Saudi Journal of Medical and Pharmaceutical Sciences **ISSN 2413-4929 (Print)**
Scholars Middle East Publishers **ISSN 2413-4910 (Online)**
Dubai, United Arab Emirates
Website: https://saudijournals.com/

Formulation and Evaluation of Flubiprofen Emulgel by Using Different Concentration CARBOPOL 974P

M. Swetha[1]*, B. Mohan[4], Dr. R. Narsimha Rao[1], Dr. J. N Suresh Kumar[2], Dr. Satyavathi[3], P. Sushma[1]
[1]Associate Professor, Holy Mary Institute of Technology and Science College of Pharmacy, keesara (M), Rangareddy, Telangana, India
[2]Narsaraopet College of Pharmacy, India
[3]Brilliant College of Pharmacy, India
[4]Sanofi India Ltd, India

Original Research Article

***Corresponding author**
M. Swetha

Article History
Received: 22.01.2018
Accepted: 11.02.2018
Published: 15.02.2018

DOI:
10.36348/sjmps.2018.v04i02.008

Abstract: The aim and objective of this study was to formulate and evaluate the Flurbiprofen emulgel as a topical drug delivery which is a novel and advantageous delivery system forhydrophobic drugs to systemic circulation via skin. Flurbiprofen is a Non-Steroidal Anti-Inflammatory Drug (NSAID) used to treat Rheumatoid Arthritis (RA). Emulgel is one of the most interesting topical delivery system. In spite of many advantages of gels a major limitation is to deliver the hydrophobic drugs. Emulgel is used topically because of its characteristic dual control release (i.e.) emulsion as well as gel it demonstrates better drug release as compared to other topical drug delivery systemdue to excess of oil bases and lack of insoluble excipients. In present work Flurbiprofen emulsion was prepared by using liquid paraffin and white soft paraffin as an oil phase prepared emulsion was gelled with different concentrations of Carbopol 974p. All 6 formulations were evaluated for Homogenicity, Extrudability, pH, Viscosity, Spreadability, swelling index, drug content determination &Invitro dissolution test out of 6 formulation F4 is optimized based on the results and optimized formulation is good at stability conditions.

Keywords: Flurbiprofen, NSAID, Rheumatoid Arthritis, CARBOPOL 974 P, Homogeneity, extrudability, pH, viscosity, Spreadability, swelling index, drug content determination & Invitro dissolution test.

INTRODUCTION

Emulgel is one of the most interesting topical delivery system. Emulgel is a combination of gel and emulsion, emulsion either O/W or W/O type, which are gelled by mixing with a gelling agent (Carbopol 974 P) which allows the formulation to stable by decreasing surface and interfacial tension at the same time increases the viscosity of aqueous phase.

In spite of many advantages of gels a major limitation is to deliver the hydrophobic drugs. Emulgel is used topically because of its characteristic dual control release (i.e.) emulsion as well as gel it demonstrates better drug release as compared to other topical drug delivery system due to excess of oil bases and lack of insoluble excipients [1-6].

Flurbiprofen is a member of the phenyl alkanoic acid derivative family of nonsteroidal anti-inflammatory drugs (NSAIDs). It is primarily indicated as a pre-operative anti miotic (in an ophthalmic solution) as well as orally for arthritis or dental pain. Mechanism of action via reversible inhibition of cyclooxygenase (COX), the enzyme responsible for the conversion of arachidonic acid to prostaglandin G2 (PGG2) and PGG2 to prostaglandin H2 (PGH2) in the prostaglandin synthesis pathway [7, 8].

Rheumatoid arthritis (RA) is a long lasting autoimmune disorder that primarily affects joints. It typically results in warm, swollen, and painful joints. Pain and stiffness often worsen following rest. Most commonly, the wrist and hands are involved, with the same joints typically involved on both sides of the body. The disease may also affect other parts of the body. This may result in a low red blood cell count, inflammation around the lungs, and inflammation around the heart. Fever and low energy may also be present. Often, symptoms come on gradually over weeks to months. While the cause of rheumatoid arthritis is not clear, it is believed underlying bone and cartilage. The diagnosis is made mostly on the basis of a person's signs and symptoms [7, 8].

X-rays and laboratory testing may support a diagnosis or exclude other diseases with similar

symptoms. Other diseases that may present similarly include systemic lupus erythematosus, psoriatic arthritis, and fibromyalgia among others. The goal of treatment is to reduce pain, decrease inflammation, and improve a person's overall functioning. This may be helped by balancing rest and exercise, the use of splints and braces, or the use of assistive devices.

MATERIALS AND METHODS

Flubiprofen was purchased from B.M.R chemicals and pharmaceuticals remaining all ingredients are analytical grade.

Method of preperation of emulgel [9]

Preparation of oil in water emulsion

Oil phase was Ceto steryl alcohol, Cetomacrogol 1000, span 60, white soft paraffin, is added and heated up to 70c and dissolve benzoic acid and aqueous phase was water the required quantity is heated to 70c.

Drug solution preparation

The exact quantity of flurbiprofen was dissolved in propylene glycol.

Preparation of gel phase

The cabopo l974p is weighed accurately and dissolve in water make a gel by neutralizing with TEA. Incorporation of gel in emulsion with continuous stirring to form emulgel.

