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Formulation and Evaluation of Phytosome and Plants Exhibiting Anti-Inflammatory Activity

Krishnaveni Manubolu[*1], Sai Yamini J[2], Charishma R[2], Neelesh Kumar P[2], Kishori O[2], Tanusha K[2], Kudipudi Harinadha Baba[3]

[1]Department of Pharmaceutics, Narayana Pharmacy College, Chinthareddy Palem, SPSR Nellore - 524 002, Andhra Pradesh, India
[2]Narayana Pharmacy College, Chinthareddy Palem, SPSR Nellore - 524 002, Andhra Pradesh, India
[3]Department of Pharmaceutical Analysis, Narayana Pharmacy College, Chinthareddy Palem, SPSR Nellore - 524 002, Andhra Pradesh, India

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ABSTRACT

The aim of the present study is formulation & evaluation of phytosome complexes from plant extracts of *Ixora coccinea*, *Chrysanthemum morifolium* & *Tinospora cordifolia*. Plants exhibiting anti-inflammatory activity (*Ixora coccinea, Chrysanthemum morifolium, and Tinospora cordifolium*) were selected. To carry out the Cold maceration process, prepare an aqueous and alcoholic extract of *Ixora coccinea, Chrysanthemum morifolium, and Tinospora cordifolia*. To perform Phytochemical screening, phytochemical evaluation, and FTIR spectral analysis. To prepare phagosomes by cholesterol complex method. Optimization of phagosomal formulations. The in vitro drug release from F1 to F9 was preserved in table below. It is executed that 8-hour drug releases time profile From the results, it was reported that F1 formulation preparation using *Ixora coccinea* exhibited 19.9% of drug release, which is less than 30%, indicating that worst release was not observed. This is the desired characteristic to be passed by the control release formula. At the end of the 4th hour, 48.9 % of drug release was observed 98.7% of Drug was released at the end of the 8th hour.

*Corresponding Author

Name: Krishnaveni Manubolu
Phone: +91 8074866545
Email: krishnaveni.manubolu@gmail.com

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INTRODUCTION

During oral and topical applications, pyrosomes enhance lipid-insoluble polarity phytoconstituent absorption, exhibiting increased bioavailability and a significantly elevated therapeutic benefit. The quantity of active compounds that must be consumed typically reduces as their rate for absorption increases [1]. Flavonoid and terpenoid compounds discovered in plant preparations were well suited toward direct binding with phosphatidylcholine. A standardized extraction, as well as polyphenolic constituents (including such simple flavonoids), were mixed with a stoichiometric amount of phospholipid (phosphatidylcholine) to generate phytosomes [2]. A lipophilic phosphatidyl moiety and an amino group make up a bifunctional compound, phosphatidylcholine. A hydrophilic moiety of choline. The choline head of the phosphatidylcholine molecule selectively attaches to these substances, and the body or tail of a lipid-soluble phosphatidyl section after that wraps this choline-bound substance. Damage is caused by gut microorganisms but also stomach secretions [3].

As a response, these phytoconstituents create a biochemical complex that's also biocompatible with lipids along with phospholipids, known as the phyto-phospholipid complex. Specific spectroscopic techniques show that molecules are anchored to the polar choline head of the phospholipids via chemical bonds. According to precise chemical analysis, the unit phytosome is typically a flavonoid molecule linked to at least one phosphatidylcholine molecule. As a result, a small microsphere or cell is formed. The phytosome technology creates a small enclosure that protects the plant extract or its active constituent [4].

MATERIALS AND METHODS

Fresh leaves were collected from fully grown flower plants of *Ixora coccinea* from Nellore, N-Hexane from NICE chemicals, Ltd., Kerala, Ethanol from Jiangsu Huaxi, Ethyl acetate from Ranbaxy fine Chemical Ltd, New Delhi, Soya lecithin is from Bakers villa, cholesterol is from S D Fine Chemicals Ltd, Mumbai, Bromine water is from Ranbaxy fine Chemical Ltd, New Delhi, and remaining reagents like Mayers reagent, Barfoeds reagent, H2So4, HCl from NICE chemicals, Ltd., Kerala.

