

Available online on 15.08.2024 at <http://jddtonline.info>

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Copyright © 2024 The Author(s): This is an open-access article distributed under the terms of the CC BY-NC 4.0 which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited



Open Access Full Text Article



Research Article

Innovative Formulation and Evaluation of Phytosomal Nanoparticles from *Ixora Coccinea* Linn and its Pharmacological Screening

Shreyash Patil ^{*}, Swarali Patil, Smita P. Kamalakar, Suraj Patil, Sujitkumar Patil, Sulaxmi Patil

R. L. Tawde Foundation's Sarojini College of Pharmacy, Kolhapur, Maharashtra, India 416013

Article Info:



Article History:

Received 18 May 2024
Reviewed 03 July 2024
Accepted 21 July 2024
Published 15 August 2024

Cite this article as:

Patil S, Patil S, Kamalakar SP, Patil S, Patil S, Patil S, Innovative Formulation and Evaluation of Phytosomal Nanoparticles from *Ixora Coccinea* Linn and its Pharmacological Screening, Journal of Drug Delivery and Therapeutics. 2024; 14(8):110-118

DOI: <http://dx.doi.org/10.22270/jddt.v14i8.6757>

*Address for Correspondence:

Shreyash Patil, Department of Pharmaceutical Chemistry, R. L. Tawde Foundation's Sarojini College of Pharmacy, Kolhapur, Maharashtra, India

Abstract

The use of herbal extracts in pharmaceutical formulations has gained significant attention due to their therapeutic potential and minimum side effects and shows pharmacological profiles as anti-inflammatory, anticancer, and antimicrobial. Thus, the intent of the current study was to develop a potential drug carrier system phytosomal nanoparticle using an extract of the plant "*Ixora coccinea*". The extract of *Ixora coccinea* was prepared by using the maceration method and it is incorporated into Phytosome nanoparticles by using the solvent evaporation method. The impact of various process parameters and material attributes on the average particle size and drug entrapment efficacy. Extract loaded Phytosomal nanoparticles were characterized by particle size determination, Zeta potential, FTIR, and UV spectroscopy. The pharmacological screening consolidated antimicrobial activity was carried out by the well diffusion method, wherein it was performed against Gram Positive (*B. Cereus*, NCIM-2703) and Gram Negative (*E. coli*, NCIM 2832) bacteria strains. Which resulted in showing phytosomal nanoparticles show good activity than the extract. The anti-inflammatory activity was carried out by the protein denaturation method, which concluded that *Ixora Coccinea* phytosomal nanoparticles show better activity. Therefore, it results in moderate anti-inflammatory activity as compared to standard Diclofenac sodium.

Keywords: Phytosome nanoparticles, Solvent evaporation method, Invitro anti-inflammatory activity.

INTRODUCTION

In the present era, there is a growing interest among scientists and researchers in creating and developing new methods for the safe and efficient delivery of drug compounds¹. Conventional dosage forms have several drawbacks, which prevent them from achieving the desired therapeutic effects and fulfilling the prescriber's intentions². The principles of novel drug delivery provide several benefits that enable a drug compound to be delivered to the target site, enhancing its effectiveness while reducing potential side effects³. Targeting the drug compound is a crucial strategy that allows for its delivery at a controlled rate over a specified time period. Novel drug delivery systems aim to reduce the side effects associated with pharmacotherapeutic agents while ensuring the drug maintains consistent therapeutic levels in the body⁴. Utilizing nano formulations is crucial for achieving effective therapeutic activity at the target site, reflecting the current demands of the field. Various nanopreparations, including solid lipid nanoparticles (SLN), liposomes, phytosomes, nano emulsions, polymeric nanoparticles, and nanocapsules, can be effectively employed to deliver the active compound to the desired location, thereby maximizing therapeutic benefits. These nano preparations offer numerous advantages, such as improved bioavailability, enhanced solubility, protection from toxicity, improved pharmacological action, increased stability, better distribution within tissue macrophages, extended release, and superior protection against physical and chemical

degradation⁵. Among the various carrier systems used for drug delivery, vesicular systems are well-organized structures composed of lipid bilayers that can exist as individual units or in concentric arrangements⁶. Amongst different vesicular systems, Phytosomes are an innovative drug delivery system that can significantly improve the effectiveness of plant-based compounds by enhancing their absorption, stability, and delivery to target sites in the body⁷.

Ixora coccinea Linn is native to southern India, Bangladesh, and Sri Lanka and cultivated universally. *Ixora coccinea* Linn is a valuable plant with numerous bioactive constituents that contribute to its medicinal properties. The combination of flavonoids, tannins, saponins, and other compounds makes it a useful plant in traditional and potentially modern medicine. Its rich composition supports its use in treating a variety of ailments, from infections to inflammation and beyond⁸.