Table-1: formulaion of emulgel

S. NO	INGREDIENTS in %	F1	F2	F3	F4	F5	F6
1	Flurbiprofen	5	5	5	5	5	5
2	Liquid paraffin	-	7	6	6	6	6
3	White soft paraffin	5	-	-	-	-	-
4	Ceto steryl alcohol.	7	7	8	8.3	10	10
5	Ceto macrogol 1000	3	3	3	3	3	3
6	Arlacel 60	1.5	1.5	1.5	1.5	1.5	1.5
7	Benzoic acid	-	0.2	0.2	0.2	0.2	0.2
8	Methyl paraben	0.2	-	-	-	-	-
9	Propyl paraben	0.02	-	-	-	-	-
10	BHT	0.05	0.05	0.05	0.05	0.05	0.05
11	Carbopol 974p	0.2	0.2	0.2	0.25	0.4	0.6
12	Propylene glycol	10	10	10	10	10	10
13	Triethanol amine	q.s	q.s	q.s	q.s	q.s	q.s
14	Menthol	0.3	0.6	0.6	0.6	0.6	0.6
15	Purified water	67.7	65.45	65.45	65.10	63.25	63.45

Raw material analysis of the flurbiprofen [8]

The raw material analysis is done as per IP 2007. The following test were conducted for Flurbiprofen.

Solubility

An excess amount of Flurbiprofen transfer to a 250ml conical flask containing 100ml of dissolution media. The solubility study was performed at 25^0c. The flask was shaken for 24 hours by keeping conical flask on rotary shaker at 200 rpm. A portion of drug solution dissolved in buffer solution was filtered and absorbance was taken at 247 nm by UV visible. The amount of drug dissolved in dissolution medium where calculated and reported. The tests were prepared in triplicate in the selected buffer of dissolution medium (Ph 1.2, 4.4, 6.8 and 7.4 buffers) [8].

Determination of standard calibration curve

100 mg of Flurbiprofen was accurately weighed and dissolved with 10ml of methanol and make up the final volume up to 100 ml with phosphate buffer (PH 6.8) to prepare stock solution. The 10 ml of stock solution was further diluted with phosphate buffer (6.8pH) in 100ml to get 100µg/ml (working standard). Then 0.2,0.4,0.6.0.8, and 1 ml of working standard was taken in 10 ml standard volumetric flask and made up the volume with phosphate buffer to prepare 2µg,4µg,6µg,8µg, and 10µg drug per ml solution. Then the absorbance was measured in a UV spectrophotometer at 249 nm against phosphate buffer (pH 6.8) as blank [10].

Assay

Weigh accurately about 60mg of drug (flurbiprofen) in 100ml standard flask and add 20ml of methanol to dissolve and make up the volume with methanol. Dilute 10ml of this solution to 100ml with Ph6.8phosphate buffer further dilute 10ml of this solution to 100ml with phosphate buffer [10].

Sample preparation

Weigh accurately about 1200mg of drug sample in100ml standard flask and add 20ml of methanol to dissolve sonicate for 10 minutes and make up the volume with methanol. Dilute 10ml of this

solution to 100ml with Ph 6.8phosphate buffer further dilute 10ml of this solution to 100ml with phosphate buffer [10].

Fourier transform infrared spectrophotometer (FTIR)

The FTIR spectra of Flurbiprofen formulations were recorded between 400 and 4000/cm with FTIR spectrometer detects the drug-excipients interactions. The FTIR spectra for the test samples were obtained using KBr disk method; the resultant spectra were compared for any possible changes in the peaks of the spectra.

Evaluation of emulgel [11-13]

Homogenicity: The formulations were tested for their homogeneity by visual appearance after the emulgel applied as a thin layer on the slide.

Extrudability: It is a usual empirical test to measure the force required to extrude the material from tube. The method applied for determination of applied shear in the region of the rheogram corresponding to a shear rate exceeding the yield value and exhibiting consequent plug flow [14].

In the present study, the method adopted for evaluating emulgel formulation for extrudability is based upon the quantity in percentage of emulgel and emulgel extruded from lacquered aluminum collapsible tube on application of weight in grams required to extrude at least 0.5 cm ribbon of emulgel in 10seconds. More quantity extruded better is extrudability. The measurement of extrudability of each formulation is in triplicate and the average values are presented. The extrudability is than calculated by using the following formula:

$$\text{Extrudability} = \frac{\text{Applied weight to extrude emulgel from tube (in g)}}{\text{Area (in cm2).}}$$

pH: The PH of emulgel selected for the study are determined by the use of the pH meter (Digisun electronics system). study the where done for all the six formulation there were selected for the DOE Study.

Viscosity

The viscosity of different emulgel formulation was determined at 25^0c using a Brookfield viscometer with spindle no 96 at 1.5 rpm.

Spreadability

Spread ability is determined by apparatus suggested by Mutimer *et al.*, [15] 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 2gm) 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 1kg 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. The top plate is then subjected to pull of 80gm. 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. Lesser time indicates better spreadability.

