WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 15, 2412-2426. Research Article ISSN 2277–7105

FORMULATION AND EVALUATION OF HERBAL MICROSPHERES LOADED WITH PAPAYA LEAF AND GUDUCHI STEM EXTRACT FOR ANTI THROMBOCYTOPENIC ACTIVITY

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Article Received on 05 July 206,
Article Revised on 25 July 2026,
Article Published on 04 August 2026,

https://doi.org/10.5281/zenodo.21820517

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How to cite this Article: Challa Sravanthi*, Madharam Swapna, Garuda Karthik, G. Tulja Rani (2026). Formulation And Evaluation Of Herbal Microspheres Loaded With Papaya Leaf And Guduchi Stem Extract For Anti Thrombocytopenic Activity. World Journal of Pharmaceutical Research, 15(15), 2412–2426

1. ABSTRACT

Thrombocytopenia is a hematological disorder characterized by a reduced platelet count, which increases the risk of bleeding and other serious complications. Herbal medicines have gained considerable attention as safer and cost-effective alternatives due to their diverse pharmacological properties. The present study aims to formulate and evaluate herbal microspheres containing Carica papaya leaf and Tinospora cordifolia (Guduchi) stem extracts for their potential anti-thrombocytopenic activity. The herbal extracts were incorporated into microspheres using the ionotropic gelation technique with sodium alginate as the polymer. The prepared microspheres were evaluated for percentage yield, particle size, entrapment efficiency, swelling index, surface morphology, and in vitro drug release. Their antioxidant potential was assessed using the membrane stabilization studies were performed to investigate their anti-thrombocytopenic potential, which is associated with protection of blood cells. The optimized formulation demonstrated satisfactory physicochemical characteristics, sustained drug release, and promising antioxidant and membrane stabilization activities. These findings suggest that microsphere-based delivery of papaya leaf and Guduchi extracts may improve the efficacy and controlled release of phytoconstituents, thereby enhancing their therapeutic potential. Overall, this study highlights the promise of herbal microspheres as an effective drug delivery approach for the management of thrombocytopenia and provides a foundation for future in vivo and clinical investigations.

KEYWORDS: Thrombocytopenia, Herbal Microspheres, Carica Papaya Leaf Extract, Tinospora Cardifolia, Ionotropic Gelation, Membrane Stabilization Assay.

2. INTRODUCTION

Thrombocytopenia is a common hematological disorder characterized by a platelet count below the normal physiological range of 150,000–450,000 platelets/µL of blood. Platelets play an essential role in maintaining hemostasis by preventing excessive bleeding through clot formation. A reduction in platelet count can lead to symptoms ranging from mild bruising and petechiae to severe internal bleeding and life-threatening hemorrhage. Thrombocytopenia may occur due to decreased platelet production, increased platelet destruction, or abnormal sequestration of platelets in the spleen. It is associated with several conditions, including dengue fever, viral infections, autoimmune disorders, bone marrow diseases, chemotherapy, and certain medications. Despite the availability of conventional therapies such as corticosteroids, immunoglobulins, thrombopoietin receptor agonists, and platelet transfusions, these treatments are often expensive, associated with adverse effects, or provide only temporary relief. Therefore, there is a growing need to explore safer, affordable, and effective therapeutic alternatives.

Medicinal plants have been used for centuries in traditional systems of medicine to treat a variety of diseases. Their therapeutic effects are mainly attributed to the presence of bioactive phytochemicals such as flavonoids, alkaloids, phenolic compounds, tannins, glycosides, saponins, and terpenoids. These naturally occurring constituents exhibit a wide range of biological activities, including anti-inflammatory, immunomodulatory, antimicrobial, and tissue-protective properties. Herbal medicines are increasingly being recognized for their potential in the management of blood disorders due to their comparatively lower toxicity and better patient acceptance.

Among medicinal plants, Carica papaya (papaya) has attracted considerable attention because of its beneficial effects on platelet recovery. Papaya leaf contains several phytoconstituents, including flavonoids, alkaloids, vitamins, minerals, and phenolic compounds. Previous studies have suggested that papaya leaf extract may stimulate platelet production, improve bone marrow function, and protect blood cells from damage. It has also been widely used as a supportive therapy in dengue-associated thrombocytopenia, where a rapid decline in platelet count is frequently observed. Clinical and experimental studies have reported improvement in

platelet counts following administration of papaya leaf preparations, making it one of the most promising herbal candidates for thrombocytopenia management.

