken to separate the slides.

Extrudability study (Tube Test) [18]

The emulgel formulation were filled in standard caped collapsible lami-tube and sealed. The tube was weighted recorded. The tube was placed between two glass slides and was clamped. A 500 g weight was placed over the glass slide and then capwas opened. the amount of emulgel were collected and weighed. The % of emulgel extruded was calculated; and grades were allotted (+ + + excellent, + + Very good, + Good)

Viscosity[19]

The viscosity of the formulated batches was determined using a Brookfield Viscometer (Brookfield DV-2 + pro) with spindle S64. The formulation whose viscosity was to be determined was added to the beaker and was allowed to settle down for 30 min. at the assay temperature (25±1ºC) before the measurement was taken. Spindle was lowered perpendicular in to the Centreof Emulgel taking care that spindle does not touch bottom of the jar and rotated at a speed of 60 rpm for 10 minutes. The viscosity reading was noted down.

***In vitro* drug release studies**[19]

The *in vitro* drug release studies were performed by using Franz diffusion cell with cellophane paper. The water jacketed recipient compartment had total capacity of 22.5 ml and it had 2 arms, one for sampling and another for thermometer. The donor compartment had internal diameter of 2 cm. The donor compartment was placed in such a way that it just touches the diffusion medium in receptor compartment. The receptor compartment contained IPA and phosphate buffer pH 6.8 (80:20) that was maintained at 320C ± 10C. The membrane was equilibrated before application of the equivalent to 1 gm of emulgel onto the donor side. Samples were periodically withdrawn from the receptor compartment, replacing with the same amount of IPA and phosphate buffer 6.8 (80:20), and assayed by UV spectrophotometer at 320 nm.

Table 3: In Vitro drug release conditions

Apparatus	**Franz diffusion cell**
Medium	IPA + pH 6.8 phosphate buffer (80:20)
Diffusion medium volume	22.5 ml
Temperature	32 ºC ±1 ºC
Speed	50 RPM
Sampling volume	1 ml
Sampling interval	1 hour

Evaluation of Optimized batch F10

Skin irritation Test of Optimized batch F10 [20, 21]

As the formulation was intended for dermal application, skin irritancy should be tested. Skin irritation tests were conducted at Albino rabbits (New Zealand white variety) to determine irritancy after single application of Topical Emulgel. The room temperature was maintained at 22± 3°C. Skin was prepared by removing hair of the rabbit (backside) twenty four hour.

The optimized formulation was applied on the patch of preshaved skin ($3cm^2$) for 2 second and occluded with adhesive tapes and resulting reactions such as erythema and edema were scored after 24 h. The patch was removed after 24 h and treatment sites were cleaned with wet gauze to remove any residual test substance. Exposed skin was graded for formation of edema and erythema. Based on the scoring, the formulation was graded as 'non-irritant', 'irritant' and 'highly irritant'. The irritation scores of the test area were obtained by judging the extent of erythema and edema. Erythema and edema were graded as 0 for no visible reaction, 1 for just present reaction, 2 for slight reaction, 3 for moderate reaction and 4 for severe reaction. Eventually, the total scores for irritation test in each formulation were calculated using the following equation.

Table 4: Experimental Animal DetailsSpecies	**Weight**	**Gender**	**Number to be used**
Albino Rabbit	1.5-2.5kg	Female	2

Table 5: Experimental group of Skin irritation test for Optimized Batch F10

Group No	**Name of Group**	**Tretment**
1	Group 1:No application (control)	Vehicle for 24 hr
2	Group 2:Topical Emulgel of Adapalene	for 24 hr

$$\text{Primary irritation index} = \frac{(\text{Erythema reaction scores} + \text{Edema reaction scores})}{\text{Time interval (h)}}$$

Table 5: score of Erythema and Erythema and Edema formation

score of Erythema and Erythema and Edema formation	**Score**
No	0
Very slight	1
Well defined	2
Moderate to severe	3
Severe	4

