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Formulation and Evaluation of Crisaborole Topical Nanoemulgel for the Treatment of Dermatitis

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ABSTRACT

Nanoemulsion is a promising alternative to increase drug delivery system penetration and targeting poorly soluble drugs. Nanoemulsion with globules in nano-scale size of an emulsion do not relay on the emulsion physical properties itself. The small size of particles, the more amount of drug is able to be incorporated in the formulation, which subsequently increases the thermodynamics towards the skin.Drug delivery through the skin to the systemic circulation is convenient for a number of clinical conditions. It offers the advantage of steady state-controlled drug delivery over extended periods of time. An extra advantage is the total absence of gastrointestinal side effects like irritation and bowel ulcers associated with oral delivery. Crisaborole is a novel oxaborole approved by FDA on December 14, 2016 as Eucrisa, a topical treatment of for mild to moderate atopic dermatitis. Its structure contains a boron atom, which facilitates skin penetration and binding to the phosphodiesterase 4 enzyme. Crisaborole (2% w/w) in the form of emulgel, containing Nanoemulsion of the drug. Almond oil was found to be better with the drug diffusion. Optimized formulation compared with marketed formulation for in- vitro drug release. Nanoemulsion loaded emulgel prepared with the tween 80, Almond oil was found to be better with the drug diffusion. When the optimized formulation was compared with marketed formulation for in- vitro drug release, it showed controlled release for optimized batch (F1) in 24 hours and marketed formulation in 12 hours.

Keywords: *Nanoemulsion, dermatitis, Crisaborole, drug release, drug diffusion.*

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INTRODUCTION

Topical drug delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorders (e.g. acne) or the cutaneous manifestations of a general disease. Skin is one of the most readily accessible organs on human body for topical administration and is main route of topical drug delivery system [1.2,3].Emulsions are biphasic system in which immiscible liquid is dispersed into other which makes system unstable and is stabilized by emulsifying agents. Gels are the semisolid systems consisting of dispersions of small or large molecules in an aqueous liquid vehicle rendered jelly like by the addition of a gelling agent [4,5].Atopic dermatitis (eczema) is a condition that makes your skin red and itchy. It's common in children but can occur at any age. No cure has been found, but treatments and self-care measures can relieve itching and prevent new outbreaks. Repeated scratching that breaks the skin can cause open sores and cracks, which can lead to infections [6,7].

MATERIAL AND METHODS

Materials:

Crisaborole was obtained as kind gift sample from Metrochem API Pvt. Ltd., Hyderabad. Almond Oil, Tween 80, Methanol, Ethanol, Triethanolamine, Potassium dihydrogen phosphate and Potassium Phosphate (monobasic) were procured from Research -Lab Fine Chem Industry, Mumbai. Potato dextrose Agar was acquired from Himedia Lab Pvt. Ltd., Mumbai.

Methods:

High pressure homogenization:

High pressure homogenization is a highly efficient method, available at both laboratory and large scale but consumes a large amount of energy. In this method, two liquids along with surfactants are made to pass through a small orifice at high pressure (500-5000 psi) to produce nanoemulsions [8,9,10].

Microfluidization:

Liquids (oil and water) from two opposite microchannels are made to collide with each other at a common interface. This mixing technique makes use of a high pressure displacement pump (500– 20000 psi) to produce fine nanoemulsions[8,9,10].

Sonication:

Sonication is the process of bringing liquid droplets together to generate mechanical vibration and cavitation, which provides the necessary energy input for formation of small sized droplets. This method can be widely used to prepare nanoemulsions on small scale however care must be taken to prevent shear induced coalescence[8,9,10].

Phase inversion temperature technique:

In this technique a mixture of oil, water and nonionic surfactants at room temperature exhibiting a positive curvature are taken on increasing the temperature. The polyethoxylated surfactant becomes lipophilic and gets solubilized in the oily phase. This results in the phase inversion and o/w emulsion changes to w/o emulsion exhibiting a negative curvature[8,9,10].

Preformulation Study:

In drug development it is essential that certain fundamental physical and chemical properties of a drug molecule and other derived properties of the drug be determined. This provides a framework for the drug combination with pharmaceutical excipients in the dosage form[11,12,13].

Organoleptic Properties:

The drug sample of Crisaborole was evaluated for its organoleptic properties such as appearance, color, odour.

Melting Point:

The melting point of the drug was determined by using open capillary method using the melting point apparatus. The melting point done in triplicate[11,12,13].