Preparation of Phytosome

Phytosomes are prepared using the cholesterol complexation method [5]. The different molar ratio of the pyrosomes was designed by the selected optimize working method as mentioned in Table 1.

Preformulation Studies

Organoleptic Evaluation

The samples of plant extracts [Table 2] *Ixora coccinea, Tinospora cordifolia, and Chrysanthemum morifolium*, were studied for organoleptic characteristics such as color, odor, & solubility [6].

Melting Point

Plant extracts *Ixora coccinea*, *Chrysanthemum morifolium*, and *Tinospora cordifolia* has been established using such melting point equipment as well as the capillary technique [7].

FTIR Spectroscopy

Using a Shimadzu-8400S FT-IR Spectrophotometer, the medications' ft-or range was obtained (Tokyo, Japan). Each blend of Ixora +cholesterol, Ixora +soya lecithin, Tinospora + cholesterol, and chrysanthemum +cholesterol was compacted to a semisolid paste.

They were scanned using a Fourier transform infrared instrument inside a wavenumber range of 3500 to 1000 cm, and spectral analysis was performed. The software was employed to analyze the data [8] (UV PROB version 14).

Determination of Solubility

The Plant extracts *Chrysanthemum morifolium, Tinospora cordifolia, and Ixora coccinea* were determined in various organic solvents like ethyl acetate, ethanol, dichloro methane, DMSO, and distilled water was done [9].

UV Spectroscopy Study (Determination of λm max)

The standard stock solution of 50μg/ml of *drug Ixora coccinea, Chrysanthemum morifolium, and Tinospora cordifolia* was filtered between 200 - 800 nm using a UV spectrophotometer in water & ethanol, respectively.

Evaluation of Phytosomes

The phytosomes of plant extract were characterized by FTIR and Calibration studies [10–12] and assessed for percent yield, percent entrapment efficiency, particle size, and in vitro drug release [13–15].

Optimization of a Final Batch of Phytosomes

Based on in-vitro dissolution parameters, formulations were optimized.

Determination of % Yield

The simultaneous equation calculated assurance of % yield of formulations:

$$(\%)\ Yield = \frac{Practical\ yield}{Theoretical\ yield} \times 100$$

Determination of the Average Particle Size

The results of optical microscopy were conducted to identify. The average particle size of the phytosomal formulation of *Ixora coccinea, chrysanthemum morifolium & Tinospora cordifolia* was determined.

Drug Entrapment Efficiency

Each of the produced phytosomes' drug entrapment effectiveness was determined as a percentage. A 100 ml volumetric flask containing 100 ml of phosphate-buffered saline (pH 6.8) with 100 mg of a product has been measured accordingly and set aside.

A volumetric flask was stirred continuously at 35° C for two hours that following day to release all medicament from formulations.

After that, using an ultraviolet (UV) spectrophotometer, 1 ml of a solution was diluted upto 10 ml and then evaluated for drug entrapment efficiency 286, 256, 410 nm, respectively for *Ixora, Chrysanthemum & Tinospora,* respectively. Drug entrapment was calculated using the formula.

$$\%\ of\ Drug\ Entrapment\ Efficiency = \frac{Actual\ drug\ content}{theoretical} \times 100$$

Drug Release Kinetic Model

Zero-order release (cumulative percent drug released vs. time) equation [Figure 4]

$$Q = K_0 t \quad (1)$$

First order release (cumulative log percentage of Drug remaining vs. time) equation [Figure 5]

$$Log\ Q_t = Log\ Q_0 + K_1 t/2.303 \quad (2)$$

Higuchi's (cumulative percent drug released Vs. square root of time) equation [Figure 7]

$$Q = K_H\ t^{1/2} \quad (3)$$

Korsmeyer and Peppa's (Log cumulative percent drug released versus log time equation) [Figure 6]

$$F = (M_t / M) = K_m\ t^n \quad (4)$$

Where,

'Q' is the number of Drugs released at the time; 'M_t' is drug release at the time; 'M' is the total amount of the Drug in dosage form; 'F' is a fraction of the drug released at the time; 'K_0' is zero order release rate constant; 'K_H' is Higuchi's square root of the time release rate regular; 'K_m' is constant and depends on the geometry of the dosage form.

