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Formulation And Evaluation of Morinda Citrifolia Plant Extract Containing Phytosomes

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ABSTRACT

Rheumatoid Arthritis (RA) is a substantial worldwide health challenge, prompting the investigation of alternative medicines to enhance traditional therapy. This systematic study assesses the efficacy of herbal remedies in the treatment of rheumatoid arthritis (RA). Natural plant extracts and phytoconstituents have significant in vitro bioactivity; however, their in vivo bioactivity is diminished due to inadequate lipid solubility, the presence of large multi-ring compounds, or gastrointestinal degradation. Polyphenolic phytoconstituents were complexed with phospholipids, primarily phosphatidylcholine, which facilitates molecular attachment of components to create innovative drug delivery systems such as phytosomes. The essential components of the herbal extract are formulated to safeguard against disruption by stomach acids and gut bacteria, since phytosomes possess the capability to traverse lipid-rich biomembranes and enhance bioavailability. The primary aim of this work is to construct a phytosome combination derived from Morinda citrifolia to improve bioavailability relative to conventional pharmaceuticals. The research also seeks to investigate the characteristics of phytosomes for the prospective creation of a herbal gel system for rheumatoid arthritis therapy.

Key words: *Rheumatoid arthrhitis, inflammatory disorder, phytosomes, morinda citrifolia, herbal treatment*

1. INTRODUCTION

Rheumatoid arthritis is a chronic, systemic inflammatory disorder characterized by the autoimmune attack of the body's tissues and joints, resulting in inflammatory synovitis that frequently leads to joint destruction, ankylosis, and degradation of articular cartilage. An autoimmune illness is a disorder that results from an aberrant reaction of the immune system. The immune system is a defensive mechanism consisting of a complex arrangement of cells and antibodies that typically functions to identify and eliminate bodily intruders. The synovium, a fragile lining inside joints, acts as a crucial source of nutrition for cartilage. In rheumatoid arthritis (RA), this lining thickens, leading to inflammation and discomfort in and around the joints. Furthermore, synovial cells produce joint lubricants that facilitate smooth movement, including collagens, fibronectin, and hyaluronic acid, which provide the structural framework of the synovial interstitial.

Inflammatory arthritis is often categorized into seropositive and seronegative classifications. The presence of rheumatoid factor, an immunoglobulin that interacts with gamma globulin, is seen in the blood of most patients with seropositive illness and in a small proportion of those with seronegative disease. The prototypical seropositive kind of arthritis is rheumatoid arthritis. Additional members include the category of illnesses known as collagen vascular diseases, including systemic lupus erythematosus, scleroderma, vasculitis, and Sjögren's syndrome. This category comprises ankylosing spondylitis, psoriatic arthritis, reactive arthritis, and arthritis associated with inflammatory bowel illness. Alongside the presence of rheumatoid factor, there are extra-articular characteristics that differentiate seropositive from seronegative types of inflammatory arthritis [3].

Phytosomes are recently developed structures that encapsulate the active constituents of herbs, enveloped and bonded by phospholipids. This is a recently patented method designed to integrate standardized plant extracts or water-soluble phytoconstituents into phospholipids, resulting in lipid-compatible molecular complexes known as phytosomes. The reaction involves a stoichiometric quantity of phospholipid, mostly phosphatidylcholine, with a standardized herbal extract in an aprotic solvent. It mostly comprises the bioactive phytoconstituents of the plant, encased by a lipid.

Phytosomes are a novel lipid-based delivery system with a structure akin to liposomes, used for encapsulating various polyphenolic phytoconstituents to enhance their absorption upon administration. The first phytosomes were created by

