TOPICAL LIPOSOMAL LOTION OF *CARDIOSPERMUM HALICACABUM* FOR ANTI INFLAMMATORY ACTION IN RHEUMATOID ARTHRITIS

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ABSTRACT:

Rheumatoid arthritis is a chronic autoimmune inflammatory disorder that primarily affects synovial joints and often requires long-term therapy, which may lead to systemic side effects. The present study focuses on the development of a topical liposomal herbal lotion containing Cardiospermum halicacabum extract to enhance localized anti-inflammatory action and improve patient compliance. The aerial parts of C. halicacabum were subjected to ethanolic extraction and evaluated for phytochemical constituents, which confirmed the presence of flavonoids, glycosides, alkaloids, and tannins. The extract was characterized using FTIR, UV–Visible spectroscopy, and thin layer chromatography to confirm functional groups and marker compounds. Liposomes were prepared using soya lecithin and cholesterol and incorporated into a herbal lotion base. The formulated liposomal lotion was evaluated for physicochemical parameters such as appearance, pH, viscosity, spreadability, skin irritation, and microscopic characteristics. In vitro anti-inflammatory activity was assessed using the protein denaturation assay, showing concentration-dependent inhibition comparable to the standard drug. Morphological studies using microscopy and SEM confirmed the formation of spherical, uniformly distributed liposomes. Molecular docking studies revealed favorable binding interactions of kaempferol with the TLR4 receptor, supporting the observed anti-inflammatory activity. Overall, the results demonstrate that liposomal encapsulation significantly enhances the therapeutic potential of Cardiospermum halicacabum, suggesting that the developed topical liposomal herbal lotion is a promising, safe, and effective alternative for the management of rheumatoid arthritis.

Keywords:

Cardiospermum halicacabum; Liposomes; Herbal lotion; Rheumatoid arthritis; Anti-inflammatory activity; Targeted drug delivery; Protein denaturation assay

INTRODUCTION:

Targeted drug delivery directs medications to diseased tissues while limiting exposure to healthy organs, improving treatment and reducing side effects. In rheumatoid arthritis (RA), it helps deliver drugs specifically to inflamed joints. Success relies on identifying RA-specific targets and using stable, biocompatible carriers. Systems such as nanoparticles and liposomes enhance solubility, stability, and precise delivery by recognizing markers on inflamed synovium. They also help retain drugs longer at the disease site. Although effective, challenges like off-target distribution and systemic toxicity remain, requiring further refinement for safer RA therapy. [1]

Liposomes are tiny, biocompatible vesicles made of phospholipids that can transport both hydrophilic and lipophilic medications. Since their identification by Bangham in 1965, they have become crucial for safeguarding drugs, enhancing stability, and facilitating safer, targeted delivery. Their dimensions, charge, and surface can be altered to extend circulation duration and improve tissue localization. In rheumatoid arthritis, liposomes aid in targeting anti-inflammatory drugs to swollen joints, minimizing side effects and enhancing treatment results. They penetrate cells via membrane fusion or absorption by phagocytes in the inflamed synovium, facilitating regulated, localized drug release.[2, 3]

A lotion is a viscous topical preparation, usually a solution, emulsion, or suspension—applied gently to unbroken or inflamed skin. It offers moisturizing, soothing, and emollient effects and may also provide anti-inflammatory, antibacterial, sunscreen, or therapeutic benefits. Lotions contain humectants, oils, sterols, and fine solids to ensure smooth, nongreasy application and are typically applied with the hands, cotton, or brushes. Cosmeceuticals combine cosmetic use with active pharmaceutical ingredients, helping in moisturization, anti-aging, skin lightening, scar care, and acne treatment, thereby supporting overall skin health and appearance.[4]

Rheumatoid arthritis (RA) is a long-lasting autoimmune condition in which the immune system targets the joints, resulting in ongoing inflammation, discomfort, rigidity, and progressive joint deterioration. It mainly influences the smaller joints, but it can also affect larger organs.

Arthritis generally indicates joint inflammation and includes over 100 rheumatic disorders that cause pain, swelling, and reduced mobility. Around 15% of India's population is impacted, with prevalent types being osteoarthritis, rheumatoid arthritis, gout, and ankylosing spondylitis.[5]

AIM:

To formulate and evaluate a topical liposomal herbal lotion containing *Cardiospermum halicacabum* for its anti-inflammatory activity in the management of rheumatoid arthritis.

OBJECTIVES:

The objectives include preparing and characterizing the liposomes, developing a stable herbal lotion, and evaluating its physicochemical properties and in-vitro anti-inflammatory activity. The performance of the liposomal lotion is compared with a conventional lotion to assess its improved therapeutic effectiveness.