Another important medicinal plant is Tinospora cordifolia (Guduchi), a well-known herb in Ayurveda. Guduchi is valued for its immunomodulatory, anti-inflammatory, antioxidant, hepatoprotective, and hematopoietic properties. The stem of Guduchi contains alkaloids, diterpenoid lactones, glycosides, steroids, and polysaccharides that contribute to its pharmacological activities. It has traditionally been used to improve immunity, enhance blood health, and support recovery from infections. The combined use of papaya leaf and Guduchi may provide complementary therapeutic benefits because both plants possess biological activities that support hematological function and protect cellular integrity.

Microspheres are one such advanced drug delivery system that offers several advantages over conventional dosage forms. They are small, spherical particles generally ranging from 1 to 1000 µm in diameter, capable of encapsulating both synthetic drugs and herbal extracts.

Microspheres provide sustained and controlled release of active constituents, protect sensitive phytochemicals from degradation, improve drug stability, and enhance therapeutic efficacy.

They also reduce dosing frequency and improve patient compliance. Because of these advantages, microsphere-based formulations have gained considerable interest in the development of herbal medicines.

Based on these considerations, the present research was designed to formulate and evaluate herbal microspheres loaded with Carica papaya leaf and Tinospora cordifolia stem extracts using the ionotropic gelation technique. The study aims to develop a stable herbal drug delivery system with improved release characteristics and to assess its membrane stabilizing potential as a preliminary indicator of its usefulness in the management of thrombocytopenia. The findings of this work may contribute to the development of an effective herbal formulation that combines the therapeutic benefits of traditional medicinal plants with the advantages of modern pharmaceutical drug delivery systems.

3. MATERIALS AND METHODS

3.1 Materials and Reagents

Plant Materials: Leaves of Carica papaya and stems of Tinospora cordifolia. Polymers: Sodium Alginate (medium viscosity).

Cross-linking Agents: Calcium Chloride (CaCl_2), Glutaraldehyde. Solvents: Tween 80, Ethanol (95% AR Grade), Distilled Water.

3.2 Collection and Authentication

Sourcing: Fresh samples will be collected from malla reddy pharmacy college garden

Authentication: The specimens will be authenticated by a Taxonomist at [government degree college Kukatpally, medchal district].

Processing: Samples are washed with deionized water to remove debris, shade-dried for 10-15 days at room temperature, and ground into a coarse powder using a mechanical grinder.

3.3 Extraction Protocol (Hydro-Alcoholic Extraction)

Maceration was selected as the method of extraction due to its simplicity, cost-effectiveness, and suitability for thermolabile compounds that degrade under high temperatures.

3.4 Materials Used

Coarsely powdered papaya leaves and guduchi stem powder, Ethanol (95%), Conical flask, Muslin cloth, Whatman No.1 filter paper, Rotary Evaporator.

PROCEDURE

Weighing: 50 grams of the dried Papaya leaf and guduchi stem powder was accurately weighed.

Soaking: The powder was transferred into a clean, dry 1000 mL conical flask, and 500 mL of ethanol (95%) was added in a 1:10 drug-to-solvent ratio.

Maceration: The flask was sealed and kept undisturbed at room temperature (25 ± 2°C) for 6 to 12 days. The mixture was occasionally shaken (3–4 times a day) to enhance solvent penetration and extraction efficiency.

Filtration: After 72 hours, the contents were first filtered through muslin cloth to remove coarse particles and then filtered again using Whatman No.1 filter paper to obtain a clear extract.

Concentration: The filtrate was concentrated using a rotary evaporator under reduced pressure at 40–45°C to remove the solvent and obtain a semisolid extract.

Drying and Storage: The concentrated extract was further dried using a water bath at 40°C to eliminate any remaining traces of ethanol. The dried extract was stored in an airtight amber colored glass container in a refrigerator (4°C) until further use in the preparation of microspheres.

Formulation Development (Ionotropic Gelation Technique)

1. Polymer Solution: Sodium Alginate is dissolved in 100 mL of distilled water to create concentrations of 1%, 2%, and 3% w/v.
2. Drug Loading: The lyophilized extract (Ratio 1:1 of Papaya and Guduchi) is added to the alginate solution under constant stirring.
3. Dropping Process: The mixture is extruded through a 22-gauge syringe needle into a chilled 5 % w/v CaCl_2 solution at a rate of 2 mL/min.
4. Curing: The droplets (microspheres) are allowed to "cure" in the CaCl_2 bath for 30, 60, or 120 minutes to optimize hardness.
5. Separation: Microspheres are collected via filtration, washed with distilled water to remove excess CaCl_2, and dried at 40^circ C in a hot air oven.