Solubility:

The solubility of Crisaborole was checked in different solvents: Water, acetonitrile, methanol, ethanol, 0.1 N HCl, Phosphate buffer 6.8. The solubility of Crisaborole in various oils, surfactants was determined by adding an excess amount of drug to 5ml of selected oils. The mixtures were kept on magnetic stirrer for 48 hrs. at 40±0.5°C (RAJ 305-C) and then kept for 24 hrs. at room temperature.

Ultraviolet - Visible Spectroscopy:

Determination of Maximum absorbance (λ max): The UV spectrum of Crisaborole was obtained using UV Shimadzu. Accurately weighed 10 mg of the drug was dissolved in sufficient quantity of methanol. Stock solutions (100 µg/ml) of Crisaborole were prepared in methanol. The UV spectrums were recorded in the range 200-400 nm by using UV-Visible double beam spectrophotometer. The wavelength of maximum absorption (λ max) was determined [14,15,16].

Standard Calibration Curve of Crisaborole in Methanol: Accurately weighed 10 mg Crisaborole and transferred to 10 ml volumetric flask. The volume was made up to 10 ml with methanol and sonicated for 5 min. to produce stock solution of 100 µg/ml. Working standard solutions of strengths 2-10 µg/ml were made from the stock solution by appropriate dilutions. The above solutions were analyzed by UV spectrophotometer at λ max 252 nm [14,15,16].

FTIR spectroscopy:

The IR spectrum of Crisaborole was recorded at wave number 4000 to 50cm-1 using Fourier transform infrared spectrophotometer (Mode- FTIR, Bruker). Method used for analysis was ATR. Attenuated Total Reflection (ATR) involves pressing the sample against high refractive index prism and measuring the infrared spectrum using infrared light that is totally internally reflected in prism [17,18].

Drug excipients compatibility study:

Spectra were recorded with FTIR instrument and the spectral analysis was done. It was performed by mixing drug with excipients like oil, surfactant and polymer in equal proportion. Small amount of the mixture was placed on the sample cell, then fitted in sample holder [17,18].

Formulation and Development of Nanoemulsion:

The quantities of drug and other ingredients were weighed by calculating equivalent amounts as per table 16 and formulations were prepared in following manner.All the glassware was washed with distilled water and then sterilized by drying at 160-165^{0}C for 1 hr. in hot air oven [19,20].

Preparation of aqueous phase 'A': Accurately weighed quantity of propylene glycol was added into distilled water (80^{0}C).

Preparation of Oil phase 'B': Weighed quantity of Almond oil and tween 80 mixed together by maintaining hot condition, simultaneously accurately weighed quantity of Crisaborole was added into it then addition of methyl paraben, propyl paraben and BHT in it.

Incorporation of solution 'A' in dispersion 'B': Both the phases were mixed properly with the help of High pressure Homogenizer maintaining the respective rpm.

Table 1: Composition of Nanoemulsion formulation

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ingredients	%								
Crisaborole (w/w)	10	10	10	10	10	10	10	10	10
Almond Oil (v/v)	3	3	3	2	2	2	1	1	1
Tween 80 (v/v)	5.25	4.50	3.75	5.25	4.50	3.75	5.25	4.50	3.75
Propylene glycol (v/v)	1.75	1.50	1.25	1.75	1.50	1.25	1.75	1.50	1.25
Methyl Paraben (w/w)	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Propyl Paraben (w/w)	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BHT	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Water Q.S (v/v)	100	100	100	100	100	100	100	100	100

Preparation of gel:

The weighed quantity of Carbopol 934 was mixed in distilled water (40^0C) further addition of Triethanolamine to maintain the desired pH range of the solution. The uniformity in the stirring was maintained and then the gel was kept in the refrigerator for 24 hrs. [21,22]

Table 2: Composition of gel

Sr. No.	Ingredients (% w/w)	Quantity (%)
1	Carbopol 934	1
2	Triethanolamine	0.1
3	Water q.s.	100

Preparation of Emulgel:

Further incorporation of 20% nanoemulsion was incorporated to obtain 100 % (w/w) emulgel which contains 2% of drug [21,22]

Filling to container:

The formulation was transferred into previously cleaned and dry containers.

Evaluation of Nanoemulsion:

Appearance:

The prepared nanoemulgel formulations were inspected visually for their colour, homogeneity, consistency and pH. The pH values of 0.1% aqueous solutions of the prepared Gellified Emulsion were measured by a pH meter.

Scanning Electron Microscopy:

The morphology of nanoemulsion can be determined by scanning electron microscopy (SEM). SEM gives a three-dimensional image of the partial. SEM samples are examined at suitable accelerating voltage, usually 20 kV, at different magnifications. A good analysis of surface morphology of disperse phase in the formulation is obtained through SEM.