MATERIALS AND METHODS:

1.Collection of plant materials:

Fresh aerial parts of *Cardiospermum halicacabum* were collected from the local regions of Tiruttani, Kanchipuram District, Tamil Nadu, during the month of September. Collected samples were cleaned to remove dust and foreign particles and then air-dried under shade until further processing.

2.Identification and authentication of plant material:

The collected plant material was submitted to the Siddha Central Research Institute (SCRI), Chennai, Ministry of AYUSH, Government of India, for taxonomic verification. The sample was identified as *Cardiospermum halicacabum* belongs to the family Sapindaceae. The specimen was authenticated as *Cardiospermum halicacabum L.* with the authentication number C04092502H dated 06.09.2025.

3.Plant profile:

Vernacular names:[6]

English	Balloon Vine
Tamil	Modakkathan
Telugu	Budda kakara
Malayalam	Ulincha, Uzhinja
Kannada	Bekkinabudde gida
Hindi	Kanphuta
Marathi	Kaanphodi
Bengali	Lata futki

Table 1: Vernacular Names of *Cardiospermum halicacabum*

Taxonomical classification:[7]

Kingdom	Plantae
Phylum	Tracheophytes

Subphylum	Angiosperms
Class	Eudicots
Order	Sapindales
Family	Sapindaceae
Genus	Cardiospermum
Species	Halicacabum

Table 2: Taxonomical Classification of *Cardiospermum halicacabum*

Figure 1: Leaves of *Cardiospermum halicacabum*

4. Extraction of plant material:[8]

The freshly collected aerial parts of *Cardiospermum halicacabum* were washed thoroughly to remove dust and impurities and then shade-dried for 10–12 days. Once completely dried, the plant material was coarsely powdered in a grinder and stored in an airtight container. *C.halicacabum* coarse leaf powder (50g) was macerated for 72hrs in 300ml of ethanol by using cold maceration extraction method. After maceration, the mixture was filtered through muslin cloth followed by Whatman filter paper to obtain a clear extract. Evaporation was carried out to concentrate the extract. The partially concentrated liquid extract was collected and stored in a well-closed container for future use in formulation work.

Figure 2: Maceration of *Cardiospermum halicacabum*

Figure 3: Filtered extract of *Cardiospermum halicacabum*

5.Phytochemical screening:[9-12]

S.No.	Identification test	Observation	Inference
1.	**Alkaloids** **a. Mayer's Test** Test extract + Mayer's reagent **b. Tannic acid Test** Test extract + Tannic acid solution	Cream coloured precipitate Buff coloured precipitate	Presence of alkaloids Presence of alkaloids
2.	**Glycosides** **a**. Extract +5ml dil.H2SO4, heat on water bath, neutralize with 5% NaOH solution,0.1ml Fehling's A and B until it becomes alkaline, heat on water bath for 2 minutes. **b**. Extract +5ml water, heat on water bath, 5% NaOH solution,0.1ml Fehling's	Red precipitate Red precipitate	Presence of Glycosides Presence of Glycosides

	A and B until it becomes alkaline, heat on water bath for 2 minutes.		
3.	**Tannins** **a. Gelatin Test** Test solution + Gelatin solution containing 10%NaCl **b. Lead acetate Test** Alcoholic extract + Lead acetate Solution.	Precipitate is formed White precipitate	Presence of Tannins Presence of Tannins
4.	**Carbohydrates** **a. Molisch's Test** Extract + Molisch's reagent, shake and add Conc.H2SO4from sides of test tube. **b. Fehling's Test** Extract + Fehling's Solution A and B reagents	Formation of Violet colour ring at junction of 2 liquids. Brick red precipitate	Presence of Carbohydrates Presence of Carbohydrates
5.	**Flavonoids** **a. NaOH test** Extract + NaOH Solution **b. Lead acetate Test** Extract + Lead acetate solution	Coloured precipitate Yellow coloured precipitate	Presence of Flavonoids Presence of Flavonoids
6.	**Terpenoids** **Test for Volatile Oils** **a**. Extract placed on filter paper **b**. Extract + Alcohol **Test for Resins** **a**. Heat the extract **b.** Burn the extract	Filter paper is permanently stained. Soluble Softens and melts Smoky flame is produced	Presence of Volatile Oils Presence of Volatile Oils Presence of Resins Presence of Resins

Table 3: Phytochemical screening of plant extracts

6.FTIR Spectral Analysis for Functional Group Identification:[13, 14]

FTIR (Fourier Transform Infrared spectroscopy) is a rapid and non-destructive analytical technique used broadly in the identification and characterization of chemical functional groups in pharmaceutical and herbal samples. The technique is based on the absorption of infrared radiation

by molecules, which causes characteristic vibrational transitions and is representative of a unique molecular fingerprint. FTIR is commonly applied for the confirmation of the presence of phytoconstituents such as flavonoids, phenolics, alcohols, and glycosides, along with drug excipient compatibility tests in pharmaceutical formulations. Moreover, FTIR analysis helps in assessing chemical stability and maintaining structural integrity during the formulation development process. In the present study, FTIR spectroscopy was employed to characterize the functional groups present in the *Cardiospermum halicacabum* extract and to support its role in anti-inflammatory activity.