Indena, a business based in Milan, Italy, in the late 1980s, with the objective of enhancing medication bioavailability by complexation with phospholipids. Phytosomes consist of standardized polyphenolic plant extracts integrated with phospholipids, mostly phosphatidylcholine (PC) [5]. The lipid vesicles of phytosomes arise from hydrogen bond interactions between the polyphenolic components of bioactive plant extracts and the phosphate groups of phospholipid matrices in non-polar solvents. The water-soluble polyphenolic rings of phytochemicals, such as flavonoids and terpenoids, exhibit a strong affinity for chemically binding to the hydrophilic component of phospholipids, specifically choline, thereby constituting the core of phytosomes. Meanwhile, the lipophilic component of phospholipids, phosphatidyl, forms a tail that integrates the water-soluble choline-bound phytoconstituents. Nonetheless, the phytoconstituents exhibit inadequate absorption, either due to their substantial molecular size, which precludes passive diffusion, or their low lipid solubility, thereby significantly restricting their transport across lipid-rich biological membranes and leading to diminished bioavailability. Morinda citrifolia L. (Rubiaceae), referred to as Noni, has been used in traditional medicine by Polynesians for more than 2000 years. It is in great demand as an alternative medicine because to its properties as an antioxidant, antifungal, antibacterial, anti-inflammatory, hepatoprotective, anticancer, analgesic, immunomodulatory, antiviral, and wound healing agent [8]. Phytochemical investigations have shown that noni contains a number of phenolic compounds, in particular, coumarins, flavonoids, and iridoids which are reported to have various pharmacological effects. So, the phytosomes are vesicular drug delivery systems which incorporate plant extracts or water solublephytoconstituents into phospholipids to produce lipid compatible molecular complexes. They provide better absorption and bioavailability than the conventional herbal extracts

2. MATERIAL AND METHODS

Procurement and Authentication of Plant material (*Morinda citrifolia*): The pharmacognostic analysis of plant material serves to verify and ascertain the identification, purity, and quality of a crude medicine. Fresh, completely mature Morinda citrifolia fruits for research were procured from locations around Bhopal, India, for pharmacognostical analysis. The fruits of Morinda citrifolia were segregated, shade-dried, powdered to 60 mesh, kept in airtight containers, and used for phytochemical and pharmacological investigations [9].

Pharmacognostical studies:

Macroscopical study:

The macroscopical description of different parts of *Morinda citrifolia* plant include size, shape, nature of outer and inner surfaces, types of fracture, and organoleptic characters like color, odour, taste etc. were studied

Microscopical study

Transverse section of *Morinda citrifolia* fruit: The transverse slices were obtained by positioning the Morinda citrifolia fruit between the thumb and index finger of the left hand. A thin section was produced by maneuvering a sharp razor held in the right hand across the item. The sections were placed in a container with water, to which chloral hydrate was added, then heated, filtered, and the transverse sections were dyed with a phloroglucinol and hydrochloric acid solution (1:1). The processed transverse segment was affixed in glycerin and examined under low magnification. Photomicrographs at various magnifications were captured. Photographs of unstained slides were taken to examine crystals and starch grains. For standard histological purposes, sections were captured using bright field microscopy [10]. The same methods were conducted using Morinda tinctoria fruit and stem for microscopic analysis.

Powder microscopy: The dried fruit of Morinda citrifolia was ground, passed through a sieve with a mesh size of 60#, and then analyzed individually. Each of the three powders was subjected to the addition of few drops of chloral hydrate and then heated for one to two minutes. Chloral hydrate was used for tissue clearing and clarity. A few drops of a 1:1 combination of phloroglucinol and HCl were added to the cleaned powder, which was then mounted with glycerin. Lignified tissue had a pink hue. To examine starch grains, powders were suspended in water with one to two drops of weak iodine, while unstained slices for observing calcium oxalate crystals were mounted alone in water [11].

Physicochemical Evaluation of *Morinda citrifolia*:

Physicochemical analysis of crude pharmaceuticals establishes standards to mitigate batch-to-batch variance and assess quality. Their research also provides insight into the characteristics of the phytoconstituents present. A physicochemical examination of Morinda citrifolia fruit powders was conducted using techniques outlined in standard literature via numerous determinations. The metrics are Total Ash, Acid Insoluble Ash, Water Soluble Ash, Extractive Value, Alcohol Soluble Extractive Value, Water Soluble Extractive Value, Loss of Moisture Content, and Swelling Index [12].

Extraction of *Morinda citrifolia*: Ten grams of air-dried powdered Morinda citrifolia were sequentially extracted using solvents of increasing polarity in a Soxhlet system. The dried Morinda citrifolia stem powder was placed in a Soxhlet extractor and subjected to extraction with petroleum ether (a non-polar solvent) for thorough extraction. The extract was filtered, and the solvent was eliminated using a rotary evaporator to get the petroleum ether extract. The desiccated Morinda citrifolia stem powder was air-dried to eliminate residual petroleum ether, thereafter repacked in a Soxhlet apparatus, extracted with ethanol, filtered, and dried to get the ethanol extract. The percent yield of the extracts, after the removal of

solvents, was determined. The extraction's completeness was verified by evaporating few drops of extract from the thimble on a watch glass, confirming that no residue persisted after the solvent's evaporation. The extracts' consistency, color, appearance, and % yield were recorded [13].

