

Preparation and Enlargement of Topical Flurbiprofen Emulgel by with Xanthan Gum

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Abstract: Flurbiprofen is non-steroidal quieting drug used for the treatment of rheumatoid joint irritation as a safe framework infection that causes diligent exacerbation of the joints. Flurbiprofen is a strong inhibitor of platelets assortment, which diminish torture, broadening and joint immovability. The objective of this study was to shape and evaluate skin flurbiprofen emulgel for the transport of hydrophobic meds to essential course. In present work flurbiprofen emulgel was prepared by using liquid paraffin (oil), eucalyptus oil (entrance enhancer) and thickener used as gelling trained professional. All definitions evaluated for homogeneity, pH, extrudability, spreadability, consistency, drug content and prescription release. In-vitro drug appearance of emulgel was evaluated by using scattering cell containing cellophane layer with phosphate support pH 7.4 as the receptor medium. The plans were improved by the three components and two levels Box-Behnken arrangement by using Design-Expert programming (structure 12). Spreadability of F6 specifying was seen (3.4 cm in distance across) which was more than various definitions. Consistency of F16 enumerating was 3067 cps. Rate Drug content of F14 (98.61%) has shown more prescription substance as pondered various subtleties. In-vitro scattering studies, the formulations F5, F6, F13, F14 and F16 has shown more than 80% of drug release for 8hrs.

Keywords: Topical emulgel, flurbiprofen, NSAID, thickener, liquid paraffin and eucalyptus oil.

I. Introduction

Skin as a movement course has been a promising evaluation for a long time because skin is easy to access and has a large surface area with_0 vast exposure to the circulatory and lymphatic structure [1]. Viable preparation has been the most notable medication estimations structures. Skin as a route of drug delivery has gained popularity because it_0 avoids first_0 pass effects, gastrointestinal exacerbation and metabolic corruption coordinated with oral association [2].

are considered: one is achieving adequate flux across the skin and the other is minimizing the_ slack time in skin infiltration [5]. Percutaneous maintenance of meds incorporates the appearance of the prescription by infiltration through skin to show up at the target tissue [6].

The major advantage of topical drug delivery system is to avoid the risk of intravenous_ treatment and gastrointestinal issues like pH changes, presence of synthetics, gastric cleansing time, it_0 reduces side effects, improve bioavailability, better patient compliance and easy end of medicine association are other advantage of the skin drug movement structure. Topical drug delivery is easy and painless. Skin is the_ largest organ of the human body, providing around 10% of the body mass of an average person, and it_0 covers an average area of 1.7m². Emulgel has a higher aqueous component, which permits better dissolution of drugs, so the gelling expert in the water stage which changes over an emulsion into an emulgel [7].

The present_0 work was to develop a topical emulgel formulation of flurbiprofen, which would help to reduce the gastrointestinal related toxicities integrated with_0 oral administration. It_ is established that_0 emulgels are superior to topical formulation over any other topical formulations, since they have better application property conversely, with gels, creams and medicines [8-9].

II. Materials and Methods

Flurbiprofen was_ received_ as_ a gift_ sample from Vasudha Pharma Chem Ltd. Andhra_ Pradesh. Xanthan_ gum, Span 20, Tween 20, liquid_ paraffin, glycerin and alpha-tocopherol received_ from_ Research_ finelab Mumbai. Benzyl alcohol and eucalyptus oil from_ Merck Life Science Pvt. Ltd. All_ other chemicals and_ reagents_ used_ were of analytical grade.

A. Method of preparation of Emulgel

1. Drug solution preparation: The exact quantity of flurbiprofen was dissolved in methanol after that a solution of benzyl alcohol and glycerin were added in this solution.

2. Preparation of oil in water emulsion: Oil time of the emulsion was prepared by dissolving length 20 in liquid paraffin while the watery stage was prepared by dissolving tween 20 in purified water. Both the oily and aqueous phases were separately heated up to 70-80°C until completed dissolution then the oily phase was added to the aqueous phase with continuous stirring until cooled to room temperature.