Particle Size Analysis:

Formulated nanoemulsion should be analyzed for their hydrodynamic particle size. Dynamic light scattering method used for the measurement of particles and further particle size distribution.

Zeta potential measurements:

Zeta potential for nanoemulsion was determined using Zetasizer hsa 3000 (Malvern instrument Ltd., UK). Samples were placed in clear disposable zeta cells and results recorded. Cuvettes were washed with methanol and rinsed with the sample to be measured before each experiment.

Entrapment efficiency:

Entrapment efficiency is defined as the percentage amount of drug which is entrapped by the Nanoemulsion. Unentrapped drug was first separated by centrifugation at 15000 rpm for 30 minutes. The resulting solution was then separated and supernatants liquid was collected.

Evaluation of Nanoemulsion based Gel:

pH determination:

pH of the formulation was determined by using digital pH meter. pH meter electrode was washed by distilled water and then dipped into formulation to measure pH and this process was repeated 3 times.

Measurement of viscosity:

Viscosity of emulgel was determined using a Brookfield Viscometer (RVDV-I Prime, Brookfield Engineering Laboratories, and USA) with spindle 63. 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.

Spreadability:

Gel was placed over one slide and the other over its top such that the gel is sandwiched between the two slides. The slides were pressed upon each other so as to displace any air present and the adhering gel was wiped off. The spreadability was determined using the formula below.

$$S=M.L/T$$

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

Drug content study:

Drug content study was done to determine the amount of the drug present in a certain quantity of the formulation. Volumetric flask was kept for 2 hrs. and shaken well in a shaker to mix it properly. Solution was passed through filter paper and filtered the mixer then measured absorbance by using spectrophotometer at 252 nm.

In-vitro Drug release study:

In-vitro drug release studies were carried out on Diffusion cell using egg membrane. Emulgel (1gm) was applied on to the surface of egg membrane dialysis membrane. Cumulative amount of drug release across the egg membrane was determined as a function of time.

Release kinetics of selected formulation:

To examine the drug release kinetics and mechanism, the cumulative release data were fitted to models representing Zero order (cumulative % drug release v/s. time), First order (log cumulative % drug retained v/s. time), Higuchi model (cumulative % drug retained v/s. Square root of time).

Accelerated stability studies of Emulgel:

Stability studies are performed by guidelines. The organized emulgel were filled in aluminum collapsible tubes (5 g) and subjected to strength learns at 5°C, 25°C/60% RH, 30°C/65% RH, and 40°C/75% RH and 60 ± 2° for a period of 3 months. Tests were pulled back at 15-day time between times and surveyed for physical appearance, pH, rheological properties and pharmaceutical substance.

RESULT AND DISCUSSION

Preformulation evaluation:

Organoleptic Properties, melting point and solubility:

Crisaborole was studied for its organoleptic properties such as appearance, colour and odour. It is crystalline powder, white in color and slight in odor. The result shows the details of Crisaborole properties are similar to those of other organic compounds such as cyanoacids and phenylcyclohexanoic acid. The reported value of melting point is 128-133^{0}C and observed value is 129^{0}C. Crisaborole was found to be soluble in methanol, acetonitrile, 0.1 N HCl and pH 6.8 phosphate buffer while slightly soluble in water.

Ultraviolet – Visible Spectroscopy study:

Determination of (λ max) of Crisaborole in Methanol: The UV spectrum of Crisaborole solution (100µg/ml) scanned between 400-200 nm using UV spectrophotometer exhibited wavelength of absorbance maxima at 252 nm. λmax of Crisaborole in Methanol is shown in figure 1.

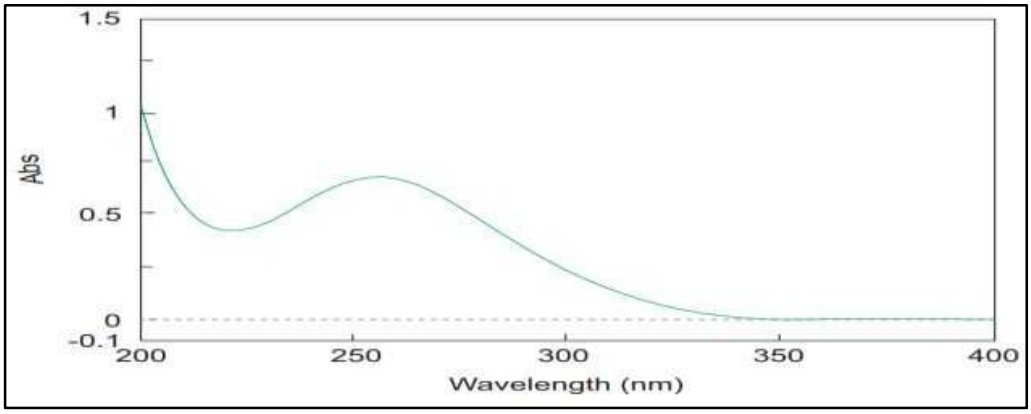

Figure 1: Ultraviolet Spectra of Crisaborole in Methanol

Calibration of Crisaborole in Methanol: Methanol solution of drug was very clear and readily analysed by the UV- visible spectrophotometer. Calibration curve of Crisaborole was found to be linear in the concentration range of 2-10 µg/ml given in figure 2.