Evaluation and Characterization

1. Drug Entrapment Efficiency

A known quantity of microspheres is crushed and dissolved in a suitable solvent. The solution is filtered and analyzed spectrophotometrically or by HPLC to determine the actual amount of drug entrapped. Entrapment efficiency is then calculated.

$$\text{Entrapment Efficiency (\%)} = \frac{\text{Actual Drug Content}}{\text{Theoretical Drug Content}} \times 100$$

2. Percentage Yield

The prepared microspheres are collected, dried, and accurately weighed. The percentage yield is calculated by comparing the practical weight obtained with the total theoretical weight of drug and polymer used in the formulation.

$$\text{Percentage } \textit{Yield} = \frac{\textit{Practical Yield}}{\textit{Theoretical Yield}} \times 100$$

3. Swelling Index

Microspheres are weighed and immersed in a suitable swelling medium such as phosphate buffer. After a predetermined period, they are removed, blotted to remove excess liquid, and reweighed. The increase in weight indicates the swelling capacity.

$$\text{Swelling } \textit{Index} = \frac{W_t - W_0}{W_0} \times 100$$

4. In-vitro Drug Release Study

Microspheres equivalent to a known amount of drug are placed in a dissolution apparatus containing dissolution medium maintained at 37 ± 0.5°C. Samples are withdrawn at regular intervals, replaced with fresh medium, and analyzed for drug content to determine the release profile.

5. Surface Morphology (SEM)

The microspheres are dried and mounted on an aluminum stub using double-sided adhesive tape. The sample is coated with a thin layer of gold and examined under a scanning electron microscope to study shape, surface texture, cracks, and porosity.

6. FTIR studies

The prepared herbal microspheres were finely powdered and analyzed using a Fourier Transform Infrared (FTIR) spectrophotometer. The spectrum was recorded over the range of 4000–400 cm^{-1} to identify the characteristic functional groups present in the formulation. The obtained FTIR spectrum was used to confirm the presence of functional groups and assess the chemical characteristics of the microspheres.

7. Tapped Density

A known quantity of herbal microspheres was transferred into a graduated measuring cylinder. The cylinder was tapped repeatedly until a constant volume was obtained. The tapped density was calculated by dividing the mass of the microspheres by the tapped volume.

Tapped density Density = Mass of Solid / Tapped Volume of Solid

8. Bulk Density

Bulk density is the mass of a powder divided by the volume it occupies before tapping. The volume includes both particles and the spaces between them. It is used to assess powder packing behavior

Bulk Density = Mass of Powder / Bulk Volume of Powder

9. Hausner's Ratio

Hausner's ratio is a measure of powder flowability. It compares tapped density with bulk density. Lower values indicate better flow characteristics.

Hausner's Ratio = Tapped Density / Bulk Density

10. Carr's Compressibility Index Carr's index measures the compressibility and flow properties of a powder. It is calculated using bulk and tapped density values. Lower values indicate better flowability.

Carr's Compressibility Index = [(Tapped Density − Bulk Density) / Tapped Density] × 100

11. MEMBRANE STABILIZATION ASSAY

- Collection of Blood Samples: Fresh blood samples were collected aseptically from healthy volunteers in anticoagulant-containing tubes.
- Preparation of Test Samples: Different concentrations of the formulation were prepared using suitable buffer solution.
- Preparation of Reaction Mixture: The collected blood samples were mixed with the prepared formulation in separate test tubes.
- Incubation: The reaction mixtures were incubated under suitable laboratory conditions for the specified duration.
- Platelet Count Estimation: Platelet count was determined before and after treatment using an automated hematology analyzer or hemocytometer method.
- Recording of Observations: The platelet count values obtained for control and formulation-treated samples were recorded carefully.
- Calculation of Percentage Change in Platelet Count: The percentage increase or maintenance of platelet count was calculated to evaluate anti-thrombocytopenic activity.

Fig No: 1. Papaya leaves and guduchi stems.

Fig No: 2 Maceration of papaya leaf powder and guduchi stem.

Fig No: 3 Microspheres formation

FORMULATION TABLE

Table no. 01.