3. Preparation of gel stage: The thickener was weighed definitively and separated in water to structure a gel by killing it with triethanolamine then this gel stage was combined in emulsion to outline emulgel.

B. Raw material analysis of Flurbiprofen

1. Solubility: Solubility is a substance property wherein solute separated in a dissolvable. It saw when most prominent proportion of solute crumbled in a dissolvable at congruity. Solubility depends on the nature of drugs as well as the solvent. Polar solutes dissolved in polar dissolvable and non polar solvents separated just non-polar solutes. The possibility of the solvent can affect the solubility of drugs. A state of dynamic equilibrium established between these two cycles and at this point, the amount of solute enters in the course of action and becomes comparable to the amount of particles leaving the plan, concentration of the solute in the solution remains constant at a given temperature and pressure conditions. A response which have no more prominent capacity to separate more solute in the solvent at a given temperature and pressure called saturated solution [10-11].

2. Determination of standard calibration curve of flurbiprofen: 10 mg of flurbiprofen taken and separated in 10 ml of methanol, made last volume up to 100 ml in volumetric flask with phosphate pad (pH 7.4) for the availability of stock course of action. The 10 ml of stock solution was further diluted with 0 phosphate buffer (7.4 pH) in 100 ml to get 10 µg/ml (working standard). Then 1.0, 2.0, 3.0, 4.0 and 0.5 ml of working standard was taken in 10 ml standard volumetric flask and made up the volume with phosphate backing to design 0.1 µg, 0.2 µg, 0.3 µg, 0.4 µg, and 0.5 µg drug per ml solution. Then the absorbance was measured in 0 a UV spectrophotometer at 247 nm against 0 phosphate buffer (pH 7.4) as blank [12].

III. Experimental design

Design expert @ software, version 12, Stat-Ease was used to find correlation between independent and dependent variables. The software itself select the suitable model on the basis of individual parameters generated from regression analysis, such as adjusted R² value, predicted R² value and p value. At 0.05% level of significance, analysis of variance was implemented. In design expert the model was screened out by analyzing adjusted R² value, which has to be < 1. The general quadratic equation for three independent variables is as follows:

$$Y = \beta_0 + X_1\beta_1 + X_2\beta_2 + X_3\beta_3 + X_1X_2\beta_4 + X_1X_3\beta_5 + X_2X_3\beta_6 + X_1^2\beta_7 + X_2^2\beta_8 + X_3^2\beta_9$$

The compelling meanings of emulgel were progressed by three factors and two levels Box-Behnken plan. Three free definition factors were evaluated: a) centralization of polymer b) concentration of oil c) concentration of penetration enhancer. At three factor, two levels Box-Behnken verifiable preliminary arrangement of the response surface methodology requires 17 runs, of which 5 are the copies. The % drug release (Y₁) and thickness (Y₂) were evaluated as the dependent elements. The one-way examination contrast (ANOVA) was applied to survey the significance of the model (P < 0.05) and individual response parameter.

Table 1: Independent variables and their corresponding levels for optimization studies

Independent variables		Levels	
		-1	+1
Concentration of xanthan gum (gm)	X ₁	0.5	1.0
Concentration of liquid paraffin (ml)	X ₂	5.0	10.0
Concentration of eucalyptus oil (ml)	X ₃	8.0	10.0

Table 2: Box-behnken design for formulation of topical flurbiprofen emulgel

Formulation number	Factor 1 (X ₁)	Factor 2 (X ₂)	Factor 3 (X ₃)
1	0	0	0
2	1	-1	0
3	1	0	-1
4	0	-1	1
5	-1	1	0
6	0	1	1
7	-1	-1	0
8	0	0	0
9	0	0	0
10	0	-1	-1
11	0	0	0
12	-1	0	-1
13	1	0	1
14	0	1	-1
15	-1	0	1
16	1	1	0
17	0	0	0

IV. Results and Discussion

A. Raw material assessment of Flurbiprofen

1.Solubility: Solubility studies were driven by using different normal solvents. Most raised solubility of flurbiprofen was found in acetone, ethanol, methanol and ether.

