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FORMULATION AND EVALUATION OF SOLID LIPID NANOPARTICLE OF HERBAL PLANT EXTRACT AND ITS ANTIMICROBIAL ACTIVITY

Jayant Prakash[1], Pinky Singh[2], Naveen Gupta[3], Dharmendra Singh Rajput[4]

[1]Student-Patel College of Pharmacy, Madhyanchal Professional University, Bhopal (M.P)

[2]Associate Professor- Patel College of Pharmacy, Madhyanchal Professional University, Bhopal (M.P)

[3]Dean- Patel College of Pharmacy, Madhyanchal Professional University, Bhopal (M.P)

[4] Head of Department- Patel College of Pharmacy, Madhyanchal Professional University, Bhopal (M.P)

Abstract:

The present research aimed to formulate and evaluate solid lipid nanoparticles (SLNs) loaded with the plant extract of Ixora coccinea, focusing on their antimicrobial activity. Preliminary phytochemical screening confirmed the presence of alkaloids, flavonoids, phenols, tannins, saponins, and glycosides, while quantitative analysis indicated high levels of phenolic and flavonoid compounds, known contributors to antimicrobial and antioxidant activity. The organoleptic assessment of the extract revealed a reddish-brown color, offensive odor, and a reddish-brown semisolid appearance. Particle size analysis using a Malvern Zeta Sizer demonstrated that the drug-loaded SLNs had an average size ranging from 51.89 to 103.97 nm, which falls within the nanometer range required for improved bioavailability and cellular uptake. Zeta potential analysis, used to predict the stability of colloidal dispersions, showed values between –11.7 mV and –22.2 mV, indicating acceptable stability of the formulations. Scanning Electron Microscopy (SEM) confirmed the spherical shape, smooth surface, and porous nature of the nanoparticles, further supporting their stability and uniformity. Accelerated stability studies conducted under conditions of 40 °C ± 2 °C/70% ± 5% RH and 25 °C ± 2 °C/60% ± 5% RH for three months demonstrated that the formulation remained chemically and physically stable. Antibacterial assays conducted using the well diffusion method revealed that SLN formulations exhibited significantly higher antimicrobial activity compared to the crude extract, attributed to the synergistic action of phytochemicals and improved delivery by the SLN system. In conclusion, the study successfully developed a stable and efficient SLN formulation of Ixora coccinea extract, demonstrating improved antimicrobial activity and long-term stability. These findings highlight the potential of SLNs as a promising herbal drug delivery platform and provide a foundation for further in vivo and clinical investigations.

Keywords: *Ixora coccinea, solid lipid nanoparticles, phytochemical screening, antimicrobial activity, nanotechnology, herbal drug delivery, stability study*

Corresponding author:

Jayant Prakash,

Student-Patel College of Pharmacy,

Madhyanchal Professional University, Bhopal (M.P)

Mail id.- sharmavihan7509@gmail.com

QR CODE

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INTRODUCTION:

Herbal medicines have been widely utilized for centuries due to their therapeutic benefits, attributed to the presence of diverse bioactive phytoconstituents. However, the direct use of crude plant extracts in modern medicine is often limited by issues such as poor solubility, instability, low bioavailability, and rapid degradation of active compounds. To overcome these drawbacks, nanotechnology-based drug delivery systems have emerged as an effective approach to enhance the pharmacological potential of plant-derived bioactive **(Dar *et al.*, 2023).**

SLNs are solid lipid based molecules that are diffused in a diameter ranging of 10 to 1000 nm. Since they include the benefits of these colloidal systems yet avoiding their drawbacks, SLNs it was first designed as an alternative to microparticles as well as liposomes there in early 1990s. Optimal biomedical applications are SLNs' key strength over polymeric micelles as the lipids that are used in preparation are internal components of the body so are well tolerated, while their increased stability makes them superior to liposomes **(Shirodkar *et al.*, 2019**). Due to their favourable characters, Utilization of SLNs in I.V., I.M., oral, intestinal, ocular, cutaneous, and other modes of therapy have been demonstrated. Solid lipid nanoparticles (SLNs), in particular, are gaining attention as novel drug delivery carriers due to their biocompatibility, ability to encapsulate and protect active compounds, and potential for controlled and sustained release **(Borges *et al.*, 2020).** These properties make SLNs suitable candidates for enhancing the pharmacological activity of plant-derived extracts. Solid lipid nanoparticles (SLNs) represent one of the most promising nanocarriers because of their unique features, including biocompatibility, non-toxicity, controlled drug release, and ability to improve the stability of encapsulated compounds. By protecting sensitive phytochemicals from environmental degradation and improving their bioavailability, SLNs can significantly enhance the therapeutic efficiency of herbal extracts **(Madkhali, 2022).**

