International Journal of Pharmacy and Biological Sciences
ISSN: 2321-3272 (Print), ISSN: 2230-7605 (Online)
IJPBS™ | Volume 8 | Issue 3 | JUL-SEPT | 2018 | 552-562
Research Article | Pharmaceutical Sciences | Open Access | MCI Approved| ज्ञान-विज्ञान विमुक्तये
|UGC Approved Journal |

DESIGN AND CHARACTERIZATION OF APREMILAST LOADED EMULGEL FOR TOPICAL TREATMENT

G.Ganarajan, Deepak Chandra Sharma*, Pranshu Tangri and Preeti Kothiyal
***Department of Pharmaceutical Sciences, Shri Guru Ram Rai University, Patel Nager, Dehradun.**

***Corresponding Author Email: sharma00deepak@gmail.com**

ABSTRACT

The aim of the present research work was to investigate the potential of emulgel in enhancing the topical delivery of Apremilast. Apremilast is Anti-psoriasis/ non-steroidal anti-inflammatory drug that has two major problems when administered orally; first is solubility of drug and has irritant effect in GIT can cause ulcerative colitis with bleeding. Apremilast emulgel were prepared using 4 types of gelling agents. The effect of different type of the gelling agent and the concentration of oil phase and emulsifying agent on the drug release was investigated. The prepared emulgel were evaluated for their physical appearance, viscosity, drug release, Spreadability, pH and stability. All the prepared emulgel showed acceptable physical properties: colour, homogeneity, consistency, spreadability, and pH value. The highest drug release from all the prepared emulgel was found to 57.82% at 24 hr. Results revealed that the emulgel formulations exhibited high drug release especially at low polymer concentration. Stability studies of all prepared emulgel showed that the physical appearance, rheological study, in vitro drug release, remained unchanged upon storage for 3 months. So, it can be concluded that topical emulgel enhanced permeation of Apremilast and possed an effective anti-psoriosis / anti-inflammatory activity, with avoidance of GIT adverse effect.

KEY WORDS

Apremilast, Topical Drug Delivery, Emulgel and Stability Study

1. INTRODUCTION

Emulgel are emulsions, either of the oil-in-water or water in oil type, which are gelled by mixing with a gelling agent. Emulsified gel is stable one and better vehicle for hydrophobic or poorly water-soluble drugs. [1] They have a high patient acceptability since they possess the advantages of both emulsions and gels. Direct (oil-in-water) systems are used to entrap lipophilic drugs, whereas hydrophilic drugs are encapsulated in the reverse (water-in-oil) systems. [2] Therefore, they have been recently used as vehicles to deliver various hydrophobic drugs to the skin. In the local market, two Emulgel are available: Voltaren emulgel (Novartis Pharma, Switzerland), containing diclofenacdiethylamine and Miconaz-H emulgel (Medical Union Pharmaceuticals, Egypt), containing miconazole nitrate and hydrocortisone. [3] 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. The emulsion gels are hydrogels containing randomly distributed oil microdroplets. [4,5] 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 effected site that mainly acts at the related regions.[6,7] On the other hand, topical delivery system increases the contact time and mean resident time of drug at the applied site leading to an increase in local drug

concentration while the pharmacological activity of Emulgel formulations may not change as rapidly as the solution form. [8] Both oil-in-water and water-in-oil emulsions are extensively used for their therapeutic properties and as vehicles to deliver various drugs to the skin. Emulsions possess a certain degree of elegance and are easily washed off whenever desired. [9, 10] They also have a high ability to penetrate the skin. In addition, the formulator can control the viscosity, appearance, and degree of greasiness of cosmetic or dermatological emulsions. Oil-in-water emulsions are most useful as water washable drug bases and for general cosmetic purposes, while water-in-oil emulsions are employed more widely for the treatment of dry skin and emollient applications. Gels for dermatological use have several favourable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, compatible with several excipients, and water-soluble or miscible. The rheological properties and the breakdown behaviour of gels filled with emulsions droplets can be varied by changing the interactions between oil droplets and gel matrix, the oil content and the oil droplet size. [11, 12]

2. MATERIALS AND METHODS

Materials

Apremilast(API) gifted from Mankind Research Center Maneshwar(Gurgua). Carbopol, Xanthan Gum, HPMC, sodium CMC Light liquid paraffin, Tween 20 Span 20, Propylene glycol, Methyl paraben, Propyl paraben, Mentha oil, Methanol, Ethanol, Glutaraldehyde and TEA were obtained from Central Drug House New Delhi. Distilled water was used for all experiments. All chemicals were pharmaceutical grade and used without further modification. [13]

METHOD:

Emulgel preparation:

The composition of emulgel formulations is shown in table 1. First, the gel was prepared by dispersing HPMC in heated purified water (80 °C), and the dispersion was cooled and left overnight. Other Emulgel (Na CMC, Xanthan Gum, carbapol) was prepared by dispersing gelling agent in cool water with moderate rotating speed (500RPM). The oil phase of the emulsion was prepared by dissolving Span 80 in liquid paraffin while the aqueous phase was prepared by dissolving Tween 80 in purified water. Methyl and Propyl parabens were dissolved in propylene glycol whereas Apremilast was dissolved in ethanol, and both solutions were mixed with the aqueous phase. Both the oily and aqueous phases were separately heated to 70 to 80 °C then the oily phase was added to the aqueous phase with continuous stirring until cooled to room temperature. The obtained emulsion was mixed with the gel in 1:1 ratio with gentle stirring to obtain the emulgel. Finally, pH of emulgel was adjusted by using triethanolamine (TEA). [13]

TABLE 1: Composition of different formulation batches (%w/w).