Table 6: score of Erythema and Erythema and Edema formation

Index	Evaluation
0.00	No irritation
0.04-0.99	Irritation barely percipitable
1.00-1.99	Slight irritant
2.00-2.99	Mild irritation
3.00-5.99	Moderate irritation
6.00-8.00	Severe irritation

Stability study[22,23,24]

The developed formulation was stored for stability testing as per ICH guidelines for1 month. Then the optimized formulation F10 was kept for accelerated stability study at 40°C± 2°C temperature and 75%RH± 5% RH for 1 month. After an interval of 1 month chemical stability of the formulations was assessed by estimation of the percent drug remaining in the formulations (Drug content), and physical stability was evaluated by monitoring any change in pH, appearance, color

Table 7: - Stability study parameter.

Stability study	Temperature (°C)	Humidity (%RH)	Time period
Accelerated Stability Study	40°C± 2°C	75%RH± 5%RH	1 month

RESULT & DISCUSSION

FTIR of Adapalene

Drug excipient compatibility study by FTIR

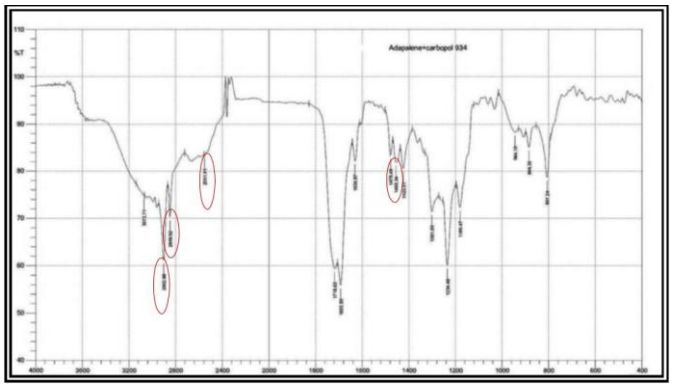


FIGURE 2 FTIR of Adapalene +Carbopol 934

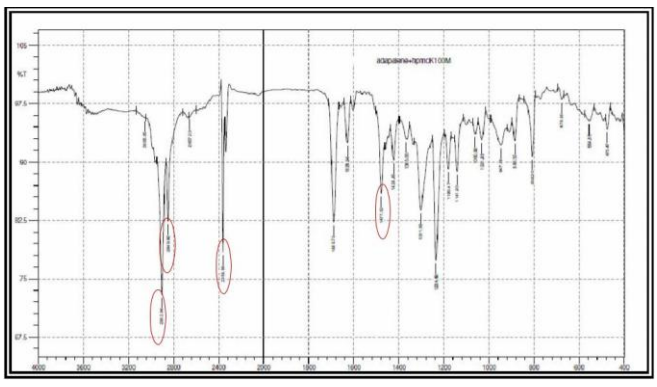


FIGURE 3 FTIR of Adapalene +HPMC K100M

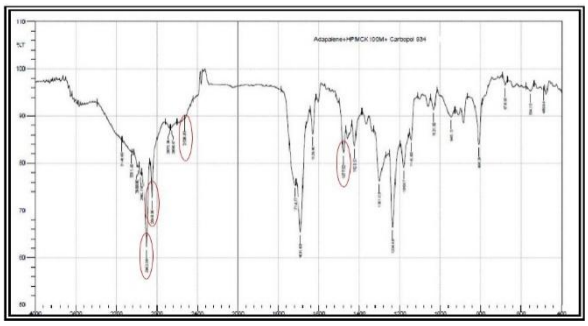


FIGURE 4 FTIR of Adapalene + Carbopol +HPMC K100M

Table 8: FTIR peak of Adapalene and Mixtures

Functional group	Reported Peak (cm^{-1})	Peak of Adapalene (cm^{-1})	Peak of Adapalene + Carbopol 934 (cm^{-1})	Peak of Adapalene + HPMC K100 (cm^{-1})	Peak of Adapalene + Carbopol 934 +HPMC K100 (cm^{-1})
C=C Stretch	1600-1500	1477.52	1478.49	1477.52	1477.52
C-H in alkanes	2850	2850.88	2849.92	2849.92	2848.96
CH in aldehyde & ketone	3000-2800	2904.89	2902.96	2902.96	2902.96
O-H stretch	3000-2500	2656.00 2573.13	2552.91	2359.98 2657.03	2526.83

Melting Point

Table 9: Melting point of Adapalene.