Table 3: Solubility of flurbiprofen

Solvent	Observation
Water	Insoluble in water
Acetone	Freely soluble in acetone
Ethanol	Freely soluble in ethanol
Methanol	Freely soluble in methanol
Ether	Freely soluble in ether
Acetonitrile	Soluble in acetonitrile

2. Drug-excipient correspondence studies: Flurbiprofen was feasible with excipients was concentrated by FTIR. The FTIR spectra of plans with excipients uncover no participation among drug and excipient. Seen tops were perceived and unraveled in the spectra. The FTIR studies from the spectra confirmed the absence of any chemical interaction between the drug and excipients. The FTIR spectra of drug and formulation shown in Figure 1, 2, 3 and 4.

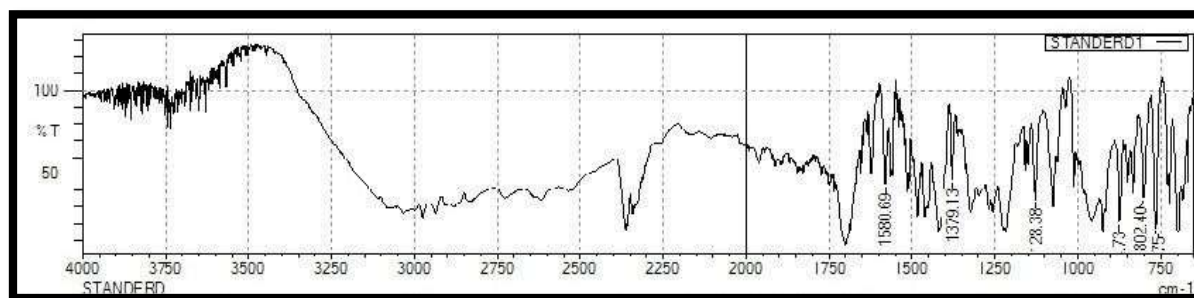


Figure1:FTIR offlurbiprofenstandard

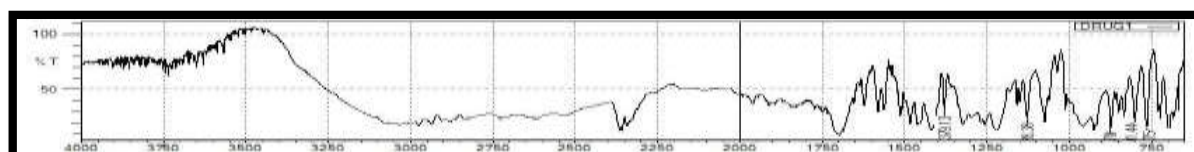


Figure2:FTIR offlurbiprofen drug sample

Figure4:FTIR_offlurbiprofen+xanthan_gum_+liquidparaffin+span_20+tween20+eucalyptus_oil+ alpha-tocopherol

3.Differential sifting calorimeter (DSC): A warm assessment of pure flurbiprofen drug was performed. It was performed to see any physico-substance coordinated effort among drug and excipients. Thermogram of pure flurbiprofen drug was inspected by using DSC (MettlerStarSW12.10)ataheatingrate10°C/minuteovera_0temperaturerangeof30-300°C.Accuratelyweighed2.0-5.0mgofthesamplewashermeticallysealedinan_aluminum dish. Nitrogen gas was scrubbed at speed of 10 ml/minutes for staying aware of latent atmosphere[24-25].