Spreadability was calculated by using the formula,

$$\mathbf{S = M.L/T}$$

Where,

S = Spreadability,
M = Weight tied to upper slide,
L = Length of glass slide;
T = Time taken to separate the slides completely from each other.

Spreadability was measured in terms of g.cm/sec.

Swelling Index

Emulgel of known weight (1 gram) was wrapped with Aluminum Foil (pricked with a pin to make holes) and placed in phosphate buffer pH 7.4 for 6 hours. After 6 hours, the gels were scrapped and the wet weight of the swollen gel was determined by first blotting the gels with filter paper to remove absorbed water on surface and then it was immediately weighed on an electronic balance. The weight of the swollen gels was determined using an electronic balance. The swelling index of was calculated using the following formula,

$$Sw = [(W_t - W_o) / Wo] \times 100$$

Sw = percentage of swelling of Emulgel
Wt = the weight (g) of the gels at time t
Wo = initial weight (g) of the Emulgel.

Drug Content Determination

Take 1g of emulgel. Mix it in suitable solvent. Filter it to obtain clear solution. Determine its absorbance using UV spectrophotometer. Standard plot of drug is prepared in the same solvent. Concentration and drug content can be determined by using the same standard plot by putting the value of absorbance.

Drug Content = (Concentration × Dilution Factor × Volume taken) × Conversion Factor.

In-vitro study

Franz diffusion cell (with effective diffusion area 3.14 cm2 and 15.5 ml cell volume) was used for the drug release studies. Jellified Emulsion (200 mg) was applied onto the surface of egg membrane evenly.

The egg membrane was clamped between the donor and the receptor chamber of diffusion cell. The receptor chamber was filled with freshly prepared PBS (pH 5.5) solution to solubilize the drug. The receptor chamber was stirred by magnetic stirrer. The sample (1.0 ml aliquots) was collected at suitable time interval. Samples were analyzed for drug content by UV visible after appropriate dilutions. Cumulative corrections were made to obtain the total amount of drug release at each time interval. The cumulative amount of drug released across the egg membrane was determined as a function of time.

Stability studies

The optimized emulgel were packed in aluminum collapsible tubes (5 g) and subjected to stability studies at 5°C, 25°C/60% RH, 30°C/65% RH, and 40°C/75% RH for a period of 3 months. Samples were withdrawn at 15-day time intervals and evaluated for physical appearance, pH, rheological properties, drug content, and drug release profile.

RESULTS & DISCUSSION

Raw material analysis of the flurbiprofen

The assay value obtained by procedure as per I.P showed a purity of 99.8 % which was found to be in the range of I.P standard as

Table-2: Identification tests

S. NO	TEST	STANDARD
1	IR Spectroscopy	As per I. P
2	UV Spectroscopy	As per I. P

Solubility

Solubility studies were conducted by using different solvents by using the flask method. Flurbiprofen is more soluble in Ethanol and DMF

Calibration curve

The calibration curve was constructed with phosphate 6.8 buffer solution and results were shown in Table-1 and Fig-5. The regression coefficient obtained was 0.99 which shows a better correlation between both axis.

Table-3: standard calibration curve

Concentration (mcg/ml)	Absorbance
2	0.149 ± 0.03
4	0.301 ± 0.07
6	0.446 ± 0.04
8	0.553 ± 0.05
10	0.665 ± 0.02