7.Absorption Spectrum Analysis Using UV–Visible Spectrophotometer:[14]

UV–Visible spectroscopy is a simple, rapid, and reliable analytical technique widely used in pharmaceutical and herbal research for the qualitative and quantitative evaluation of bioactive compounds. Many phytoconstituents such as flavonoids, phenolics, and other conjugated compounds absorb light in the ultraviolet and visible regions due to the presence of chromophores. UV–Visible spectroscopy helps in identifying these compounds, determining their absorption characteristics, and assessing extract purity and consistency. In the present study, UV–Visible spectroscopy was employed to characterize the *Cardiospermum halicacabum* extract and support its phytochemical profile related to anti-inflammatory activity.

8. Chromatographic evaluation:

Thin layer chromatography:[15]

TLC was carried out to qualitatively assess the hydroalcoholic extract of the powdered leaves. After development, the chromatographic spots were visualized under normal daylight and UV illumination. The retention factor (Rf) for each spot was calculated using the formula:

Rf = distance travelled by the sample / distance travelled by the mobile phase.

Stationary phase: Silica gel G.

Mobile phase: Toluene: Ethyl acetate: Acetic acid: Methanol (2.5:7:0.25:0.25)

Detecting agent: Iodine vapour.

9. Formulation development:

Method of preparation of herbal lotion:[16]

All ingredients were weighed according to the formulation. The ethanolic extract of *Cardiospermum halicacabum* was transferred into a beaker. Triethanolamine, glycerine, distilled

water, methyl paraben, and propyl paraben were added to form the aqueous phase, and the mixture was heated to 75°C.

S. No	Ingredients (Aqueous phase)	Quantity (50ml)
1.	*Cardiospermum extract*	20ml
2.	Triethanolamine	2ml
3.	Glycerin	2ml
4.	Distilled water	9ml
5.	Methyl paraben	0.5gm
6.	Propyl paraben	0.5gm
7.	Rose water	1ml
	Ingredients (Oil phase)	
8.	Stearic acid	8gm
9.	Coconut oil	3ml
10.	Almond oil	4ml

In a separate beaker, stearic acid, coconut oil, and almond oil were weighed and mixed thoroughly to form the oil phase, which was also heated to 75°C.

The hot oil phase was then slowly added to the hot aqueous phase with continuous stirring. After uniform mixing, rose water was added. The mixture was allowed to cool, and thus the herbal lotion was prepared.

Table 4: Formulation table for herbal lotion

Method of preparation of liposomes:[17]

A total of 1 g of soya lecithin and 0.25 g of cholesterol were added to a 100 mL beaker containing 20 mL of 70% ethanolic extract of *Cardiospermum halicacabum*. The mixture was gently heated to 60 °C with occasional stirring until a homogeneous solution was formed.

After complete dissolution, the mixture was allowed to evaporate to form a thin lipid layer. Subsequently, 20 mL of distilled water was added for rehydration of the lipid film, and the contents were shaken for 30 min to ensure complete dissolution of the thin layer.

The resulting dispersion contained liposomes along with excess water. The liposomes were separated by centrifugation at 3000 rpm for 30 min. The obtained pellet was observed under an optical microscope using a 10X objective lens, where the liposomal formulation was clearly visible.

S. No	Ingredients	Quantity
1.	Cholesterol	0.25gm
2.	Soya Lecithin	1gm

Table 5: Formulation table for liposome

Figure 4: Preparation of liposomes

Method of preparation of herbal liposomal lotion:[16, 17]

Take liposomes in a borosilicate glass beaker. The ethanolic extract of *Cardiospermum halicacabum* was transferred into a beaker. Triethanolamine, glycerine, distilled water, methyl paraben, and propyl paraben were added to form the aqueous phase, and the mixture was heated to 75°C.

In a separate beaker, stearic acid, coconut oil, and almond oil were weighed and mixed thoroughly to form the oil phase, which was also heated to 75°C.

The hot oil phase was then slowly added to the hot aqueous phase with continuous stirring. After uniform mixing, rose water was added. The mixture was allowed to cool, and thus the herbal liposomal lotion was prepared.