Ingredients (%w/w)	Formulations							
	F1	F2	F3	F4	F5	F6	F7	F8
Apremilast	1	1	1	1	1	1	1	1
Carbapol	0.5	1	-	-	-	-	-	-
HPMC	-	-	0.5	1	-	-	-	-
Na CMC	-	-	-	-	0.5	1	-	-
Xanthan gum	-	-	-	-	-	-	0.5	1
Light liquid paraffin	10	10	10	10	10	10	10	10
Span 20	2	2	2	2	2	2	2	2
Tween 20	2	2	2	2	2	2	2	2
Methyl paraben	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Propylene glycol	5	5	5	5	5	5	5	5
TEA	3	3	3	3	3	3	3	3
Ethanol	4	4	4	4	4	4	4	4
Isopropyl Myristate	5	5	5	5	5	5	5	5
Water	qs	qs	Qs	qs	qs	qs	qs	qs

3. Characterization of Emulgel

Physical Appearance

The Apremilast emulgels were inspected visually for their color, homogeneity, consistency.

pH

pH meter is used for measuring the pH value of Emulgel formulation. Before use, ph meter should be caliberated with standard solution having ph 4-7. In distilled/di-ionised water 1gm of prepared Emulgel formulation was dissolved and stirred it to form a uniform suspension, kept it for 2hr. The volume made up to 100 ml and pH of the suspension can be measure with the digital pH meter.

Spreadability:

Two glass slides was used, which is same dimension used for determination of the prepared Emulgel formulation. Prepared Emulgel was placed over one slide and the other slide was placed over its top. The slides were pressed upon each other like sandwich and remove the air bubble. Apply 2 gm of Emulgel is place between the slide and put 500 gm of weight on upper slide. Top plate was then subjected to pull of 80 grams. With the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5cm be noted. The lesser the time taken more will be the spreadability

Extrudability

Here the weight required to extrude 0.5 cm ribbon of emulgel in 10 sec from lacquered collapsible aluminium tube was determined. Test was repeated and the average values were used for the calculation.

Formula for extrudability calculation:

Extrudability= weight applied to extrude emulgel from tube(g)/Area(cm^2)

Viscosity measurement

Brookfield Viscometer was used to determine viscosity of prepared Emulgel formulation. For the determination of viscosity, prepared Emulgel formulation was added to the beaker and setteled it for 30 mintue at 25-30 °C. Adjust the spindal in that way that spindal does not touch the bottom of the jar and rotate at a moderate speed 50 and 100 RPM for 10 mintue. The viscosity reading was noted.

Drug content determination

Apremilast content in emulgel was measured by dissolving known quantity of emulgel in solvent (Methanol) by Sonication. Filtration of resulting solution was done by using whatman filter paper no.41. Absorbance was measured after suitable dilution at 340 nm using UV/VIS spectrophotometer.

Swelling Index

Formulation with maximum swelling index indicates its tendency to absorb extrudates from wound. The swelling index is calculated by placing 1 gm of Emulgel on porous aluminium foil and then it was placed in petridish containing 10 ml distilled water. Then sample were removed from dish at different time and put it on dry place for some time after it reweighed. Swelling index was calculated using following formula.

Swelling Index (SW) %=[(W_t–W_0) W_0] ×100

Where; (SW)= Equilibrium percent swelling
Wt = Weight of swollen emulgel after time t
Wo = Original weight of emulgel at zero time.

Centrifuge test

6 gm of Emulgel was taken in 10 ml graduated centrifuge tubes and were subjected tospin a t 4000 rpm for 10 min. the sample was observed for any phase separation occurrence.

Temperature swing test

Temperature swing test gives the formulator an idea about the stability of the formulation in extreme temperature conditions. Therefore, this test is frequently employed in the evaluation of topical semisolid dosage forms. For the purpose of this test, the formulations were subjected to freeze and thaw cycles. One cycle comprised of 8 h storage at -40 and another was carried out for 16 h at 400. This was performed for 2 days. The formulations were visually inspected at the end of the test to ascertain their stability

***In Vitro* Drug Release Studies**

The *in vitro* drug release studies were carried out using a modified vertical Franz diffusion cell (with effective diffusion area 4.9 cm^2 and 14 ml cell volume). The formulation was applied on egg membrane 0.45 µm (which was previously soaked in Phosphate buffer pH 7.4 for 24 hours); which was sandwiched between donor and receptor compartment of the franz diffusion cell. Phosphate buffer pH 7.4 + methanol (80:20) was used as a diffusion media. The temperature of the cell was maintained at 37±0.2 0C by kept it in water bath. This whole assembly was kept on a magnetic stirrer and the solution was stirred continuously using a magnetic

bead at 50 rpm. The samples (1.0 ml aliquots) were withdrawn at suitable time interval and analysed for drug content by UV visible spectrophotometer at 345 nm after appropriate dilutions.

Kinetic analysis of the drug release

Kinetic analysis of the drug release was done by fitting the release data to the different release model given below to describe the proper release model.

Zero order release (cumulative % drug release vs. time)

$Q=K_0T$

Where Q is the amount of drug released at time t, K0 is the zero– order release rate.