Tests	Specifications	Results
Melting Point	320º C	3 18-312°C

Determination of absorption maxima (λ max) of Adapalen e in IPA and Phosphate buffer pH 6.8 (80:20) by UV Spectroscopy

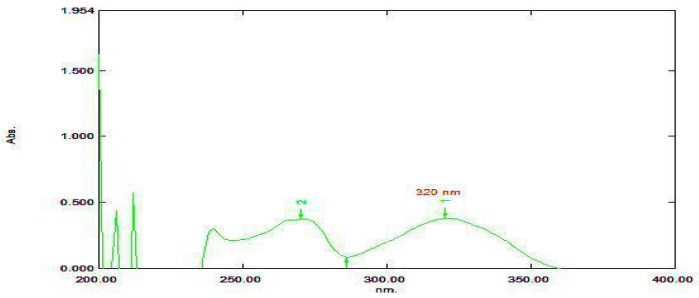
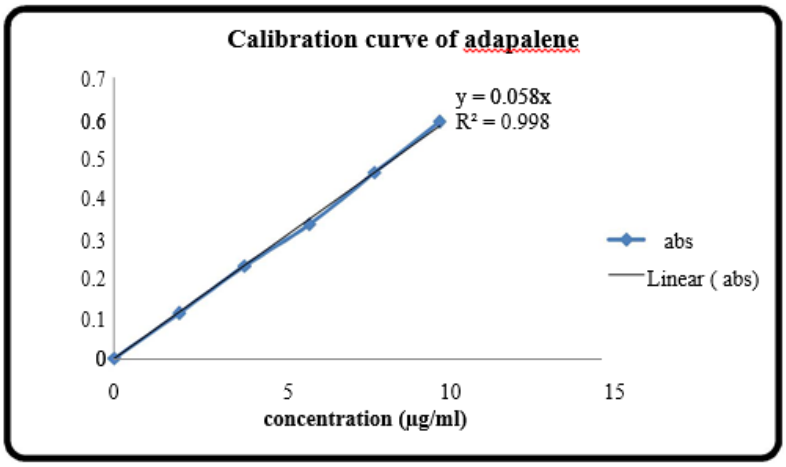


Fig 5: Determination of absorption maxima of Adapalene.

Figure 6: Calibration Curve of Adapalene in IPA and Phosphate buffer pH 6.8 (80:20)



EVALUATION OF FORMULATION

Appearance of Emulgel

Emulgel formulations were white viscous with a smooth and homogeneousappearance.

pH:

Table: 10 pH of different formulation of Emugel

Batch No.	Emulgel	Batch No.	Emulgel	Batch No.	Emulgel
F1	6.2	**F5**	6.1	**F9**	6.2
F2	6.3	**F6**	6.2	**F10**	6.3
F3	6.3	**F7**	6.3	**F11**	6.2
F4	6.3	**F8**	6.3	**F12**	6.3

Drug content of all formulations (F1-F12)

Table 11: Result of drug content of batch F1-F12 (mean, n=3)

Batch No.	% Drug Content	Batch No.	% Drug Content	Batch No.	% Drug Content
F1	98.57 ± 0.5	**F5**	98.70 ± 0.62	**F9**	97.35 ± 0.55
F2	99.63 ± 0.7	**F6**	96.56 ± 0.28	**F10**	98.20 ± 0.45
F3	98.57 ± 0.4	**F7**	95.40 ± 0.9	**F11**	97.22 ± 0.3
F4	99.87 ± 0.35	**F8**	96.75 ± 0.2	**F12**	98.30 ± 0.8