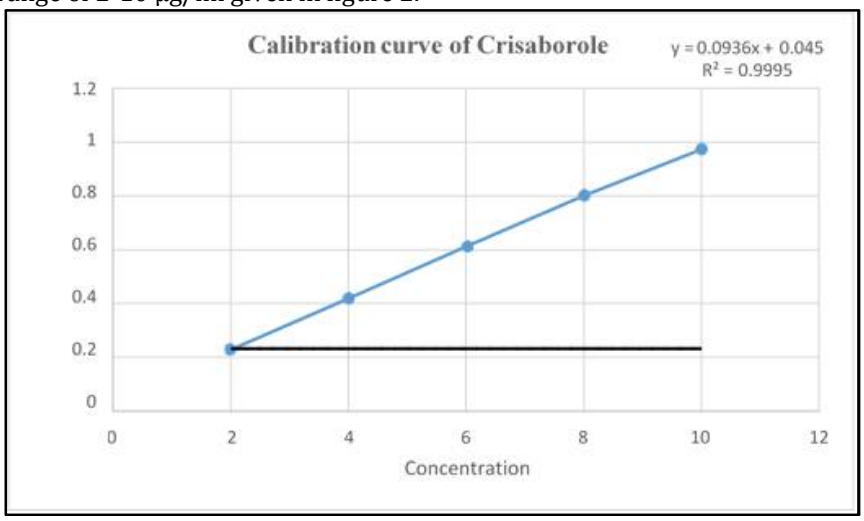

Figure 2: Calibration curve of Crisaborole in Methanol

Fourier Transform Infrared Spectroscopy:

The FTIR spectrum of Crisaborole has been shown in figure 3. The spectrum shows characteristic peaks for Crisaborole.The absorption bands shown by Crisaborole are characteristic of the functional groups present in its molecular structure.

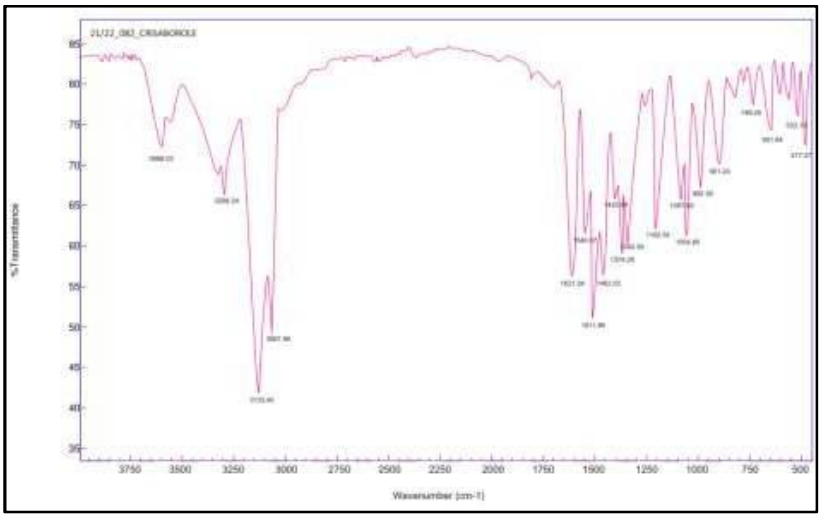

Figure 3: Representative IR spectrum of Crisaborole

Evaluation of Nanoemulsion:

Entrapment Efficiency:

The maximum Entrapment efficiency was found to be 96.5% and the minimum Entrapment efficiency was found to be 69% for F1 and F8 respectively. It has been observed that the drug entrapment efficiency was highest for optimized batch (F1).

Particle size and poly dispersibility index:

The Particle size of the Nanoemulsion of optimized batch was found to be 100 nm. It is seen with increase in concentration of Almond oil with high speed of homogenizer decrease in particle size.