Ixora coccinea Linn (Rubiaceae) is known as Jungle of Geranium (or) Flame of the woods or vetchi in Ayurveda. It is a common flowering shrub native to Asia. It is name derived from an Indian deity. It is traditionally used as hepatoprotective, Chemoprotective, antimicrobial, anti-oxidant, anti-nociceptive, anti–mitotic and anti-inflammatory activities **(Shafi, 2016).** Free radicals or oxidative injury now appears the fundamental mechanism underlying a number of human neurologic and other disorders. For instance, in diabetes, increased oxidative stress which co-exists with reduction in the anti-oxidant status has been postulated. *Ixora coccinea*, a medicinal plant widely used in traditional systems of medicine, is known for its antimicrobial, antioxidant, and anti-inflammatory properties. Phytochemical studies have revealed that it contains alkaloids, flavonoids, phenols, tannins, saponins, and glycosides, all of which contribute to its pharmacological activities. Despite its rich phytoconstituents, the direct therapeutic application of *Ixora coccinea* remains limited due to the challenges associated with conventional delivery methods **(Nadeem *et al.*, 2025).**

Therefore, the present study aims to formulate and evaluate solid lipid nanoparticles containing *Ixora coccinea* extract, with a particular focus on enhancing its antimicrobial activity. The research includes phytochemical screening, SLN formulation using suitable techniques, characterization of nanoparticles, and assessment of antimicrobial potential. This approach is expected to establish SLNs as an effective carrier system for improving the therapeutic value of *Ixora coccinea* in modern drug delivery applications.

MATERIALS AND METHODS:

Chemicals

Sodium nitrite, Ferric chloride, Ammonium sulphate, Mercuric chloride, and Lead acetate were obtained from Merck, a reputable supplier of analytical reagents. Fizmerk provided the Sodium carbonate, and Sodium citrate. Himedia provided the Follin ciocalteu's reagent and Potassium sodium tartrate. Fisher Scientific provided the Ninhydrin. Sunkem provided the Hydrochloric acid. Copper sulphate, Methanol and Petroleum ether obtained from Rankem.

Collection of Plant Material

The *Ixora coccinea* plant was harvested and permitted to dry for three days in the shade at typical temperatures. Dried plant components were stored in sealed glass containers in a dry, cool environment to prevent contamination and deterioration. A plant taxonomist has established the identity and purity of therapeutic herb *Ixora coccinea*.

Soxhlet extraction (Alara et.al., 2019)

The dried and powered *Ixora coccinea* plant part was defatted with petroleum ether before being kept in Soxhlet apparatus thimble. The procedure of extraction lasted 8-10 hours at temperature of 40-60^{o}C in the heating mantle using a methanol solvent. Following the procedure of extraction, the sample extract was filtered and concentrated till dryness. Extracts were collected in airtight containers. Extraction yield of all extracts was computed using the equation that follows:

% Yield = Weight of extract/ Weight of Plant Material usedX100

Qualitative Phytochemical Estimation of Extracts (Kokate et.al.,2006).

Total phenolic content (TPC)

The Folin-Ciocalteu Assay was used to measure the extract of Ixora coccinea's total phenolic content. The *Ixora coccinea* extracts (0.2 mL stock solution) combined with 2 milliliters of Folin-Ciocalteu Reagent and 2.5 milliliters of 7.5% sodium carbonate. This mixture diluted using purified water until it was 7 mL. The resulting solutions were let to rest at normal temperature for two hours before being spectrophotometrically analysed at 760 nm. Calibration shapes were produced using standard solutions of Gallic Acid Equivalent (GAE) mg/gm. Gallic Aid was created with 10, 20, 30, 40, and 50 µg/ml concentrations. The reagent Folin-Ciocalteu is sensitive to reducing chemicals, such include polyphenols. They produce a blue color when they react. The blue color was evaluated spectrophotometrically.