First order release (log cumulative % drug retained vs. time)

$In(100-Q) = in\ 100-K_1T$

Where Q is the percent of drug released at time t, K1 is the first– order release rate constant

Higuchi model (cumulative % drug retained vs. square root of time)

$Q=K2\sqrt{T}$

Where Q is the percent of drug released at time t, K2 is the Higuchi square root of time release constant.

Korsmeyer-peppas model (log cumulative % drug release v/s. log time)

$F=MT/M=K_mT^n$

Where,

F is fraction of drug released at time t**,**

Mt is drug release at time t,

M is the total amount of drug in dosage form**,** Km is a constant dependent on the geometry of the dosage form**,**

n is diffusion exponent indicating the mechanism of drug release, if the value of n is 0.5 it indicates fickian diffusion and if between 0.5 to 1 it is anomalous transport or Non-fickian diffusion

Stability study

Stability studies of optimized formulation were performed as per ICH guideline (International Conference on Harmonization). It can be observed that the emulgel formulation showed no major alteration in relation to the pH, microbiological study, consistency, skin irritation test and in vitro release study. The formulation shows stability for the period of 3months. No significant changes in the pH of formulations were observed for 3 months in all storage conditions.

4. RESULTS AND DISCUSSION

Physical appearance

The prepared Apremilast emulgel formulations were inspected visually for color, homogeneity, phase separation, consistency and pH. All formulations showed white color and glossy appearance. No phase separation was noticed, formulations showed suitable homogeneity and consistency. The data obtained is shown in Table 2.

Table 2. Physical parameters of formulation batches.

Formulation	Color	Homogeneity	Consistency	Phase separation
F1	Shiny White	Excellent	Excellent	None
F2	White	Excellent	Excellent	None
F3	White	Excellent	Excellent	None
F4	Shiny White	Excellent	Excellent	None
F5	White	Excellent	Excellent	None
F6	White	Excellent	Excellent	None
F7	White	Excellent	Excellent	None
F8	White	Excellent	Excellent	None

pH

The pH of the emulgel formulation was in the range of 5.12-6.46 as shown in table 3 and in fig.1. The results were in the acceptance range and can be easily apply on skin without any irritation.

Table. 3 pH data of all formulation batches.

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8
pH	5.24	5.73	4.92	5.03	5.71	5.20	4.34	4.78

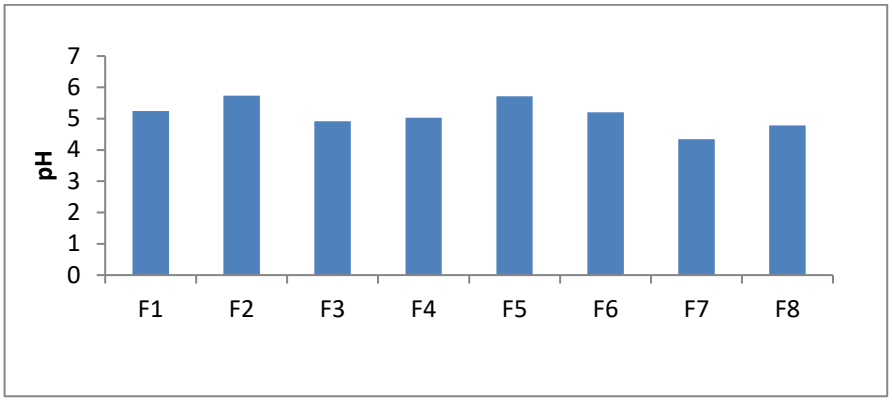

Fig.1 Graphical representation of pH

Spreadability

The spreading coefficient of various emulgel formulations are given below in table 4 and fig.2.

Table.4 Spreadability of Emulgel formulations

Formulation	F1	F2	F3	F4	F5	F6	F7	F8
Spreadability (cm^2)	27.98	23.08	17.80	15.91	21.73	20.92	18.10	17.75

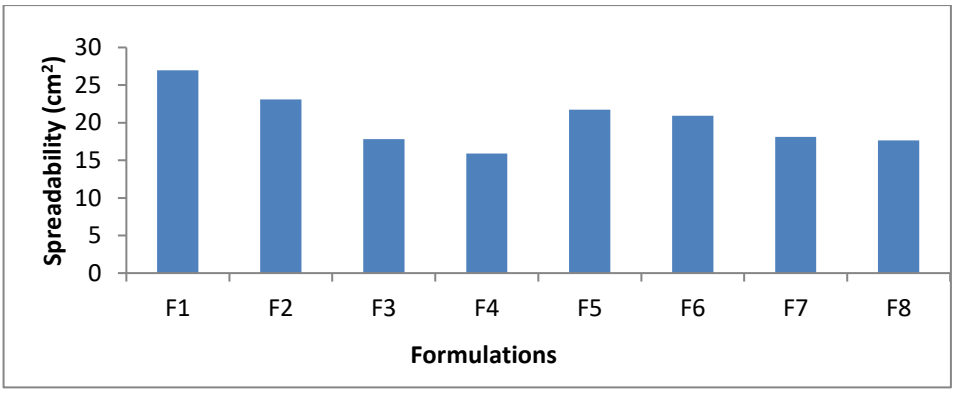

Fig.2 Graphical representation of spreadibility of Emulgels

Viscosity

The tests were performed at 50 and 100 rpm for 10 min. Results are shown in table 5 and fig.3.