RESULTS AND DISCUSSION

Organoleptic Evaluation: λ_{max}: Absorption maxima(λ_{max}) in plant extraction of Ixora coccinea leaves [Figure 1].

Calibration: Standard Calibration curve of Ixora coccinea in distilled water at 286nm [Figure 2 and Table 3].

Determination Solubility Studies: Solubility of Ixora coccinea at 286nm [Table 4].

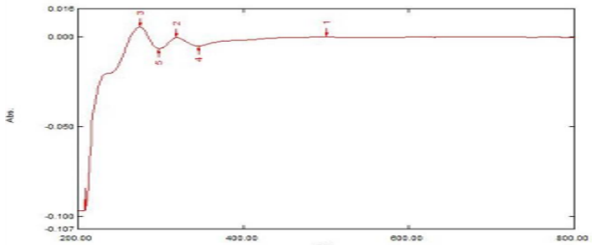

Figure 1: The λ_{max} for the Plant Extract of *Ixora coccinea* was Found to be at 286 nm

FTIR Interpretations

From the FTIR spectral analysis of *Tinospora cordifolia* extract and *Tinospora cordifolia* excipients and *chrysanthemum morifolium* and *chrysanthemum morifolium* extract + excipients. Presented

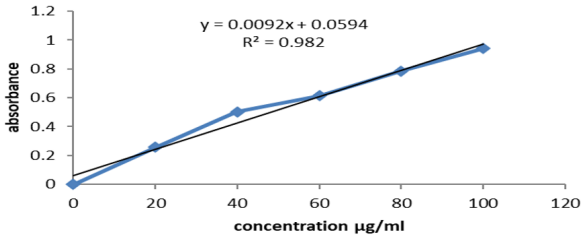

Figure 2: Standard Calibration Curve of *Ixora coccinea* in Distilled Water at 286 nm

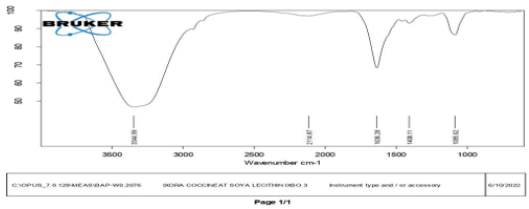

Figure 3: Fourier –Transform Infrared Spectroscopy Absorption of *Ixora coccinea*

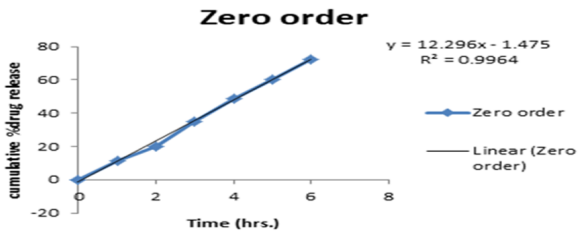

Figure 4: Zero-Order Release (Cumulative Percent Drug Released vs. Time)

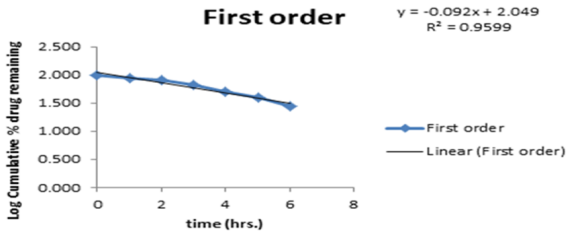

Figure 5: First Order Release (Cumulative Log Percentage of Drug Remaining vs. Time)

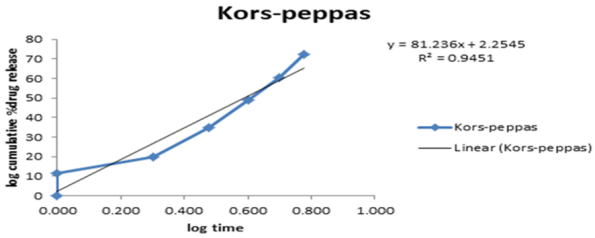

Figure 6: Korsmeyer and Peppa's (Log Cumulative Percent Drug Released vs. Log Time)