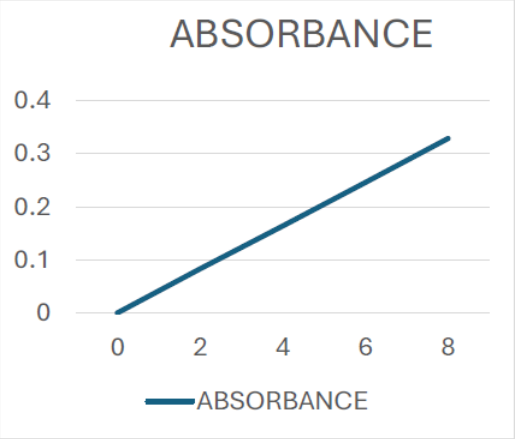
Ingredients	F1	F2	F3	F4
Papaya leaf extract	200mg	300mg	400mg	500mg
Guduchi leaf extract	100mg	200mg	300mg	400mg
Sodium alginate	2g	2g	2g	2g
Tween 80	0.5 ml	0.5ml	0.5 ml	0.5ml
Calcium chloride	6g	6g	6g	6g
Water	q.s	q.s	q.s	q.s

4. RESULTS AND DISCUSSIONS

DRUG ENTRAPMENT EFFICACY

Table no. 02.

Concentration	Absorbance
0	0.000
2	0.083
4	0.164
6	0.246
8	0.329

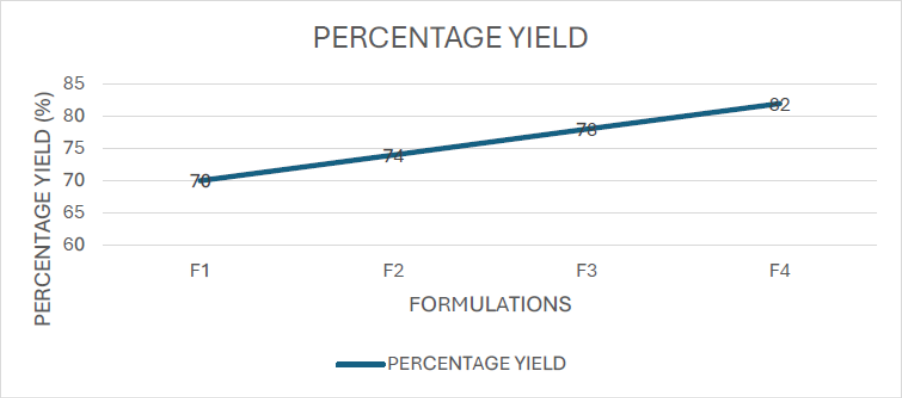


Graph No: 01 Standard Graph Of Drug Entrapment Efficacy.

PERCENTAGE YIELD

Table no. 03.

Sample	Theoretical weight (mg)	Practical weight (mg)	Percentage yield (%)
F1	2300	1610	70.00%
F2	2500	1850	74.00%
F3	2710	2106	78.00%
F4	2910	2378	82.00%

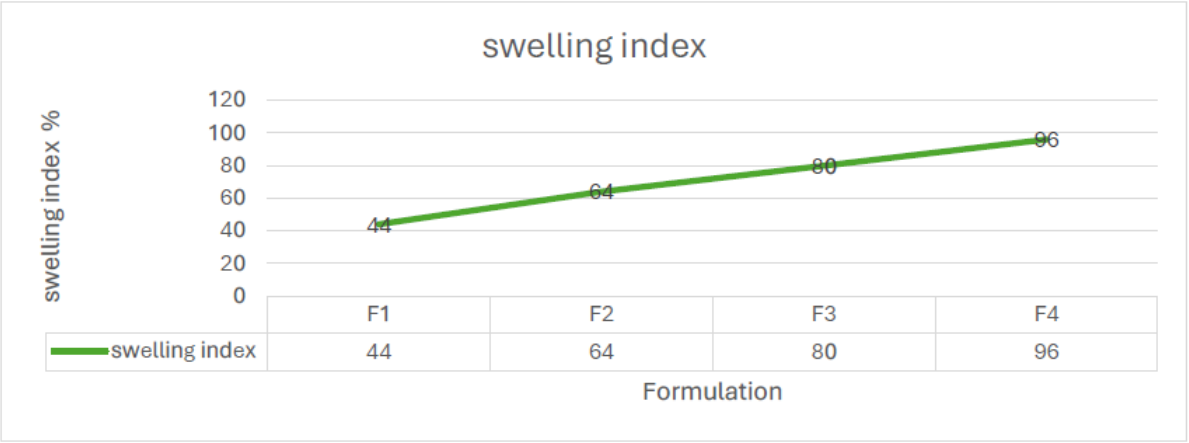


Graph No: 02 Percentage Yield.

