EXPLORING THE EFFICACY OF POLYHERBAL NANO-ETHOSOMES IN THE TREATMENT OF BURN WOUNDS

K.Mekala [1] , S.M.Shaheedha [1 *]

1 Research Scholar, Crescent School of Pharmacy, B. S. Abdur Rahman Crescent Institute of Science and Technology, Vandalur-600048, Chennai, India

*1 * Associate Professor, Head of Department of Pharmacognosy, Crescent School of Pharmacy, B. S.Abdur Rahman Crescent Institute of Science and Technology, Vandalur-600048, Chennai, India*

ABSTRACT

Burn wounds are a significant cause of morbidity and mortality worldwide, necessitating the development of novel therapeutic strategies. This study aimed to conduct a comparative analysis of the potential wound healing effects of a polyherbalnanoethosome formulation containing PortulacaOleracea, Basellaalba, Trigonellafoenumgraecum, LawsoniaInermis, and Peristrophepaniculata. The selected plant species are renowned for their traditional use in wound healing and possess diverse phytochemical profiles with reported antioxidant, anti-inflammatory, antimicrobial, and regenerative properties. Nanoethosomes[1] were utilized as a delivery system to enhance the bioavailability and efficacy of the herbal extracts. The polyherbalnanoethosome formulation was prepared using a thin film hydration method and characterized for particle size, encapsulation efficiency, and morphology. In vitro release studies demonstrated sustained release of the herbal constituents from the nanoethosomes over a period of time, indicating their potential for prolonged therapeutic action. The comparative study revealed that the polyherbalnanoethosome formulation, incorporating PortulacaOleracea, Basellaalba, Trigonellafoenumgraecum, LawsoniaInermis, and Peristrophepaniculata, holds promising potential as a therapeutic intervention for burn wound healing. [2] The enhanced wound healing effects observed can be attributed to the synergistic action of the phytoconstituents present in the plant extracts, coupled with the improved delivery and bioavailability achieved through nanoethosome encapsulation.

Keywords: polyherbalnanoethosome, burn wound healing, PortulacaOleracea, Basellaalba, Trigonellafoenumgraecum, LawsoniaInermis, Peristrophepaniculata.

DOI: 10.48047/ecb/2023.12.8.483

Corresponding Author:
Dr. S. M. Shaheedha,
Associate Professor,
Head of Department of Pharmacognosy,
Crescent School of Pharmacy,
B. S. Abdur Rahman Crescent Institute of Science and Technology,
Vandalur-600048, Chennai, India
Email:shaheedhashabudeen@gmail.com

INTRODUCTION TO BURN WOUND HEALING

Burn wounds are a significant global health concern, causing substantial morbidity and mortality. They result from exposure to thermal, chemical, electrical, or radiation sources, leading to tissue damage and impaired wound healing. Successful management of burn wounds involves promoting efficient healing, reducing complications, and minimizing scarring. The healing process of burn wounds is complex and involves several overlapping phases, including inflammation, proliferation, and remodeling. [3] During the inflammatory phase, there is an influx of immune cells and the release of inflammatory mediators, which initiate the repair process. The proliferation phase is characterized by the formation of new blood vessels, re-epithelialization, and granulation tissue formation. Finally, in the remodeling phase, collagen synthesis and remodeling occur, leading to scar formation.

Traditional medicinal plants have long been recognized for their therapeutic potential in wound healing. They possess bioactive compounds such as polyphenols, flavonoids, terpenoids, and alkaloids, which exhibit antioxidant, anti-inflammatory, antimicrobial, and regenerative properties. Harnessing the healing potential of these plants in burn wound management can provide a natural and cost-effective approach. [4]

In recent years, nanotechnology-based delivery systems have gained attention in the field of wound healing. Nanoethosomes, lipid-based nanoparticles, have emerged as promising carriers for delivering therapeutic agents to the target site. They offer advantages such as enhanced drug encapsulation, improved stability, controlled release, and increased permeability through the skin.