While most herbal dosage forms are effective, they have some drawbacks, such as toxicity, poor solubility, lack of stability, low pharmacokinetics, reduced bioavailability in renal clearance, and difficulty in reaching the target site. To address these issues, it is important to incorporate herbal materials into vesicular drug delivery systems like Phytosomes. Phytosomes are a valuable tool in modern medicine and health products, providing enhanced bioavailability, stability, and targeted delivery of plant-derived compounds. Their ability to improve therapeutic outcomes while minimizing side effects makes them a powerful option in drug delivery systems⁹. Therefore,

the current study was to design and develop the *Ixora coccinea* Linn extract encapsulation into phytosomes¹⁰. The study aimed to maximal amount of extract of *Ixora coccinea* Linn leaves loading and further protects the same from degradation to improve its solubility¹¹. In the end, research work was designed to Phytosomal nanoparticles to improve their efficacy against inflammation and microbial bacteria while minimizing side effects in healthy tissues.



Figure 1: Plant of *Ixora coccinea* Linn

Separation of Extract from *Ixora coccinea* plant leaves

The plant, *Ixora coccinea*, was collected from a rural area from Morewadi, Kolhapur, Maharashtra, INDIA (416013) and authenticated by the department of botany, New College, Kolhapur, INDIA (416013). After collecting the leaves, they were dried at room temperature, shade dried for 72 hrs. The completed dried leaves were powdered using an automatic grinder, and a phytochemical test was done, and the Ash value was determined by using a muffle furnace, after that extraction done by the maceration method, and 50 grams of the resulting powder were soaked with 95% ethanol for 24 hours. After that it filtered and the extracts were concentrated into crude solid forms by using the evaporation method with a magnetic stirrer at a temperature of $60 \pm 2^\circ\text{C}$ ¹². The yield of *Ixora coccinea* leaves extract was recorded as 10 gm and stored in an airtight container. extract was preformulated by using UV-spectroscopy, IR.

Phytochemical Screening of Extract

From the Phytochemical Screening Glycoside, Phenol, Alkaloid, Flavonoids and Tannins was identified into extract.

Preformulation Study for Extract

FTIR Spectroscopy

The ethanolic extract of *Ixora coccinea* leaves FTIR was carried out at the Common Facility Centre (CFC)-Sophisticated Analytical Instrument Facilities (SAIF) Kolhapur, under the Department of CFC-SAIF-DST Center, Shivaji University, and Kolhapur 416004, using the ALPHA FTIR (2734625) from Bruker, Germany; obtain information about the functional groups, which were observed from 4000 to 400 cm^{-1} .

UV-Spectroscopy

Determination of λ max for extract

To get a concentration of 100 mg/mL^{-1} , 1 mg of pure extract was weighed and diluted in 10 mL of ethanol (stock solution). To achieve a final concentration of 10 mg/mL^{-1} , from this 1 mL of solution was further diluted with 10 mL of same solvent in

MATERIALS AND METHODS

Materials

The plant, *Ixora coccinea*, was collected from a rural area in Morewadi, Kolhapur, Maharashtra, Research-Lab Fine Chem. Industries, Islampur, Maharashtra, supplied Soya lecithin and cholesterol, and LOBA PVT. LTD supplied ethanol and Dichloromethane. **Fig no 2.1.** Plant of *Ixora coccinea* Linn.

another volumetric flask. The UV spectra of the solution were then measured between 400 and 200 nm after it had been filtered¹³.

Calibration Curve

A stock solution with a concentration of $10\text{ }\mu\text{g/mL}$ was prepared, and 0.2 mL of this solution was diluted with 10 mL of ethanol. Further dilutions were performed to create solutions with concentrations of 0.2, 0.4, 0.6, 0.8, and $1\text{ }\mu\text{g/mL}$, each adjusted to a final volume of 10 mL with the solvent. The solutions were filtered and analyzed using a UV spectrophotometer over a wavelength range of 400-200 nm. A standard curve was then constructed, and the slope intercept were calculated^{13,14}.

Preparation of *Ixora coccinea* leaves extract loaded Phytosome

For the development of *Ixora coccinea* leaves extract loaded Phytosome nanoparticles solvent evaporation method was employed. In a round-bottom flask, 10 ml each of dichloromethane and ethanol were combined, followed by the addition of 150 mg of soya lecithin and 100 mg of cholesterol, which were thoroughly mixed. to this, 10 mg of extract were mixed, in a rotary evaporator set to 100 rpm and maintained at $60 \pm 5^\circ\text{C}$. The mixture was evaporated until a thin film developed in the round-bottom flask. The film was then hydrated with a buffer solution (pH 7.4) for 60 min at 250 rpm. Following this, the preparation was subjected to ultrasonic waves using a bath sonicator for 30 minutes to reduce particle size, and the resulting Phytosome was stored overnight at room temperature^{15,16}.

Characterization of *Ixora coccinea* leaves extract loaded Phytosome nanoparticles

FTIR of Phytosome Nanoparticle

Ixora coccinea leaves extract containing Phytosomes FTIR was carried out at the Common Facility Centre (CFC)-Sophisticated Analytical Instrument Facilities (SAIF) Kolhapur, under the Department of CFC-SAIF-DST Center, Shivaji University, and

Kolhapur 416004, using the ALPHA FTIR (2734625) from Bruker, Germany; obtain information about the functional groups, which were observed from 4000 to 400 cm^{-1} . The obtained results were compared with conventional data for comparison.