Total flavonoid content (TFC)

The flavonoid content was determined utilizing the process of aluminum chloride. Two milliliters of distilled water were combined with 0.5 milliliters of *Ixora coccinea* extract solution. After that, 0.15 ml of 5% sodium nitrite was added and thoroughly combined. After that, wait 6 minutes before adding 0.15 mL of 10% aluminum chloride and letting it stand for 6 minutes. Then, 2 milliliters of 4% sodium hydroxide were added. They shook the mixture and well mixed. The combination's measurements of absorbance were made at 510 nm with a UV spectrophotometer. Calibration curves were generated using standard Rutin Equivalent (RE) mg/gm solutions. Rutin concentrations ranged from 10–50 µg/ml. The calibration curve was employed to ascertain the total flavonoid concentration, which was represented in mg Rutin corresponding to one gram of dry extract weight.

Organoleptic Properties

The organoleptic studies of *Ixora coccinea* extract like general appearance like appearance, color, odor, state etc. were performed and observed.

Formulation of Solid Lipid

The SLNs were made by the hot homogenization method. To produce the phase of lipids, stearic acid, lecithin, and extract were melted at temperatures 80 to 90°Cover the lipid melting point, which for stearic acid is 69°C. Tween 80 was dissolved in deionized water and heated to the same temperature as the lipid phase to produce the aqueous phase. The hot aqueous phase was then progressively added to the lipid phase in a water bath that was set at 90°C above the lipid's melting point. For 30 minutes, the aqueous phase was constantly agitated using a magnetic stirrer. The solution was then subjected to 5–10 minutes of sonication. The dispersions that were produced were gathered in glass containers and kept in the refrigerator for use in other experiments **(Badawi et. al.,2020).**

Table 1: Composition of Solid lipid nanoparticle formulation

Required chemicals	SLNs 1	SLNs 2	SLNs 3	SLNs 4	SLNs 5
Ixora coccinea (Extract) (mg)	300	300	300	300	300
Stearic acid (lipid) (mg)	50	100	150	200	250
Tween 80 (Surfactant)	0.1	0.2	0.3	0.4	0.5
Lecithin (co-surfactant) (mg)	25	50	75	100	125
Sonication time (min.)	15	15	15	15	15
Temperature (^{0}C)	80-90	80-90	80-90	80-90	80-90
Distilled water (ml)	30	30	30	30	30

Evaluation parameter of Solid Lipid Nanoparticles formulation

Particle size

Particle size is one of the most essential parameters for SLNs characterization. The SLNs' sizes were computed using the Malvern Zeta sizer (Malvern Instruments). **(Balla and Goli 2020).**

Zeta potential

In the current study, SLNs were diluted ten times using purified water before being examined making use of Zetasizer Malvern equipment. **(Penjuri et al.,2016).**

Scanning Electron Microscopic (SEM)

The morphological attributes of SLNs that were optimized were achieved utilizing an electron beam from a scanning electron microscope, which was covered in a thin layer (2-20 nm) of metal (s) such as gold, palladium, or platinum using a vacuum sputter coater. The pretreatment specimen was then exposed to an electron beam, which produced secondary electrons known as augers. From this interaction between the beam of electrons and the specimen's atoms, only the electrons scattered at 90°C were chosen and further processed based on Rutherford and Kramer's Law to create images of surface topography **(Ahmed et al.,2020).**

Anti-microbial activity of SLNs by Well diffusion assay

- **Preparation of Nutrient Agar Media**

  100 milliliters of purified water were utilized to

dissolve 2.8 grams of Nutrient Media. The acidity of media was measured before sterilization. The media was sterilized in an autoclave at 121ºC and 15 psi for 15 minutes. Nutrient media was transferred on plates and put in a laminar airflow until the agar solidified.

