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FORMULATION AND EVALUATION OF CRISABOROLE OINTMENT BY CO-SOLVENCY METHOD

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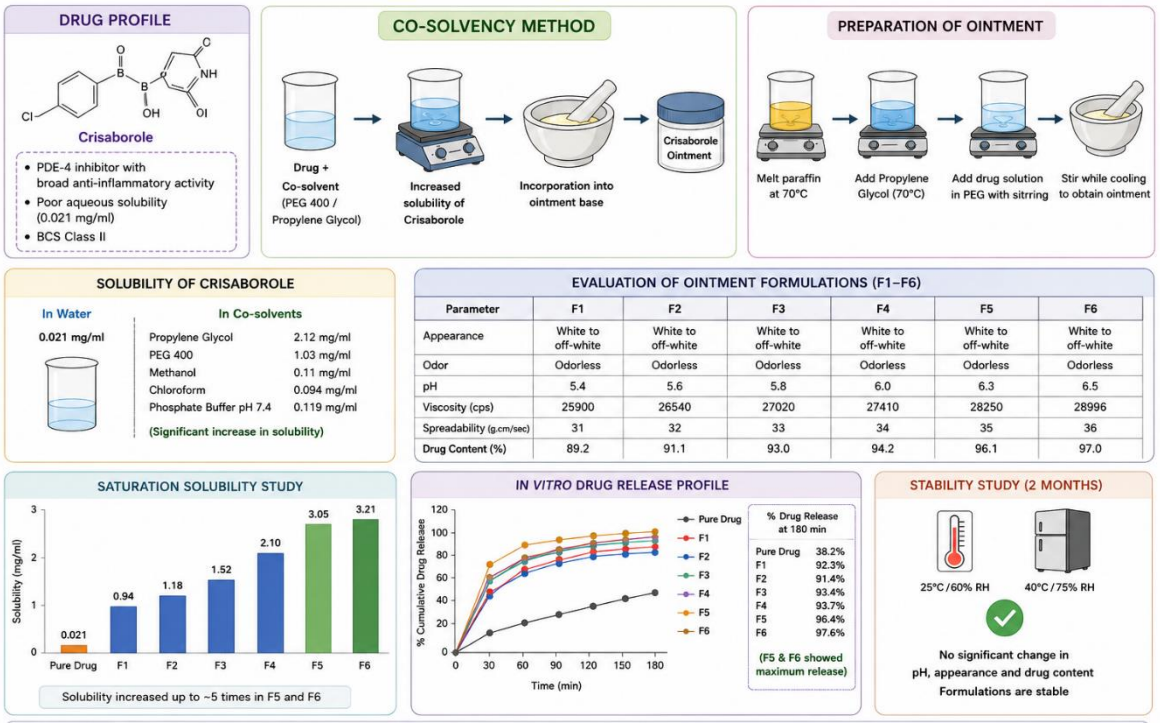
ABSTRACT

Crisaborole is a potent anti-inflammatory drug that acts by inhibiting phosphodiesterase-4 (PDE-4) enzyme and is widely used in the treatment of inflammatory skin disorders such as psoriasis and other dermatological conditions. However, its therapeutic effectiveness is limited due to its poor aqueous solubility (0.021 mg/ml) and low dissolution rate. The present study was aimed to improve the solubility of Crisaborole by using the co-solvency technique and to formulate a topical ointment with enhanced drug release characteristics.Pre-formulation studies were carried out to determine the physicochemical properties of the drug. Crisaborole was identified as a white to off-white crystalline, odorless, and bitter powder with a melting point of 132°C. The λmax was found to be 250 nm, and the calibration curve showed good linearity with an R^2 value of 0.999. Solubility studies revealed higher solubility of Crisaborole in co-solvents such as propylene glycol and PEG 400 compared to water.Crisaborole ointment formulations (F1–F6) were prepared using the co-solvency method and evaluated for various parameters including appearance, pH, viscosity, spreadability, drug content, solubility enhancement, and in-vitro drug release. All formulations showed acceptable physical characteristics, with pH ranging from 5.4 to 6.5 and uniform drug content between 89% and 97%. The formulations containing higher concentrations of propylene glycol and PEG 400 (F5 and F6) demonstrated approximately five-fold improvement in drug solubility and achieved maximum drug release of 96.4% and 97.6%, respectively.The stability study of optimized formulations showed minimal changes in their properties over two months, indicating good stability. Therefore, the co-solvency technique was found to be a simple, economical, and effective approach for improving the

solubility and release profile of poorly water-soluble Crisaborole in topical ointment formulations.