Formulation of phytosomes:

The phytosomes were synthesized using the thin-layer hydration technique. Precisely measured amounts of Morinda citrifolia extract were introduced into a round-bottom flask and dissolved in 100 mL of 100% ethanol at 60 °C under reflux and magnetic stirring until a homogenous suspension was achieved. Soy phosphatidylcholine (PC) and lecithin (LC) were individually solubilized in 25 mL of 100% ethanol and gradually introduced under reflux and agitation to the solubilized extract, which reacted for 2 hours at 60 °C. Ethanol was then evaporated at reduced pressure using a rotary evaporator. The resultant viscous, transparent, orange-hued substance was dehydrated under a nitrogen stream to eliminate any solvent residues. The desiccated MCP were rehydrated with 80 mL of water, and the particle size was modified using sonication in a water bath for 30 minutes [14].

Table 1: Composition of Morinda citrifolia extract containing phytosomal gel

F. Code	Morinda citrifolia extract (gm)	Phosphatidylcholine (PC) (gm)	Lecithine (LC) (gm)	Absolute ethanol (ml)	Sonication time (min)
MCP1	1	1	0	25	15
MCP2	1	0	1	25	15
MCP3	1	0.5	0.5	25	15
MCP4	1	0.25	0.75	25	15
MCP5	1	0.75	0.25	25	15

Evaluation of phytosomes:

The examination of physical attributes (Percentage Practical Yield, size distribution, PDI index, zeta potential), encapsulation efficiency, and drug content was performed subsequent to 30 minutes of sonication in a water bath.

Percentage Practical Yield: To ascertain the percent yield or efficiency of any operation, the percentage practical yield was calculated, aiding manufacturers in selecting the optimal production method. To determine the practical yield, phytosomal gel was generated, collected, and weighed using the following equation.

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

Particle Size & PDI index: Particle size distribution of phytosomal gel was measured using zetasizer with a computerized system (Malvern, Zetasizer).

Zeta Potential: The stability increases with heightened electrostatic repulsion among the particles. The zeta potential of the improved phytosome was assessed using the Zetasizer Nano ZS90 (Malvern Instruments Ltd., Malvern, UK). The sample was diluted with water to a volume of 10 mL; thereafter, 5 mL of this diluted sample was transferred to a cuvette for the determination of Zeta potential.

Encapsulation Efficiency and Drug content: The encapsulated drug fraction was assessed by centrifuging 0.5 mL of the phytosomal gel formulation at 14,000 rpm for 90 minutes at ambient temperature [15]. The supernatant was meticulously extracted using a pipette. The pure supernatant was then diluted in ethanol to rupture the vesicles, followed by suitable dilution for the measurement of GA concentration using UV spectrophotometry at 260 nm. Entrapment efficiency was calculated by the equation below:

The encapsulation efficiency (EE, %) and drug loading (%) were calculated using the following formulas:

$$\%\ EE = \frac{\text{Total GA in suspension - GA concentration in the superrnatan}}{\text{Total GA in the suspension}} \times 100$$

Results and Discussion:

The pharmacognostic analysis of plant material serves to validate and ascertain the identification, purity, and quality of a crude medicine. Morinda citrifolia is an evergreen shrub or diminutive, irregularly shaped tree with a conical crown, reaching

heights of 3-8(-10) m, characterized by a deep taproot; the bark is greyish or yellowish-brown, shallowly fissured, and glabrous; the branchlets are quadrangular. The fruit is an ovoid syncarp, yellow-white in color, consisting of pyramidal, 2-seeded drupes measuring 4-11 cm by 2-3 cm. It has a strong, caustic odor and a harsh flavor (Figure 1).

Figure 1: Morphology of *Morinda citrifolia* fruits

Microscopical study: The microscopic analysis of the powder revealed the existence of individual acicular calcium oxalate crystals, lignified cells, starch granules, and oil globules. The transverse slice of fresh Morinda citrifolia fruits exhibited a unilayered epidermis and a mucilaginous hypodermis area with oil glands. The mesocarp was recognized by the existence of vascular bundles (Figure 2).