UV-Spectroscopy

Determination of λ max for Phytosome Nanoparticle

To get a concentration of 100 mg/mL^{-1} , 1 ml of phytosome nanoparticles was diluted in 10 mL of ethanol (stock solution). To achieve a final concentration of 10 mg/mL^{-1} , from this 1 mL of solution was further diluted with 10 mL of the same solvent in another volumetric flask. The UV spectra of the solution were then measured between 400 and 200 nm after it had been filtered¹⁷.

Calibration Curve

A stock solution with a concentration of 10 $\mu\text{g/mL}$ was prepared, and 0.2 mL of this solution was diluted with 10 mL of ethanol. Further dilutions were performed to create solutions with concentrations of 0.2, 0.4, 0.6, 0.8, and 1 $\mu\text{g/mL}$, each adjusted to a final volume of 10 mL with the solvent to achieve final concentrations between 2 and 5 $\mu\text{g/mL}$. The solutions were filtered and analyzed using a UV spectrophotometer over a wavelength range of 400-200 nm. A standard curve was then constructed, and the slope, intercept, were calculated¹⁷.

Particle Size and Zeta Potential Analysis

Nano ZS90, make: MALVERN, UK was utilized to measure the particle size and zeta potential of Phytosome nanoparticles. The measurement of particle size and Zeta potential is influenced by both the strength of the particle and the size of the particle center.

Drug Entrapment Efficiency

The drug entrapment efficiency of the Phytosome solution loaded with *Ixora coccinea* leaf extract was evaluated by centrifuging the solution for 45 minutes at 2500 rpm, which left the supernatant containing the free extract. The extract

quantity was then determined spectrophotometrically at a wavelength of 280 nm in a buffer solution with a pH of 7.4. The amount of Phytosomes was calculated using the formula provided below,

$$\% \text{ Entrapment efficiency} = (\text{Entrapped drug} / \text{Total drug}) \times 100$$

Invitro-Anti-inflammatory Activity

A mixture of 5.6 mL of phosphate-buffered saline (PBS, pH 6.4) and 4 mL of an extract solution and Phytosome (1000 $\mu\text{g/mL}$) was prepared separately. An equivalent volume of double-distilled water was used as a control. The both mixtures were incubated in an incubator at $37^\circ\text{C} \pm 2$ for 15 minutes and then heated at 70°C for 5 minutes. After cooling, the absorbance was measured at 660 nm, using the vehicle as a blank. Diclofenac sodium at a concentration of 1000 $\mu\text{g/mL}$ was used as a reference drug and was treated in the same way for absorbance measurement. The percentage inhibition of protein denaturation was calculated by using the following formula.

$$\% \text{ Inhibition} = \frac{\text{Absorbance of control} - \text{Absorbance of test}}{\text{Absorbance of control}} \times 100$$

RESULTS AND DISCUSSION

Determination of Ash Value

By the calculation the total ash value of *Ixora coccinea* plant leaves was found to be 6%

Separation of Extract from *Ixora coccinea* plant leaves

By the Maceration method *Ixora coccinea* plant leaves ethanolic extract was found to be 10 mg

Phytochemical Screening of Extract

Phytochemical screening is a foundational step in both scientific research and the development of natural products, offering insights into the potential applications and benefits of plant extracts. By performing the test following results are observed **Table no. 1**

Table 1: Phytochemical Screening of Extract

Sr. No	Test	Observation	Inference
1	Glycoside: 5ml of extract + glacial acetic Acid + few drops of ferric chloride	Brown ring at the junction	Glycoside present
2	Phenol: 5ml of extract + few drops of Ferric chloride solution	Bluish black color	Phenol present
3	Saponin: 1 ml Solution of Powder and Extract Was Diluted with Distilled Water To 20 ml And Shaken For 10 Minutes Presence Foam	No Foam Generation	Saponin absent
4	Alkaloid: 5ml Sample + Iodine Potassium Sol.	Reddish Brown Ppt.	Alkaloids Present
5	Flavonoid: Alcoholic Sol. + HCl	Orange Or Red Color Ppt.	Flavonoid Present
6	Tannins: Aq. Sol of Sample + 5% FeCl_3	Dark Color	Tannin Present

Preformulation Study for Extract

FTIR Spectroscopy

Table no.2, Fig.no.2 Shows a strong peak was observed between 3500-2500 cm^{-1} , indicating O-H and C-H stretching, which suggests the presence of carboxylic and alkane groups. The peak at 1517.74 cm^{-1} indicates the presence of a nitro compound, and the peak at 1084.09 cm^{-1} suggests the presence of a primary alcohol.