Table.5 Viscosity of Emulgel formulations

RPM	Viscosity(cp)							
	F1	F2	F3	F4	F5	F6	F7	F8
50	7314	7145	7247	7174	7114	7201	7184	7207
100	5348	5093	5021	5207	5343	5277	5273	5273

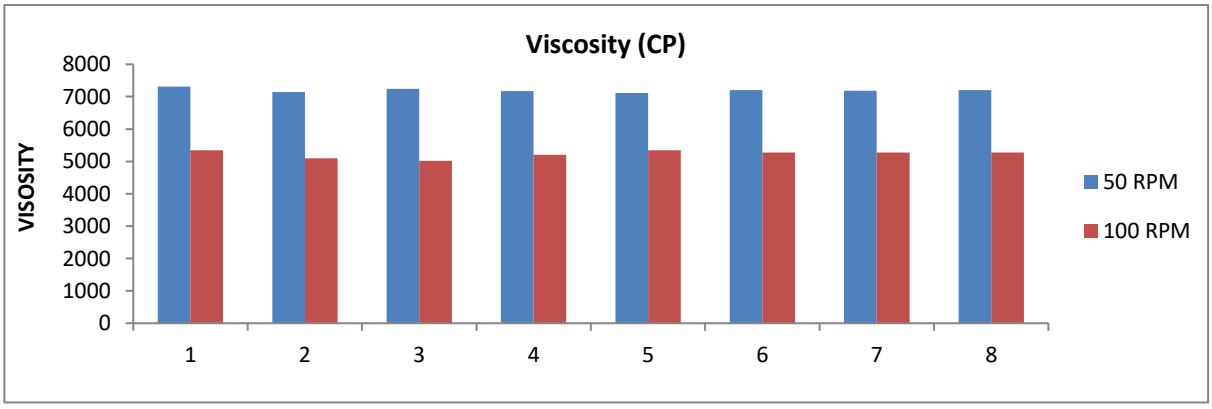

Fig.3 Graphical representation of Viscosity of Emulgels

Drug content

The drug content of different emulgel formulations was estimated and the results were in official limits with range of 94.77 to 98.45 % (as shown in table.6 and fig. 4) which indicate uniform distribution of the drug throughout the emulgel.

Table.6 Drug content of Emulgel formulations

Formulation	F1	F2	F3	F4	F5	F7	F7	F8
Drug content (%)	99.87	99.71	97.51	95.12	101.27	100.98	98.43	97.49

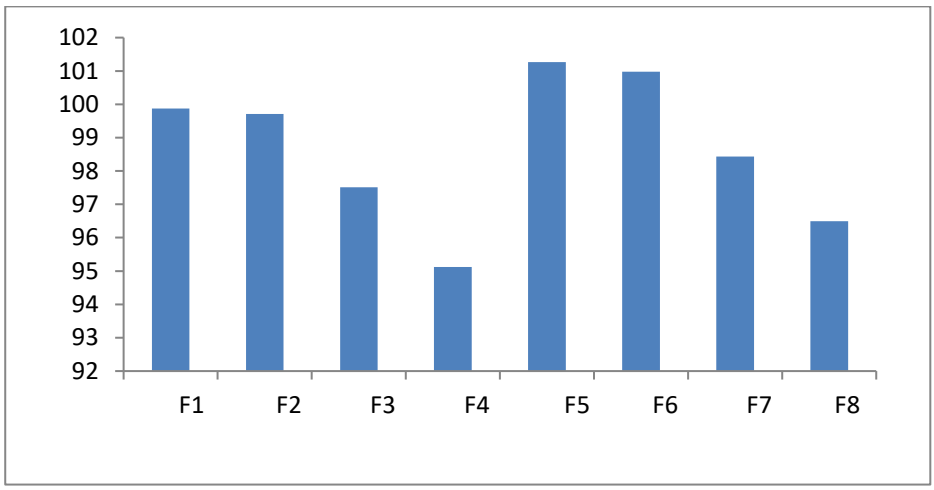

Fig.4 Graphical representation of Drug content of Emulgel

Extrudability

The gel formulations were filled into collapsible metal tube or aluminium collapsible tube. The tube was pressed to extrude the material and the extrudability of formulation was observed. Results are shown in table 7 and fig.5.

Table.7 Extrudability of Emulgel formulations

Formulation	F1	F2	F3	F4	F5	F6	F7	F8
Extrudability (g/cm^2)	17.54	15.87	19.77	18.98	17.28	18.11	20.73	21.59