Swelling index

Table no 04.

Formulation	Initial weight (mg)	After 1 hr (mg)	After 2hrs (mg)	After 3 hrs (mg)	After 4hrs (mg)	Swelling index (%)
F1	50	60	65	70	72	44.00
F2	50	65	72	78	82	64.00
F3	50	68	76	84	90	80.00
F4	50	72	80	88	98	96.00



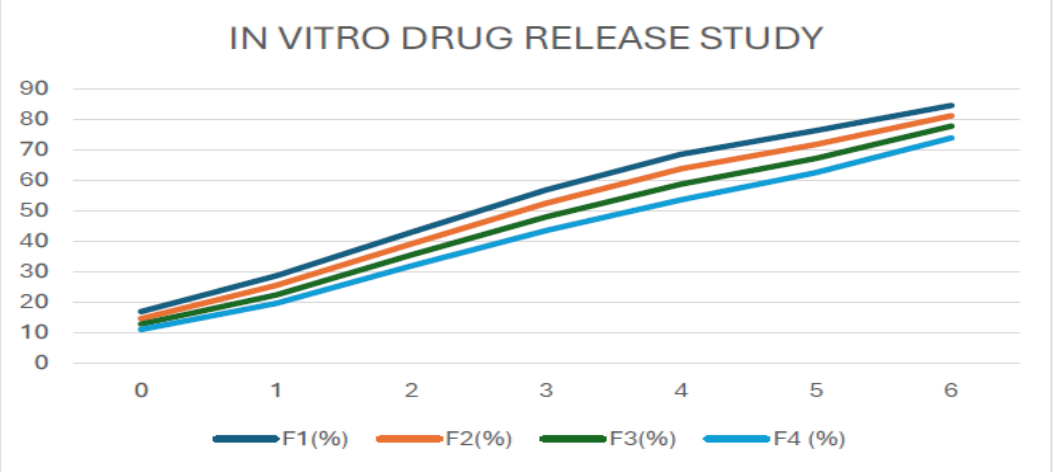
Graph No: 03 swelling index.

IN VITRO DRUG RELEASE STUDY

Table no. 05.

TIME (hrs)	F1(%)	F2(%)	F3(%)	F4(%)
0	16.8	14.5	12.7	10.9
1	28.6	25.4	22.3	19.5
2	42.9	39.1	35.4	31.8
3	56.8	52.4	47.9	43.5
4	68.5	63.8	58.7	53.6

5	76.4	71.8	67.2	62.5
6	84.6	81.2	77.8	73.9



Graph no. 04 in vitro drug release.

SEM (SURFACE MORPHOLOGY)

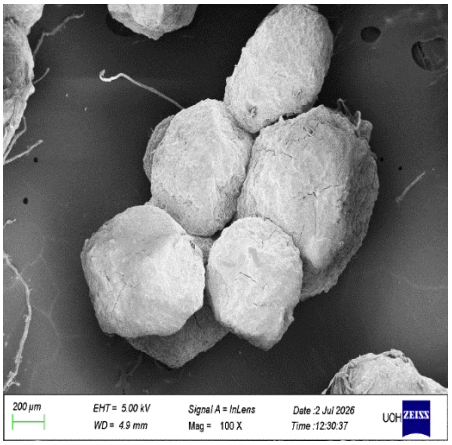


Fig No: 4. Shows Overall Shape And Size Of Microspheres

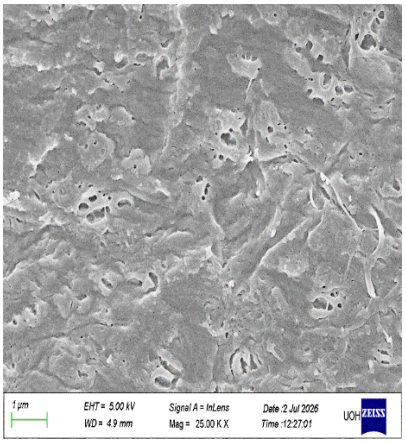


Fig No: 5 shows surface morphology (roughness and porosity).