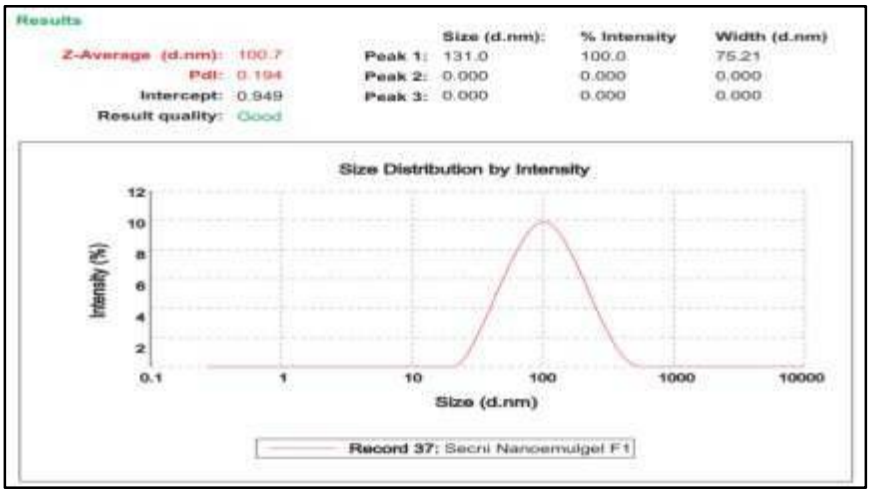

Figure 4: Particle size and PDI of optimized formulation (F1)

Particle size was found to be 100 nm and poly dispersibility index was found to be 0.194 for optimized formulation F1. The particle size and PDI for optimized batch F1 is shown in figure 4.

Zeta Potential:

Zeta potential shows the stability of the (colloidal dispersion) nanoemulsion under the stress testing condition. Zeta potential is affected by particle size, lowest particle size in nano size i.e. 100, shows -32 mV. This indicates thermodynamic instability of the dispersion. The zeta potential for optimized batch F1 is shown in figure 5.

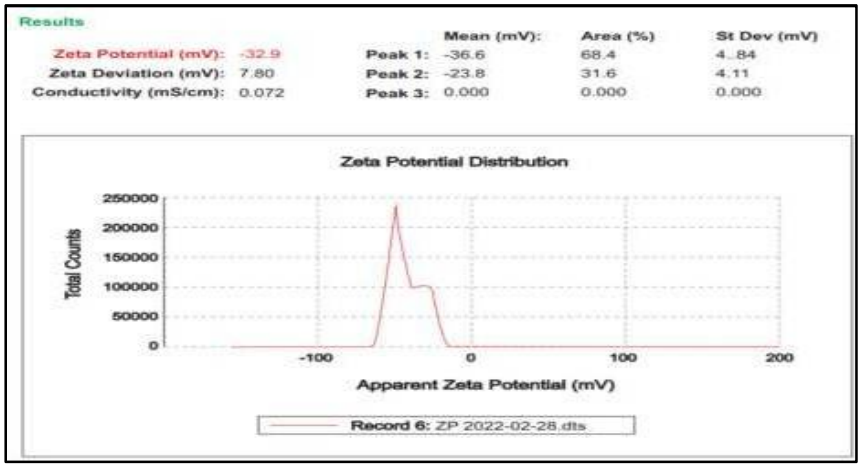

Figure 5: Zeta potential of optimized formulation (F1)

Scanning Electron Microscopy:

Scanning electron microscopy of nanoemulsion has revealed that the Nanoemulsion was spherical in shape and had a size below micrometer range. Some agglomeration might be due to the evaporation of water present in formulation during sample preparation prior to SEM analysis. SEM of nanoemulsion of Batch F1 is shown in figure 6.

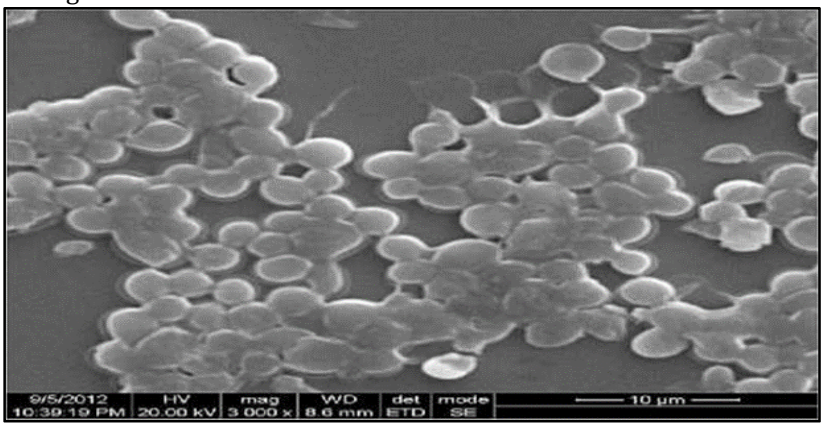

Figure 6: Scanning Electron Microscopy of optimized formulation (F1)

Evaluation of emulgel:

Physical appearance:

The emulgel was translucent homogeneous and consistent gel.

pH:

The pH values indicate the suitability of emulgel for topical application, so as to minimize discomfort or irritation due to acidic pH and microbial growth due to basic pH. pH values in the range of 5.31 to 5.75 are shown in the following table 3.