KEYWORDS: Crisaborole, Co-solvency Technique, Ointment Formulation, Solubility Enhancement, Phosphodiesterase-4 (PDE-4) Inhibitor.

Graphical Abstract



INTRODUCTION

Skin inflammatory disorders such as psoriasis, eczema, and dermatitis are common chronic conditions characterized by redness, itching, swelling, and irritation of the skin. These disorders involve the activation of various inflammatory pathways and the release of pro-inflammatory cytokines.**[1]** The management of such conditions generally involves the use of topical therapeutic agents that can provide targeted drug delivery directly at the site of action while reducing systemic side effects.Crisaborole is a novel non-steroidal anti-inflammatory drug that belongs to the boron-containing phosphodiesterase-4 (PDE-4) inhibitor class.**[2]** PDE-4 plays a crucial role in regulating the production of inflammatory mediators in keratinocytes and immune cells. By inhibiting the PDE-4 enzyme, crisaborole decreases the production of inflammatory cytokines and provides effective anti-inflammatory activity.**[3]** Due to its localized action, topical administration of crisaborole is considered a suitable approach for the treatment of various inflammatory skin diseases.Despite its significant

therapeutic potential, the formulation of crisaborole presents certain challenges because of its poor aqueous solubility. It is categorized as a Biopharmaceutical Classification System (BCS) Class II drug, exhibiting high permeability but low solubility, with an aqueous solubility of approximately 0.021 mg/ml.**[4]** Poor solubility results in a slower dissolution rate, which may limit drug availability at the target site and can affect the overall therapeutic performance of the formulation. Therefore, improving the solubility and dissolution behavior of crisaborole is essential for developing an effective topical dosage form.Various techniques have been explored for improving the solubility of poorly water-soluble drugs, including particle size reduction, solid dispersion, complexation, nanotechnology, and the use of co-solvents. Among these approaches, the co-solvency technique is considered a simple, economical, and effective method for enhancing the solubility of hydrophobic drugs.**[5]** This technique involves the use of water-miscible organic solvents such as propylene glycol and polyethylene glycol (PEG 400), which increase the solubility of poorly soluble drugs by improving their wettability and dissolution characteristics.**[6]**Topical ointments are widely used semi-solid dosage forms due to their ability to remain in contact with the skin for a prolonged period and provide sustained drug release. The incorporation of co-solvents into ointment formulations can significantly improve drug solubilization, uniform distribution, and release from the dosage form. Additionally, ointments provide advantages such as ease of application, better patient compliance, and minimized systemic exposure.**[7]**Therefore, the present research work was undertaken to develop, characterize, and evaluate crisaborole ointment using the co-solvency method. The study focused on enhancing the aqueous solubility of crisaborole using suitable co-solvents, namely propylene glycol and PEG 400, followed by the preparation of different ointment formulations.**[8,9]** The prepared formulations were evaluated for their physicochemical properties, including appearance, pH, viscosity, spreadability, drug content, solubility enhancement, in vitro drug release, and stability studies. The findings of the study are expected to provide an effective and economical approach for improving the performance of topical crisaborole formulations.**[10,11]**

MATERIALS AND METHODS

Materials

Crisaborole was obtained as a gift sample from a pharmaceutical industry. Propylene glycol, polyethylene glycol (PEG 400), white soft paraffin, liquid paraffin, and other analytical grade

chemicals and solvents used in the study were procured from approved chemical suppliers. Distilled water was used throughout the experimental work.