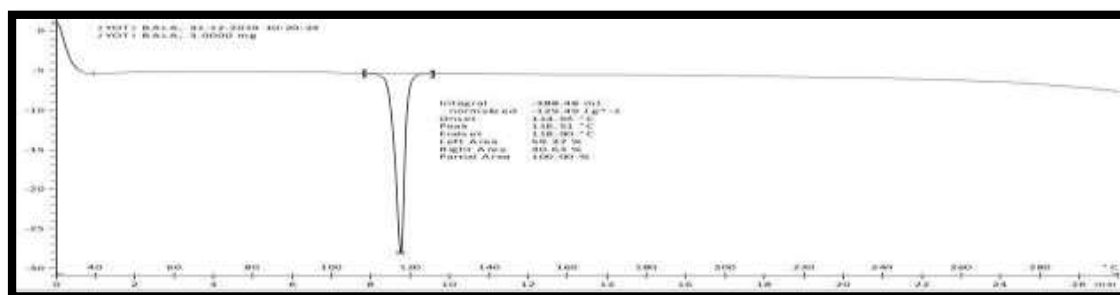
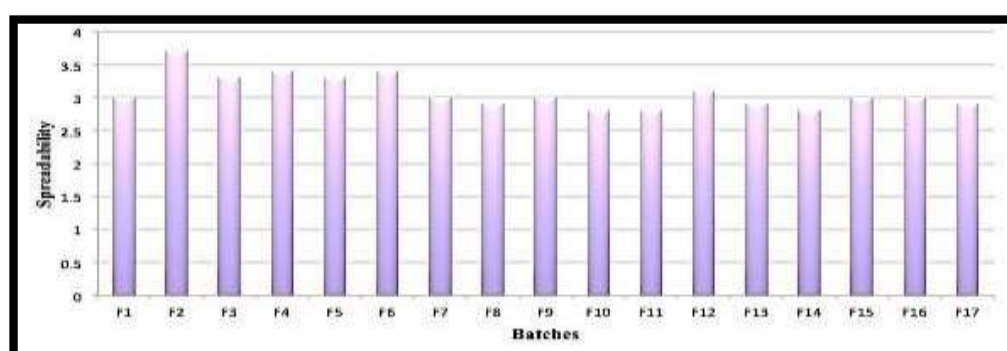


Figure5:Differentialscanning_calorimeterofflurbiprofen

4.X-Ray Diffraction (XRD): Powder XRD was performed to investigate the crystallinity of the medicine, as a matter of fact. The diffraction illustration of pure drug showed its incredibly clear nature as shown by different undeniable tops at 2θ under following conditions: Ni-channel Cu-Kα radiation, 40 KV voltages: 30 mA current, channel speed at 6°C/minutes and clear reach 10-80°C.



Figure_ 8:Spreadabilityofallformulations

5.Extrudability: Extrusion of emulgel from tube is critical during its application and in open minded affirmation.

6. Drug content of flurbiprofen: The content of drug in 1 gm of emulgel ranged from 81.12% to 98.61% as given in Table 4, which indicates that efficient drug loading and uniform distribution of drug in the formulations. F14 (98.61%) formulated by using gelling agent xanthan gum and penetration enhancer eucalyptus oil in the concentration of 0.75% and 8% respectively has shown more drug content as compared to other formulations.

Table 4: Percentage Drug content of all formulations

Batch no.	Drug content %	Batch no.	Drug content %
F1	96.67 ± 0.69	F10	90.74 ± 0.72
F2	93.47 ± 0.26	F11	97.21 ± 0.97
F3	92.01 ± 0.13	F12	91.33 ± 0.48
F4	98.36 ± 0.50	F13	96.20 ± 0.17
F5	84.67 ± 0.58	F14	98.61 ± 0.41
F6	94.80 ± 0.42	F15	93.74 ± 0.83
F7	81.12 ± 0.38	F16	96.93 ± 0.52
F8	95.60 ± 0.74	F17	95.33 ± 0.75
F9	96.07 ± 0.85		

V. Conclusion

Flurbiprofen emulgel was actually arranged as a successful plan. The oral plans seem to have hostile effects on avoid such issues skin emulgel was organized for the delivery of hydrophobic drug. Formulations contained xanthan gum as a polymer and eucalyptus oil as an entry enhancer gave transcendent medicine release results. The definitions were progressed by the three components and two levels Box-Behnken arrangement using Design-Expert programming. The definitions F5, F6, F13, F14 and F16 had shown more than 80 % of drug release for 8 hrs. Drug release affected by the concentration of polymer and penetration enhancer. From this study, it was concluded that the Box-Behnken design had the ability to obtain an optimized formula of viscosity and 0 percentage drug release.

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