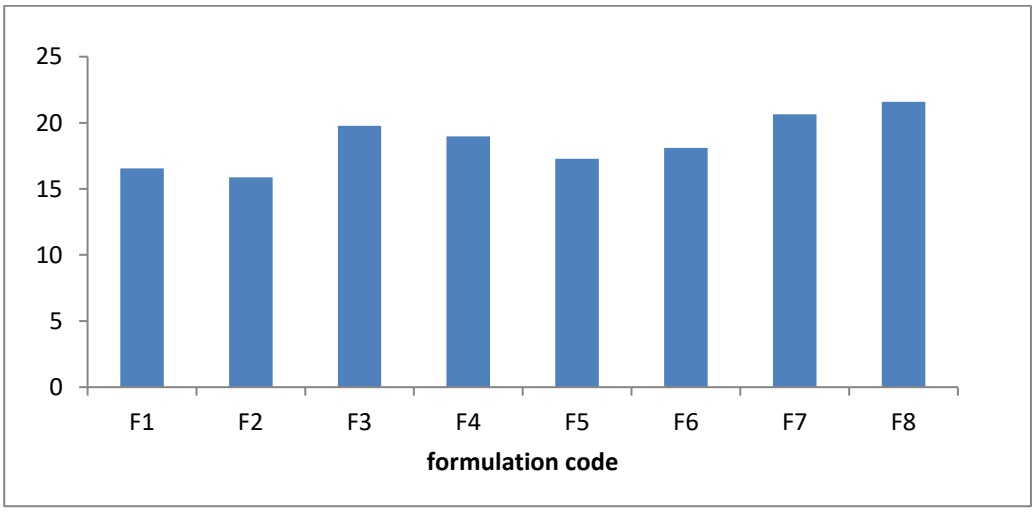

Fig.5 Graphical representation of Extrudability of Emulgels

***In vitro* drug release**

1gm of Emulgel was applied uniformly to egg membrane. The membrane was mounted between the compartments of the Frantz diffusion cell with stratum corneum facing the donor compartment. Reservoir compartment was filled with phosphate buffer of pH 6.8. The study was carried out at 37 ± 1°C and speed was 50 rpm. 1ml of sample was withdrawn from reservoir compartment at 1hr interval and absorbance was measured spectrophotometrically at 340 nm. Each time the reservoir compartment was replenished with the 1 ml volume of phosphate buffer pH 6.8 to maintain constant volume. The results are given in table 8 and fig.6.

Table 8: *In-vitro* drug release study of emulgel formulations

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
30	7.01	4.30	5.03	4.59	7.99	5.34	5.79	3.89
70	12.84	10.44	9.80	8.49	13.70	9.84	11.73	8.93
120	21.70	18..33	17.89	15.70	21.93	19.73	17.80	15.43
180	29.33	23.70	21.43	19.79	29.43	25.41	24.78	19.78
240	34.83	27.93	27.83	22.43	35.77	27.33	27.92	23.03
300	37.91	31.83	33.7	27.12	39.92	34.92	30.01	25.48
370	43.34	37.90	37.90	30.83	43.98	38.72	33.98	28.58
420	48.59	40.88	40.78	34.27	49.77	40.13	38.72	30.12
480	57.49	43.97	45.37	39.98	57.32	43.98	43.87	33.24

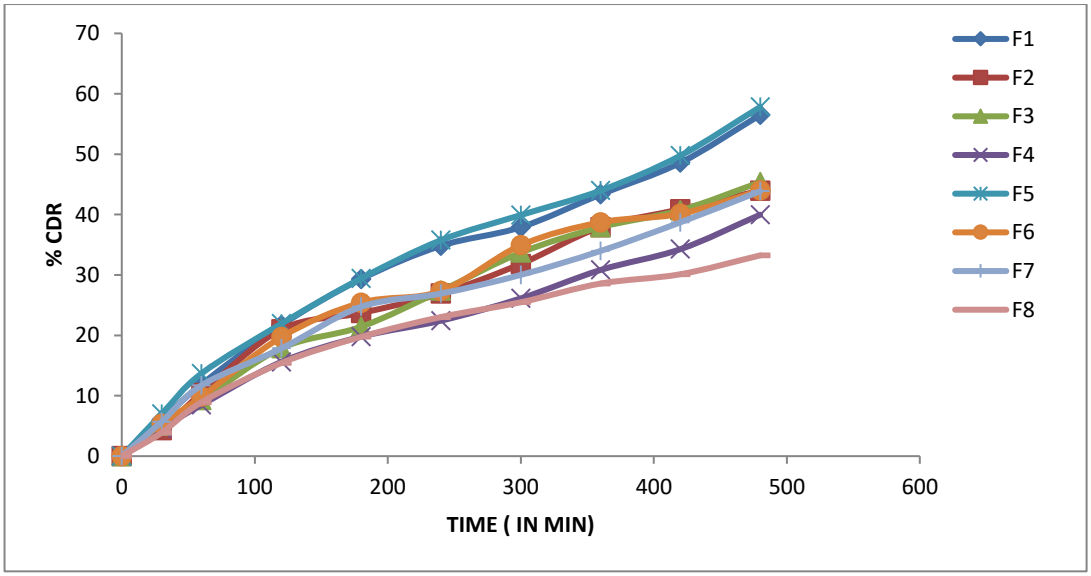

***Fig.6 In –Vitro* Cumulative % Drug Release Profile of Emulgel Formulations**

Kinetic Analysis of drug release

The results of In vitro release from formulations were plotted in different kinetic models like Zero order, first order, Higuchi plot and Korsmeyer Peppas plot and are represented in Figure 7.18, 7.19, 7.20, 7.21 respectively. The regression coefficient value R^2 is reported for all formulation. The release data of best formulation F1 and F5 follows Korsmeyer Peppas model. All the formulation follows anomalous or non fickian diffusion for drug release. The regression coefficients of all formulations are listed in Table 9,10 and 11 while release profile is shown in fig.7,8 and 9.