Pre-formulation Studies

Organoleptic Evaluation

The physical appearance of Crisaborole was examined for color, odor, and physical state by visual inspection.

Determination of Melting Point

The melting point of Crisaborole was determined by the capillary method to assess its purity and identity.

Determination of λmax and Calibration Curve

The maximum absorption wavelength (λmax) of Crisaborole was determined using UV–Visible spectrophotometry by scanning the drug solution in methanol. A calibration curve was prepared at λmax 250 nm using different concentrations, and the absorbance values were recorded to evaluate linearity according to Beer–Lambert's law.

Solubility Studies

Qualitative and quantitative solubility studies of Crisaborole were performed in various solvents including distilled water, methanol, chloroform, propylene glycol, PEG 400, and phosphate buffer pH 7.4. The saturation solubility of the drug in different solvents was determined by preparing saturated solutions and analyzing the drug concentration using UV spectrophotometry.

Preparation of Crisaborole Ointment by Co-solvency Method

Crisaborole ointment was prepared by the fusion and co-solvency technique. The required quantity of paraffin base was melted at approximately 70°C. Propylene glycol was heated separately and added to the molten ointment base with continuous stirring. Crisaborole was dissolved in PEG 400 to obtain a clear drug solution, which was gradually incorporated into the molten base. The mixture was stirred continuously during cooling until a smooth and homogeneous ointment was formed. Different formulations (F1–F6) containing varying concentrations of co-solvents were prepared.

Evaluation of Crisaborole Ointment

Physical Examination

The prepared ointments were visually inspected for color, odor, consistency, and homogeneity.

Determination of pH

The pH of each formulation was measured using a calibrated digital pH meter to ensure compatibility with the skin.

Viscosity Measurement

The viscosity of the prepared formulations was determined using an appropriate viscometer at controlled temperature conditions.

Spreadability Study

The spreadability of ointments was determined by applying a specific amount of formulation between two glass slides and measuring the ease and extent of spreading under an applied weight.

Drug Content Determination

The drug content of each formulation was estimated by dissolving an accurately weighed amount of ointment in a suitable solvent and analyzing the sample using UV–Visible spectrophotometry at 250 nm to ensure uniform distribution of Crisaborole.

Table: Evaluation Parameters of Crisaborole Ointment Formulations.

Table No. 1: ***Evaluation parameters and methods used for characterization of Crisaborole ointment formulations.***

S. No.	Evaluation Parameter	Method/Description
1	**Physical Examination**	The prepared ointment formulations were visually inspected for color, odor, consistency, appearance, and homogeneity to evaluate their physical characteristics.
2	**Determination of pH**	The pH of each ointment formulation was measured using a calibrated digital pH meter to ensure compatibility with the normal skin pH.
3	**Viscosity Measurement**	The viscosity of the formulations was determined using a suitable viscometer under controlled temperature conditions to assess the flow behavior of the ointments.
4	**Spreadability Study**	Spreadability was determined by placing a fixed quantity of ointment between two glass slides and measuring the ease and extent of spreading under an applied weight.
5	**Drug Content Determination**	An accurately weighed amount of ointment was dissolved in a suitable solvent, and the drug content was estimated using UV–Visible spectrophotometry at λmax 250 nm to determine uniform distribution of Crisaborole.

Identification of drug sample by UV Spectroscopy

The λmax of Crisaborole was obtained at 250 nm. This found to be similar as given in the reference[48]. Which shows that drug is pure.TheUVspectrum of crisaborole drug is shown in the fig. 1.