Viscosity:

An emulgel made from Almond oil and a homogenizer has been shown to be shear thinning in nature, showing decrease in viscosity at increasing shear rate. Viscosity is resistance to flow, which is an important property for topical preparations because it influences Spreadability and drug release.The viscosity values at 50 rpm was noted for all formulations and is shown in table 3.

Spreadability:

Formulation F1, having optimum viscosity and spreadability of this formulation is 17.77 gm.cm/sec. Spreadability shows the inverse relationship with the viscosity of the emulgel. Formulation with higher viscosity are very thick in nature, difficult to spread. Both the extremes are not suitable for any of the topical preparation. The spreadability of formulations F1 to F9 is shown in table 3.

Drug Content:

The percentage drug content of all prepared emulgel formulations was found to be in the range of 64 to 96%. Therefore, uniformity of content was maintained in all formulations. The F1 Formulation drug content was found to be 96%.Table 3 depicts drug content of F1 to F9.

Table 3: pH, Viscosity, Spreadability and Drug content for prepared emulgel

Formulation code	pH(±SD)	Viscosity(cP)at RT	Spreadability(g.cm/sec)±S.D.	Drug content(%)±SD
F1	5.60±0.025	12350	17.77±0.025	96±0.5
F2	5.75±0.018	10420	16±0.035	91.91±0.7
F3	5.55±0.011	11520	15.38±0.028	95±0.7
F4	5.45±0.011	11250	15.68±0.018	93.91±0.7
F5	5.43±0.0158	10950	15.09±0.032	94±0.7
F6	5.33±0.011	10504	14.81±0.012	72±0.7
F7	5.31±0.005	12520	15.53±0.012	68±1.09
F8	5.40±0.018	11200	15.23±0.011	82±1.07
F9	5.53±0.026	9320	15.84±0.018	64.91±1.43

***In-vitro* drug diffusion study:**

The *in-vitro* diffusion of Crisaborole from its various emulgel formulations batch F1 to F9 at 0 to 24 hrs. Total amount of Crisaborole that diffused (%) through the egg membrane using all of the emulgel formulations was measured using a modified Franz diffusion cell and is shown in table 4.

Table 4: Drug diffusion (%) of various formulation at 0 to 24 hours

Time (hrs.)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	9 ±0.70	8.17 ±0.76	7.14 ±0.22	6.25 ±0.071	6.13 ±0.75	5.34 ±0.82	5.01 ±0.70	3.41 ±0.85	2.31 ±0.53
2	17 ±0.70	14.08 ±0.73	12.96 ±0.51	15.22 ±0.24	11.13 ±0.75	12.96 ±1.06	16.74 ±0.97	19.15 ±0.75	16.24 ±0.79
3	25 ±1.07	24.21 ±0.74	23.01 ±0.16	22.11 ±0.17	23.12 ±0.74	19.6 6±0.39	21.30 ±0.81	18.12 ±0.74	20.11 ±0.74
4	34 ±1.06	32.65 ±0.38	31.09 ±0.12	28.23 ±0.79	26.61 ±0.84	25.66 ±0.64	23.49 ±0.88	22.44 ±0.31	20.66 ±0.94
5	41 ±0.70	40.42 ±0.85	40.97 ±0.52	35.49 ±0.88	30.99 ±0.50	32.67 ±0.95	34.69 ±095	39.45 ±0.69	39.41 ±0.85
6	50 ±0.53	48.57 ±0.38	47.87 ±0.47	45.66 ±0.72	45.35 ±0.83	40.19 ±0.19	38.09 ±0.75	35.66 ±0.94	30.11 ±0.74
7	59 ±1.06	57.45 ±0.31	55.13 ±0.94	52.79 ±0.99	48.49 ±0.88	44.09 ±0.10	41.49 ±0.88	38.09 ±0.73	37.71 ±0.96
8	68 ±1.07	65.15 ±0.27	62.14 ±0.16	60.49 ±0.32	57.18 ±0.76	54.66 ±1.2	51.78 ±0.66	48.83 ±1	49.89 ±1.03
12	78 ±1.41	72.30 ±0.28	74.25 ±0.32	64.49 ±0.33	62.16 ±0.75	58.19 ±0.19	56.99 ±1.07	54.97 ±1.04	52.31 ±0.81
16	85 ±1.04	81.89 ±0.50	73.41 ±0.64	70.89 ±1.05	68.12 ±0.74	64.69 ±0.45	61.44 ±0.86	58.10 ±0.73	54.14 ±0.54
24	96 ±0.66	90 ±0.38	87.42 ±0.30	78.94 ±0.50	72.09 ±0.73	69.99 ±1.0	65.05 ±0.72	61.19 ±0.76	58.45 ±1.21