Trials were done by triplicate

Table-4: statistical analysis of the calibration curve

s. no	Factors	Value
1	y-intercept	0.6394x+0.0376
2	R square	0.99
3	Slope	0.6394

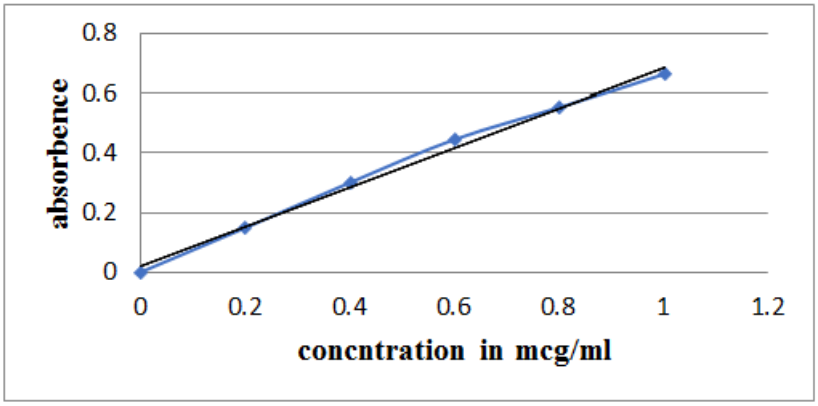

Fig-1: calibration curve of flurbiprofen

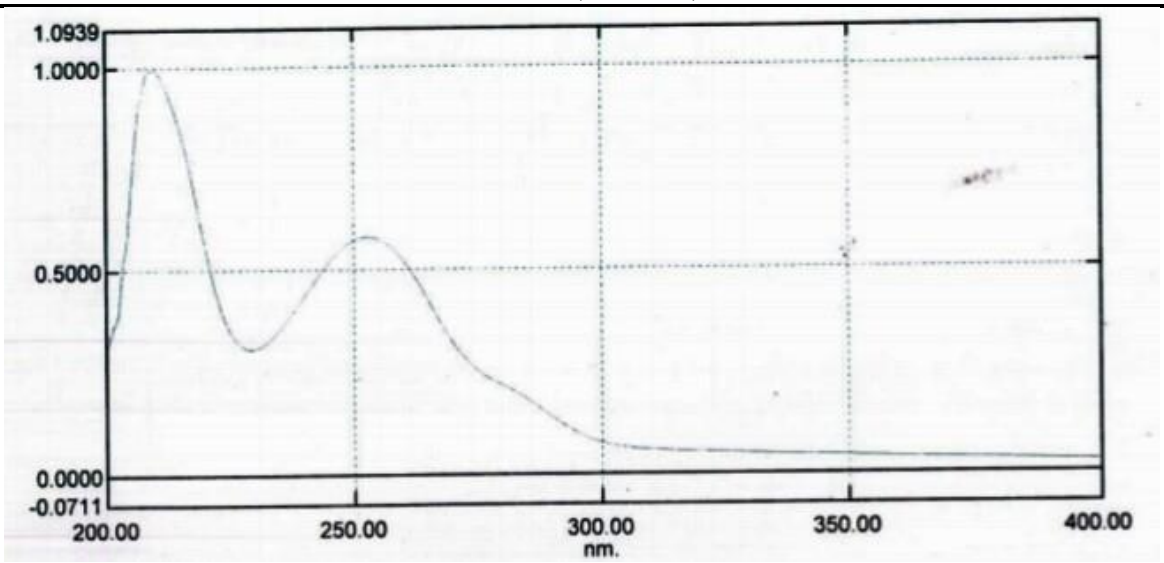

Fig-2: Assay of flurbiprofen pure drug by UV

Drug – excipients interaction studies: The test for interaction between drug and the excipients are necessary for the stability of the formulation.

FTIR: The FTIR was conducted for pure drug and all excipients used in study results were shown in figure 3&4. There are no significant changes in drug peaks were observed in the mixture of drug and excipients.so there is no incompatibility.

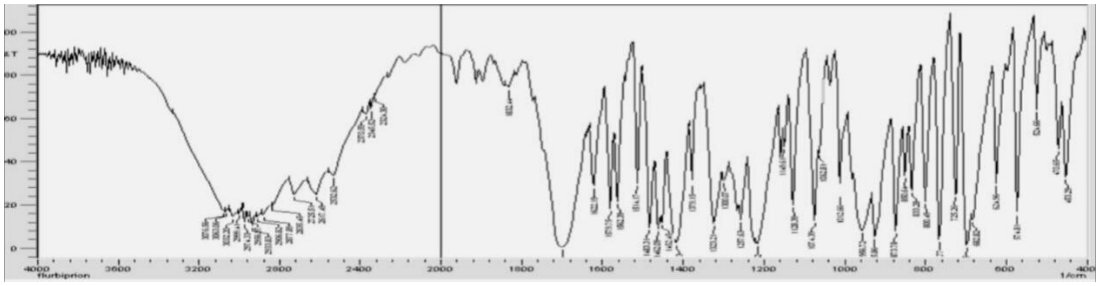

Fig-3: FTIR spectrum of Flurbiprofen

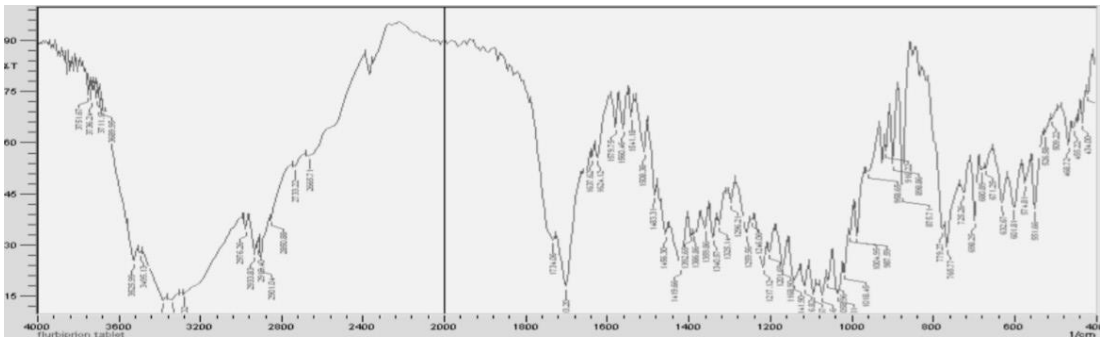

Fig-4: FTIR spectrum of physical mixture of final formulation

Evaluvation of emulgel

Homogenisity

All formulations were tested for their homogeneity by preparing a smear of emulgel on the slide and observed under electronic microscope results was shown in fig no 5 all formulations were having the good homogenicity.