Table 1: Preparation of Phytosomes

Plant extract phytosomes	Molar ratios	
	Extract	Cholesterol
F1	1	1
F2	1	2
F3	2	1
F4	1	1
F5	1	2
F6	2	1
F7	1	1
F8	1	2
F9	2	1

Table 2: Organoleptic Evaluation of *Ixora coccinea*, *Chrysanthemum morifolium* and *Tinospora cordifolia*

S.no	Name of the Plant	Colour	Odour	Solubility
1	*Ixora coccinea*	Brown	Fragrant	Freely soluble
2	*Tinospora cordifolia*	Green	Characteristic odor	Freely soluble
3	*Chrysanthemum morifolium*	Yellow	Fragrant	Freely soluble

Table 3: Calibration Values of *Ixora coccinea* in Distilled Water at 286 nm

Concentration (μg/ml)	Absorbance
0	0
20	0.258
40	0.502
60	0.614
80	0.786
100	0.942

Table 4: Solubility of *Ixora coccinea*

S.no	Solvents	Solubility
1	Water	Partially soluble
2	Ethanol	Partially soluble
3	Ethyl acetate	Immiscible
4	DMSO	Completely soluble

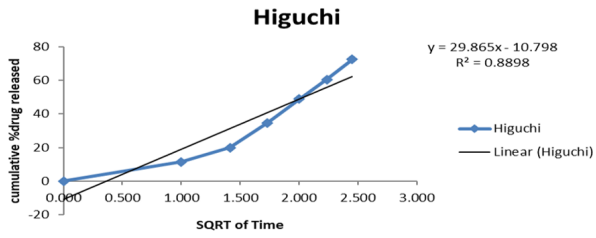

Figure 7: Higuchi's (Cumulative Percent Drug Released vs. Square Root of Time)

shifts of valence vibration bands of flavonoids carboxyl group according to the number of -OH groups and strong bonds relating to a characteristic of aromatic ring vibration appeared in the range of 1448.95 - 1449.50 Cm^{-1}.

And also indicated the presence of C-OH stretching Nitrations. After observation of results in comparison with plant extract & Plant extract + excipients didn't exhibit new peaks appearance and existing peaks disappearance. It showed good compatibility between plant extract and excipients [Figure 3 & Table 5].

Table 5: Fourier – Transform Infrared Spectroscopy Absorption of *Ixora coccinea*

S.no	Functional groups of *Ixora coccinea*	Infrared absorption of plant extract	Infrared absorption of drug & soya lecithin	Infrared absorption of Drugs & cholesterol
01	OH – Stretching; O-H stretching; OH – Stretching	3338 cm^{-1}	3344 cm^{-1}	3338 cm^{-1}
02	CΞC stretching; CΞC stretching; CΞC stretching	2114 cm^{-1}	2114 cm^{-1}	2114 cm^{-1}
03	C=C stretching; C=C stretching; C=C stretching	1636 cm^{-1}	1636 cm^{-1}	1636 cm^{-1}
04	S=O stretching; S=O stretching; S=O stretching	1407 cm^{-1}	1408 cm^{-1}	1407 cm^{-1}
05	C-O stretching; C-O stretching; C-O stretching	1095 cm^{-1}	1085 cm^{-1}	1095 cm^{-1}

Table 6: Percentage Yield of Phytosomal Formulations

Formulation	Percentage yield(%)
F1	80%
F2	70%
F3	40%
F4	50%
F5	46%
F6	53%
F7	40%
F8	33%
F9	40%

Table 7: Drug Entrapment Efficiency

Formulation code	% Entrapment efficiency
F1	90.90
F2	85.91
F3	83.31
F4	81.17
F5	83.64
F6	90.01
F7	92.91
F8	72.34
F9	76.79

Determination of Percentage Yield

The following equation was used to calculate the assurance of the percentage yield of formulations [Table 6].

$$\%Yield = \frac{Practical\ yield}{Theoretical\ yield} \times 100$$

Determination of Particle Size

Optical microscopy was used to determine particle size, and the particle size of ixora coccinea formulations was 63μm. Optical microscopy was used to determine particle size, and the size of chrysanthemum morifolium fomulations was found to be 56μm.