Table 2: FTIR of Extract

Sr. No	Wavelength(cm)	Group	Compound
1	3282.89	OH-Stretching	Carboxylic Acid
2	3018.41	CH-Stretching	Alkane
3	1517.74	N=O Stretching	Nitro Compound
4	1084.09	C-O Stretching	Primary Alcohol
5	1378.44	C-H Bending	Aromatic Compound

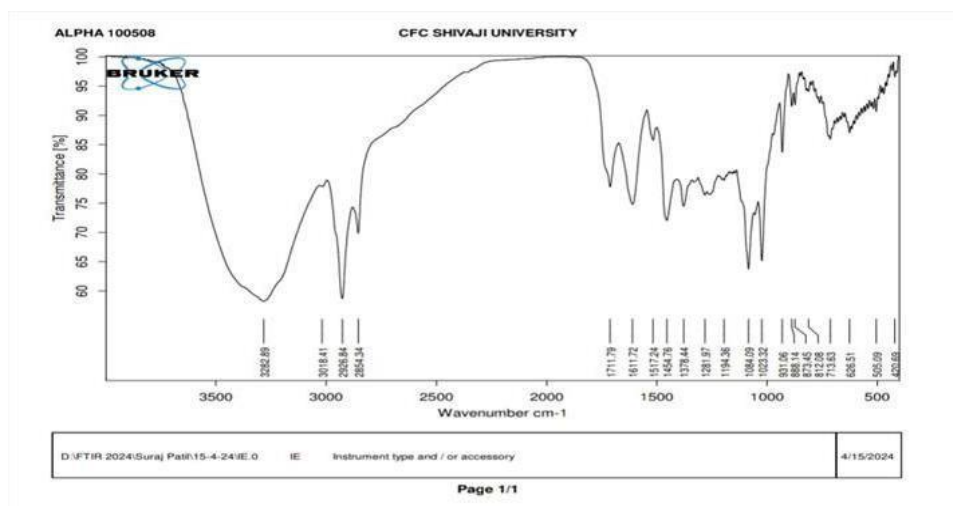


Figure 2: FTIR of Extract

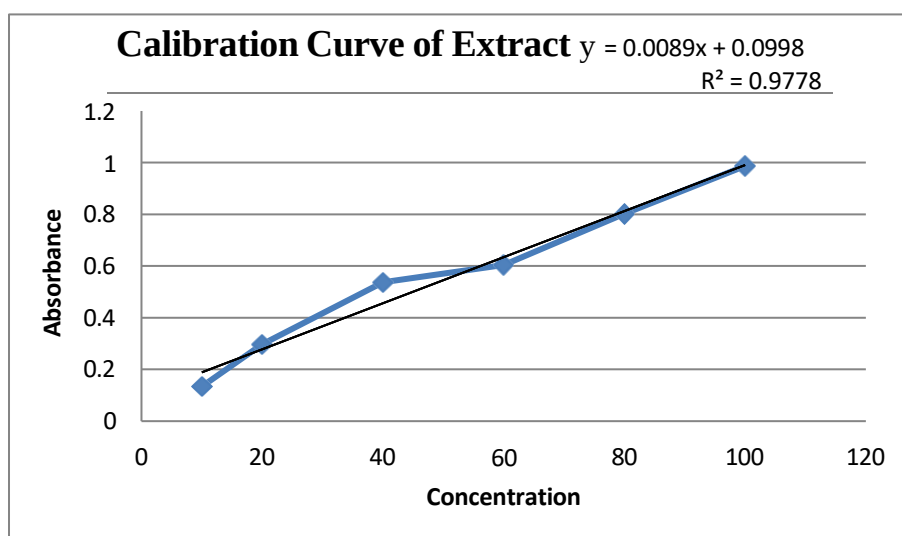
UV-Spectroscopy of Extract

Determination of λ_{max} for Extract

The *Ixora coccinea* extract solution was dissolved in DMSO and scanned using UV spectroscopy in the range of 400–200 nm. The maximum absorbance (λ_{max}) for the *Ixora coccinea* extract was found to be at 266 nm.

Determination of Slope and Intercept through Calibration Curve

Calibration curves for *Ixora coccinea* extract were prepared and tested using conventional methods, and absorbance at different concentrations was measured at 10–100 $\mu\text{g ml}^{-1}$. **Fig.No.3** shows the calibration correlation coefficient was found to be 0.977 using Lambert Beer's law.

Figure 3: Calibration curves for *Ixora coccinea* extract

FTIR of Phytosomes

Fig no.4, Table No.3 Shows FTIR analysis of *Ixora coccinea* extract-loaded phytosomes revealed strong bands at 2054 shows the O-H stretching, indicates the presence of Carboxylic

Acid. Strong peak at 1728 shows C=O stretching indicates presence of aldehyde and ketone group. The peak at 1655 shows the presence of C=C stretching indicates alkene group. Peak at 1466 shows presence of C=C stretching, indicates presence of aromatic group.