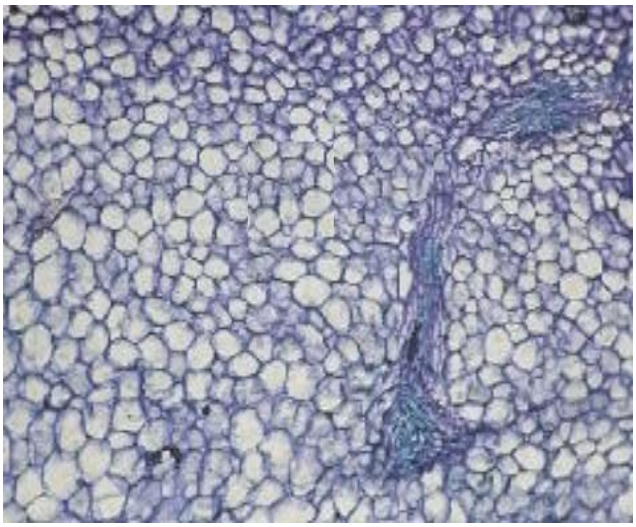

Figure 2: Transverse section of fruit of Morinda citrifolia

Physicochemical parameters: The total ash content of M. citrifolia fruit was determined to be 6.81%. Water-soluble ash was measured at 4.07%, whereas acid-insoluble ash was recorded at 1.13%. The ethanol-soluble extractive value was determined to be 11.32% w/w, while the water-soluble extractive value was discovered to be 13.34%. The moisture content of the powder, determined as percentage loss on drying (LOD), was 7.31% w/w.

Extraction of Pharmaceuticals: The coarse powder of Morinda citrifolia fruit underwent sequential solvent extraction using solvents of increasing polarity. Following extraction, the % yield of each extract was determined based on the air-dried medication used in the research. The percentage yield in petroleum ether is 5.31% w/w, while in ethanol it is 12.32% w/w, respectively.

Characterization of phytosomes: To ascertain the percent yield or efficiency of any operation, the percentage practical yield was evaluated; this assisted producers in selecting the optimal production method. The phytosomes MCP4 had the highest practical yield percentage of 93.72%. The particle size distribution of the phytosomal gel was assessed using a computerized zetasizer device. The particle size of all phytosomal gels ranged from 129.11 nm to 131.11 nm. The polydispersity index of all phytosomal gels ranged from 0.213 to 0.224 (Figure 3). The amplitude of zeta potential indicates the possible stability of the colloidal dispersion. If the particles possess significant positive or negative charge, it indicates that they oppose one another, resulting in dispersion stability. The zeta potential of the improved formulation indicated that the sample is extremely stable. The formulation MCP4 had a stability value of -23.91, indicating that it is more stable than the other formulations (Figure 4). The ratio of encapsulated medication was assessed for the phytosome formulation. The Percentage Entrapment Efficiency of all formulated gels ranged from 66.15% to 89.71%. The phytosomes of Morinda

citrifolia, designated as MCP4, exhibited the greatest percentage at 89.71%.