The particle size of *Tinospora cardifolia* formulations was determined using optical microscopy and was 76μm.

Drug Entrapment Efficiency

Virtues for such efficiency of drug entrapment within produced phytosomes with *Ixora coccinea,*

Table 8: Invitro Drug Release Studies

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	11.5	20.6	12.6	36.9	38.1	12.3	13.5	10.3	13.3
2	19.9	31.5	19.7	39.4	42.5	24.6	27.7	17.1	18.9
3	34.7	39.6	33.8	45.3	45.6	38.2	39.1	28.4	31.4
4	48.9	42.3	46.8	49.7	51.1	40.2	42.9	30.5	40.6
5	60.4	58.4	57.2	61.2	55.6	53.9	54.5	52.7	53.8
6	72.5	71.5	70.8	66.4	61.3	75.9	68.3	64.2	67.2
7	83.2	80.5	80.6	69.1	65.4	89.5	74.6	75.2	76.5
8	98.7	92.3	96.5	70.1	78.9	92.5	80.2	82.5	81.3

Table 9: Data of Drug Release – Kinetics of Optimized Formulation

Time (Hr)	Cumulativ % drug released	% Drug remaining	Square root time	Log Cumu % drug remaining	Log time	Log Cumu % drug released	% Drug released	Cube Root of % drug Remaining(Wt)	Wo-Wt
0	0	100	0.000	2.000	0.000	0.000	100	4.642	0.000
1	11.5	88.5	1.000	1.947	0.000	1.061	11.5	4.456	0.186
2	19.9	80.1	1.414	1.904	0.301	1.299	8.4	4.311	0.331
3	34.7	65.3	1.732	1.815	0.477	1.540	14.8	4.027	0.615
4	48.9	51.1	2.000	1.708	0.602	1.689	14.2	3.711	0.931
5	60.4	39.6	2.236	1.598	0.699	1.781	11.5	3.409	1.233
6	72.5	27.5	2.449	1.439	0.778	1.860	12.1	3.018	1.624
7	83.2	16.8	2.646	1.225	0.845	1.920	10.7	2.561	2.081
8	98.7	1.3	2.828	0.114	0.903	1.994	15.5	1.091	3.551

Chrysanthemum morifolium, and Tinospora cardifolia, F1 to F9, are shown in the above table and thus are found appropriate for each formulation [Table 7].

Therefore, formulations developed by this provide superior value cholestrol complexation – F1 to F3.

Invitro Drug Release Studies

The in vitro drug release from F1 to F9 was preserved in Table 8. It is executed that 8-hour drug releases time profile From the results, it was reported that F1 formulation preparation using Ixora coccinea exhibited 19.9% of drug release, less than 30% indicating that worst release was not observed.

This is the desired characteristic to be passed by the control release formula. At the end of the 4th hour, 48.9 % of drug release was observed 98.7% of Drug was released at the end of the 8th hour.

Release Kinetics

The Drug's release from phytosomes indicates the mechanism of hixon drug release (R2 = 0.9976), which involves dissolution factors from the amphiphilic nature of cholesterol. The Information from dissolution experiments have been modelled using a variety of Kinetics equation the results of kinetic models was present in Table 9. The data were plotted according to the mathematical models results exhibited that optimized phytosomes followed zero order kinetics with regression value (0.9993).

Optimization of Phytosomes

Phytosomes (F1) formulation showed better percentage yield, EE, particle size, and drug release than other phytosomes. From the results, F1 was selected as optimized phytosomes.