- **Well Diffusion Assay**

  Make four wells in both agar plates with a sterilized cork borer. A spreader was used to spread a lawn culture of *E. coli* and *S. aureus* bacteria on Nutrient Agar media. Then, in each well, add varying amounts of extract-loaded SLNs. For twenty-four hours, the plate is incubated at 37^{O} degrees Celsius. The zone of inhibition surrounding each well is determined after incubation. A larger zone suggests more antibacterial action, and the absence of a zone signifies no antimicrobial effect **(Manandhar et al.,2019)**

Stability study

The formulation evaluated for the presence of solid lipid nanoparticles stability at accelerated temperatures ($25^0C\pm2^0C$ and 60 ± 5% RH) and $40^0C\pm2^0C$ and 70 ± 5% for three months. After30, 45, 60, and 90 days, the formulation's physical characteristics—such as color, order, appearance, and particle size were assessed. The composition was tested for stability under accelerated storage settings for three months in line with International Conference on Harmonization (ICH) standards. The formulation was tested for physical appearance alterations such as color, odor, look, and particle size. All findings were in contrast to the final formulation at 0 days as a benchmark **(González-González *et al.*, 2022).**

RESULTS:

Plant Collection Table 2: Plant collection

Plant name	Plant part used	Weight
Ixora coccinea	flower	300 gm

Percentage yield

Table 3: Percentage yield of extract

Plant name	Solvent	Color of extract	Theoretical weight (gm)	Yield (gm)	% Yield
Ixora coccinea	Pet. Ether	Greenish Brown	300	2.45	0.816
	Methanol	Green	285	4.24	1.48

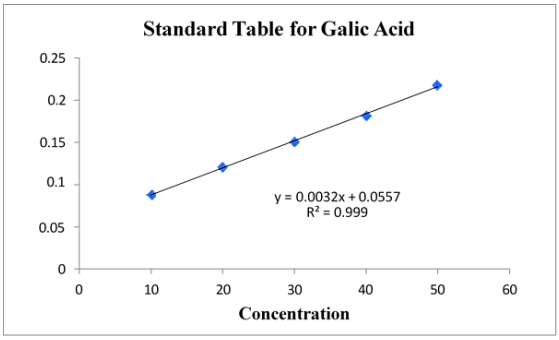
Table 4: Phytochemical analysis of *Ixora coccinea* Extract

S. No.	Experiment	Result	
		Petroleum ether	Methanolic
Test for Carbohydrates			
1.	Molisch's Test	-	+
2.	Fehling's Test	-	+
3.	Benedict's Test	-	+
4.	Bareford's Test	-	+
Test for Alkaloids			
1.	Mayer's Test	-	-
2.	Hager's Test	-	-
3.	Wagner's Test	-	-
4.	Dragendroff's Test	-	-
Test for Terpenoids			
1.	Salkowski Test	-	+
2.	Libermann-Burchard's Test	-	+
Test for Flavonoids			
1.	Lead Acetate Test	-	+
2.	Alkaline Reagent Test	-	+
3.	Shinoda Test	-	+
Test for Tannins and Phenolic Compounds			
1.	FeCl3 Test	+	+
2.	Lead Acetate Test	+	+
3.	Gelatine Test	+	+
4.	Dilute Iodine Solution Test	+	+
Test for Saponins			
1.	Froth Test	+	+
Test for Protein and Amino acids			
1.	Ninhydrin Test	-	+

2.	Biuret's Test	-	+
3.	Million's Test	-	+
Test for Glycosides			
1.	Legal's Test	-	-
2.	KellerKillani Test	-	-
3	Borntrager's Test	-	-

Quantitative Analysis

A preliminary phytochemical study of crude extracts revealed the presence of phenols and flavonoids in



plant material. TPC and TFC levels were determined using assays.**Total Phenolic content (TPC) estimation**

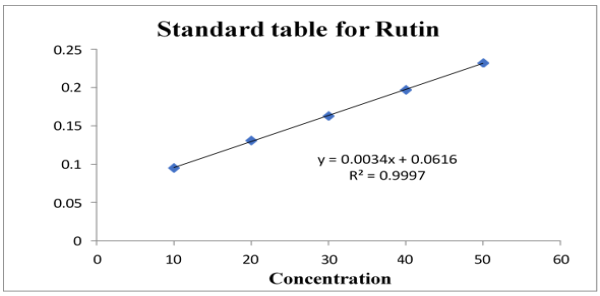
Graph 1: Represent standard curve of Gallic acidTotal Phenolic Content in extract Table 5: Total Phenolic Content