S. No	Ingredients	F1	F2
1.	*Cardiospermum* extract	20ml	-
2.	Liposomal loaded extract	-	20ml
3.	Triethanolamine	2ml	2ml
4.	Glycerin	2ml	2ml
5.	Distilled water	9ml	9ml
6.	Methyl paraben	0.5gm	0.5gm
7.	Propyl paraben	0.5gm	0.5gm
8.	Rose water	1ml	1ml
9.	Stearic acid	8gm	8gm

10.	Coconut oil	3ml	3ml
11.	Almond oil	4ml	4ml

Table 6: Formulation table for Lotion

9.Anti-inflammatory activity – Protein Denaturation Assay:[18, 19]

Material Required:

Acetyl salicylic acid, BSA was purchased from Sigma Aldrich, USA. 10X PBS was purchased from Himedia, India.

Procedure:

The primary reason for inflammation is the denaturation of proteins. The method of Mizushima and Kobayashi and Sakata et al. was used with minor adjustments to assess the inhibition of protein denaturation. 500 µL of 1% bovine serum albumin was incorporated into CH Sample (500, 250, 100, 50, and 10 µg/mL) of the test sample. This blend was maintained at room temperature for 10 minutes, then heated at 51°C for 20 minutes. The resulting solution was allowed to cool to room temperature, and absorbance was measured at 660 nm. Acetylsalicylic acid served as a positive control. The experiment was conducted in triplicate, and the percentage inhibition for protein denaturation was determined using:

% Inhibition=100−((A1-A2)/A0)* 100)

Where A1 represents the control's absorbance, A2 denotes the test sample's absorbance, and A0 indicates the absorbance of the positive control.

An IC50 value determination involved plotting a dose response curve. IC50 is the concentration needed to achieve 50% of the maximum scavenging capability. All tests and analyses were conducted in triplicate and averaged.

Figure 5: Protein denaturation assay

10. Evaluation Tests:[20, 21]

A. Physical examination:

Physical examination was carried out to assess the appearance, colour, odour, and homogeneity of the formulation.

The lotion showed a smooth, uniform texture without any phase separation or grittiness.

These observations indicate good physical stability.

B. pH evaluation:

The pH of the liposomal herbal lotion was measured using a calibrated pH meter.

The formulation showed a pH within the skin-compatible range (5.0–6.5), indicating it is safe and non-irritating for topical application.

C. Viscosity measurement (brookfield viscometer):

Viscosity was evaluated using a Brookfield viscometer with a suitable spindle and set speed.

The lotion showed consistent and stable viscosity, indicating good flow properties.

D. Spreadability test:

Spreadability was evaluated using the slip-and-drag method.

The herbal lotion showed good spreadability, indicating easy application on the skin.

Better spreadability improves uniform distribution of liposomes and enhances therapeutic action.

E. Skin irritation test:

The test was performed on a small area of skin to check for redness, itching, or swelling.

The liposomal herbal lotion showed no signs of irritation, indicating good skin compatibility.

F. Microscopical examination:

The liposomal formulation was examined under a microscope, where vesicles appeared spherical with smooth, well-defined boundaries.

The vesicles were uniformly distributed without aggregation, confirming proper liposome formation and stability.

11. Scanning Electron Microscopy (SEM):[22]

Introduction:

Scanning Electron Microscopy (SEM) is a powerful analytical technique used to study the surface morphology and structural characteristics of particulate systems at high magnification. In pharmaceutical research, SEM is widely employed to examine the size, shape, surface texture, and distribution of carriers such as liposomes. In the present study, SEM was used to observe the morphological features of the liposomal-loaded herbal lotion of *Cardiospermum halicacabum* and to confirm the formation and uniformity of liposomes.

Procedure:

A small amount of the liposomal formulation was placed on a clean aluminium stub and allowed to dry at room temperature. The dried sample was then coated with a thin layer of gold using a sputter coater to enhance electrical conductivity. The coated sample was examined under a scanning electron microscope at appropriate accelerating voltage, and micrographs were recorded at different magnifications to study the surface morphology and structural characteristics of the liposomes.

12. Molecular docking study: [23, 24]

A silicon-based protein-ligand docking software named Autodock Vina 1.5.6 was used to evaluate the binding affinities and interaction patterns between the compound CG and its proposed targets. The molecular structure of Kaempferol (PubChem Compound CID 5280863) was retrieved from the PubChem database. The 3D coordinates for the target proteins TLR4 were sourced from the PDB website. The molecular and protein files were converted into PDBQT format by eliminating water molecules and adding polar hydrogen atoms. Grid boxes were created to cover the protein domains and permit the free movement of the molecules. Autodock Vina 1.5.6 was utilized for conducting the docking studies. We extracted the lowest binding energies and estimated inhibition constants (pKi) from the docking log files (dlg).