Table.9 Release kinetics of Emulgel formulation F1, F2, F3& F4

Time (min)	√t	Log t	Cumulative % drug release				Log %cumulative drug release			
			F1	**F2**	**F3**	**F4**	**F1**	**F2**	**F3**	**F4**
30	5.47	1.47	7.01	4.32	5.03	4.59	0.701	0.432	0.503	0.459
60	7.74	1.77	11.89	10.44	9.27	8.49	1.189	1.044	0.927	0.849
120	10.95	2.07	21.7	20.99	17.89	15.7	2.17	2.099	1.789	1.57
180	13.41	2.25	29.33	23.7	21.43	19.79	2.933	2.37	2.143	1.979
240	15.49	2.38	34.83	27.93	27.38	22.43	3.483	2.793	2.738	2.243
300	17.32	2.47	37.91	31.83	33.7	27.12	3.791	3.183	3.37	2.712
360	18.97	2.55	43.34	37.92	37.91	30.83	4.334	3.792	3.791	3.083
420	20.49	2.72	48.59	40.88	40.72	34.27	4.859	4.088	4.072	3.427
480	21.90	2.78	57.49	43.97	45.37	39.98	5.749	4.397	4.537	3.998

Table.10 Release kinetics of Emulgel formulation F5, F6, F7, F8

Time (min)	√t	Log t	Cumulative % drug release				Log %cumulative drug release			
			F5	**F6**	**F7**	**F8**	**F5**	**F6**	**F7**	**F8**
30	5.47	1.47	5.34	7.99	5.69	3.89	0.459	0.534	0.569	0.389
70	7.74	1.77	9.84	13.7	11.73	8.93	0.849	0.984	1.173	0.893
120	10.95	2.07	19.73	21.93	17.84	15.43	1.57	1.973	1.784	1.543
180	13.41	2.25	25.41	29.43	24.73	19.76	1.979	2.541	2.473	1.976
240	15.49	2.38	27.33	35.77	26.92	23.03	2.243	2.733	2.692	2.303
300	17.32	2.47	34.92	39.92	30.01	25.48	2.712	3.492	3.001	2.548
370	18.97	2.55	38.72	43.98	33.98	28.58	3.083	3.872	3.398	2.858
420	20.49	2.72	40.13	49.77	38.72	30.12	3.427	4.013	3.872	3.012
480	21.90	2.78	43.98	57.32	43.87	33.24	3.998	4.398	4.387	3.324

