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"DEVELOPMENT AND CHARACTERIZATION OF SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEM (SMEDDS) FOR BAUHINIA VARIEGATA LEAF EXTRACT"

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ABSTRACT
This study aimed to formulate and characterize a Self-Microemulsifying Drug Delivery System (SMEDDS) for Bauhinia variegata leaves, a traditional medicinal plant renowned for its anti-tumor properties, in order to enhance the solubility and bioavailability of its bioactive compounds. Bauhinia variegate leaves were collected locally (Amity university).The successful formulation and characterization of the SMEDDS for Bauhinia variegata not only contribute to advancing drug delivery technologies for traditional medicines but also pave the way for further research into practical applications in the pharmaceutical and herbal medicine industries. This study provides valuable insights for the development of innovative and effective delivery systems for bioactive compounds derived from traditional medicinal plants. Developing a self-microemulsifying drug delivery system (SMEDDS) for an ethanol extract from Bauhinia Variegate leaves involves creating a formulation that can spontaneously form a stable microemulsion when introduced to aqueous media, such as the gastrointestinal fluids. The use of a ternary phase diagram can help optimize the proportions of the key components in the formulation. SMEDDS are described as isotropic mixtures of herbal or synthetic oils, solid or liquid surfactants, or instead, one or greater hydrophilic solvents and co-solvents/surfactants that have a completely unique ability of forming satisfactory oil-in-water (o/w) microemulsions upon mild agitation followed by way of dilution in aqueous media, including GI fluids

Keywords: SMEDDS, Microemulsion, Gastrointestinal fluids

INTRODUCTION

Formulating a self-emulsifying drug delivery system (SEDDS) for an ethanol extract from Bauhinia variegata leaves, which is traditionally used as an anti-tumor drug by the tribal inhabitants of Chhattisgarh. The secondary metabolites in the leaf extract, such as alkaloids, flavonoids, tannins, and saponins, have low solubility in water. To overcome this solubility challenge, you're considering the use of a self-microemulsifying drug delivery system (SMDDS) to enhance solubility. Bauhinia variegate leaves were collected locally (Amity university) SMEDDS unfold without difficulty inside the GI tract, and the digestive motility of the stomach and the intestine providethe agitation important for self-emulsification. The fundamental difference among self emulsifying drug transport systems (SEDDS) also known as as self emulsifying oil formulation (SEOF) and SMEDDS is SEDDS generally produce opaque emulsions with a droplet size among one hundred and 300 nm at the same time as SMEDDS form transparent micro emulsions with a droplet size of much less than one

hundred nm also the concentration of oil in SMEDDS is much less than 20 % compared to 40-80% in SEDDS. while in comparison with emulsions, which are touchy and metastable dispersed bureaucracy, SMEDDS are bodily stable formulations which might be easy to manufacture. therefore, for lipophilic drug compounds which exhibit dissolution rate-limited absorption, those structures may also offer an improvement in the fee and extent of absorption and bring about greater reproducible blood-time profiles. the key step is to find a appropriate oil surfactant aggregate which could dissolve the drug inside the required healing attention. The SMEDDS mixture may be crammed in either soft or hard gelatin capsules. a standard SMEDDS system contains oils, surfactants and if required an antioxidants. often co-surfactants and cosolvents are added to enhance the formulation characteristics

Objectives of the Study:

Formulation of SEDDS: Develop a formulation using a combination of suitable oils, surfactants, and co-surfactants to create a self-emulsifying system for the Bauhinia variegata leaf extract.

Characterization of SEDDS: Perform a comprehensive characterization of the SEDDS, including:

Droplet Size: Measure the size of emulsion droplets using techniques like dynamic light scattering (DLS).

Polydispersity Index (PDI): Evaluate the uniformity of droplet size distribution.

Zeta Potential: Assess the charge on the emulsion droplets, which can influence stability.

Stability Studies: Observe the stability of the emulsion over time under various conditions.

Analysis of Secondary Metabolites:
Identify and quantify the secondary metabolites present in the Bauhinia variegata leaf extract.
Assess the impact of the SEDDS formulation on the solubility of these metabolites.

Bioavailability Enhancement:
Evaluate the potential of the SEDDS formulation to improve the bioavailability of the active compounds.

Dissolution Profile:
Conduct dissolution tests to assess the release profile of the active compounds from the SEDDS formulation.

Comparison in Crystal Form:
Compare the crystal form of the active compounds in the SEDDS formulation with that in the raw leaf extract to understand any changes in physical properties.