Absorbance	TPC in mg/gm equivalent of Gallic Acid
0.131	33.66 mg/gm
0.158	
0.179	

Table 6-Total Phenolic Content of extract *Ixora coccinea*

Extracts	Total Phenolic content (mg/gm equivalent of Gallic acid)
Methanol	33.66

Total Flavonoids content (TFC) estimation



Graph 2: represent standard curve of Rutin

Total Flavonoid Content in extract

Table 7: Total Flavonoid Content

Absorbance	TFC in mg/gm equivalent of Rutin
0.153	32.76 mg/gm
0.172	
0.195	

Table 8: Total Flavonoid Content of extract *Ixora coccinea*

Extracts	Total Flavonoid content (mg/gm equivalent of rutin)
Methanol	32.76

Organoleptic properties

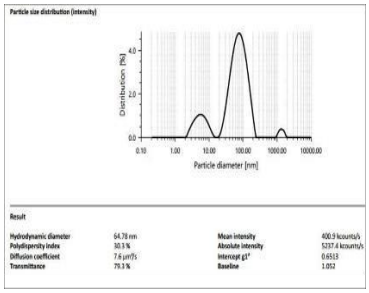
Table 9: Organoleptic properties of *Ixora coccinea*

Ixora coccinea	Study
Colour	Reddish brown
Odour	Offensive

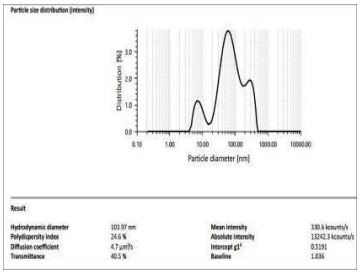
Appearance	Reddish semisolid

Characterization of SLN

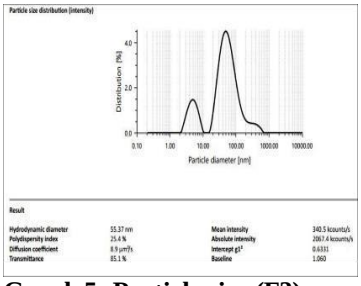
Particle Size determination



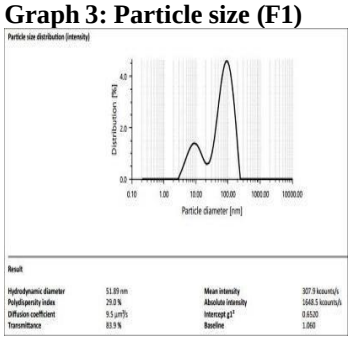
Graph 3: Particle size (F1)



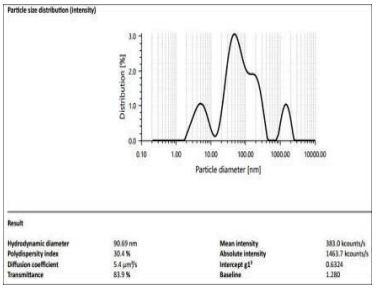
Graph 4:- Particle size (F2)



Graph 5: Particle size (F3)



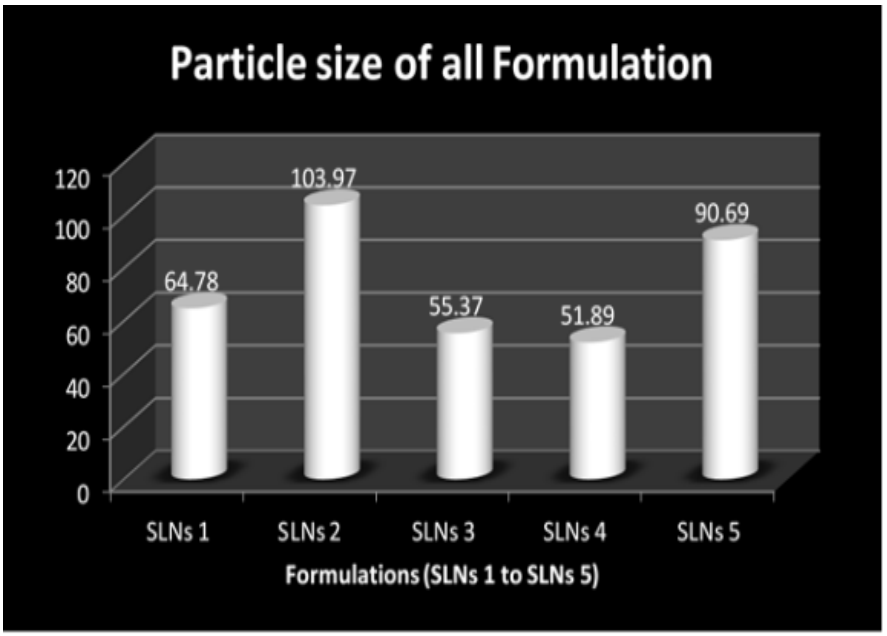
Graph 6: Particle size (F4)