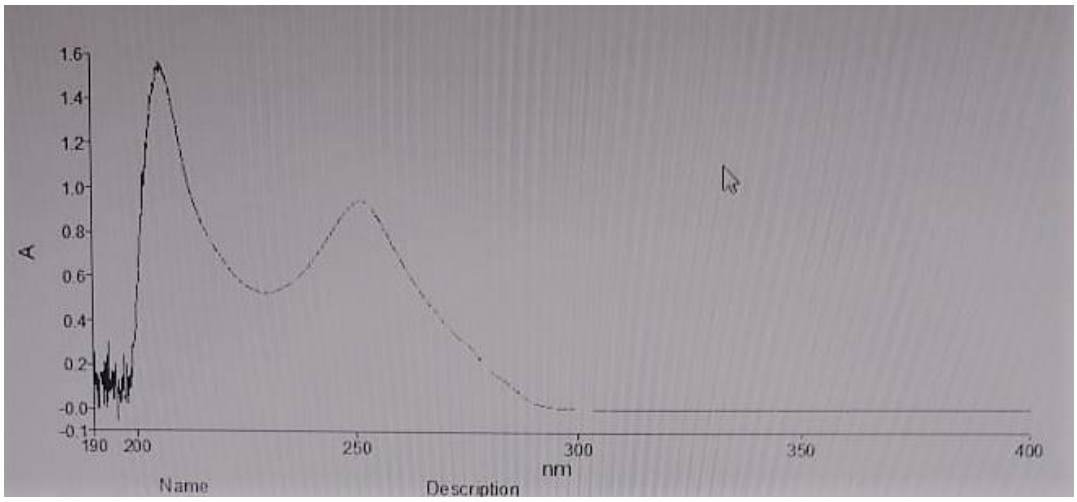


Fig 1: Spectrum of crisaborole by UV Spectroscopy.

e. Preparation of standard Calibration curve of crisaborole in methanol(λmax 250nm)

Calibration curve ofcrisaborolewas prepared in methanol at 250 nm. The absorbance values (mean of three determinations) with their standard deviation at different concentration in the range of 5-50 µg/ml for methanolaretabulated. The drug obeysBeer'sLambert law in the concentration range. Linear regression analysis for all calibration curves of crisaborole is given in Table. So, this equation was used for the calculation of the solubility of the drug in different solvent, drug content and drug release. The calibration curve of crisaborole is shown in fig.5.3.7.

Table: Data of standard calibration curve of crisaborole in methanol.

Concentration(µg/ml)	Absorbance
0	0
5	0.127
10	0.231
15	0.327
20	0.439
25	0.533
30	0.645
35	0.756
40	0.846
45	0.959
50	1.046

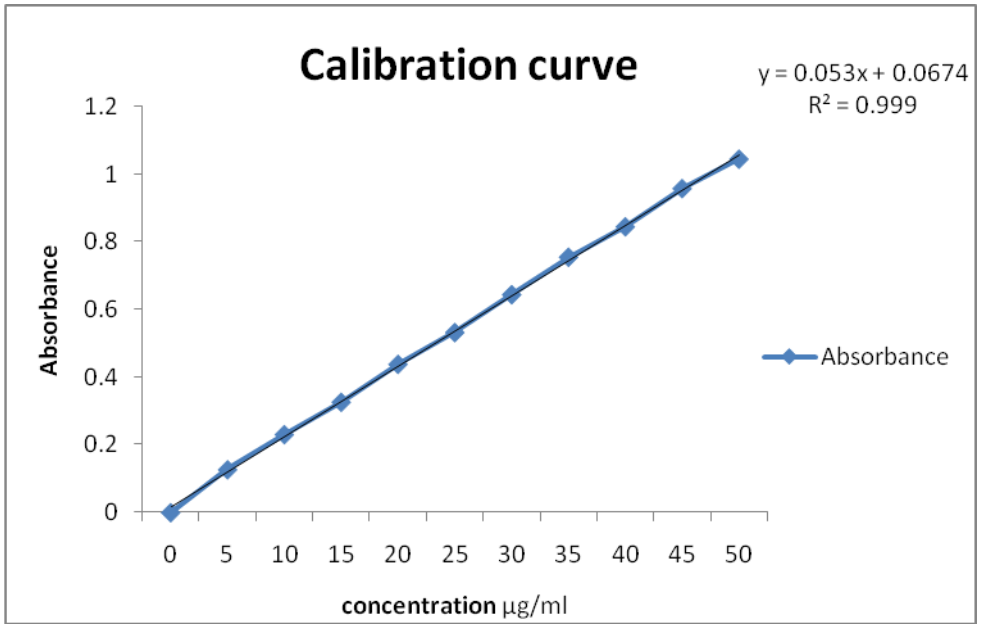


Fig 2: Calibration curve of crisaborole in methanol.