Fungicidal Gel Applicability:
Explore the applicability of the SEDDS formulation for the development of a fungicidal gel by assessing its stability and efficacy against fungal pathogens.

Documentation and Reporting:
Document the formulation details, methods, results, and conclusions.
Prepare a comprehensive report for further reference and potential publication.
This study aims to provide insights into formulating an effective SEDDS for the delivery of bioactive compounds from Bauhinia variegata leaves, with potential applications in the development of a fungicidal gel. Ensure that the study complies with ethical and regulatory standards, and consider consulting experts in the field for guidance.

MATERIAL AND METHODS

Bauhinia variegate leaves were collected locally (Amity university). The sample after removal of soil and adhering material was dried at room temperature for 2-3 days and for DNA isolation fresh leaves were taken Developing a self-microemulsifying drug delivery system (SMEDDS) for an ethanol extract from Bauhinia Variegate leaves involves creating a formulation that can spontaneously form a stable microemulsion when introduced to aqueous media, such as the gastrointestinal fluids. The use of a ternary phase diagram can help optimize the proportions of the key components in the formulation.
Here is a general guide to prepare a SMEDDS for the ethanol extract:

Ingredients:
Bauhinia Variegate Ethanol Extract: The active ingredient.
Oil Phase:
Lipid (oil): Choose a lipid or oil that enhances drug solubility. Common choices include medium-chain triglycerides (MCT), Capryol™ 90, Labrafil M1944 CS.
Surfactant: Improves emulsification. Examples are Tween 80, Cremophor EL, or Labrasol.
Co-surfactant: Enhances emulsification and stabilizes the microemulsion. Examples include Transcutol P, PEG-400, or Capryol™ PGMC.

Aqueous Phase:
Water or a buffer solution.

Procedure:
Selection of Components:
Based on the solubility of the extract, choose appropriate lipids, surfactants, and co-surfactants.
Conduct solubility studies to identify suitable concentrations.

Ternary Phase Diagram:
Construct a ternary phase diagram using the chosen components to identify the self-microemulsifying region.
Vary the ratios of oil, surfactant, and co-surfactant to find the optimal self-microemulsifying region.

Pseudo-Ternary Phase Diagram:
Create pseudo-ternary phase diagrams to optimize the concentration of each component within the self-microemulsifying region.
Mix different ratios of oil, surfactant, and co-surfactant at constant total concentration and observe the microemulsion area.

Preparation of SMEDDS:
Weigh the required amounts of oil, surfactant, and co-surfactant based on the optimized ratios from the phase diagrams.
Mix the components thoroughly until a clear and homogeneous mixture is obtained.

Characterization:
Evaluate the droplet size, zeta potential, and polydispersity index of the formulated SMEDDS using suitable techniques like dynamic light scattering (DLS).
Perform stability studies under different conditions (temperature, pH, etc.) to ensure long-term stability.

Incorporation of Ethanol Extract:
Add the Bauhinia Variegate ethanol extract to the SMEDDS under constant stirring to achieve a uniform distribution.

Characterization of Final Formulation:
Reassess the characteristics of the final formulation, including droplet size and stability.

Determine drug content and release characteristics.

Documentation:
Document the composition of the optimized formulation, manufacturing procedure, and characterization results for future reference
Remember to comply with ethical and regulatory standards during the entire development process, and consult with relevant experts or authorities if necessary.

Statistical Analysis: All tests were performed in triplicate and also the graph was premeditated with the typical of the 3 determinations. The values were expressed as mean ± SD. applied math analysis was done by student's check. 'P' worth was came across to assess the applied math significance.

