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Brucine Nano-Emulgel Drug Delivery System

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ABSTRACT: *Nanoemulgel is an advanced drug delivery system that combines the advantages of both emulsions and gels, offering controlled drug release for topical applications. Compared to traditional ointments and creams, gels typically enhance drug release due to their hydrophilic nature. Brucine, a well-known anti-inflammatory agent, faces limitations in solubility and systemic toxicity when delivered orally, making topical delivery a preferred alternative.* ***Objectives****: The objective of this study was to develop a Brucine-loaded nanoemulgel for enhanced solubility, skin penetration, and sustained topical delivery, and to improve therapeutic efficacy while minimizing systemic side effects and safe topical administration.* ***Methods****: Nano emulsions of Brucine were prepared by ultra sonication method as described by Kaushal Kumar with minor modifications subsequently characterized for their Self emulsification time, Particle size, Zeta potential, in vitro drug release study. These SNEDDS were integrated into an Carbapol 940 gel base. The optimized formulation underwent comprehensive evaluation, including physical appearance, drug content, swelling index, spreadability, viscosity, homogeneity, rheology, skin irritation, and in vivo drug release studies*

KEYWORDS: *SNEDDS, Nanoemulgel, Brucine, Skin irritation study.*

1. INTRODUCTION

Brucine, a bioactive alkaloid derived from *Strychnos nux-vomica*, is recognized for its potent anti-inflammatory and analgesic effects. However, its clinical use is limited due to poor water solubility and potential systemic toxicity when administered orally[1]. To overcome these challenges, topical drug delivery offers a safer alternative by enabling localized action while minimizing systemic exposure. Nanoemulgel systems, which merge the benefits of nanoemulsions and gels, have emerged as effective carriers for poorly soluble drugs. They enhance drug penetration through the skin, provide sustained release, and improve patient compliance. In this context, the present study aims to develop and evaluate a Brucine-loaded nanoemulgel for topical application, utilizing suitable oils,surfactants, and gelling agents to optimize drug delivery and therapeutic efficacy[2,3].

MATERIALS & METHODS

Materials

Brucine, from Alican pharmaceutical Pvt.. Tween 80, PEG 400,Arachis oil was parches arochemical. Carbapol 940, TEA,Propyl paraben, Methyl paraben, Gycerin, was parches vajrachem.

Methods

Nano emulsions of Brucine were prepared by ultra sonication method as described by Kaushal Kumar with minor modifications. In this method preselected quantity of the drug (Brucine) was separately dissolved in accurately measured quantity of each oily phase. On the basis of solubility studies 2chosen oily phases were-Arachis oil, Sesam oil, Castor oil. Chosen surfactant was Tween 80, Tween 20 and co-surfactant Labrafil M2125, PEG400. For different formulations varying quantities of co-surfactant were taken in beaker and mixed with drug containing oily phase under continuous stirring. That's how oil phase was prepared. For the preparation of aqueous phase Tween 80 was dissolved in distilled water. Aqueous phase was placed on the magnetic stirrer and then the oil phase was added to it drop wise with continuous stirring 500 rpm for 15 minutes. The solution was then ultrasonicated for 20 min[4,5].

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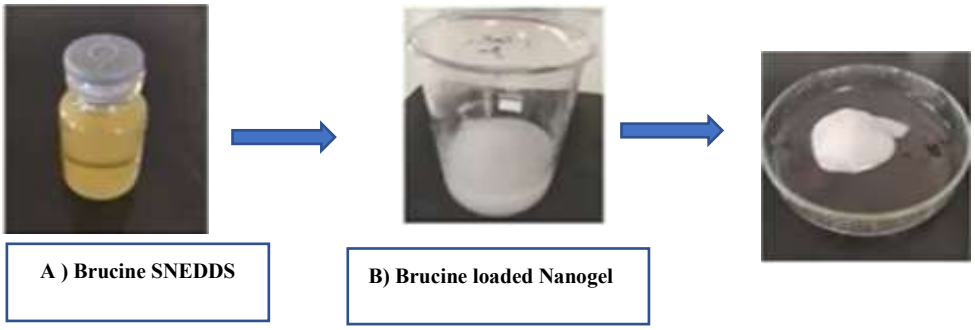


Fig.1: Optimized formulation and Evaluation of SNEDDS convert in to Nanoemulgel

The prepared nanogel was evaluated for various parameters to uncover whether the final optimized Brucine nanoemulgel was suitable for topical application.