Table 12: Result of Viscosity of batch F1-F12

Batch No.	Viscosity at 60 RPM (CPS) Spin dle S64	Batch No.	Viscosity at 60 RPM (CPS) Spindle S64	Batch No.	Viscosity at 60 RPM (CPS) Spindle S64
F1	4,038	**F5**	2,789	**F9**	4,219
F2	4,089	**F6**	2,794	**F10**	4,225
F3	6,501	**F7**	3,409	**F11**	6,771
F4	6,518	**F8**	3,419	**F12**	6,782

The viscosities of formulations were increased with increased in the polymers concentration

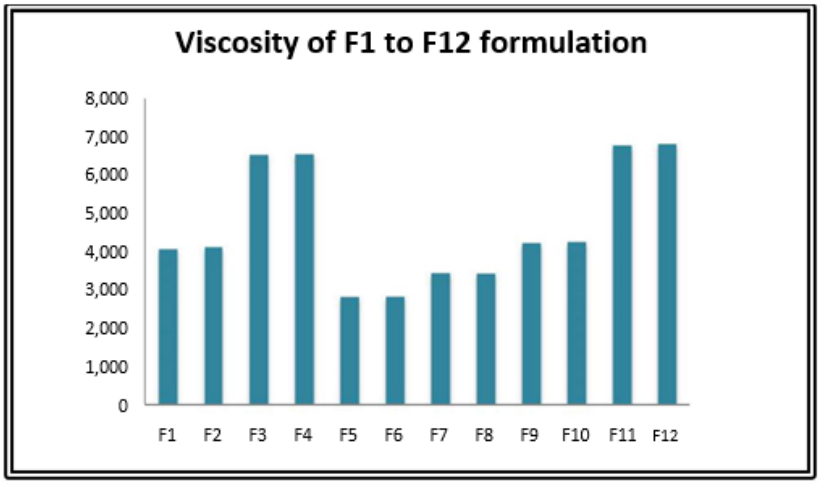


Figure 7: Viscosity of F1 to F12 formulation at 60 rpm

Spreadability and Extrudability of the Formulation (F1-F12)

Table 13: Result of Spreadability and Extrudability of batch (F1-F12)

Formulation	Spreadability test (gm*cm/sec)	Extrudability Test
F1	16.44	+++
F2	17.85	+++
F3	10.25	++
F4	11.5	++
F5	7.22	++
F6	8.12	++
F7	3.87	++
F8	4.76	++
F9	15.16	+++
F10	16.09	+++
F11	6.2	++
F12	7.66	++

Where: +Good, ++Very good, +++Excellent

The formulations with the highest viscosity had the minimum spredability.

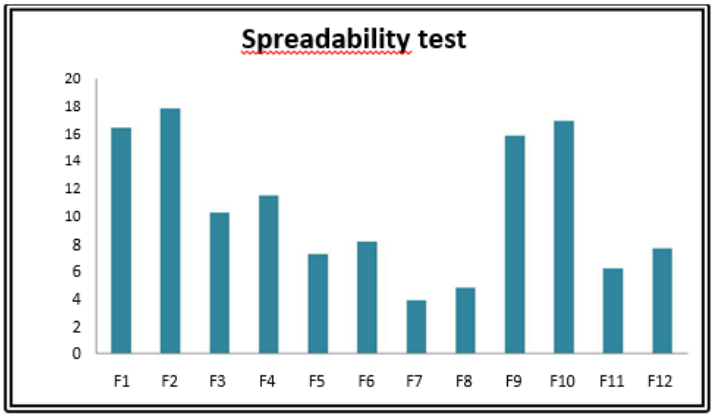


Figure 8: Spreadability of F1 to F12 formulation.