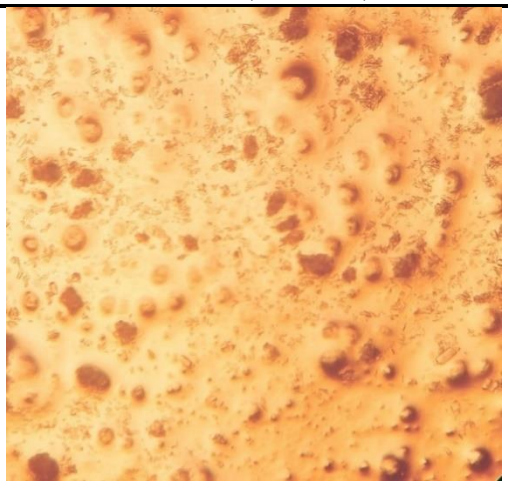

Fig-5: homogenicity

Extrudability

Extrudability was performed according to the given method for all formulations and results were shown in Table-5 & Figure-6 among all formulations F4 is having good Extrudability.

Table-5: measurement of extrudability

S. No	Formulation	Extrudability
1	F1	0.97 ± 0.02
2	F2	1.32 ± 0.05
3	F3	1.03 ± 0.01
4	F4	1.56 ± 0.06
5	F5	1.35 ± 0.03
6	F6	1.20 ± 0.05

Trials were done by triplicate

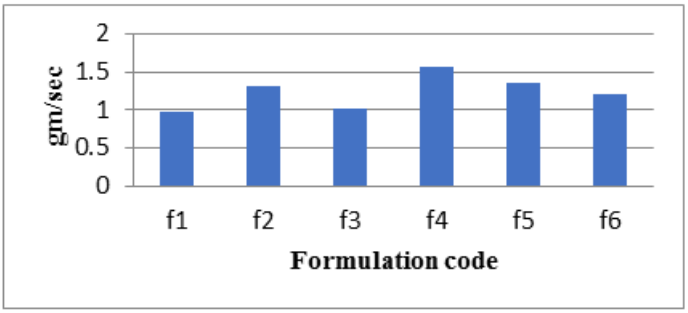

Fig-6: extrudability

pH

pH is an important variable for topical preparations to avoid the skin problems the ideal pH is 4.5 to 6 .All 6 formulation pH is determined by the given method and results were shown in table no 6 .

In F1 & F3 pH is more than 6 for other formulations pH is within the limit but compare to all formulations F4 is having ideal pH

Table-6: ph for six formulations

S. No	Formulation	Ph
1	F1	6.9 ± 0.1
2	F2	4.7 ± 0.3
3	F3	6.2 ± 0.5
4	F4	4.9 ± 0.2
5	F5	5.9 ± 0.3
6	F6	4.8 ± 0.1

Trials were done by triplicate

Viscosity

Viscosity plays a major role in stability of emulgel. For all 6 formulations viscosity is determined by Brookfield viscometer. F1is having more viscosity and less extrudability compare to all formulations F4 is having ideal viscosity and extrudability were shown in Table-7.

Table-7: measurement of the viscosity for six formulations

S. No	Formulation	Viscosity in cps
1	F1	34500 ± 20
2	F2	13000 ± 10
3	F3	20120 ± 20
4	F4	15300 ± 20
5	F5	20000 ± 10
6	F6	15700 ± 10

Trials were done by triplicate

Spreadability

Spreadbility is very important for the absorption of drug through the skin it is measured on the basis of 'Slip' and 'Drag' characteristics of emulgels. And results were shown in Table-8. All 6 formulations are having good spreadbility.

Table-8: measurement of the spread ability

S. No	Formulation	Spread ability
1	F1	22 ± 0.4
2	F2	30 ± 0.6
3	F3	15 ± 0.2
4	F4	21 ± 0.7
5	F5	26 ± 0.3
6	F6	20 ± 0.5

Trials were done by triplicate

Swelling index

The swelling index was performed by using the specified method it is based on the amount of liquid material that can be absorbed. Among all six formulations F4 formulation is having more swelling index were shown in Table-9.

Table-9: measurement of the swelling index

FORMULATION CODE	SWELLING INDEX
F1	80
F2	95
F3	108
F4	113
F5	88
F6	70

TIME in Hrs	ABSORBANCE	CONCENTRATION	AMOUNT OF DRUG	% OF DRUG RELEASE
0	0	0	0	0
1	0.09	0.14	0.75	15.03 ± 0.08
2	.17	0.27	1.44	28.71 ± 0.36
3	0.24	0.37	2.00	40.03 ± 0.71
4	0.30	0.47	2.55	51.01 ± 0.23
5	0.38	0.60	3.23	64.52 ± 0.64
6	0.43	0.68	3.65	72.97 ± 0.41
7	0.50	0.79	4.24	84.79 ± 0.12
8	0.58	0.91	4.91	98.14 ± 0.50

Trials were done by triplicate

Drug Content Determination

The assay value obtained for formulation (F4) showed a purity of 101.2 % which was found to be in the range of I.P standard. The results were shown in Fig-7.