Solubility studies of drug

Solubility studies for the drug crisaborolewereperformed and explained as follow:

1. Qualitative solubility study

Qualitative solubility analysis for drug crisaborole was determined in different solvents. The crisaborole was found to be slightly soluble in methanol, octanol and PEG 400 and soluble in propylene glycol and PEG 400. This shows that drug is soluble only in organic solvents, which shows the lipophilic nature of the drug. The results are found to be similar as given in the reference[49].Results are disclosed in the table 5.3.9.

Table 5.3.7: Qualitative solubility study in various solvents.

S.No	Solvents	Solubility
1.	Water	Insoluble
2.	Methanol	Slightly soluble
3.	Octanol	Slightly soluble
4.	Propylene Glycol	Soluble
5.	PEG	Soluble
6.	Chloroform	Slightly soluble

2. Quantitative solubility study

Quantitative solubility analysis of crisaborole was determined in different solvents. The crisaborole drug was found to be more soluble in Methanol, propylene glycol and PEG 400 and chloroform.This shows that drug is soluble only in organic solvents, which shows the

lipophilic nature of the drug. The results are found to be similar as given in the reference[49].The results are disclosed in table 5.3.10.

Table 5.3.8: Quantitative solubility analysis.

S.no	Solvents	Solubility mg/ml
1.	Water	0.021
2.	Methanol	0.11
3.	Octanol	1.09
4.	Propylene Glycol	2.12
5.	PEG	1.03
6.	Chloroform	0.094

In Vitro Drug Release Study

The in vitro drug release study was carried out using a suitable dissolution apparatus and appropriate dissolution medium. Samples were withdrawn at predetermined time intervals, analyzed spectrophotometrically at 250 nm, and the cumulative percentage drug release was calculated.

Stability Studies

The optimized formulations were subjected to stability studies as per ICH guidelines for a period of two months under different storage conditions. The formulations were periodically evaluated for changes in physical appearance, pH, and drug content to assess their stability.

CONCLUSION

The present study successfully developed Crisaborole has broad-spectrum anti-inflammatory activity by mainly targeting phosphodiesterase 4 (PDE4) enzyme that is a key regulator of inflammatory cytokine production. As this enzyme is expressed in keratinocytes and immune cells, crisaborole mediates an anti-inflammatory effect on almost all inflammatory cells. Topical application of this drug is useful as it potentiates the localization of this drug in the skin and this anti-inflammatory activity is in the low micromolar range.It belongs to class II under BCS and exhibit low and variable oral bioavailability due to its poor aqueous solubility 0.0234 mg/ml. Hence it is necessary to increase the solubility of drug in order to improve to increase bioavailability to show effective pharmacological action. The drug is having poor aqueous solubility 0.0234 mg/ml.Crisaborole is an efficacious drug in the management of skin disease and psoriasis. But the major drawback is its poor aqueous solubility.Moreover, recent studies evidenced its efficacy in patients with skin disease and psoriasis. But it's very low aqueous solubility and poor dissolution can cause formulation problems and limit its