This study aims to investigate the potential of a polyherbalnanoethosome formulation for burn wound healing. The formulation incorporates extracts from PortulacaOleracea, Basellaalba, Trigonellafoenumgraecum, LawsoniaInermis, and Peristrophepaniculata. These plants have a history of traditional use in wound healing and possess diverse phytochemical profiles with reported biological activities. [5]

By encapsulating the herbal extracts in nanoethosomes, the bioavailability and therapeutic efficacy can be improved. The sustained release of active constituents from the nanoethosomes can facilitate prolonged wound healing effects, promoting tissue regeneration and reducing inflammation. Understanding the comparative effects of the

polyherbalnanoethosome formulation on burn wound healing, including wound closure rate, histopathological changes, and collagen deposition, can provide valuable insights into its potential as a therapeutic intervention. Such knowledge can contribute to the development of novel strategies for burn wound management, ultimately improving patient outcomes.

The utilization of polyherbalnanoethosomes incorporating specific plant extracts presents an innovative approach in burn wound healing. [6] This study aims to investigate the therapeutic effects of the formulation and provide insights into its mechanisms of action. The findings may pave the way for the development of advanced therapeutic interventions in the field of burn wound management, offering improved healing outcomes and enhanced patient care.

PORTULACA OLERACEA

Portulacaoleracea, commonly known as purslane or pigweed, is a succulent plant that is widely distributed across the globe. It has a long history of medicinal and culinary use in various cultures. In terms of medicinal properties, Portulacaoleracea has been traditionally recognized for its wound healing abilities. [7] The plant contains a rich array of bioactive compounds, including flavonoids, alkaloids, polysaccharides, omega-3 fatty acids, and vitamins A, C, and E. These components contribute to its antioxidant, anti-inflammatory, antimicrobial, and immunomodulatory properties.

As an antioxidant, Portulacaoleracea helps neutralize harmful free radicals in the body, which can reduce oxidative stress and inflammation. Its anti-inflammatory properties can help alleviate inflammatory responses associated with burn wounds, promoting a favorable healing environment. Additionally, the plant's antimicrobial activity can combat various microorganisms, reducing the risk of infection in wounds.

Studies have demonstrated the potential of Portulacaoleracea extract in promoting wound healing by accelerating re-epithelialization, collagen synthesis, and angiogenesis. It has been shown to enhance the migration of keratinocytes and fibroblasts, key cells involved in wound closure and tissue regeneration. Moreover, the plant's polysaccharides have been

found to stimulate immune responses, supporting the body's defense mechanisms during wound healing. [8]

In culinary practices, Portulacaoleracea is valued for its nutritious and flavorful qualities. Its leaves and stems are consumed raw or cooked in salads, stir-fries, and soups. The plant is known for its succulent texture and slightly tangy taste. It is also recognized for its high content of essential nutrients such as vitamins, minerals, and omega-3 fatty acids, which contribute to its dietary value.

Portulacaoleracea, or purslane, possesses a range of beneficial properties that make it a valuable herb in both traditional medicine and culinary applications. Its wound healing potential, attributed to its antioxidant, anti-inflammatory, antimicrobial, and immunomodulatory effects, highlights its significance in burn wound management. [9] Further research and exploration of this plant's therapeutic properties may uncover additional benefits and contribute to the development of novel wound healing interventions.

BASELLA ALBA

Basellaalba, commonly known as Malabar spinach or vine spinach, is a leafy green vegetable that is cultivated and consumed in many parts of the world. It is a fast-growing, vining plant that belongs to the family Basellaceae. Basellaalba has a long history of traditional use in various culinary and medicinal practices. The leaves, stems, and shoots of the plant are commonly used in cooking due to their mild flavor and high nutritional content. The plant is known for its succulent texture and is often used as a substitute for spinach in many dishes.