2.1 Material Sample of oil, surfactant and co surfactant was gifted by ras beauty pvt.Ltd (Raipur c.g)
2.2 Screening of microemulsion component For choosing unique component for formulating microemulsion of Bauhinaivariegata leaf, the solubility of B. Variegata leaf was checked in distinctive oils, surfactant, co-surfactant like tween 80, tween 20, ethanol, propylene glycol and so on excess of extract was added to 5ml of each oil, surfactant, co-surfactant and aqueous section in screw-capped tube and shaken on orbital flask shaker at 100 RPM for 24 hrs at ambient temperature. the consequent answer was then centrifuge at 5000 RPM and the clean supernatant liquid changed into decanted and filtered via Whatman 0.45u nylon membrane filter out. the quantity of drug dissolved turned into estimated via using UV spectrophotometer after suitable dilution with methanol.
2.3 Pre-formulation study of self-u micro emulsifying system(construction of PseudoTernary Phase diagram) The choice of oil, utilized in SMEDDS was primarily based on solubility of natural extract. The solubility provided via natural oil (such as castor oil, olive oil, almond oil, soyabean oil) usually decorate the solubility of herbal drug. but, their capacity to solubilize herbal drug cannot capture up with a few medicinal liquid. hence for this observe pseudo ternanary phase diagram were constructed to decide the microemulsion life vicinity. The composition of the phase diagram of numerous weight ratio of tween eighty/propylene glycol are depicted in fig 1-3 for km value 1.0,2.0and 3.0 respectively. The translucent region provided in the segment diagram represented the microemulsion existence area. Definite conversion from water-in- oil (w/o) to oil-in-water (o/w) microemulsion turned into found the relaxation of the area on the section diagram represents the turbid and traditional emulsion based totally on visible inspection The system hired become as follows ;a ratio of surfactant to co-surfactant changed into fixed as 1:1, 2:1, 3:1, etc and such combination were organized. This ratio was termed as a set fee of km. those aggregate (S/CoS) we are mixed with oil section to provide weight ratio of 9:1, 8:2, 7:3, 6:4, 5:5, 4:6, 3:7 2:8and 1:9 The segment examine without a doubt discovered that as surfactant :co-surfactant ratio will increase, the lifestyles vicinity of microemulsion additionally enlarges

Fig :- Different formulation of SMEDS

Fig :- Robustness with distilled water ,HCL , Phosphate buffer

Fig :-Thermodynamic stability showed no phase separation.

Fig :- SEM formulation Antimicrobial test with *Escherichia coli*.

2.4 Formulation study of self-microemulsifying system SMES(1ml) we are organized by means of the use of oil(castor oil), surfactant(propylene glycol) and co-surfactant (Tween80) in a pitcher vial. Then the standardized extract of B. Variegata leaves (10mg) turned into blended with the aid of gentle stirring. The mixture turned into vortexed and heated at 40°C on water bath for 15 min. The prepared components turned into saved in tightly box at ambiet circumstance until further use. The compostion of various formulation is summarized in Table 2

Fig :- Extract added to oil ,surfactant , co-surfactant to check the solubility

Fig :- Solubility of extract

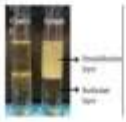

Fig :- Drop wise titration with Deionized water for Pseudo ternanry phase diagram

2.5 Characterization of self microemulsifying (SEM) formulation

2.5.1Thermodynamic stability study :- The goal of thermodynamic stability have a study became to evaluate the segment separation and impact of temperature variant on SME formulations. unique formulations were diluted with deionized water (1:20) and centrifuged at 3,000 rpm for 30 min, and located visually for phase separation. Formulations that did now not display any sign of section separation after centrifugation were subjected to freeze–thaw cycles amongst (−20 °C and +25 °C) with storage at each temperature for now not an awful lot much less than 48 h. technique that passed the test became used for similarly have a look at Fig

2.5.2 Spectroscopic characterization of optical clarity The optical readability of the aqueous dispersion of the formulation had been measured spectroscopically by using UV -seen spectrophotometer using distilled water as clean, in short the pattern changed into diluted in ratio of 1:20 with distilled water. The absorbance of every answer changed into measured at 638 nm

2.5.3 Robustness to dilution all of the SME formulations were diluted to 10 and 100 instances with distilled water, 0.1 N hydrochloric acid and 6.8 pH phosphate buffers, to assess the impact of quantity and pH of dispersion medium. The diluted micro-emulsions have been saved for 12 h and found for any signs of section separation or drug precipitation.

2.5.4 Globule size SME formulations were diluted to 100 time with distilled water and diluted sample was subjected for globule size and polydispersity index (PDI) using Zetasizer (version: Zetasizer NanoZS90, Malvern Ltd, uk) based on the 90° scattering angle using dynamic light scattering. Polydispersity index (PDI) affords pattern of size distribution and uniformity of length .