In-vitro drug release studies of formulations (F1-F12)

Table 14: Result of % Drug release of batch F1-F12 (%w/w)

Time (hour)	% cumulative drug release ±SD (n=3)											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	7.37	10.28	2.32	5.43	4.07	6.20	2.52	3.49	9.89	11.05	4.07	6.012
2	14.09	15.58	6.11	9.22	10.65	12.3	6.12	9.46	15.76	17.56	7.16	9.38
3	21.11	22.27	13.56	17.33	14.61	17.1	13.56	14.53	21.29	24.91	13.68	17.74
4	28.6	30.38	20.74	25.44	19.88	22.09	19.19	19.42	32.27	33.72	20.86	26.06
5	33.28	37.27	26.85	31.17	28.47	30.18	22.72	23.72	37.86	40.35	26.86	31.03
6	40.64	45.56	33.59	37.1	34.88	37.23	27.53	29.73	47.56	49.74	33.71	37.34
7	48.26	55.33	40.19	44.4	41.71	44.15	32.12	39.65	55.47	57.34	40.31	44.85
8	58.48	66.53	49.35	52.35	49.57	56.94	45.47	45.68	62.87	66.93	49.47	53.01
20	68.49	74.3	61.75	64.34	64.68	70.22	59.53	61.43	75.55	79.38	63.81	67.66
24	76.13	80.70	71.13	72.56	73.59	77.4	70.69	71.28	79.96	83.73	73.67	75.31

Formulation batch F10 release drug faster than the other formulation due to the lower concentration of combination of both polymers 0.5% (Carbopol 934+HPMC K100M) and higher amount of emulsifiers. Increasing concentration of Polymers leads to decreased drug release from formulation due to increase in viscosity of formulation.

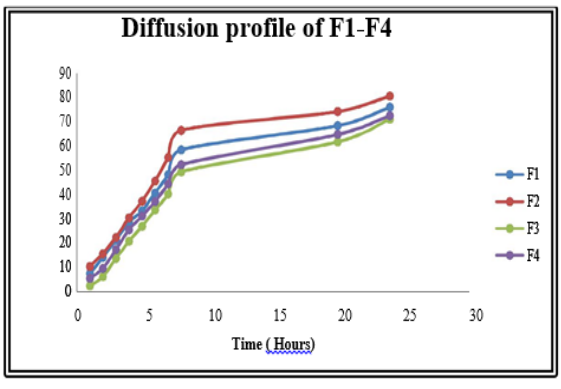


Figure 9: Release profile of batch F1 to F4

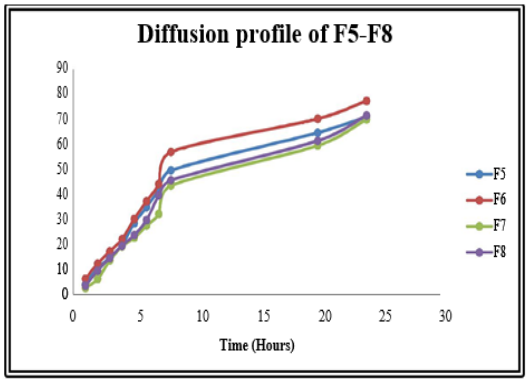


Figure 10: Release profile of batch F5 to F8

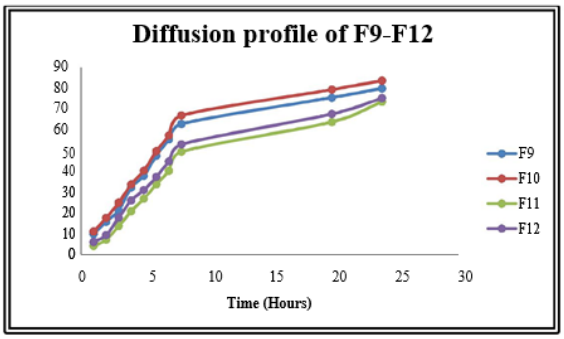


Figure 11: Release profile of batch F9 to F12

Statistical Data Analysis for Batch F10

To ascertain the exact release mechanism of drug from developed formulations, the release data were subjected to various kinetic models. A variety of mathematical models have been used to describe drug release mechanism, viz. zero order, Higuchi and Korsmeyer and Peppas model.