RESULTS AND DISCUSSION:

1.Phytochemical screening:

It has been verified that the leaves of *Cardiospermum halicacabum* possess numerous phytochemical compounds. Consequently, establishing a standard is essential to uphold their quality. The samples underwent initial phytochemical analysis to identify the different phytochemical components. The examination showed the existence of alkaloids, glycosides, flavonoids, tannins, and additional substances.

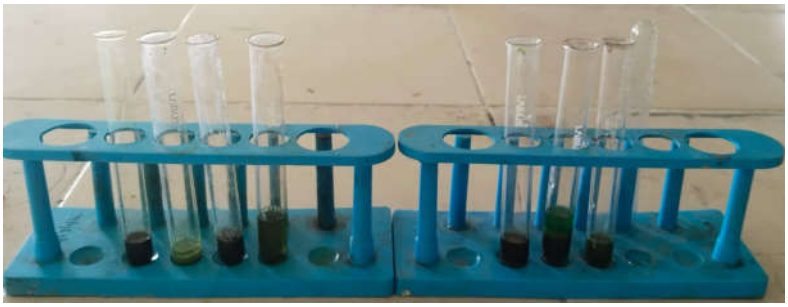

Figure 6: Phytochemical screening of *Cardiospermum helicacabum* extract

Preliminary phytochemical analysis of *Cardiospermum halicacabum* leaves extract

S. No	Test	Ethanolic extract of *Cardiospermum halicacabum*
1.	Alkaloids	+
2.	Glycosides	+
3.	Tannins	+
4.	Carbohydrates	+
5.	Flavonoids	+
6.	Terpenoids	_

Table 7: Phytochemical screening of plant extracts

(+) Presence (-) Absence

2. FTIR:

FTIR analysis of the *Cardiospermum halicacabum* extract revealed a broad peak at 3322.8 cm^{-1}, indicating O–H stretching of phenolic and flavonoid compounds. Peaks at 2975–2926 cm^{-1} correspond to C–H stretching of aliphatic groups. A strong band at 1650 cm^{-1} confirmed C=O stretching of flavonoids. Aromatic C=C stretching appeared between 1600–1580 cm^{-1}, while peaks at 1276–1210 cm^{-1} indicated C–O stretching of flavonoid glycosides. The band at 1080–1030 cm^{-1} corresponded to C–H bending of aromatic structures.

These peaks collectively confirm the presence of flavonoids, phenolics, and glycosides in the extract.

Peak (cm-1)	Functional group	Interpretation
3322.8	O-H stretch	Phenols and Flavonoids
2928.9	C-H stretch	Aliphatic compounds
1650.9	C=O / C=C stretch	Conjugated carbonyl compounds
1451.4	Aromatic C-H bending	Aromatic phenolic compounds
1028	C-O stretch	Glycosides / Polysaccharides

Table 8: FTIR Data for herbal extract

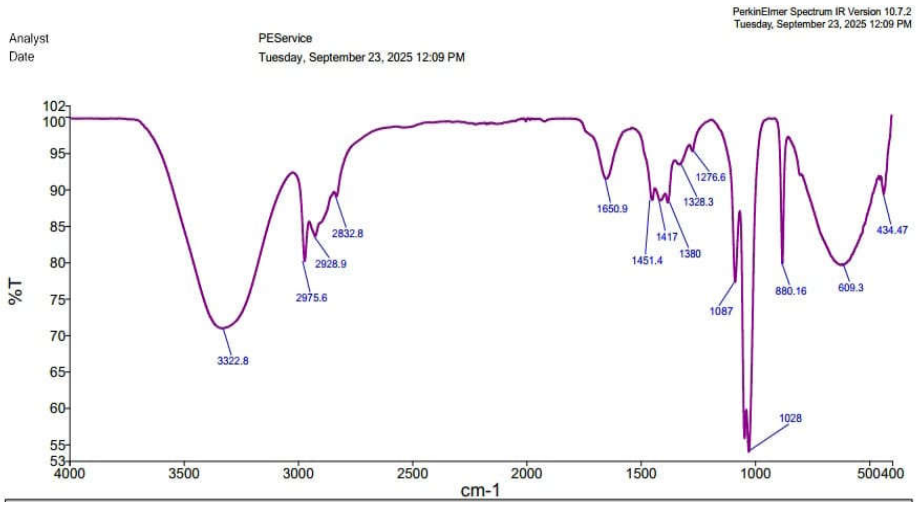

Figure 7: FTIR spectrum of *Cardiospermum halicacabum*

3.UV:

The UV–Visible spectrum of the sample was recorded in the range of 200–800 nm using a JASCO V-730 spectrophotometer. The spectrum showed three characteristic absorption peaks at 349 nm (λmax), 460 nm, 669 nm.