Design of Experiments

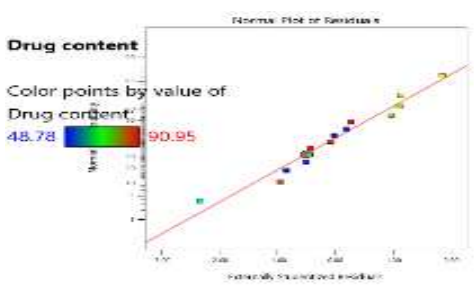
Brucine SNEDDS-loaded Nanoemulgel were formulated by the box-bhenkan models. The effect of Carbopol 934, TEA concentration on the responses such as % drug content were statistically analyzed by using design expert software and the results were shows in tables[6,7].

Brucine loaded Nanoemulgel formulated by the box- bhenkan models

Table.1: Brucine loaded Nanoemulgel formulated by the box- bhenkan models

Std	Run	Factor 1	Factor 2	Factor 3	Response 1
		A: Carbapol 940	B: TEA	C: Water	Drug content %
1	1	1.5	4	10	49.27
13	2	1.5	2.5	30	60.78
9	3	1.5	1	10	48.78
4	4	2	4	30	75.25
3	5	1	4	30	65.86
11	6	1.5	1	50	88.45
12	7	1.5	4	50	89.14
7	8	1	2.5	50	90.95
2	9	2	1	30	79.23
6	10	2	2.5	10	50.12
8	11	2	2.5	50	90.56
1	12	1	1	30	76.23
5	13	1	2.5	10	50.45
14	14	1.5	2.5	30	79.85

ANOVA for Quadratic model



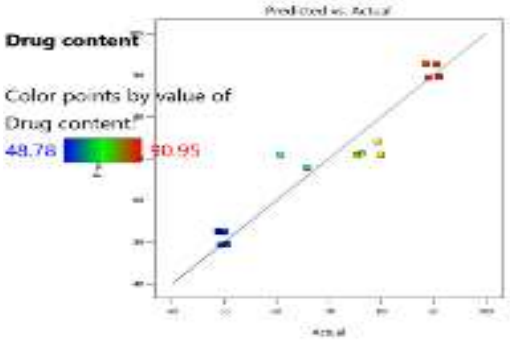


Fig.2: ANOVA for Quadratic model for Drug content %

2. Characterization

Evaluation of nanoemulsion

Gels were evaluated for their clarity. pH, Viscosity, Spread ability, in vitro and by using standard procedure. All studies were carried out in triplicate and average values along with standard deviation were reported.

Physical appearance

The prepared nanoemulgel formulations are inspected visually for their colour, and phase separation and consistency.

Drug content

Nanoemulsion based gel equivalent to 2.0% brucine was taken in 100ml volumetric flask containing 10ml methanol and stireed for 30min. then appropriate dilutions were made. The resultant solution was filtered through 0.45um membrane filter. The absorbance of the solution was measured spectrophotometrically at 265nm[13,14].

Determination of pH

2.5g of gel was accurately weighed and dispersed in 25 ml. of distilled water. The pH of dispersion was measured by using digital pH meter[8].

Homogeneity

All the developed gels were tested for hommogeneity by visual inspection after the gels have been set in the container for their appearance and presence of any aggregate[9].