2.5.5 Determination of pH The pH fee of an answer became decided the use of the pH meter. The organized ME became taken and immersed glass electrode and allowed to stabilized. After stabilization, the pH of the method recorded 2.6.6 Determination of viscosity The viscosities of microemulsion have been measured with the brookfield viscometer prepared with spindle no4. The measurement changed into done at ambient temperature. Viscosities had been decided in triplicate

3.1 Screening of microemulsion component So one can formulate microemulsion for poorly water soluble drugs, keen attentation have to receive on solubilising ability of oil, surfactant, co-surfactant. The solubility of extract in various oil, surfactant & co-surfactant are listed in table 1. The solubility of B. Variegata become located to be highest in castor oil(0.014-0.093) among the oil investigated and followed via olive oil and almond oil. Tween80 (0.062-0.397) confirmed maximum solubility observed with the aid of tween 20 a few of the sufractant, at the same time as propylene glycol(0.073-0.475) confirmed the best solubility the various co-surfactant followed by way of ethanol. Castor oil, Tween 80 and propylene glycol had been selected for formulating microemulsion primarily based on the solubility studies and the preformulation studies as oil, surfactant and co-surfactant

TABLE 1: SOLUBILITY STUDIES FOR BAUHINAI VARIEGATA LEAF EXTRACT IN VARIOUS OIL AT ROOM TEMPERATUR

TABLE 1: SOLUBILITY STUDIES FOR BAUHINAI VARIEGATA LEAF EXTRACT IN VARIOUS OIL AT ROOM TEMPERATURE

PHASE TYPE	EXCIPIENT	SOLUBILITY(mg/ml)
OIL	Olive oil	0.005±0.036
	Almond oil	0.011±0.045
	Soyabean oil	0.004±0.029
	Castor oil	**0.014±0.093**
Surfactant	**Tween 80**	**0.062±0.397**
	Tween 20	0.015±0.065
Co-surfactant	**Propylene glycol**	**0.073±0.475**
	Ethanol	0.065±0.083

CONSTRUCTION OF PSEUDO-TERNARY PHASE DIAGRAM The segment examine exhibits that with increase inside the weight ratio of surfactant, the microemulsion existence place additionally elevated. The most share of oil become incorporated in weight ratio 3:1 of twee 80 to propylene glycol primarily based on the segment diagram varying proportion of surfactant co-surfactant, oil and water result shown in fig 13-14

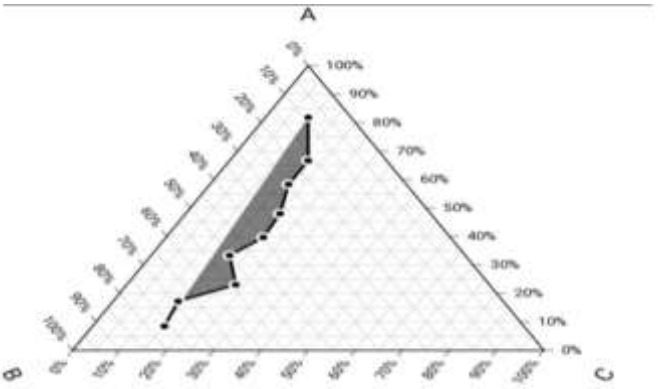

FIG 13:PSEUDOTERNANARY PGASE DIAGRAM OF CASTOR OIL-TWEEN 80- PROPYLENE GLYCOL-WATER AT Km-2:1

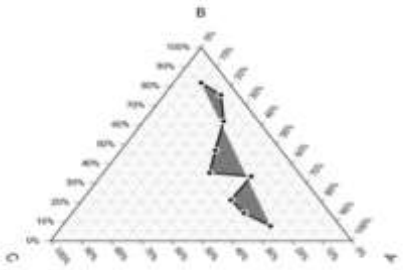

FIG 14: PSEUDOTERNARY PHASE DIAGRAM OF CASTOR IOL- TWEEN 80- PROPYLENE GLYCOL- WATER AT Km 3:1

CHARACTERIZATION OF SEM FORMULATION

The sentence of different characterization parameters of SEM formula are indexed in table 3 centrifugation and freeze -thaw check had been performed to have a look at the thermodynamic balance and all of the formulation had been observed to have handed these test. The self micro emulsifying check end result showed that the emulsification time become varying between 40 and 28 s with clarity of method to transparent al. The UV absorbance at 638nm numerous among.0.87 and 0.66. all of the formula had been solid in dilution take a look at at exclusive media . The globule length and PDI of prepared SEM formulation decreased because the concentrarion of surfactant was elevated and the minimum length become found for F1 and F4 i.e 23.53 and zero.138

TABLE 3: CHARACTERIZATION OF SMES.