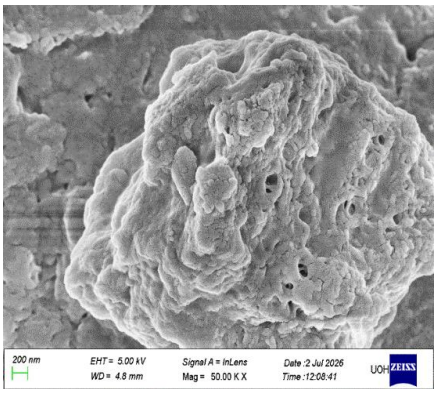


FIG NO: 6 Herbal microspheres at 200nm showing detailed surface.

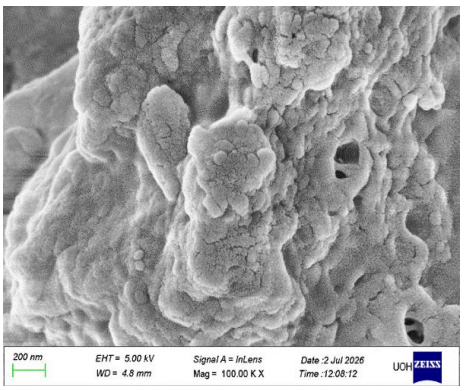
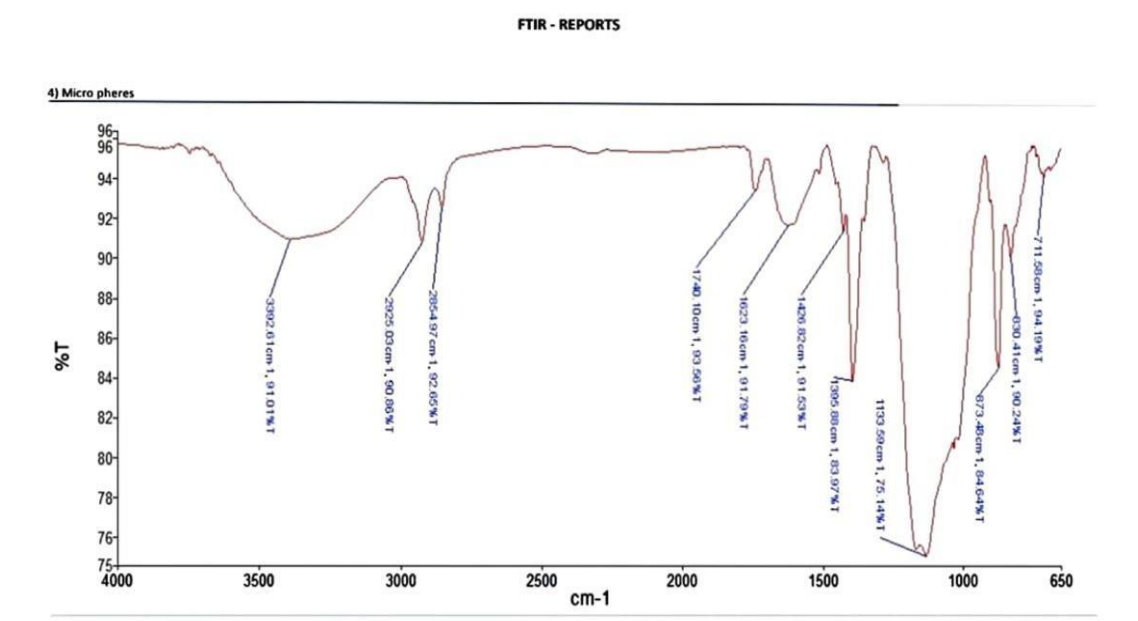


FIG NO: 7 Herbal microspheres showing morphology and porosity.

FTIR STUDIES

Table no. 06.

SN	Peak	Functional group
1	3332	OH stretching
2	2925	CH stretching
3	1740	C=O stretching
4	1603	Coo Stretching
5	1429	Coo symmetric stretching
6	1139	Co stretching
7	1030	Co stretching



Graph No: 05 Ftir Studies.

Tapped density

Table no: 07.

Formulation	Weight (mg)	Tapped volume	Tapped density
F1	100	0.106	0.94
F2	100	0.103	0.97
F3	100	0.100	1.00
F4	100	0.097	1.03

BULK DENSITY

Table no: 08.