Viscosity

Viscosity of the gel was dtermined using a bookfield digital viscometer. It is an instrument used for measuring the viscosity of liquids. The instrument measures the shearing stress on spindle rotating at adefinite, constant thixotropic nature speed while immersed in the sample. The degree of spindle lag is indicated on a rotating dial. This reading is muliplied by a conversion factor based on spindle size and rotational speed, gives a value for viscocity in centi[oises. By taking measurements at different rotational speeds, an indication of the degree of thixotrophy of the sample is obtained[10].

Spreadability:

Spreadability is a term expressed to denote the extent of area to which the gel readily spreads on application to skin. The therapeutic efficiency of a formulation also depends on its spreading value. A special apparatus has been designed to study the spreadability of formulations. Spreadability is expressed in terms of time in seconds taken by two slides to slip oil from formulation, placed between, under the application of a certain load lesser the time taken for the separation of the two solids better spreadability[11].

Homogeneity and pH

The prepared nanoemulgel formulation was evauated for homogeneity, which was visually inspected for clarity and colour.

The pH of the formulation was found to be 6.0 as determined by the pH meter.

Table 2: Characterization of Homogeneity and pH

Formulation	Homogeneity	pH
F2	Homogenous	6.8
F4	Homogenous	6.7
F10	Homogenous	5.5
F11	**Homogenous**	**6.0**
F14	Homogenous	6.8
F16	Homogenous	6.6

Viscosity and spreadability

The viscosity and spreadability was found to be 3367.2412cps and 16.2 respectively table- indicating ease of application.

Table 3: Characterization of Viscosity and Spreadability

Formulation	Viscosity	Spreadability
F2	686.8913	18.9
F4	4788.1223	25.2
F11	**3367.2412**	**16.2**
F14	6932.9574	18.4
F14	4783.1845	33.1
F16	6123.1621	17.4

Drug permeation study of novel formulation of Brucine using diffusion cell

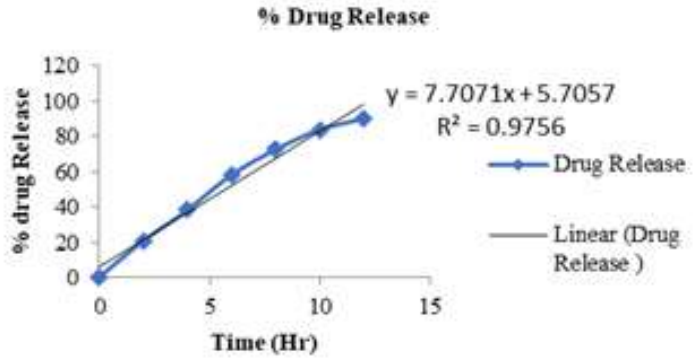


Fig.3. Drug release at various time intervals

Skin Irritation study of novel formulation of Brucine in New Zeland white Rabbits

Table 4: Confirmatory test

Animal 2 (2nd Rabbit) removal of patch after 4 hours				
	Erythema and Eschar Formation	**Scores**	**Edema formation**	**Scores**
1	No erythema	0	No oedema	0
2	Very slight erythema (barely perceptible)	0	Very slight oedema (barely perceptible)	0
3	Well defined erythema	0	Slight oedema (edges of area welldefined by definite raising)	0
4	Moderate to severe erythema	0	Moderate oedema (raisedapproximatel y 1 mm)	0
5	Severe erythema (beef redness) to eschar formation preventing grading of erythema	0	Severe oedema (raised more than 1 mm and extending beyond area of exposure)	0

Interpretation of the results and conclusion

No lesions were observed after any patch removal and throughout the observation period of 7 days. The details photographs have been presented in Figure 1. It was observed that no skin irritation or any lesions

due to the test formulation of Brucine were seen at the site of application to the rabbit skin. Further, after removal of the 2nd patch after 1 hour and the 3rd patch after 4 hours did not exhibit any sign of irritation, skin reactions, or erythema and edema. In addition, observations continued for up to 72 hours periodically for any possible effects. Thus, based on the aforementioned finding of the present study, it can be concluded that the test formulation of Brucine was found to be non-irritant or non-corrosive (no skin irritation) to the rabbit skin[15].