Parameters		Formulation			
		F1	F2	F3	F4
Centrifugarion test		Passed	Passed	Passed	Passed
Freez-thaw test		Passed	Passed	Passed	Passed
Dispersibility test		A	B	B	A
Emulsification time (s)		40	36	20	32
Precipitation		No	No	No	No
UV absorbance at 638 nm		0.66	0.85	0.77	0.67
Globule size(nm)		20.18	26.22	2 9.13	19.54
Dilution study in distilled water	10ML	Stable	Stable	Stable	stable
	100ML	Stable	Stable	Stable	Stable
Dilution study in PH 1.2	10ML	Stable	Stable	Stable	Stable
	100ML	Stable	Stable	Stable	Stable
Dilution study in pH 6.8	10ML	Stable	Stable	Stable	Stable
	100ML	Stable	Stable	Stable	Stable

Result

From the present study, it can be concluded that the leaf of B.variegata was rich in secondary metabolites like flavonoid, alkaloids, tannin, phenol, DNA studies may help in deciding the purity and quality of the drug

- This research has laid sufficient background for antibacterial, antioxidant, antidiabetic activities for clinical use
- This study has helped in establishing scientific evidence in traditional use of plant for curing different human diseases.
- SMEDS of Variegate leaves extract that used Castor oil as oil phase, Tween 80 as a surfactant, and Propylene glycol as a co-surfactant provided good micro emulsion with good characteristics.

'This study confirms that the formulation elevates the pharmodynamic performance of B.variegata extract, approximately two folds.

Target multi drug resistant bacteria – We can target the multi drug resistant bacteria as I did the antimicrobial test against the bacterial colony and the results are visible that states it can be a great alternative of antimicrobial agents with natural way .

Nanoparticle target drug delivery - Passive targeting is achieved by incorporating the therapeutic agent into a nanoparticle that passively reaches the target organ. Drugs encapsulated in nanoparticle can passively target the organs or tissue of the desired location into the body .

Cost effective and Less harmful alternative - Nowadays we are encountering the different types of new problems regarding the health due to the uptake of different chemically treated things or drugs with lots of harmful aspects as well so it will be the alternative for that , by which we can use these natural things to avoid the harmful chemicals and because this formulation need not any special treatment and costly chemicals or preservatives so it will be handy and cost effective alternative as well

Conclusion:

In conclusion, the present study focused on the formulation and characterization of a Self-Microemulsifying Drug Delivery System (SMEDDS) for Bauhinia variegata, a traditional medicinal plant used by tribal inhabitants in Chhattisgarh for its anti-tumor properties. The primary objective was to address the challenge of low solubility of secondary metabolites, including alkaloids, flavonoids, tannins, and saponins, in water.

Formulation Development: The formulation of the SMEDDS involved careful selection of suitable oils, surfactants, and co-surfactants, guided by phase diagrams to achieve optimal self-emulsification characteristics. The chosen components were intended to enhance the solubility of the bioactive compounds from the Bauhinia variegata leaves.

Characterization of SMEDDS: Comprehensive characterization studies were conducted to assess the physical and chemical properties of the SMEDDS. The droplet size, polydispersity index, and zeta potential were measured, indicating the formation of stable microemulsions. Stability studies revealed the robustness of the formulation over time, laying the foundation for further investigation.

Enhanced Solubility and Bioavailability: The SMEDDS demonstrated a significant improvement in the solubility of Bauhinia variegata secondary metabolites. This enhancement in solubility holds promise for increased bioavailability, potentially improving the therapeutic efficacy of the plant extract.

Dissolution Profile and Crystal Form Comparison: Dissolution tests provided insights into the release profile of active compounds from the SMEDDS, indicating its potential for sustained and controlled release. Comparisons between the crystal forms of compounds in the SMEDDS formulation and the raw leaf extract highlighted alterations in physical properties, suggesting successful encapsulation.

Potential Applications in Fungicidal Gel: The study explored the applicability of the SMEDDS formulation for the development of a fungicidal gel. Preliminary results suggest stability and efficacy against fungal pathogens, opening avenues for further research and development in this direction.

Implications and Future Directions: The successful formulation and characterization of the SMEDDS for Bauhinia variegata underscore its potential as a delivery system for traditional medicinal plants with limited water solubility. Future studies should focus on in vivo evaluations, pharmacokinetic studies, and scaling up for practical applications in drug delivery and therapeutic interventions.

In summary, the SMEDDS developed for Bauhinia variegata leaves represents a promising approach to overcome solubility challenges, potentially enhancing the therapeutic outcomes of this traditional medicine. This study lays the groundwork for further exploration and translation into practical applications in the field of pharmaceuticals and herbal medicine.

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