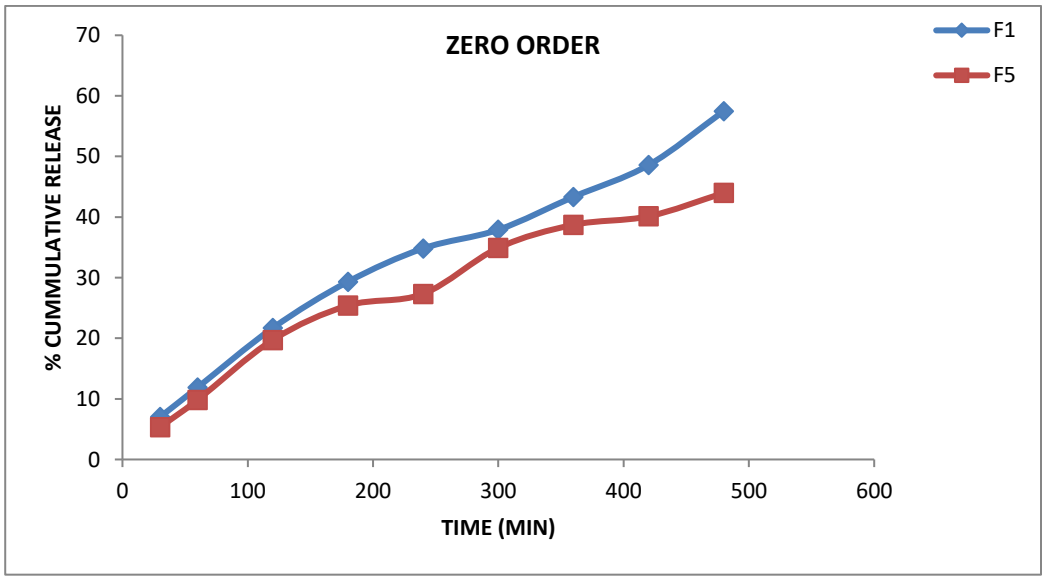

Fig.7 Zero order release plot of Emulgel formulations

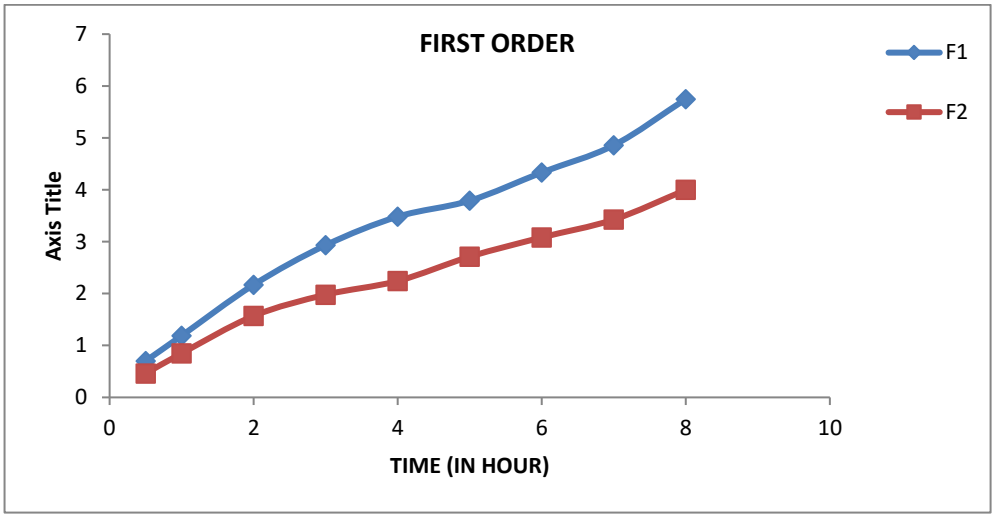

Fig.8 First order release plot of Emulgel formulations

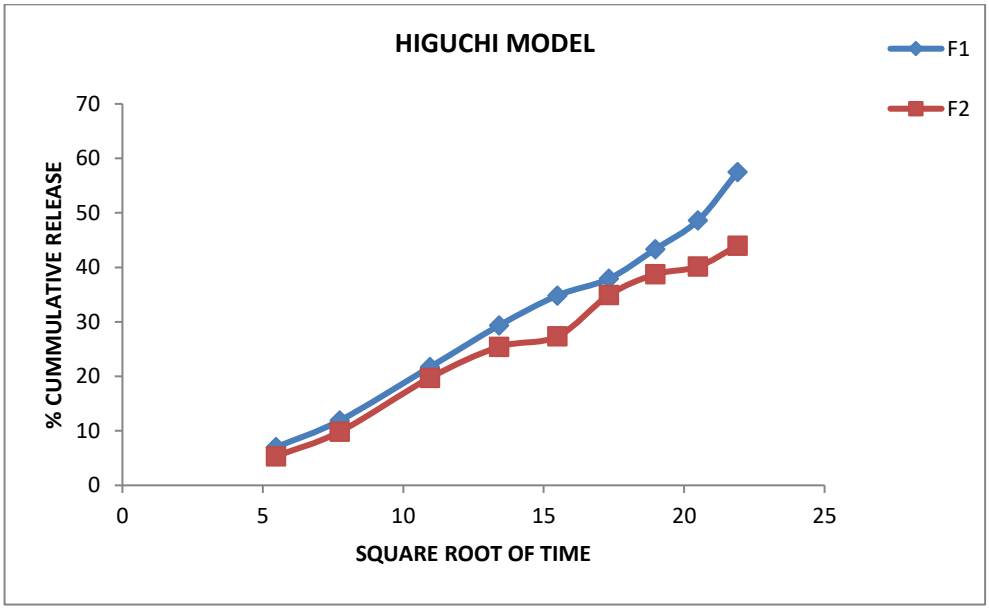

Fig.9 Higuchi release plot of Emulgel formulations

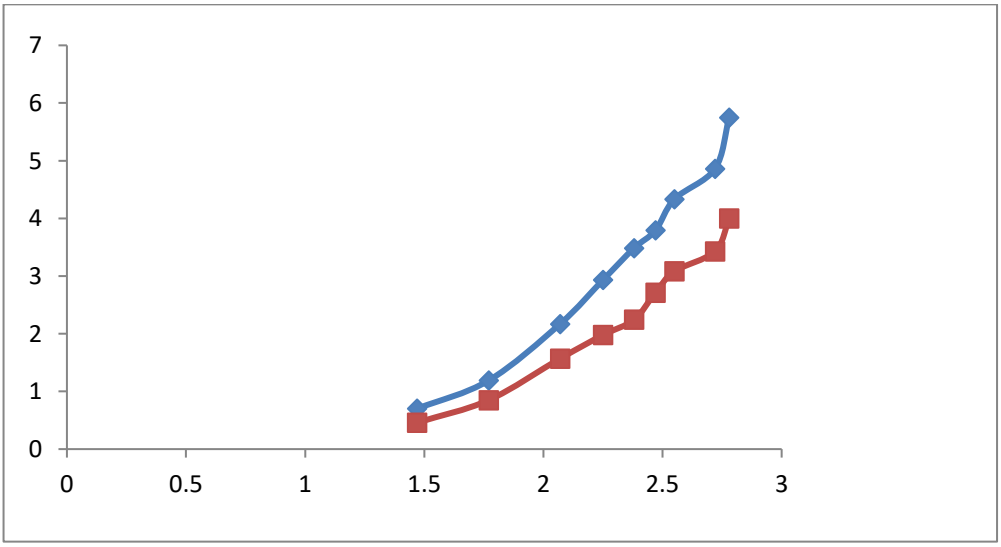

Fig.10 Korsmeyer Peppas release plot of Emulgel formulation

Table. 11 Release Kinetic Result of Emulgel Formulations

Formulation	Zero order	First order	Higuchi plot	KorsmeyerPeppas plot		Possible mechanism of drug release
	R^2	R^2	R^2	R^2	n	
F1	0.9747	0.9889	0.9230	**0.9952**	0.9821	KorsmeyerPeppas model, Non-Fickian
F2	0.9610	0.9829	0.9270	**0.9897**	0.9819	KorsmeyerPeppas model, Non-Fickian
F3	0.9806	0.9947	0.9239	**0.9923**	0.8904	KorsmeyerPeppas model, Non-Fickian
F4	0.9808	0.9893	0.9181	**0.9929**	0.8564	KorsmeyerPeppas model, Non-Fickian
F5	0.9556	0.9789	0.9275	**0.9892**	0.9651	KorsmeyerPeppas model, Non-Fickian
F6	0.9753	0.9892	0.9193	**0.9972**	0.9380	KorsmeyerPeppas model, Non-Fickian
F7	0.9642	0.9824	0.9187	**0.9968**	0.8087	KorsmeyerPeppas model, Non-Fickian
F8	0.9442	0.9660	0.9287	**0.9941**	0.8514	KorsmeyerPeppas model, Non-Fickian