Graph 7: Particle size (F5)

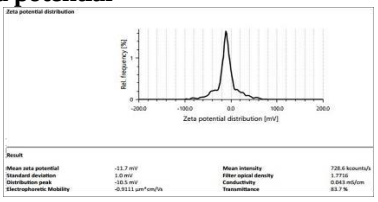
Table 10: Particle size

Formulation code	Particle size (nm)	PI Value
Solid Lipid Nanoparticle SLNs 1	64.78 nm	30.3%
Solid Lipid Nanoparticle SLNs 2	103.97 nm	24.6%
Solid Lipid Nanoparticle SLNs 3	55.37 nm	25.4%
Solid Lipid Nanoparticle SLNs 4	**51.89 nm**	**29.0%**
Solid Lipid Nanoparticle SLNs 5	90.69 nm	30.4%

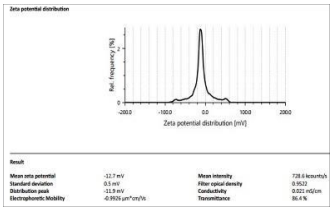


Graph 8: Graphical representation of Particle size

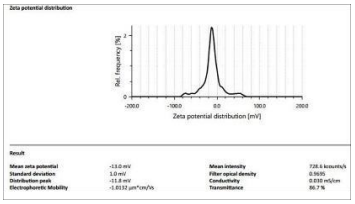
Zeta potential



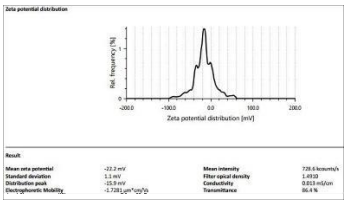
Zeta potential (F1)



Zeta potential (F2)

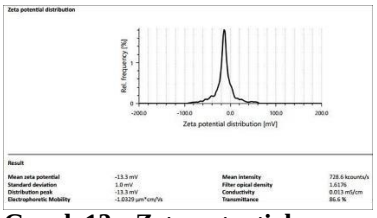


Zeta potential (F3)



Graph 12: Zeta potential

(F4)

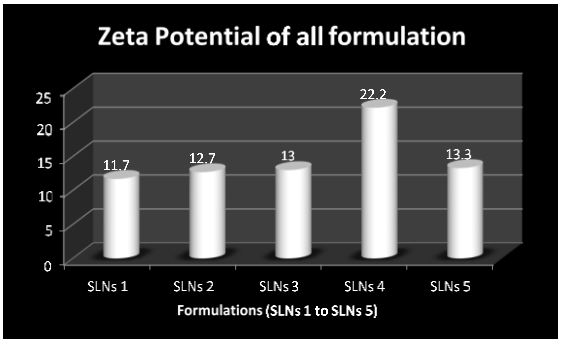


Graph 13: Zeta potential

(F5)

Table 11: Zeta potential

Formulation Code	Zeta potential
Solid Lipid Nanoparticle SLNs 1	-11.7 mV
Solid Lipid Nanoparticle SLNs 2	12.7 mV
Solid Lipid Nanoparticle SLNs 3	-13.0 mV
Solid Lipid Nanoparticle SLNs 4	-22.2 mV
Solid Lipid Nanoparticle SLNs 5	-13.3 mV



Graph 14: Graphical representation of zeta potential

Scanning electron microscope (SEM) of F4 Formulation (Optimized)