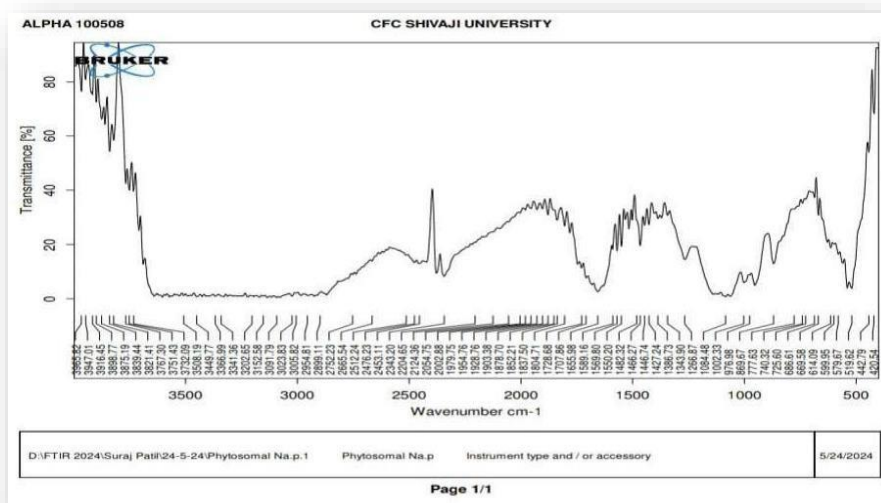


Figure 4: FTIR of Phytosomes

Table 3: FTIR of Phytosomes

Sr. No	Wevelenght(cm)	Group	Compound
1	2054	O-H stretching	Carboxylic Acid
2	1728	C=O stretching	Aldehyde and Ketone group
3	1655	C=C stretching	alkene group
4	1466	C=C stretching	aromatic group

UV-Spectroscopy

Determination of λ max for Phytosome Nanoparticle

The Ixora coccinea extract loaded Phytosome nanoparticle solution was dissolved in DMSO and scanned using UV spectroscopy in the range of 400–200 nm. The maximum absorbance (λ max) for the Ixora coccinea extract-loaded Phytosomes was found to be at 306 nm.

Determination of Slope and Intercept through Calibration Curve

Calibration curves for Ixora coccinea extract loaded Phytosome nanoparticles solutions were prepared and tested using conventional methods, and absorbance at different concentrations was measured at 10-100 μ g ml⁻¹. **Fig.No.5** shows the calibration correlation coefficient was found to be 0.992 using Lambert Beer's law.

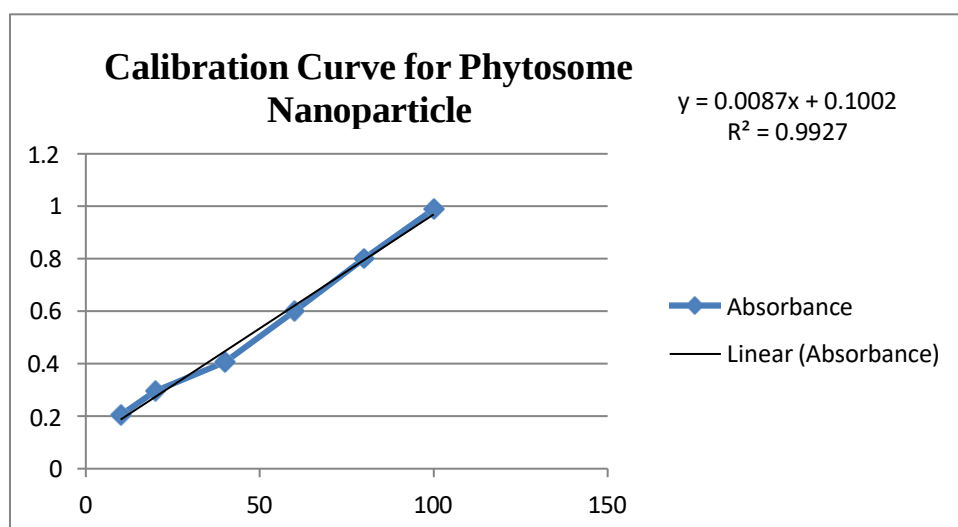


Figure 5: Calibration curves for Phytosome nanoparticles

Particle Size and Zeta Potential Analysis

Particle size and Zeta potential Analyzer used to measure particle size of the optimized Phytosomal Nanoparticles which were measured on the Malvern instrument by the dynamic light scattering method. It was observed that average Particle size was 424.3 nm with a PI value of 0.025. Zeta potential analysis

was used to evaluate the change in surface charge following the development of the prepared system of Ixora coccinea extract-loaded Phytosomes. It exhibited a negative value (-52.8 mV) in the zeta potential graph. Negative values of zeta potential are possible for a capping agent primarily composed of anionic groups that coat the surface of Ixora coccinea extract. (**Fig.No.6 &7**)