STABILITY TEST:

Stability test were performed according to ICH guideline. Every sample was subjected to drug content and physical appearance. All prepared formulations were found to be physically stable and no effect was seen on drug content**.** The stability data are given in Table: 12, 13 and 14.

Table. 12 Physical characteristics of all formulation batches

Sr.No.	Formulation code	Colour	Grittiness
1.	F1	White	None
2.	F2	White	None
3.	F3	White	None
4.	F4	White	None
5.	F5	White	None
6.	F7	White	None
7.	F7	White	None
8.	F8	White	None

Table.13 drug content of prepared emulgel

Formulation	F1	F2	F3	F4	F5	F7	F7	F8
Drug content (%)	100.92	95.71	100.51	99.12	95.27	101.98	97.43	99.49

Table.14 Phase separation of prepared emulgel

Formulation	F1	F2	F3	F4	F5	F7	F7	F8
Phase separation	---	---	---	---	---	---	---	---

5. CONCLUSION

From the above results we can conclude that emulgel will be a solution for incorporating hydrophobic drugs in water soluble gel bases. Apremilast emulgel formulations prepared using carbopol 934, HPMC 2910, xanthan gum, and Na CMC showed acceptable physical properties, pH, drug content, viscosity and antifungal activity. Stability studies revealed no significant differences before and after storage for the selected formula. As compared to carbopol 934 based formulations; Xanthan Gum based formulations showed more promising results so natural gelling agent. Xanthan gum is better gelling agent than Synthetic gelling agent Carbopol 934.

ACKNOWLEDGMENT

The authors are thankful to Director and Principal of SGRRITS, Dr. Preeti Kothiyal for permitting the use of the college facilities. I admit my sincere thanks to my guide Prof. G.Ganarajan and co-guide Pranshu Tangri for their support and encouragement. I would also like to thanks my friend Sakshi Negi for her love and support.

REFERENCE

1. Sarah Dubois Declercqet all. Promising new treatments for psoriasis. Hindawi in an emergent novel drug delivery technology: Emulgel. *Journal of controlled release* 2013;171: 122-32.

2. Baibhav J, Singh Gurpreet S, Rana AC, Seema S and Singla V. Emulgel: A comprehensive review on recent advancement on topical drug delivery. *International Research journal of pharmacy* 2011; 2: 77-70.
3. Rathbone MJ, Hadgraft J, Roberts MS, Lane ME. *Modified –release drug delivery technology* 2nd ed. Informa healthcare; 2: 273-271.
4. HibaHarshan, Krishnapillai M. Emulgel: An Advance Technique for Penetration OfHydrophobic Drugs. *World Journal of Pharmaceutical sciences* 2017; 5: 344-357.
5. Singh RP, Parpani S, Narke S, Chavan R. Emulgel: A Recent Approach for Topical Drug Delivery System. *Asian Journal of Pharmaceutical Research and Development* 2014; 2: 112-123.
6. Surender Kumar, Neeraj Singh and Satish Chander Arora. Emugel: an insight. *european journal of pharmaceutical and medical research* 2015,2(4): 1178-1187.
7. Shivam Rao, Nimrata Seth. Emulgel: A Novel Approach for Topical Drug Delivery. *International Journal of Universal Pharmacy and Bio Science* 2017,5(3): 381-387.
8. Ashwin B. Kuchekaretall.Psoriasis: A comprehensive review. *International journal of pharmacy & life science* 2011.2(7):857-877.
9. Raymond C R, Paul J S, Paul J W, *Handbook of Pharmaceutical Excipients*, 4th Ed, New York: Pharmaceutical Press; 2003: pp 110-114, 229-231, 307-309, 428-430, 473-475, 494-497, 498-499, 775-79.
10. Khan S, Tiwari T, Tyagi S, Bhowmik M, Joshi A, Dubey B. Preformulation Studies and Preparation Of Dithranol Loaded Solid Lipid Nanoparticles. *International Journal of Research and Development in Pharmacy and Life Sciences* 2012;1: 183-88.
11. Tomar S, Singhal T. Preformulation Studies of Niosomal Gel of Prednisolone &Azithromycin for Topical Drug Delivery System. *JIPBS* 2015;2: 312-21.
12. Bhatt Preeti, Ganarajan G. Emulgels: A noval formulation approach for topical delivery of hydrophobic drug. *International research journal of pharmacy* 2013;4(2): 12-15.
13. Md. SarfarazAlamet all. Design and Characterization of Nanostructure Topical Gel of Betamethasone Dipropionate For Psoriasis. *Journal of Applied Pharmaceutical Science* 2012,2(10): 148-158.

Received:04.05.18, Accepted: 07.06.18, Published:01.07.2018

***Corresponding Author:**
Deepak Chandra Sharma*
Email: sharma00deepak@gmail.com