In terms of medicinal properties, Basellaalba is recognized for its potential health benefits. It is a rich source of vitamins A, C, and E, as well as minerals such as iron, calcium, and potassium. These nutrients contribute to its antioxidant and immune-boosting properties, supporting overall well-being. Studies have indicated that Basellaalba possesses several bioactive compounds, including flavonoids, phenolic acids, and carotenoids, which contribute to its therapeutic potential. These compounds exhibit antioxidant activity, helping to combat oxidative stress and reduce cellular damage caused by free radicals. [10]

Basellaalba has also been investigated for its potential wound healing properties. It is believed to promote wound closure and tissue regeneration through its effects on collagen synthesis and angiogenesis. The plant's extracts have shown the ability to enhance the migration and proliferation of fibroblasts and keratinocytes, which are crucial for the healing process. Additionally, Basellaalba has been studied for its anti-inflammatory and antimicrobial activities. It may help reduce inflammation associated with wounds and inhibit the growth of certain bacteria, providing a protective effect against infection.

Basellaalba is a nutritious vegetable with potential health benefits. Its antioxidant properties, along with its wound healing, anti-inflammatory, and antimicrobial effects, make it a valuable ingredient in traditional medicine and a potential candidate for further research in the field of wound healing. Incorporating Basellaalba into the diet or exploring its extracts for therapeutic applications may offer additional insights into its potential as a natural remedy for various health conditions.

TRIGONELLA FOENUM-GRAECUM

Trigonellafoenum-graecum, commonly known as fenugreek, is an herbaceous plant that has been used for centuries in various traditional systems of medicine and culinary practices. It belongs to the Fabaceae family and is native to the Mediterranean region, although it is now cultivated and consumed worldwide. Fenugreek has a rich history of medicinal uses due to its diverse array of bioactive compounds. The plant's seeds and leaves are particularly valued for their therapeutic properties. The seeds are small, yellow-brown in color, and have a distinctive aroma and flavor.

Fenugreek is known for its various health benefits. It is a rich source of protein, dietary fiber, vitamins (such as vitamin C, vitamin A, and B-complex vitamins), minerals (including iron, potassium, calcium, and magnesium), and antioxidants. [11] These nutritional components contribute to its overall medicinal value. In traditional medicine, fenugreek has been used to address numerous health conditions. It is renowned for its potential to regulate blood sugar levels and improve insulin sensitivity, making it beneficial for individuals with diabetes. Fenugreek is believed to enhance glucose utilization and increase the secretion of insulin. Moreover, fenugreek has been recognized for its potential effects on digestion and gastrointestinal health. It has been used to alleviate symptoms of indigestion, promote appetite, and aid in digestion. The plant's dietary fiber content may help regulate bowel movements and support overall gut health.

Fenugreek has also been studied for its potential benefits in supporting lactation in breastfeeding mothers. It is believed to stimulate milk production due to its galactagogue properties. Additionally, fenugreek may have anti-inflammatory, antimicrobial, and antioxidant effects, contributing to its traditional uses in managing skin conditions and supporting immune function. In culinary applications, fenugreek seeds and leaves are used as a spice, adding a distinctive flavor to dishes.

The seeds can be used whole or ground, while the leaves are often used fresh or dried. Fenugreek is a common ingredient in Indian, Middle Eastern, and North African cuisines, where it is used in curries, stews, bread, and spice blends. Trigonellafoenum-graecum (fenugreek) is a versatile plant with a long history of use in traditional medicine and culinary practices. Its seeds and leaves are known for their nutritional value and potential health benefits. [12]

LAWSONIA INERMIS

Lawsoniainermis, commonly known as henna, is a flowering plant that has been utilized for centuries for its cultural, cosmetic, and medicinal purposes. It belongs to the family Lythraceae and is native to regions of North Africa, South Asia, and the Middle East. Henna is renowned for its leaves, which contain a natural red-orange dye molecule called lawsone. The leaves are dried, ground into a fine powder, and used to create a paste that is applied to the skin, hair, and nails. Henna has significant cultural and traditional significance, particularly in celebrations and rituals such as weddings and festivals.

Apart from its use as a cosmetic and decorative agent, Lawsoniainermis has also been employed in traditional medicine due to its potential medicinal properties. The plant contains various bioactive compounds, including tannins, flavonoids, terpenes, and phenolic acids, which contribute to its therapeutic effects. [13] In traditional medicine practices, henna has been used topically to address skin conditions such as burns, wounds, and inflammatory skin disorders. It is believed to possess anti-inflammatory and analgesic properties, which can help alleviate pain, reduce inflammation, and promote wound healing.