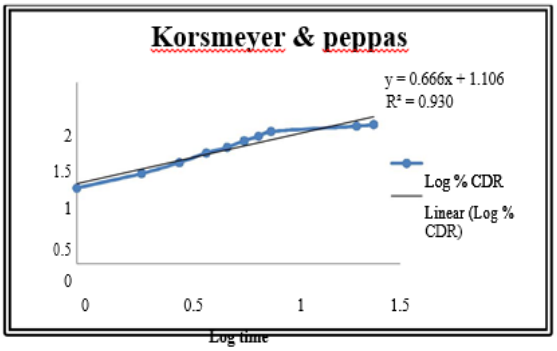


Figure 12: - Log of % cumulative drug released Vs. Log Time Korsmeyer peppas equation

The correlation coefficient (R^2) of the korsmeyer-peppas model was found to be 0.930 as mentioned in table 6.15, slightly higher when compared to the other plot. Hence the release of drug from the F10 batch followed korsmeyer-peppas (non fickian) model for diffusion.

Table 15: - Diffusion kinetic data for F10 batch.

Diffusion Kinetic	R^2
Zero order plot	0.366
First order plot	0.601
Korsmeyer & peppas plot	0.930
Hisxon-crowell plot	0.877
Higuchi plot	0907

Skin Irritation Test optimized Batch F10

Skin irritation test was performed on rabbit back side. Control (without adapalene) and Test formulation (with Adapalene) were observed for 24 hour after application. The total scores for irritation test of optimized formulation was calculated using the following equation and result shown in Table 6.18

Primary irritation index= (Erythema reaction scores + Edema reaction scores) / Time interval (h)

Table 16: Skin Irritation Test optimized Batch F10

Groups	**Primary Irritation Index**	
	8h	24h
Without Adapalene (control)	0	0
Adapalene topical Emulgel (Test)	0	0

Figure 13:- Control after 24 h.

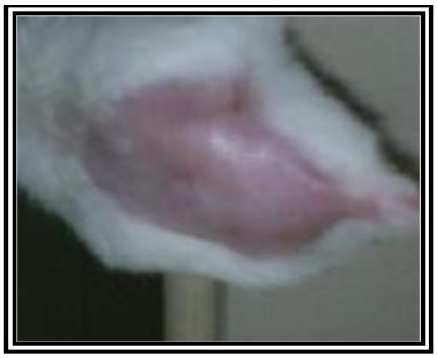


Figure 14:- Test after 24 h.

The primary irritation index of Adapalene topical Emulgel was calculated to be 0.00. No erythema or edema were found in the primary skin irritation studies of the optimized formulations F10 on the rabbits hence found to be safe and non irritant for topical application. The formulation developed was more efficient for a period of 24hr after application.

Stability studies data of the optimized formulation F10 at 40°C± 2°C temperature and 75%RH± 5%RH.

Table 17: Result of Stability Study for Optimized Batch F10

Parameter Evaluated	**Initial**	**After 1 Month**
Appearance	White viscous creamy	White viscous creamy
pH	6.3±0. 05	6.6± 0.07
% Drug content	98.20 % ± 0.45	96.12% ± 0.28

Mean± SD; n=3

Stability studies showed that formulation was stable and there were no significant change in Appearance, pH, and % drug content under accelerated storage condition.

CONCLUSION

On the basis of the previous finding the following could be concluded that the formulation F10 was the most promising formulation. A comparision was done with the marketed formulation Adapalene gel 0.1% (Differin) in which drug is as such and result were found that F10 0.5% (Carbopol 934 + HPMC K100M) shown 83.73 % release and marketed formulation shown 77.56 % release in 24 hours. The result was revealed that F10 shown better drug release as compared to the marketed formulation. Skin irritation study was performed by using rabbit. No skin irritation was produced by optimized formulation F10. Stability test was performed for 1 month at 40°C ±2°C temperature and 75% RH±5%RH. The optimized formulation F10 batch was selected for 1 month stability study; there were no significance change in colour, pH, and % drug content which indicated the selected formulation is stable. Hence, topical Adapalene Emulgel would have to be a better alternative as a topical drug delivery system for treatment of acne.

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