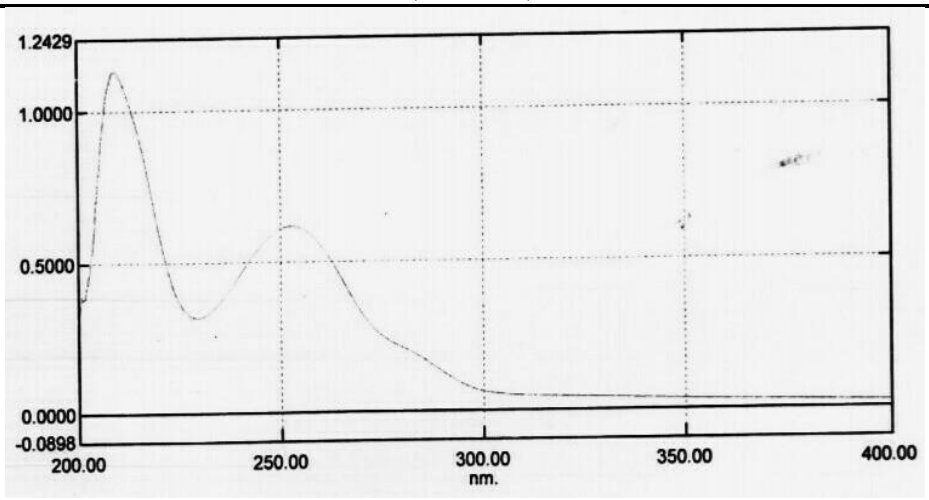

Fig-7: DRUG CONTENT ANALYSIS OF FLURBIPROFEN EMULGEL (F4)

***In-vitro* drug release study**

The drug release study was done using Franz's diffusion cell .The study was done for 10 hrs with an optimum interval of sampling. Results were shown in Table-10 & Fig-8. for all 6 formulation *In vitro* release is 80 to 98 at the end of 8th hour but among all six formulation F 4 is having 98.14 ± 0.50 % drug release at the end of study.

Table-10: *In-vitro* drug release study

TIME in Hrs	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	7.26 ± 0.22	7.26 ± 0.31	7.26 ± 0.53	15.03 ± 0.08	7.60 ± 0.23	2.20 ± 0.43
2	21.11 ± 0.53	21.11 ± 0.19	15.20 ± 0.61	28.71 ± 0.36	19.76 ± 0.31	13.51 ± 0.60
3	31.42 ± 0.19	31.42 ± 0.63	23.14 ± 0.36	40.03 ± 0.71	30.07 ± 0.26	20.44 ± 0.52
4	46.45 ± 0.37	46.45 ± 0.48	35.98 ± 0.22	51.01 ± 0.23	44.76 ± 0.54	33.27 ± 0.46
5	54.22 ± 0.62	54.22 ± 0.27	48.98 ± 0.45	64.52 ± 0.64	52.36 ± 0.42	43.24 ± 0.32
6	67.23 ± 0.44	67.23 ± 0.71	65.37 ± 0.21	72.97 ± 0.41	62.83 ± 0.64	53.54 ± 0.21
7	80.40 ± 0.36	80.40 ± 0.33	78.54 ± 0.12	84.79 ± 0.12	72.29 ± 0.12	65.71 ± 0.13
8	95.77 ± 0.28	95.77 ± 0.51	84.96 ± 0.09	98.14 ± 0.50	82.26 ± 0.31	71.45 ± 0.45

Trials were done by triplicate

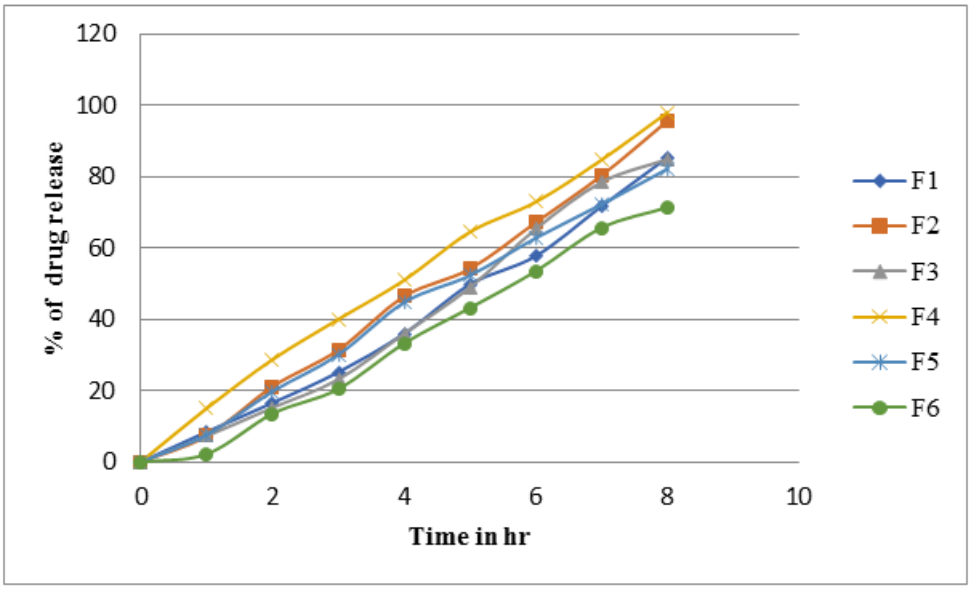

Fig-8: *In-vitro* drug release study N

Comparative Study of Emulgel Formulation with marketed product

By the data obtained from the results F 4 is optimized as a good formulation it is compared with the marketed formulation results were shown in Table-11 & Fig-9.

Drug release of marketed formulation is 99.82 ± 0.35% and F4 is having almost 98.14 % at the end of the study.