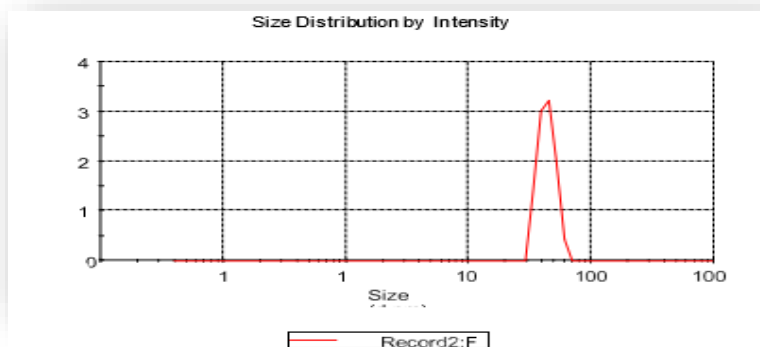


Figure 6: Particle Size of Phytosome

Calculation Results		
Peak No.	Zeta Potential	Electrophoretic Mobility
1	-52.8 mV	-0.000272 cm ² /Vs
2	---	---
3	---	---
Zeta Potential (Mean)		: -52.8 mV
Electrophoretic Mobility Mean		: -0.000272 cm ² /Vs

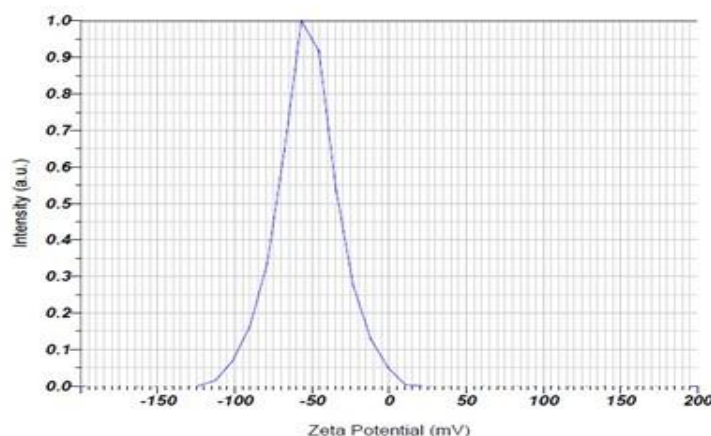


Figure 7: Zeta Potential of Phytosome Nanoparticles

Percentage Drug Entrapment Efficacy

Drug entrapment efficacy is a crucial parameter in drug delivery systems, particularly for nanoparticle-based and encapsulation technologies. By performing drug entrapment,

the following results was observed, at concentration 80 mg/ml shows maximum drug entrapment percentage 69.38% and by intercepting slope R2 value found to be 0.931. (**Table no.4, Fig no.8**)

Table 4: Percentage Drug Entrapment Efficacy

Conc. Mg/ml ⁻¹	sorbance of Supernant	sorbance of Sediment	entrapment efficiency
20	0.045	0.097	34.00
40	0.084	0.102	50.37
60	0.106	0.120	52.40
80	0.204	0.20	69.38

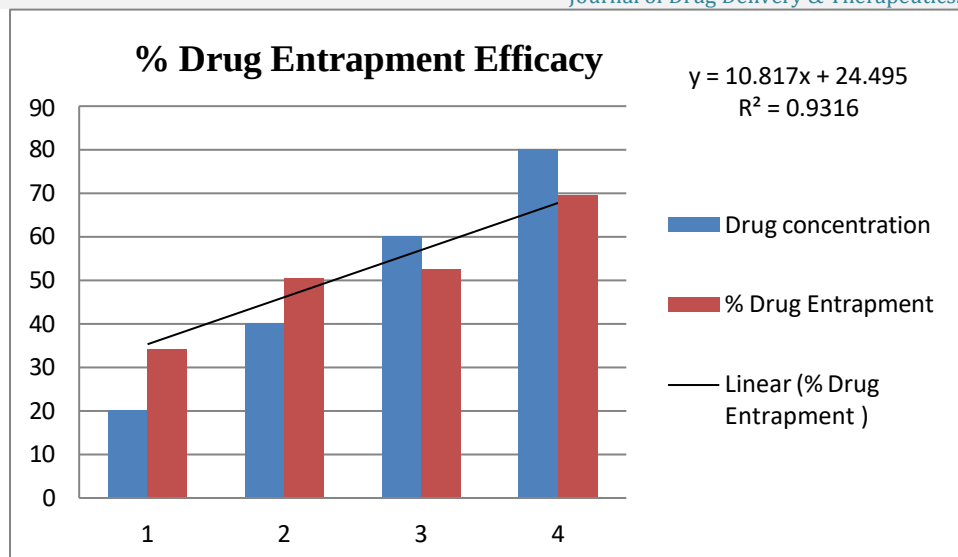


Figure 8: % Drug entrapment efficacy

Invitro-Anti-inflammatory Activity

The in-vitro results from the current study confirmed the anti-inflammatory effectiveness of a new series of Phytosomes. This is significant because many anti-inflammatory drugs are known to have a dose-dependent effect on inflammation. Our findings indicate that Phytosome nanoparticles exhibit significantly more anti-inflammatory activity than the extract alone, likely

due to their ability to dissolve and release anti-inflammatory compounds. The percentage of protein denaturation suppression at various doses is presented in **(Table no.5 Fig no.9 & 10)**, demonstrating that *Ixora coccinea* extract-loaded Phytosome shows superior in-vitro anti-inflammatory activity compared to the pure drug extract. Maximum protein denaturation shows 34.88 at concentration 1000 ug/ml.