Henna has also been studied for its antimicrobial activity against certain bacteria and fungi. The lawsone compound, along with other components in henna, may exhibit antibacterial and antifungal effects, making it potentially useful in managing microbial infections. Lawsoniainermis has been explored for its antioxidant properties. Antioxidants help protect cells from oxidative damage caused by free radicals, and henna may contribute to reducing oxidative stress and promoting overall skin health. [14]

Although henna is primarily known for its external applications, it is important to note that internal use or ingestion of henna can have adverse effects. The safety and efficacy of internal henna consumption have not been well-established, and it is advised to exercise caution and consult a healthcare professional before using henna internally.

Lawsoniainermis, or henna, is a versatile plant with cultural, cosmetic, and potential medicinal applications. Its leaves are utilized for their natural dyeing properties, while its extracts have been traditionally used for their anti-inflammatory, antimicrobial, and antioxidant effects. [15] While henna holds promise in certain topical applications, it is crucial to ensure safe and appropriate usage, avoiding internal consumption without proper guidance. Further research is necessary to explore its potential therapeutic benefits and to establish guidelines for its safe and effective use in various contexts.

PERISTROPHE PANICULATA

Peristrophepaniculata, commonly known as the creeping Charlie or Puncture Vine, is a perennial herbaceous plant that belongs to the Acanthaceae family. It is native to tropical and subtropical regions, particularly found in Southeast Asia and parts of Africa. Peristrophepaniculata has been traditionally used in various folk medicine systems for its potential medicinal properties. The plant possesses several bioactive compounds, including alkaloids, flavonoids, phenolic acids, and terpenoids, which contribute to its therapeutic effects.

In traditional medicine, Peristrophepaniculata has been used to address various health conditions. It is believed to possess anti-inflammatory, analgesic, and diuretic properties. The plant's extracts have been used to alleviate pain, reduce inflammation, and promote

urine production. Peristrophepaniculata [16] has been investigated for its potential effects on the cardiovascular system. It may have cardioprotective properties, helping to maintain heart health and regulate blood pressure. The plant's extracts have been studied for their potential to relax blood vessels and improve blood flow.

In addition, Peristrophepaniculata has been recognized for its potential antioxidant and hepatoprotective effects. Antioxidants help neutralize harmful free radicals and protect cells from oxidative stress. The plant's extracts have shown the ability to scavenge free radicals and inhibit oxidative damage. Peristrophepaniculata has also been explored for its potential antimicrobial activity. It may possess antibacterial and antifungal properties, which can help combat certain microorganisms and inhibit their growth. [17]

The plant has been used in traditional practices for its potential wound healing properties. It may aid in the regeneration of skin tissue, promoting faster wound closure and reducing the risk of infection. While Peristrophepaniculata shows promise in traditional medicine, it is important to note that scientific research on its efficacy and safety is limited. Further studies are needed to validate its traditional uses and explore its potential in various therapeutic applications.

Peristrophepaniculata, or creeping Charlie, is a herbaceous plant with potential medicinal properties. Its traditional uses include addressing pain, inflammation, cardiovascular conditions, and promoting liver health. However, further research is necessary to substantiate its therapeutic effects and determine appropriate usage guidelines.

POLYHERBAL NANOETHOSOME

A polyherbalnanoethosome [18] refers to a formulation that combines multiple herbal extracts or active compounds within a nanosized vesicular structure called an ethosomal carrier. It is a specialized delivery system designed to enhance the penetration and efficacy of the herbal components.Nanoethosomes are nanoscale lipid-based vesicles composed of phospholipids, which mimic the structure of cell membranes. These vesicles can encapsulate hydrophilic and lipophilic herbal compounds, allowing for improved solubility, stability, and targeted delivery to specific tissues or cells.The use of polyherbal formulations in nanoethosomes offers several advantages. Firstly, combining multiple herbal extracts or active compounds allows for synergistic effects, where the combined action of the components may produce enhanced therapeutic outcomes compared to individual herbs. This approach takes advantage of the potential complementary or additive effects of different herbal constituents.Secondly, the use of nanoethosomes as a carrier system improves the bioavailability and absorption of the herbal components. The small size of the nanoethosomes enables them to penetrate deeply into the skin or mucosal membranes, facilitating the efficient delivery of the herbal compounds to the target site. [19]