therapeutic application by delaying the rate of absorption and the onset of action. Therefore, improvements in solubility and/or dissolution rate of Crisaborole may be achieved through the preparation of Co-solvency technique.Different solubility enhancement techniques have been developed till present out, nowadays researchers are mainly focusing on novel solubility enhancement technique to improve solubility of drug. Bioavailability of oral preparation is highly depending on the solubility.Co-solvency is a novel and most important method to increase solubility of water insoluble solid drug (BCS Class II) for formulation of semi-solid dosage form. It can enhance dissolution rate as well as bioavailability of drug.Rapid release rate can be obtained and this can be efficiently used for water insoluble/poorly water soluble drugs.The objective of present research work is to enhance the aqueous solubility of poorly water soluble drug Crisaborole using Co-solvency technique.Thepre-formulation study of crisaborole was conducted and λmax was found at 250nm. Melting point was found 1320C. The standard curve of crisaborole was prepared in methanol (λmax 250nm) and r2 value was obtained 0.999, which are shows the the linearity of absorbance and follows beer's lambert law.Organoleptic properties was determined and observed that the crisaborole is white-off crystalline powder, odorless, bitter in taste. Quantitative solubility study shows that the crisaborole is poorly water soluble drug (0.021 mg/ml) and quantitative solubility of crisaborole determined in different solvents and the result were found to be more soluble in methanol(0.11 mg/ml), chloroform(0.094mg/ml), Propylene glycol (2.12mg/ml), PEG 400(1.03mg/ml) and Phosphate buffer 7.4 pH (0.119 mg/ml). Qualitative solubility study shows that the drug is practically insoluble in water and soluble in organic solvents.

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Conflict of Interest

The authors announce that there is no disagreement of interest associated with this research work.

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REFERENCES

1. Amit Kumar Nayak and PrachiPravaPanigrahi Solubility Enhancement of Etoricoxib by Co-solvency Approach International Scholarly Research Network ISRN Physical Chemistry Volume 2012, Article ID 820653, 5 pages doi:10.5402/2012/820653
2. VajirSandip, Vishal Sahu, NileshGhage, Pavan Bang and BukdeBV,Enhancement of Dissolution Rate of Poorly Water Soluble Diclofenac Sodium By Liquisolid Technique International Journal of Pharmaceutical And Chemical Sciences Vol. 1 (3) Jul-Sep 2012
3. Kapadiya N, Singhvi I, Mehta K, Karwani G, and Dhrubo J, "hydrotropy: a promising tool for solubility enhancement: a review." Int. J. D. Dev. Res. 2011, 3(2), 24-30.
4. Praveen C and Pramodkumar S, "Solubility enhancement of hydrophobic drugs using synergistically interacting cyclodextrin and co solvent." Current sci.2007, 92(11), 110-120.
5. Purwa J and Achhrish G, "Solubility enhancement techniques with special emphasis on hydrotrophy." Int. J. Pharm. Prof. Res. 2010, 1(1), 34-45
6. S.P.BhilegaonkarandR.SGaud, Improved Wetting For Improved Solubility and Dissolution of Candesartan Cilexetil, Comparative Study Of Surfactant And Modified Surfactant In Varying Ratios IOSR Journal Of Pharmacy Volume 4, Issue 12 (December 2014), PP. 01-09
7. Kapadiya N, Singhvi I, Mehta K, Karwani G, and Dhrubo J, "hydrotropy: a promising tool for solubility enhancement: a review." Int. J. D. Dev. Res. 2011, 3(2), 24-30
8. Kapadiya N, Singhvi I, Mehta K, Karwani G, and Dhrubo J, "hydrotropy: a promising tool for solubility enhancement: a review." Int. J. D. Dev. Res. 2011, 3(2), 24-30.
9. Sudhir Singh*1, Anand Singh1, Anil Bhandari2, Satish Kumar Sharma1, Sumer Singh1,Dinesh Kumar Formulation and Evaluation of Ointment of Valproic Acid Asian Journal of Pharmaceutical Research and Development 2020; 8(3):246 -251.
10. Pradeep Kumar Bolla 1,2 , Bradley A. Clark 2, Abhishek Juluri 3,Hanumanth Srikanth Cheruvu 4 and JwalaRenukuntla 2 Evaluation of Formulation Parameters on Permeation of Ibuprofen from Topical Formulations Using Strat M® Membrane Pharmaceutics 2020,12,151;doi:10.3390/pharmaceutics12020151
11. AVISH D MARU*, SWAROOP R LAHOTI FORMULATION AND EVALUATION OF OINTMENT CONTAINING SUNFLOWER WAX Asian J Pharm Clin Res, Vol 12, Issue 8, 2019, 115-120