Comparison of *in-vitro* drug release with marketed formulation:

The release of drug from optimized (F1) emulgel formulation was higher than the commercial gel. This indicates that this formulation would show better contact with biological membrane. The drug is entrapped in the oil phase, hence when formulation was applied on egg membrane the penetration takes place upto 24 hrs. The Cumulative drug release of formulation F1 and Marketed formulation is shown in table 5.

This may be due to one of the following mechanism:

Adsorbed medications on nanoemulsions will rapidly diffuse through the stratum corneum and become accessible to the epidermis. Due to the greater amount of free drug present on the surface, the formulation with lower entrapment efficiency would adopt this strategy.

The Nanoemulsion, which exhibits quick drug availability in the epidermal region due to its low entrapment efficiency, works by following principle A above. By diffusing onto the skin's surface, the medicine incorporated in the nanoemulsion may leach, and this leached drug may then diffuse through the stratum corneum.

The Nanoemulsion is a gel made up of an entrapped drug that moves towards the skin of higher water concentration across the stratum corneum because of longer time of hydration. From the epidermal region further the drug would be released in controlled fashion which ultimately improves the antibacterial activity.

Table 5: Comparison of cumulative drug release of formulation F1 and Marketed formulation (Eucrisa Ointment)

Time (hrs.)	% CDR ± Sd (F1 formulation)	Time (hrs.)	% CDR ±SD Marketed formulation (Eucrisa ointment)
0	0	0	0
1	9±0.70	1	8±0.77
2	17±0.70	2	15±0.707
3	25±1.07	3	24±0.70
4	34±1.06	4	34±0.70
5	41±0.07	5	42±0.72
6	50±0.77	6	55.57±0.91
7	59±0.70	7	60.45±0.83
8	68±0.71	8	69±0.707
12	78±0.70	9	76.90±705
16	85±0.77	10	82±0.73
24	96±0.71	12	92±0.76

Drug release Kinetics:

Best fit kinetic model for the optimized formulation with highest R2 value and least slope value was the Higuchi model. The classical zero order release curve was found be linear, while the curve plotted for Higuchi release model was found to be linear. Which indicate that the formulation shows the drug release probably by diffusion.

Stability study:

Optimized batch F1 was stable at Accelerated temperature conditions ($40^0C\pm 2^0C$, 75% RH ± 5% RH) and Room Temperature. Results have been given in table 6. The optimized formulation was evaluated after storage accelerated condition and room temperature.

Table 6: Stability Study data for F1 formulation at $40^0C\pm 2^0C$, 75 % RH±5% RH)

Parameter		0 month	3rdmonth
Clarity		Translucent	Translucent
pH		5.60±0.006	5.41±0.025
% Drug content		96±0.5	95.97± 0.5
Viscosity	**10**	14960	14846
	20	14200	14152
	30	13050	12948
	40	13000	12794
	50	12350	12015

CONCLUSION

Antibacterial therapy is one of most effective mechanism to eradicate the Bacterial infection for improving quality of life. Systemic treatment is usually reserved for infections of the nails, extensive cutaneous infections or those which have not responded to topical therapy. Conventional topical formulations are unable to retain and controlled the delivery of the drug over the skin for a prolonged period.

Nanoemulsion were prepared by high speed homogenization and studied for different parameters. Organoleptic properties, melting point, solubility testing, UV spectroscopy studies and FTIR were performed for the Crisaborole. Drug loaded emulgel were evaluated for physical appearance, pH, viscosity, drug content, in vitro drug release study (diffusion study) and antibacterial activity.
Nanoemulsion loaded emulgel prepared with the tween 80, Almond oil was found to be better with the drug diffusion than other preparations. Scanning electron microscopy shows spherical shape and size below as well as the micrometric range.