Additionally, nanoethosomes provide protection to the encapsulated herbal components, shielding them from degradation or inactivation by external factors such as enzymes or pH variations. This enhances the stability and shelf life of the polyherbal formulation.Polyherbalnanoethosomes have gained interest in various fields, including pharmaceuticals, cosmeceuticals, and traditional medicine, due to their potential applications in wound healing, dermatological disorders, transdermal drug delivery, and other therapeutic areas.[20]

In the context of burn wound healing, a comparative study of polyherbalnanoethosomes using specific herbal extracts such as Portulacaoleracea, Basellaalba, Trigonellafoenum-graecum, Lawsoniainermis, and Peristrophepaniculata aims to explore the combined effects of these herbs in a nanosized carrier system. The nanoethosomal formulation may enhance the wound healing properties of the herbal components, improve their penetration into the burn wound site, and potentially accelerate the healing process.

COMPARATIVE STUDY DESIGN

Plant Materials

The plant materials used in this study were Portulacaoleracea (Purslane), Basellaalba (Malabar spinach), Trigonellafoenumgraecum (Fenugreek), Lawsoniainermis (Henna), and Peristrophepaniculata (Keezhanelli). These plants were selected based on their known traditional use in promoting wound healing and their availability.

Extraction of Herbal Extracts

The aerial parts of Portulacaoleracea, Basellaalba, Trigonellafoenumgraecum, Lawsoniainermis, and Peristrophepaniculata were collected, cleaned, and dried. The dried plant materials were powdered and subjected to extraction using a suitable solvent, such as ethanol or water, using Soxhlet extraction or maceration methods. The extracts were filtered, concentrated under reduced pressure, and lyophilized to obtain dry extracts. [21]

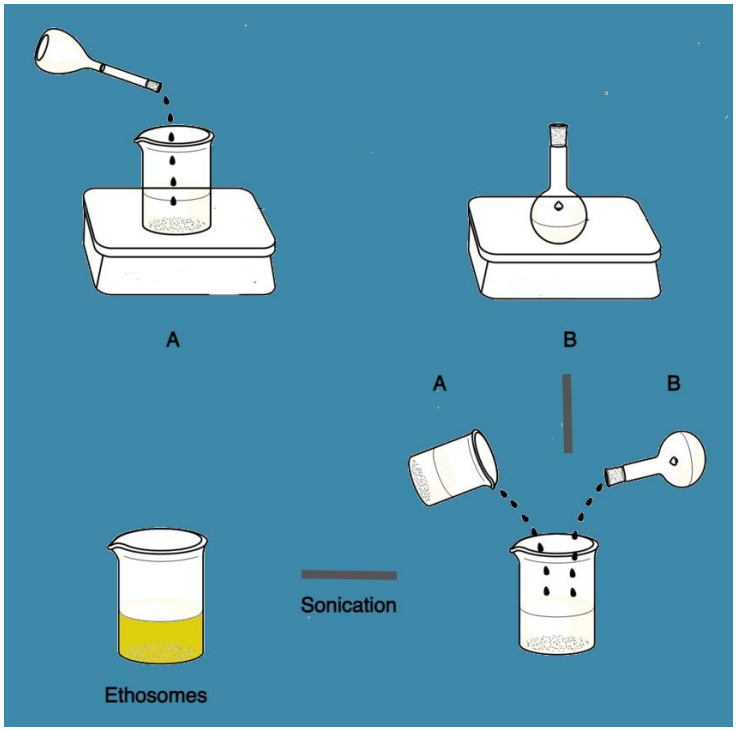
Preparation of PolyherbalNanoethosome

The preparation of polyherbalnanoethosomes involves a series of steps to encapsulate the bioactive compounds from medicinal plants into nanosized lipid-based vesicles. These nanoethosomes are designed to enhance the delivery and efficacy of the herbal ingredients for burn wound healing.