The major absorption maximum at 349 nm indicates the presence of flavonoid compounds, which typically show strong π→π* transitions in the range of 320–380 nm. The minor peak at 460 nm corresponds to n→π* transitions usually associated with conjugated polyphenols, while the peak at 669 nm may be attributed to the presence of chlorophyll derivatives or extended conjugation within the extract.

These characteristic peaks confirm the presence of UV-active phytoconstituents such as flavonoids and polyphenolic compounds in the sample.

Wavelength (nm)	Absorbance (Abs)	Observation
349 nm	2.6975	Major peak (maximum absorbance)
460 nm	1.7860	Secondary peak
669 nm	0.8995	Minor peak

Table 9: UV Absorbance for herbal extract

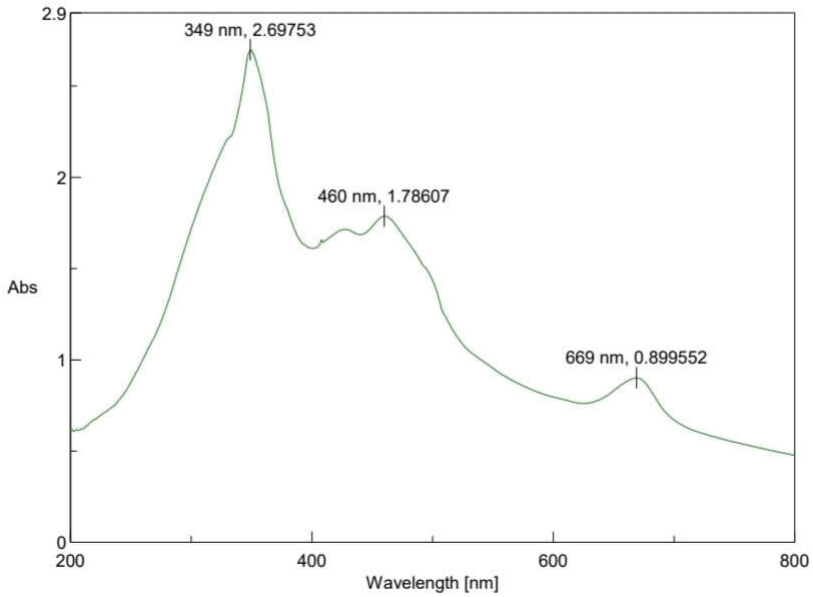

Figure 8: UV-Visible absorption spectrum of *Cardiospermum halicacabum*

4.TLC:

Thin layer chromatography was performed to detect quercetin in the hydroalcoholic leaf extract (HAEAM) using silica gel plates. A solvent system of toluene, ethyl acetate, acetic acid, and methanol (2.5:7:0.25:0.25) was used, and spots were visualized with iodine vapor. The standard quercetin showed an Rf value of 0.65, while the extract showed an Rf value of 0.63. The close similarity in Rf values confirms the presence of quercetin in the extract.

Mobile phase composition (v/v)	Detection method	Sample	Rf value	Observation
Toluene: Ethyl acetate: Acetic acid: Methanol (2.5: 7: 0.25: 0.25)	Iodine vapor	Quercetin (Standard)	0.65	Distinct spot
Toluene: Ethyl acetate: Acetic acid: Methanol (2.5: 7: 0.25: 0.25)	Iodine vapor	HAEAM (Extract)	0.63	Spot like standard

Table 10: TLC

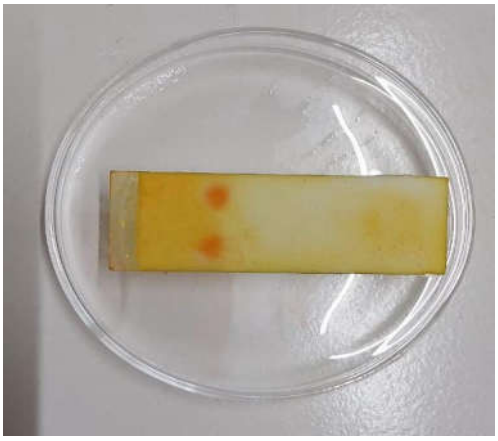

Figure 9: TLC profile of Cardiospermum halicacabum

4. Anti-inflammatory activity – Protein Denaturation Assay:

Concentration (µg / ml)	% Inhibition of protein denaturation
10	35.99
50	45.87
100	52.64
250	61.28
500	69.76