Table-11: comparative study of formulation f4 with marketed emulgel

TIME in Hrs	Formulation F4	Marketed emulgel
0	0	0
1	15.03 ± 0.08	17.23 ± 0.23
2	28.71 ± 0.36	35.81 ± 0.50
3	40.03 ± 0.71	54.05 ± 0.41
4	51.01 ± 0.23	67.06 ± 0.26
5	64.52 ± 0.64	74.32 ± 0.34
6	72.97 ± 0.41	84.12 ± 0.45
7	84.79 ± 0.12	89.86 ± 0.14
8	98.14 ± 0.50	99.82 ± 0.35

Trials were done by triplicate

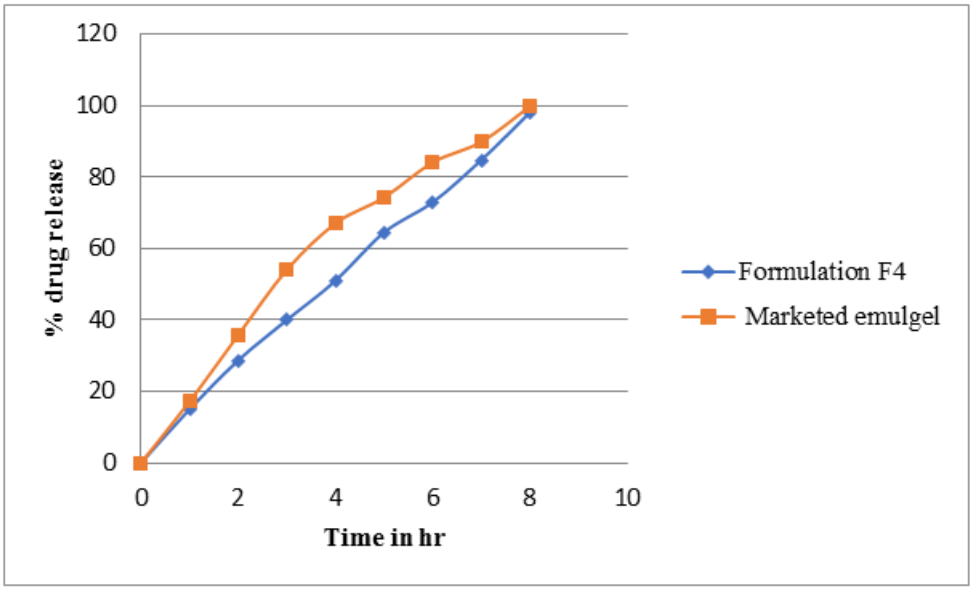

Fig-9: comparative study of emulgel formulation f4 with marketed emulgel

Stability studies

The optimized emulgel F4 were packed in aluminum collapsible tubes (5 g) and subjected to stability studies at 5°C, 25°C/60% RH, 30°C/65% RH, and 40°C/75% RH for a period of 3 months. Samples were withdrawn at 15-day time intervals and evaluated for physical appearance, pH, rheological properties, drug content, and drug release profile and results were shown in Table-12 & Fig-10.

The result indicate that Optimized formulation have good stability.

Table-12: stability study of formulation f4

Parameters	Initial	First month	
		400 ± 2°C/75 ± 5% (RH)	300 ± 20C/55 ± 5%(RH)
Ph	4.9 ± 0.2	4.9 ± 0.8	4.9 ± 0.3
Rheological properties	Good	Good	Good
Drug content	101.2%	101.06%	101.1%
In-vitro drug release study	98.14 ± 0.50	97.94 ± 0.43	98.04 ± 0.21

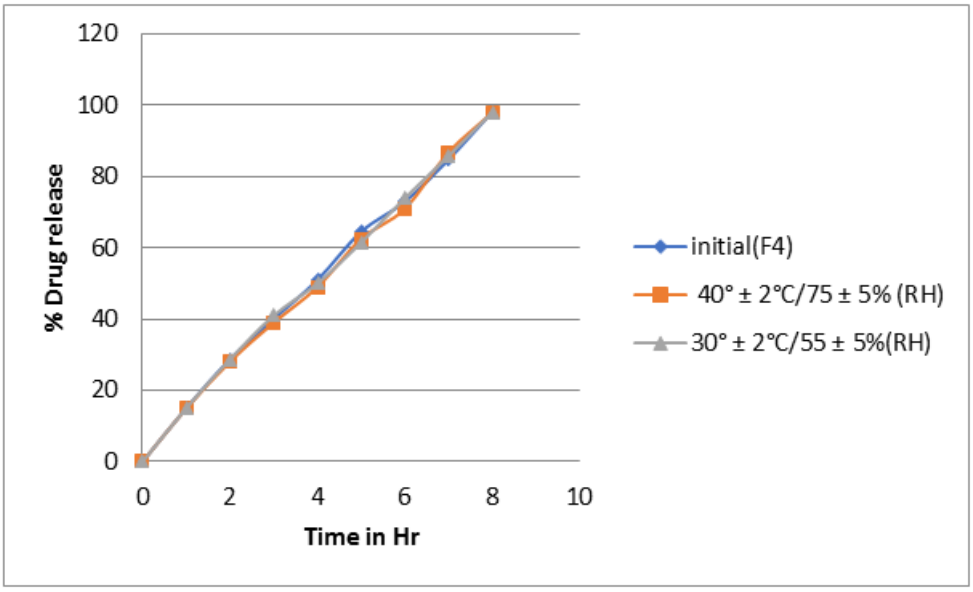

Fig-10: stability study of formulation f4

Summary

The general introduction presenting an overview about the emulgel as a topical drug delivery .it was also justified that emulgel is efficient in delivering hydrophobic drugs where comparison to other system.