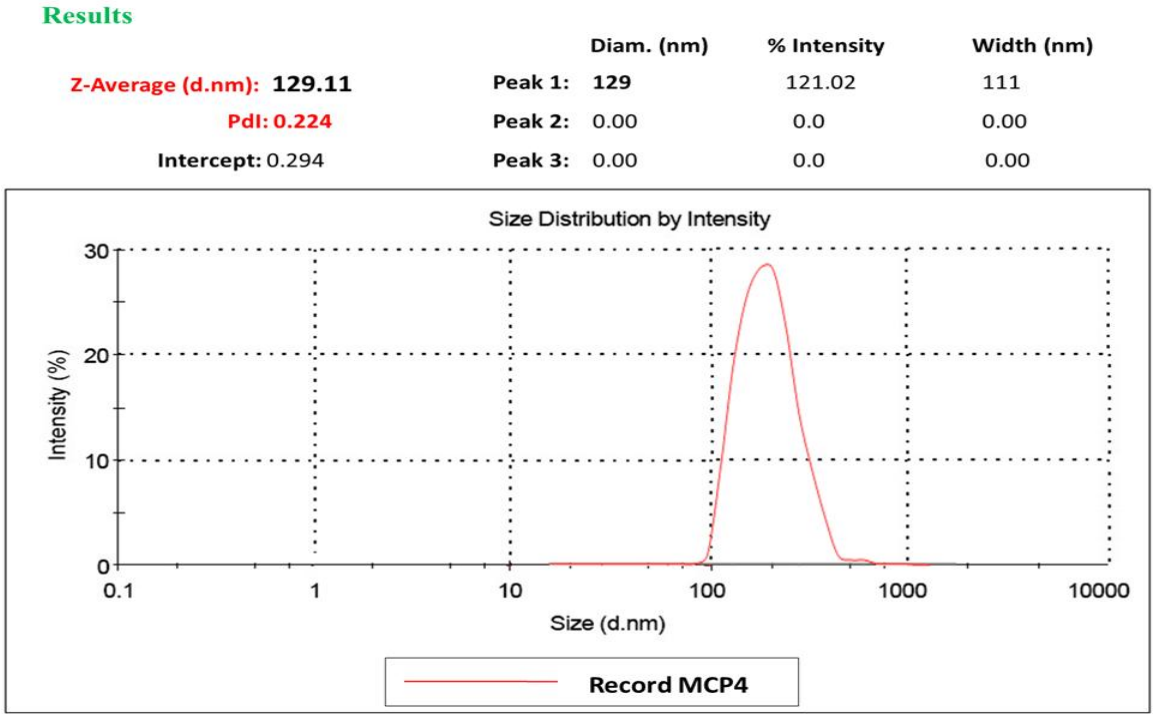

Figure 3: Particle size distribution & Polydispersity Index (PDI) of Morinda citrifolia phytosomal gel (MCP4)

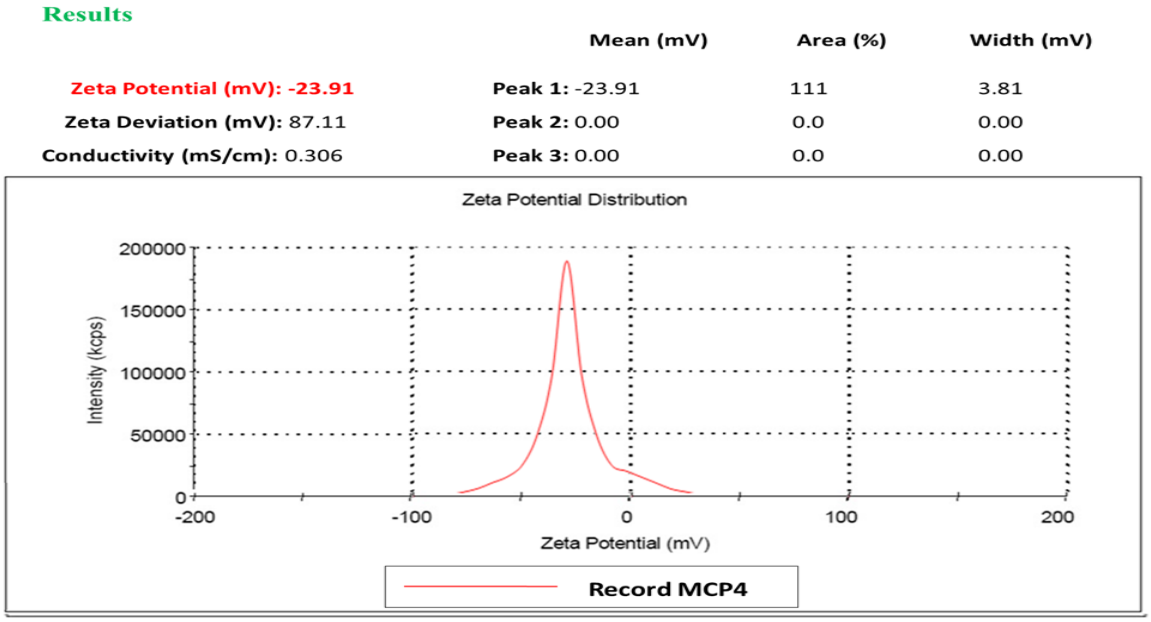

Figure 4: Zeta potential (mV) of Morinda citrifolia phytosomal gel (MCP4)

3. CONCLUSION

This research focused on the formulation and assessment of combination phytosomes derived from Morinda citrifolia to improve bioavailability and facilitate targeted medication administration in the treatment of rheumatoid arthritis. The new phytosome system exhibited the effective generation of homogeneous vesicles with favorable attributes, including high yield, exceptional entrapment efficiency, tiny particle size, and suitable zeta potential. These characteristics demonstrate the capability of phytosomes for the effective transport of herbal extracts. The developed herbal phytosomes demonstrated appropriate characteristics for topical use, including pH compatibility with the skin and ideal viscosity

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