REFERENCES

1. Bhowmik D, Harish GB, Kumar P, Duraivel S, Kumar SKP. (2012). Recent Advances in Novel Topical Drug Delivery System. The Pharma Innovation;1(9): 12- 30.
2. verma A, Singh S, Kaur R, Jain UK. (2013). Topical Gels as Drug Delivery Systems. A Review: International Journal of Pharmaceutical Sciences Review and Research;23(2):374-382.
3. Sonaje S, Gondkar SB, Saudagar RB. (2013). Gellified Emulsion A New Born Formulation for Topical Delivery of Hydrophobic Drug. World Journal of Pharmacy and Pharmaceutical Science;1(3):233-251.
4. Basera K, Bhatt G, Kothiyal P, Gupta P. (2015). Nanoemulgel A Novel Formulation Approach for Topical Delivery of Hydrophobic Drugs. World Journal of Pharmacy and Pharmaceutical Science ;4(10):1872-1876.
5. Aulton M.E., (2007). Aulton's Pharmaceutics, The Design and Manufacture of Medicine. 3rded., Churchil Livingstone :390.
6. Herbert A. (2005). Liberman, Pharmaceutical Dosage Forms, Disperse Systems, Published by Marcel Dekkar, 2nd, Page No. 1, 57.
7. Katiyar BS, Katiyar SS, Mishra PS, Sailaja DL. (2013). Microemulsions: A Novel Drug Carrier System. International Journal of Pharmaceutical Sciences Review and Research ;20(2):139.
8. Haritha, Sayed PB, Koteswara RP, Chakravarthi V. (2006). A Brief Introduction To Methods of Preparation, Applications and Characterization of Nanoemulsion Drug Delivery Systems. Indian Journal of Research in Pharmacy and Biotechnology;1(1):25-28.
9. Pingale PL, Amrutkar SV, Telange DR. (2021). Formulation, Characterization and In-Vitro Dissolution Studies of Metadoxine Tablets Prepared by Various Granulation Methods. Journal of Medical Pharmaceutical and Allied Sciences. 2712-9.
10. Christofori M. R. R. Nastiti, Thellie Ponto, (2017). Emanabd, Topical Nano and Microemulsions for Skin Delivery, Pharmaceutics, Volume 9, Issue 37, Page No. 3.
11. Form and Drug Delivery System, 7th ed, New York Lippincoott Williams and Wilkins. 1999: 394-400,278-280,405-407.
12. Setya S, legaonkar S, Razdan BK.(2014). Nanoemulsion: Formulation Method and Stability aspect. World Journal of Pharmacy and Pharmaceutical Sciences;3(2):2218, 2214, 2222.
13. Modi VJ, Pingale PL. (2012). Development and validation of analytical method for estimation of prasugrel hydrochloride in bulk and in pharmaceutical formulations. International journal of pharma and biosciences. ;3(4):292-8.
14. Thakur N, Garg G, Sharma PK, Kumar N. (2012). Nanoemulsion A Review on Various Pharmaceutical Application. Global Journal of Pharmacology ;6(3):222- 225.
15. Challepa P, MohmedAT, Keleb EI. Assad, Nanoemulsion and Nanoemulgel as Topical Formulation. IOSR Journal of Pharmacy 2015;5(10):43-47.
16. Nikhilitha P. (2021). Effect of Natural Polymer on Release Retarding Rate of Glimepiride Sustained Release Tablet. Journal of Advanced Scientific Research. 31;12(01 Suppl 1):145-50.
17. Rathod HJ, Mehta DP. (2015). A Review On Pharmaceutical Gel, Actascientifica, International Journal of Pharmaceutical Science;1(1):35.
18. Patel MA, Pingale PL. (2014). Comparative effect of different high functionality excipients on various characteristics of vardenafil HCl tablets (BCS II drug). International Journal of Pharmaceutical Sciences and Research. 1;5(12):5447.
19. Kaur J, Kaur J, Jaiswal S, Gupta GD. (2016). A Review on Novel Approach of Antifungal Emulgel for Topical Delivery in Fungal Infections. Indo American Journal of Pharmaceutical Research;6(7):2231-6876.
20. Pingale PL, Rajput AP, Bagade SB. (2020). Use of natural superdintegrants in formulation of fast disintegrating tablet of atenolol. European Journal of Molecular & Clinical Medicine.;7(9):3743-52.
21. Malay NJ, Patel CP, Prajapati BG. (2018). Nanoemulgel Innovative Approach for Topical Gel Based Formulation Research and Reviews on Healthcare;1(2):1-2.
22. Dev A, Chodankar R, Shelke O. (2015). Emulgels: A Novel Topical Drug Delivery System. Pharmaceutical and Biological Evaluations. Pharmaceutical And Biological Evaluations. vol. 2 (Issue 4): 64-75.

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