Standard (Aspirin)	80.93

Table 11: Protein denaturation assay

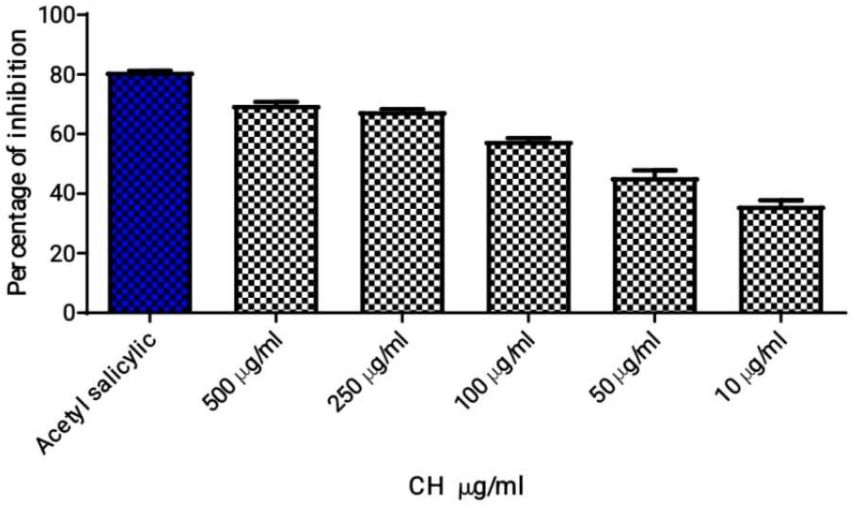

Figure 10: Protein denaturation inhibitory activity of *Cardiospermum helicacabum* extract compared with acetyl salicylic acid

5. Evaluation Test:

S. No	Physiochemical parameters	Herbal lotion	Liposomal loaded herbal lotion
1.	Appearance	Smooth, uniform lotion	Smooth, uniform lotion
2.	Colour	Dark green	Light green
3.	Odour	Pleasant, characteristic	Pleasant, characteristic
4.	Texture	Non-greasy, smooth	Non-greasy, smooth
5.	Phase separation	No phase separation	No phase separation
6.	pH	5.63	6.06
7.	Viscosity	1673cPs	2320cPs

8.	Spreadability	Good spreadability, spreads easily on skin	Improved spreadability, uniform spreading
9.	Skin irritation test	No redness or irritation	No redness or irritation

Table 12: Evaluation test of Lotion

F. Microscopical examination:

Liposomes observed under microscope. Spherical and uniform vesicles seen. Confirms successful liposome formation. Size range of liposome 0.01-5.0 micrometer.