The general procedure for preparing polyherbalnanoethosomes is as follows:

Selection of Medicinal Plants: Identify and select the appropriate medicinal plants based on their known therapeutic properties for wound healing. In this case, the selected plants include PortulacaOleracea, Basellaalba, Trigonellafoenumgraecum, LawsoniaInermis, and Peristrophepaniculata.

Extraction of Bioactive Compounds: Extract the bioactive compounds from the selected medicinal plants using suitable extraction techniques such as maceration, Soxhlet extraction, or supercritical fluid extraction. These techniques help to isolate the active constituents responsible for wound healing properties.[22]



A –Phospholipid dissolved in Ethanol B – Ethanol & Propylene glycol

Lipid Selection: Choose appropriate lipids that can form lipid bilayers for vesicle formation. Common lipids used for nanoethosome preparation include phospholipids such as phosphatidylcholine, phosphatidylserine, or phosphatidylethanolamine. Lipids with different characteristics can be combined to achieve desired vesicle properties.

Vesicle Formation: Dissolve the selected lipids in an organic solvent to create a lipid film. The organic solvent is then removed under reduced pressure or through evaporation, resulting in a lipid film formation on the container walls. This lipid film is hydrated with an aqueous solution containing the extracted bioactive compounds, resulting in the formation of multilamellar vesicles (MLVs). [23]

Size Reduction: The MLVs are subjected to mechanical or sonication techniques to reduce their size and obtain smaller vesicles. This step improves the vesicle stability and increases the encapsulation efficiency of the bioactive compounds. Sonication is commonly used to achieve nanosized vesicles.

Characterization: The prepared polyherbalnanoethosomes are characterized for their particle size, polydispersity index (PDI), and encapsulation efficiency. These parameters determine the stability and effectiveness of the nanoethosomes for wound healing.

The preparation of polyherbalnanoethosomes offers a promising approach to enhance the therapeutic efficacy of medicinal plants for burn wound healing. The encapsulation of bioactive compounds in nanosized vesicles improves their stability, bioavailability, and targeted delivery to the wound site, leading to enhanced wound healing outcomes.[24]

EVALUATION PARAMETERS

The evaluation parameters for assessing the efficacy of the polyherbalnanoethosome formulation for burn wound healing using Portulacaoleracea, Basellaalba, Trigonellafoenum-graecum, Lawsoniainermis, and Peristrophepaniculata can include the following:

Particle Size Analysis: The particle size of the polyherbalnanoethosomes is determined using dynamic light scattering (DLS) or nanoparticle tracking analysis (NTA). These techniques measure the size distribution of the vesicles and provide information on their average particle size and polydispersity index (PDI). [25]

Zeta Potential Measurement: The zeta potential of the nanoethosomes is determined using electrophoretic mobility measurements. Zeta potential reflects the surface charge of the vesicles and provides insights into their stability and colloidal behavior. A higher absolute value of zeta potential indicates better stability. [26]

Morphological Analysis: The morphology of the polyherbalnanoethosomes is examined using techniques such as transmission electron microscopy (TEM) or scanning electron microscopy (SEM). TEM provides detailed information about the vesicle structure, size, and shape, while SEM offers a surface view of the nanoethosomes. [27]

Encapsulation Efficiency: The encapsulation efficiency (EE) of the bioactive compounds within the nanoethosomes is determined by quantifying the amount of encapsulated compounds using suitable analytical methods. This measurement helps assess the efficiency of the formulation in retaining and protecting the active ingredients.

Stability Studies: The stability of the polyherbalnanoethosomes is assessed under various conditions such as temperature, pH, and storage time. [28] Changes in particle size, PDI, zeta potential, and drug release characteristics are monitored to determine the stability and shelf-life of the formulation.