Photographs of test site after removal of patches from rabbit skin.

Fig.4 : Photographs of test site after removal or patches from rabbit skin

Histopathology

Fig.5: Histopathology study

Analysis of the toxic potential of a chemical agent on target organs is incomplete without gross and histopathological evaluation. Histopathological examination of selected organs of both treated and control animals showed normal architecture, suggesting no abnormal findings in the histological evaluation.

Stability Study

The appearance, phase separation, pH, and % transmittance of formulated nanogel were observed to be consistent with no. Signs of separation and deterioration over 90 days. The results indicated that the optimized formulation was found to be physically and chemically stable during the study period [16]

Stability studies of optimized Self-Nanoemulsion gel at different time intervals and temperature/humidity conditions.

Table 5: Physical appearance of Nanoemulgel at 4°C and room temperature

Parameter	4°C			RT		
	0 day	30 days	90 days	0 day	30 days	90 days
Physical Appearance	Milky white gel	Milky white gel	Milky white gel	Milky white gel	Redispersible flocculation	Colour change

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Fig.6: Physical appearance of Nanoemulgel after 90 days

Stability studies of optimized Self-Nanoemulgel at different time intervals and temperature/humidity conditions.

Table.6: Summary of stability testing of Nanoemulgel at 4°C and RT for 0, 30 & 90 days

parameters	(4° C)			RT		
	0 Day	30 Days	90 Days	0 Day	30 Days	90 Days
Physical appearance(Colour changes)	Milky white gel	Milky white gel	Milky white gel	Milky white gel	Redispersible flocculation	Redispersible flocculation and colour change
Drug Content	92..63	93.23	93.96	92..63	89.23	88.12
pH	5.9	5.9	5.8	5.9	6.8	7.0

The stability study of Brucine-loaded Nanoemulgel showed that Nanoemulgel stored at 4°C preserved their physical properties, Drug content and pH with minimal changes. In contrast, nanoemulgel stored at room temperature caused particle aggregation, reduced Drug content and change pH, emphasizing the need for refrigeration to maintain stability[17,18].

DISCUSSIONS

Brucine-loaded nanoemulgel combines the benefits of a nanoemulsion and gel base to enhance the topical delivery of Brucine, a poorly water-soluble alkaloid known for its anti-inflammatory and analgesic properties. The nanoemulsion improves drug solubility, skin penetration, and stability, while the gel base offers better patient compliance due to its non-greasy texture and ease of application. This dual system allows sustained drug release, targeted delivery, and minimizes systemic side effects. Overall, the nanoemulgel formulation is a promising approach for effective topical delivery of Brucine in inflammatory conditions.

Conclusion

Prepared Brucine SNEDDS (Self-Nanoemulsifying Drug Delivery Systems) successfully demonstrated their potential as an effective drug delivery system for Brucine, offering enhanced stability and improved therapeutic properties. The SNEDDS formulation exhibited favorable physicochemical characteristics, including optimal particle size and high encapsulation efficiency, which contributing to prolonged release and improved bioavailability. Stability studies revealed that Brucine SNEDDS maintained their integrity and efficacy over time at 4^0C.Additionally, Skin Permeation study indicated that Brucine Nano emulgel maintained its efficacy while potentially reducing toxicity. The formulation also showed promising results in skin irritation teste and histopathological studies, suggesting that brucine nanoemulgel is a viable and safe

option for topical drug delivery. This research higlights the potential of brucine Nanoemulgel as an advanced delivery system that significantly enhances the therapeutic properties of Brucine. Future research should focus on in vivo studies to validate these in vitro findings, investigate the molecular mechanisms behind the enhanced efficacy, and explore the possibility of combining Brucine Nanoemulgel with other therapeutic agents or employing targeted delivery strategies to maximize its therapeutic benefits in the treatment of various diseases.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

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Data availability

Data will be made available on request.

Disclosure

The authors report no conflicts of interest in this work.

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