Formulation	Weight (mg)	Bulk volume	Bulk density (g/cm 3)
F1	100	0.119	0.84
F2	100	0.116	0.86
F3	100	0.114	0.88
F4	100	0.111	0.90

HAUSNERS RATIO

Table no: 09.

FORMULATION	TAPPED DENSITY	BULK DENSITY	HAUSNERS RATIO
F1	0.94	0.84	1.12
F2	0.97	0.86	1.13
F3	1.00	0.88	1.14
F4	1.03	0.90	1.14

CARR'S COMPRESSIBILITY INDEX

Table no. 10

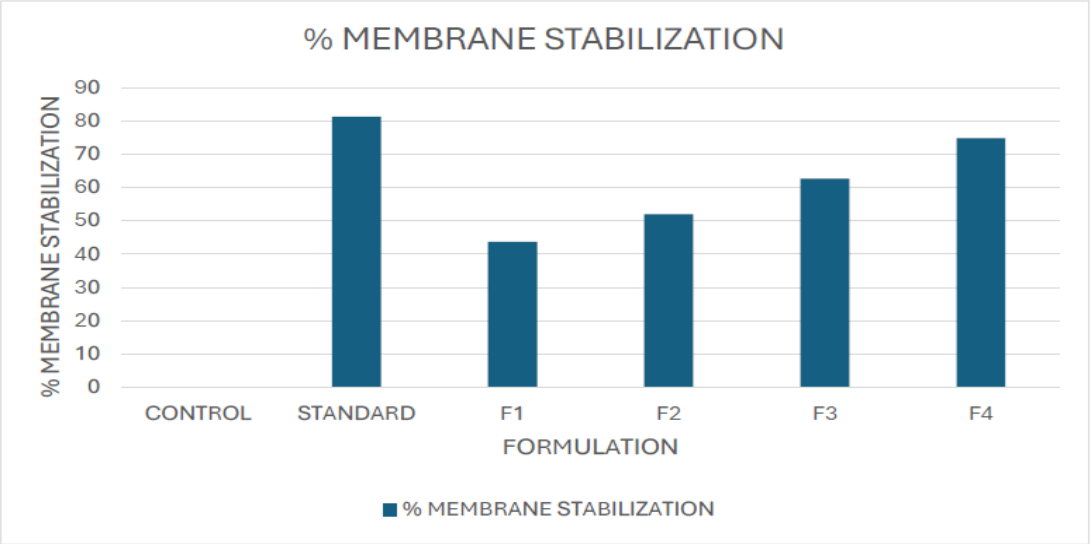
FORMULATION	TAPPED DENSITY	BULK DENSITY	CARRS COMPRESSIBILITY INDEX
F1	0.94	0.84	10.64
F2	0.97	0.86	11.34
F3	1.00	0.88	12.00
F4	1.03	0.90	12.62

MEMBRANE STABILIZATION ASSAY

Membrane Stabilization Assay

Table no. 11:

SN	Formulation	Absorbance(560nm) (mean ± SD)	% membrane stabilization mean ± SD
1	CONTROL	0.742 ± 0.006	0.00± 0.00
2	STANDARD	0.138± 0.004	81.40± 0.56
3	F1	0.418± 0.005	43.67± 0.68
4	F2	0.356± 0.004	52.02± 0.54
5	F3	0.276± 0.005	62.80± 0.67
6	F4	0.186± 0.004	74.93± 0.54



Graph No. 06: Membrane Stabilization Assay.

5. CONCLUSION

The present study successfully formulated herbal microspheres containing Carica papaya leaf extract and Tinospora cordifolia (Guduchi) stem extract using the ionotropic gelation technique. The prepared microspheres exhibited satisfactory physicochemical properties, including acceptable percentage yield, bulk density, tapped density, flow properties, swelling index, and controlled drug release characteristics. The membrane stabilization assay demonstrated promising membrane protective activity, suggesting the potential anti-inflammatory and supportive anti-thrombocytopenic effects of the herbal formulation. Among the prepared formulations, the optimized formulation showed the best overall performance based on the evaluated parameters. The results indicate that herbal microspheres can serve as an effective carrier system for the controlled delivery of papaya and Guduchi extracts.

However, further in vivo pharmacological studies and clinical investigations are necessary to confirm their therapeutic efficacy and safety in the management of thrombocytopenia.

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