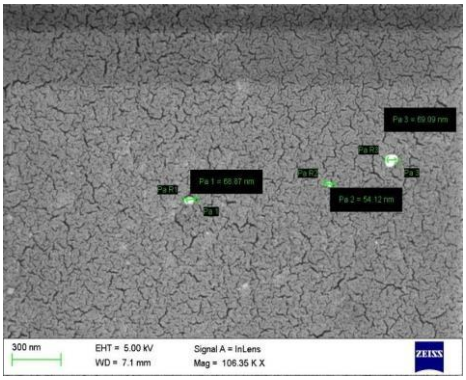


Figure 4: Scanning electron microscope

Antimicrobial activity of Solid Lipid Nanoparticle formulation of against *E.coli* and *S.aureus*

Table 12: Antimicrobial activity of Solid Lipid Nanoparticle against *E.coli* and *S.aureus*

Sample name	Zone of inhibition (mm) against E.coli	Sample name	one of inhibition (mm) against of S. aureus
Extract F1	7 mm	Extract C1	6 mm
Solid lipid nanoparticles (0.5 mg/ml) F2	**11 mm**	Solid lipid nanoparticles (0.5 mg/ml) C2	**10 mm**
Solid lipid nanoparticles	**14 mm**	Solid lipid nanoparticles	**16 mm**
(1mg/ml) F3		(0.5 mg/ml) C3	

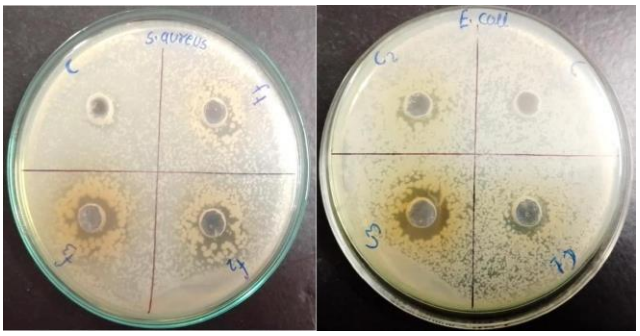


Figure 5: Antimicrobial activity against (A) *E.coli* and (B) *S.aureus*

Stability study

Table 13: Stability Study of optimized formulation (Solid Lipid Nanoparticle)

Time (Days)	25^0C±2 ^{0}C and 60 ± 5% RH		40^0C±2 ^{0}C and 70 ±5% RH	
	Particle Size (nm)	Zeta potential (mV)	Particle Size (nm)	Zeta potential (mV)
0	51.89 nm	-22.2 mV	51.89 nm	-22.2 mV
30	51.93 nm	-22.3 mV	52.97 nm	-22.4 mV
45	53.75 nm	-21.7 mV	53.54 nm	-22.5 mV
60	52.98 nm	-22.9 mV	52.78 nm	-22.9 mV
90	51.80 nm	-21.9 mV	51.71 nm	-23.1 mV

CONCLUSION:

The present study successfully formulated and evaluated solid lipid nanoparticles (SLNs) incorporating the extract of *Ixora coccinea*, with a focus on enhancing its antimicrobial potential. Phytochemical analysis confirmed the presence of bioactive constituents such as alkaloids, flavonoids, phenols, tannins, saponins, and glycosides, which are known to exhibit antimicrobial, antioxidant, and anti-inflammatory properties. Quantitative estimation revealed a significant content of phenolic compounds and flavonoids, further supporting the rationale for their integration into SLN systems.

The prepared SLNs demonstrated desirable physicochemical characteristics, including nanometer particle size, adequate zeta potential, and uniform spherical morphology, ensuring stability, effective bioavailability, and controlled release. Antibacterial evaluation revealed that the SLN-based formulation exhibited stronger inhibitory effects against selected microbial strains compared to the crude extract, highlighting the synergistic effect of phytochemicals and the enhanced delivery mechanism of SLNs. Stability studies further confirmed the long-term integrity and bioactivity of the formulation under different storage conditions.

Overall, this work establishes the potential of SLN-based formulations as an effective strategy for improving the therapeutic value of *Ixora coccinea*. The findings not only demonstrate enhanced antimicrobial efficacy but also lay a strong foundation for future in vivo and clinical investigations, thereby advancing the application of nanotechnology in herbal drug delivery systems.

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