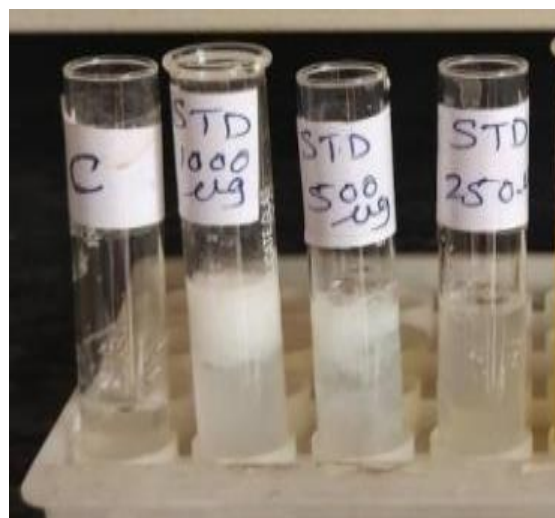


Figure 9: Invitro-Anti-inflammatory Activity (Protein Denaturation)

Table No .5. % Inhibition protein denaturation

Sr. No	Concentration	% Inhibition protein denaturation		
		250 ug/ml	500 ug/ml	1000 ug/ml
1	<i>Ixora coccinea</i> extract	10.05	20.00	25.06
2	<i>Ixora coccinea</i> extract-loaded Phytosome nanoparticle	13.95	25.58	34.88
3	Standard	72.09	79.06	86.04

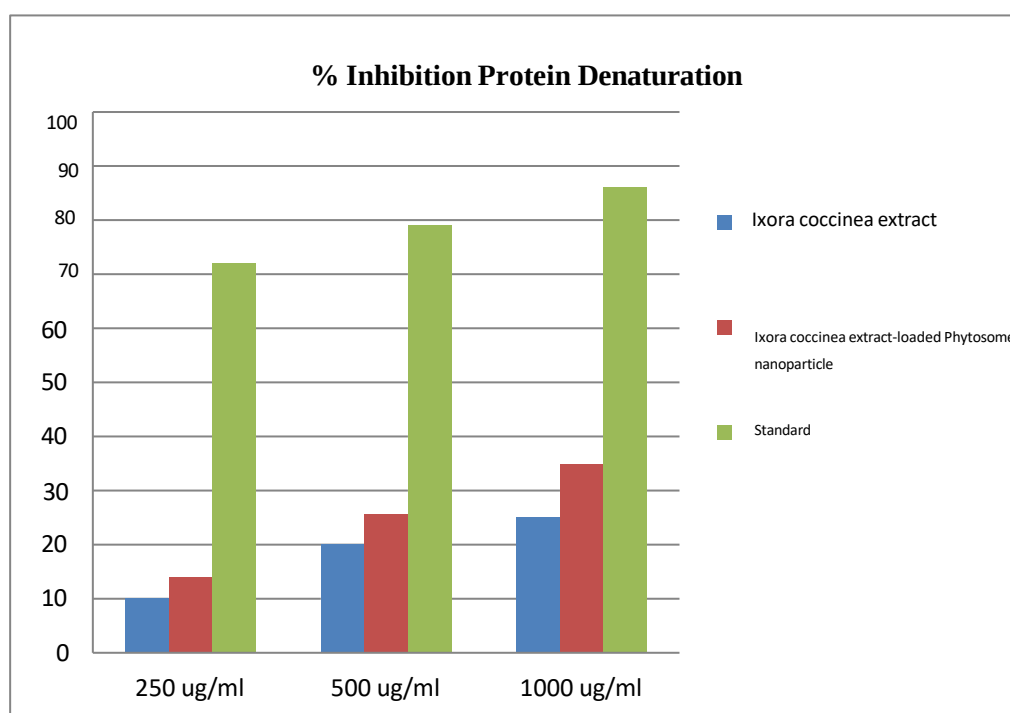


Figure 10: % Inhibition protein denaturation

CONCLUSION

The preparation of Phytosomes is a promising approach for maximizing the therapeutic potential of plant-based compounds. By improving the delivery and efficacy of these natural substances, Phytosomes hold great promise for applications in pharmaceuticals and nutraceuticals, offering a novel and effective strategy for the treatment of various inflammatory conditions. Future research should focus on optimizing formulation parameters and exploring the full range of therapeutic applications for Phytosome technology.

The prepared *Ixora coccinea* extract-loaded Phytosome nanoparticles have remarkable influence on the average Particle size and % Drug Entrapment Efficacy. The prepared Phytosome demonstrated excellent drug entrapment efficiency, which can be attributed to the higher amounts of soya lecithin, cholesterol and shows better anti-inflammatory activity than extract. so, it is novel system to minimize problems related to herbal drugs and shows target specific action through using Phytosome nanoparticles system.