6. SEM:

The Particle size of drug is 3µm

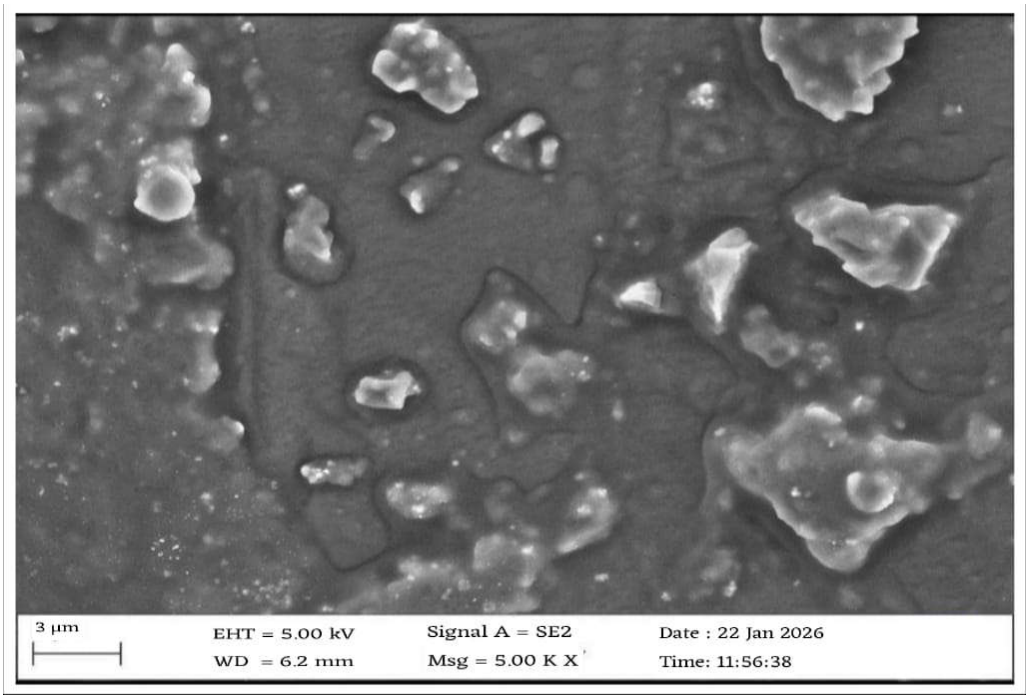

Figure 11: SEM images of drug particles

7. Molecular docking:

Molecular docking studies of the phytoconstituent kaempferol from *Cardiospermum halicacabum* were conducted with the Antiarthritic-related protein using Autodock. The docking results revealed a binding energy of -6.59 Kcal/mol for TLR4, suggesting a moderate interaction between

kaempferol and the active site of the protein. The inhibition constant (Ki) values were found to be 1 4.77 µM for TLR4, indicating a moderate binding affinity for the respective active site.

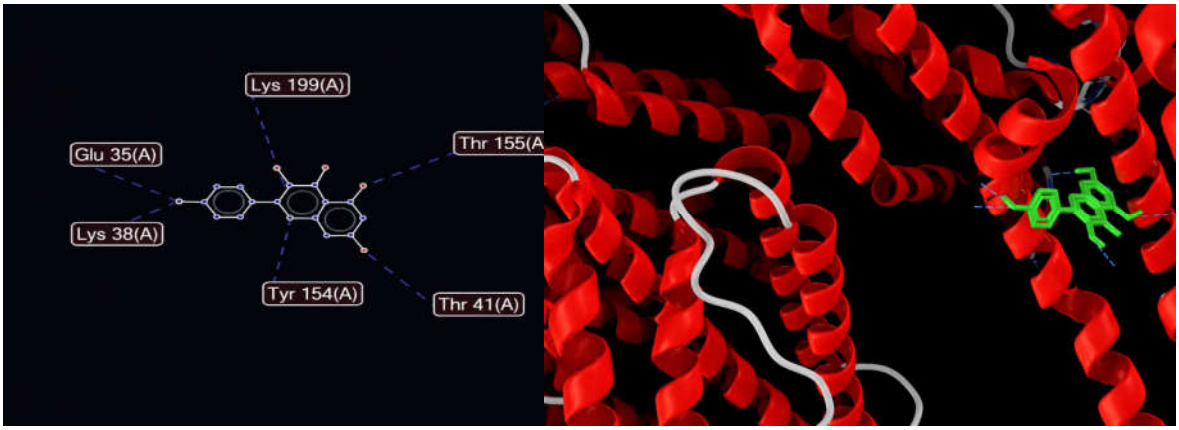

Figure 12: Molecular docking interaction of Kaempferol with TLR4

S. No	Parameter	TLR4
1.	Binding energy (Kcal /mol)	-6.59
2.	Ligand efficiency	-0.31
3.	Inhibition constant (µM)	14.77

Table 13: Docking studies using TLR4 with Kaempferol

CONCLUSION:

The current study effectively illustrated the development and assessment of a topical liposomal lotion containing Cardiospermum halicacabum extract for the treatment of inflammatory disorders linked to rheumatoid arthritis. By increasing stability, skin penetration, and retention at the application site, the adoption of a liposomal carrier system greatly improved the delivery of phytoconstituents. The liposomal formulation demonstrated superior physicochemical properties, such as appropriate pH, increased viscosity, improved spreadability, and outstanding homogeneity, when compared to the traditional herbal lotion, demonstrating its suitability for topical application. A concentration-dependent inhibitory impact was found in an in vitro anti-inflammatory evaluation utilizing the protein denaturation assay, showing successful suppression of inflammation-related protein denaturation. The liposomal formulation's increased activity demonstrates how vesicular encapsulation enhances medicinal efficacy. The developed formulation's safety and biocompatibility are further supported by the lack of skin irritation. The creation of spherical, uniformly dispersed liposomes within a suitable size range was successfully confirmed by microscopical and SEM investigations, guaranteeing effective drug loading and release. Furthermore, because kaempferol exhibited a good binding affinity with the TLR4 receptor, a

crucial mediator in inflammatory pathways involved in rheumatoid arthritis, molecular docking studies offered mechanistic support for the reported anti-inflammatory effect. Overall, this work shows that the anti-inflammatory potential and topical application of Cardiospermum halicacabum extract are significantly increased by liposomal inclusion. With a lower risk of systemic side effects, the created herbal liposomal lotion is a viable, non-invasive, and patient-friendly substitute for traditional anti-inflammatory treatments. To confirm its long-term effectiveness and therapeutic potential in the treatment of rheumatoid arthritis, more in vivo research and clinical assessments are required.

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