CONCLUSION

Numerous chronic diseases are thought by experts to be influenced by inflammation. An illustration of this would be the metabolic syndrome, which encompasses diabetes, type 2 cardiovascular disease, and being overweight. People with these

illnesses typically have higher concentrations or markers of inflammation within their organs. A body's natural defense response involves inflammation, which further assists recovery. A foreign substance, such as a thorn, an irritation, or even an infection, may be the assailant. Pathogens usually cause diseases, including bacteria, viruses, and other creatures. Your body sometimes perceives its very own tissues or cells as harmful. Autoimmunity problems such as type 1 diabetes may develop due to such a reaction. According to specialists, inflammation might play a part in various chronic illnesses. This metabolic syndrome mainly encompasses type two diabetes, cardiovascular disease, and overweight is an instance of all this. Inflammatory mediators were typically found in higher concentrations inside the bodies of individuals with all these disorders.

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Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

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REFERENCES

[1] M S Baliga and P J Kurian. Ixora coccinea Linn.: Traditional uses, phytochemistry and pharmacology. *Chinese journal of integrative medicine*, 18(1):72–79, 2012.

[2] T O Idowu, A O Ogundaini, A O Salau, E M Obuotor, M Bezabih, and B M Abegaz. Doubly linked, A-type proanthocyanidin trimer and other constituents of Ixora coccinea leaves and their antioxidant and antibacterial properties. *Phytochemistry*, 71(17-18):2092–2098, 2010.

[3] S Saha and S Ghosh. Tinospora cordifolia: One plant, many roles. *Ancient science of life*, 31(4):151, 2012.

[4] N Thakur, P Mittal, R Kaur, and M Goswami. Phytochemical screening of gum extracted from curcuma amada. *International Journal of Pharmacognosy*, 2(8):419–425, 2015.

[5] A L Thakur and K S Patil. Formulation of Alkaloid Loaded Phytosomes from Tinospora cordifolia and ex-vivo Intestinal Permeability Study. *Indian Journal of Pharmaceutical Education and Research*, 55(2):474–482, 2021.

[6] W D Ratnasooriya, S A Deraniyagala, G Galhena, S S P Liyanage, S D N K Bathige, and J R A C Jayakody. Anti-inflammatory Activity of the Aqueous Leaf Extract of Ixora coccinea. *Pharmaceutical biology*, 43(2):147–152, 2005.

[7] Z Asadi, T Ghazanfari, and H Hatami. Anti-inflammatory effects of Matricaria chamomilla extracts on BALB/c mice macrophages and lymphocytes. *Iranian Journal of Allergy, Asthma and Immunology*, pages 63–73, 2020.

[8] S Karole and G K G S Gupta. Preparation and evaluation of phytosomes containing ethanolic extract of leaves of Bombax ceiba for hepatoprotective activity. *Evaluation*, 6(2):1–5, 2019.

[9] C Y Ragasa, F Tiu, and J A Rideout. New cycloartenol esters from Ixora coccinea. *Natural product research*, 18(4):319–323, 2004.

[10] S A Salmataj, S U Kamath, V R Murty, and S R Pai. Amelioration of arsenic-induced oxidative stress in CHO cells by Ixora coccinea flower extract. *Biotech*, 8(3):1–7, 2018.

[11] A M Ghazi and M A Bayati. Anti-proliferative of the phytosome propolis, phytosome lycopene and synergistic effect on the benign prostatic hyperplasia cells in-vitro. *Plant Arch*, 20:6579–6589, 2020.

[12] R E Sasongko, S Surini, and F C Saputri. Formulation and characterization of bitter melon extract (momordica charantia) loaded phytosomes. *Pharmacognosy Journal*, 11(6):1235–1241, 2019.

[13] S Surini, H Mubarak, and D Ramadon. Cosmetic serum containing grape (Vitis vinifera L.) seed extract phytosome: Formulation and in vitro penetration study. *Journal of young pharmacists*, 10(2s):51–55, 2018.

[14] M A Versiani, A Ikram, S Khalid, S Faizi, and I A Tahiri. Ixoroid: a new triterpenoid from the flowers of Ixora coccinea. *Natural product communications*, 7(7), 2012.

[15] C Y Ragasa, F Tiu, and J A Rideout. New cycloartenol esters from Ixora coccinea. *Natural product research*, 18(4):319–323, 2004.

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