Conflict of Interest: The authors declare no conflict of interest.

Author's Contribution: All authors contributed to the preparation of the manuscript. All authors read and approved the final manuscript.

Funding: None

Acknowledgment: We are grateful to Guide Ms. Smita P kamalakar of Department of Pharmaceutical Chemistry, Sarojini College of pharmacy, Kolhapur for providing the necessary guidance chemical and facilities for completing the project work.

REFERENCES

1. Khan I, Saeed K, Khan I. Nanoparticles: Properties, applications and toxicities. *Arabian journal of chemistry*. 2019 Nov 1;12(7):908-31. <https://doi.org/10.1016/j.arabjc.2017.05.011>
2. Seema A. Recent development of herbal formulation-a novel drug delivery system. *International Ayurvedic Medical Journal*. 2014 Nov;2(6):952-8.
3. Anju Dhiman AD, Arun Nanda AN, Sayeed Ahmad SA. Novel herbal drug delivery system (NHDDS): the need of hour.
4. Srujana S, Anjamma M, Alimuddin, Singh B, Dhakar RC, Natarajan S, Hechhu R. A Comprehensive Study on the Synthesis and Characterization of TiO₂ Nanoparticles Using Aloe vera Plant Extract and Their Photocatalytic Activity against MB Dye. *Adsorption Science & Technology*. 2022;2022 <https://doi.org/10.1155/2022/7244006>
5. Maurya SD, Prajapati S, Gupta A, Saxena G, Dhakar RC, Formulation Development and Evaluation of Ethosome of Stavudine, *Indian J.Pharm. Educ. Res.* 2010;44(1)
6. Amit PY, Tanwar YS, Rakesh S, Poojan P. Phytosome: Phytolipid drug delivery system for improving bioavailability of herbal drug. *J Pharm Sci Biosci Res*. 2013;3(2):51-7.
7. Patil PS, Salunkhe VR, Magdum CS, Mohite KS, Phytosome: Increasing Bioavailability of Phytoconstituents, *IntJ UniPharma Bio Sci*.2016;5(4):82-90.
8. Bhattacharjee A. An overview on Phytosome as a novel drug delivery system for herbal drugs. *International journal of innovative pharmaceutical sciences and research*. 2015;3(6):730-9.
9. Singh RP, Gangadharappa HV, Mruthunjaya K. Phytosome loaded novel herbal drug delivery system: A review. *Int Res J Pharm*. 2016;7(6):15-21. <https://doi.org/10.7897/2230-8407.07656>
10. Sahu AR, Bothara SB. Formulation and evaluation of phytosome drug delivery system of boswellia serrata extract. *Int J Res Med*. 2015;4(2):94-9.
11. Elumalai A, Eswaraiiah C, Venkatesh Y, Narendar C. Phytochemical and pharmacological profile Of *Ixora coccinea* Linn. *International Journal of Pharmacy & life sciences*. 2012 Mar 1;3(3).

12. Joshi AB, Surlikar PM, Bhobe M. *Ixora coccinea* Linn: phytochemical investigation. *Journal of Drug Delivery & Therapeutics*. 2024; 14(8):110-118
13. Selvaraj N, Lakshmanan B, Mazumder PM, Karuppasamy M, Jena SS, Pattnaik AK. Evaluation of wound healing and antimicrobial potentials of *Ixora coccinea* root extract. *Asian Pacific Journal of Tropical Medicine*. 2011 Dec 1;4(12):959-63. [https://doi.org/10.1016/S1995-7645\(11\)60226-5](https://doi.org/10.1016/S1995-7645(11)60226-5) PMid:22118031
14. Jain N, Gupta BP, Thakur N, Jain R, Banweer J, Jain DK, Jain S. Phytosome: a novel drug delivery system for herbal medicine. *Int J Pharm Sci Drug Res*. 2010 Oct;2(4):224-8.
15. Prajapati SK, Maurya SD, Das MK, Tilak VK, Verma KK, Dhakar RC. Dendrimers in drug delivery, diagnosis and therapy: basics and potential applications, *Journal of Drug Delivery and Therapeutics*. 2016;6(1):67-92 <https://doi.org/10.22270/jddt.v6i1.1190>
16. Patel P, Modi C, Patel H, Patel UD, Ramchandani DM, Patel HR, Paidia BV. Phytosome: An emerging technique for improving herbal drug delivery. *The Journal of Phytopharmacology*. 2023;12:51-8.
17. El-Saber Batiha G, Magdy Beshbishy A, G. Wasef L, Elewa YH, A. Al-Sagan A, Abd El-Hack ME, Taha AE, M. Abd-Elhakim Y, Prasad Devkota H. Chemical constituents and pharmacological activities of garlic (*Allium sativum* L.): A review. *Nutrients*. 2020 Mar 24;12(3):872. <https://doi.org/10.3390/nu12030872> PMid:32213941 PMCID:PMC7146530