The review of the literature carried out for drug and also delivery system. The information provides the scientific nucleus for design and evaluation of emulgel. The review upholds the various attempts made for the topical emulgel with different oil phase and surfactant.

The motive and the aim behind the development of the emulgel are delivering of Flurbiprofen drug through the topical drug delivery.

The detailed description was given about the drug profile and the excipients profile. It has overviews the plane of work for the project.

The method deal with Flurbiprofen emulgel was begins with raw material analysis followed by screening of excipients and interaction with drug. A detailed description for the preparation of emulgel was developed with incorporation of carbopol gel in emulsion.

The results and discussion gives the formulation F4 shows the better pH 4.9 it's almost nearly skin pH. So it does not produce any irritation on skin. The drug release was controlled for 8 hours was shown in Table and Fig. Which reduce the patient compliance. Drug diffusivity study was done and it gives better drug diffusion through the membrane.

CONCLUSION

Flurbiprofen was successfully formulated as a topical emulgel preparation. Oral formulation seems to have adverse effect even topical have adverse effects even gel has a limitations of delivering the hydrophobic drugs. So emulgel is most preferred topical delivery of hydrophobic drugs.

The study shows above the six formulations F4 shows a good Homogeneicity, pH, Extrudability, Viscosity, Spreadability and the percentage of drug release. The formulation F4 demonstrates that it is stable after a period of one month.

REFERENCES

1. latha Samala, M., & Sridevi, G. (2016). Role of Polymers as Gelling Agents in the Formulation of Emulgels. *Polymer Sciences*, *2*(1).
2. Hardenia, A., Jayronia, S., & Jain, S. (2014). Emulgel: An emergent tool in topical drug delivery. *International Journal of Pharmaceutical Sciences and Research*, *5*(5), 1653.
3. Kute, S. B., & Saudagar, R. B. (2013). Emulsified gel A Novel approach for delivery of hydrophobic drugs: An overview. *J. Adv. Pharm. Edu. & Res*, *3*(4).
4. Ambala, R., & Vemula, S. K. (2015). Formulation and Characterization of Ketoprofen Emulgels.
5. Meenakshi, D. (2013). Emulgel: A novel approach to topical drug delivery. *Int J Pharm Bio Sci*, *4*(1), 847-856.
6. Singla, V., Saini, S., Joshi, B., & Rana, A. C. (2012). Emulgel: A new platform for topical drug delivery. *International Journal of Pharma and Bio Sciences*, *3*(1), 485-498.
7. Vats, S., Saxena, C., Easwari, T. S., & Shukla, V. K. (2014). Emulsion Based Gel Technique: Novel Approach for Enhancing Topical Drug Delivery of Hydrophobic Drugs. *International Journal for Pharmaceutical Research Scholars*, *3*(2), 650-653.
8. Chen, S., Pang, X., Song, J., Shi, L., Yao, H., Han, J., & Leon, C. (2014). A renaissance in herbal

medicine identification: from morphology to DNA. *Biotechnology advances*, *32*(7), 1237-1244.

9. Wesley, Z. (2015). D'Souza1, Rajashree Gude. Formulation, design, development and evaluation of emulgel for topical delivery of meloxicam in the treatment of rheumatoid arthritis. Indo Am J Pharm Res; 5(3):1271-1279.
10. Abdellatif, A. A. H., El Hamd, M. A., & Saleh, K. I. (2016). A Formulation, Optimization and Evaluation of Controlled Released Alginate Beads Loaded-Flurbiprofen. *J Nanomed Nanotechnol*, *7*(357), 2.
11. Nishizawa, E. E., Wynalda, D. J., Suydam, D. E., & Molony, B. A. (1973). Flurbiprofen, a new potent inhibitor of platelet aggregation. *Thrombosis Research*, *3*(5), 577-588.
12. Hardenia, A., Jayronia, S., & Jain, S. (2014). Emulgel: An emergent tool in topical drug delivery. *International Journal of Pharmaceutical Sciences and Research*, *5*(5), 1653.
13. Jasmeen, K., Jotinder, K., Sandhya, J., Das, G. G. (2016). A review on novel approach of antifungal emulgel for topical delivery in fungal infections. Indo Am J Pharm Res; 6(7): 6312-6324.
14. Basha, B. N., Prakasam, K., & Goli, D. (2011). Formulation and evaluation of gel containing fluconazole-antifungal agent. *International Journal of Drug Development and Research*, *3*(4).
15. Mutimer, M. N., Riffskin, C., Hill, J. A., & Marry, E. (1956). Cyr., NG and Glickman, G. *J. Amer. Pharm. Asso. Sci*, *45*.