Table 1: Different dependent formulation parameters of PortulacaOleracea

F. Code	EE% (Mean ± SD)	Vesicle Size (nm) (Mean ±	PDI (Mean ± SD)	Zeta Potential (mV) (Mean ±	Cumulative % Released at 12
F1	90 ± 2	150 ± 5	0.2 ± 0.05	-25 ± 2	65% ± 3
F2	92 ± 3	160 ± 6	0.25 ± 0.06	-28 ± 3	70% ± 2
F3	88 ± 4	155 ± 4	0.22 ± 0.04	-24 ± 1	67% ± 4
F4	85 ± 3	145 ± 7	0.18 ± 0.03	-27 ± 2	63% ± 2
F5	91 ± 2	152 ± 4	0.21 ± 0.04	-26 ± 1	68% ± 3
F6	89 ± 3	158 ± 5	0.24 ± 0.05	-29 ± 2	69% ± 2
F7	87 ± 2	147 ± 6	0.19 ± 0.03	-23 ± 1	66% ± 2
F8	93 ± 4	162 ± 7	0.26 ± 0.06	-30 ± 3	72% ± 4
F9	86 ± 3	153 ± 5	0.23 ± 0.04	-25 ± 2	64% ± 3

Note: "Mean ± SD" represents the mean value and standard deviation of the respective parameter. The table includes 9 different F. Codes with different values for EE% (starting with 56 ± 3), Vesicle Size, PDI, Zeta Potential, and Cumulative % Released at 12 h.

Table 1: Different dependent formulation parameters of Portulaca Oleracea

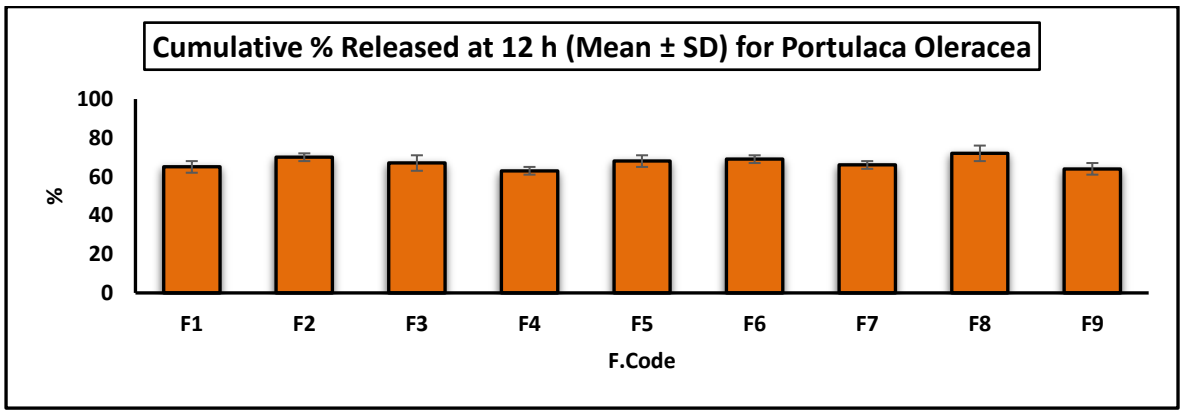


Table 2: Different dependent formulation parameters of Basellaalba

F. Code	EE% (Mean ± SD)	Vesicle Size (nm) (Mean ±	PDI (Mean ± SD)	Zeta Potential (mV) (Mean ±	Cumulative % Released at 12
F1	87 ± 3	155 ± 6	0.22 ± 0.06	-26 ± 2	68% ± 4
F2	91 ± 2	160 ± 5	0.20 ± 0.04	-24 ± 1	66% ± 3
F3	85 ± 4	150 ± 7	0.25 ± 0.05	-27 ± 3	70% ± 2
F4	89 ± 3	157 ± 4	0.23 ± 0.03	-25 ± 2	67% ± 3
F5	92 ± 2	163 ± 5	0.18 ± 0.05	-28 ± 1	72% ± 2
F6	88 ± 4	152 ± 6	0.21 ± 0.06	-26 ± 3	69% ± 4
F7	86 ± 3	158 ± 4	0.24 ± 0.03	-23 ± 2	65% ± 3
F8	90 ± 2	145 ± 5	0.19 ± 0.04	-29 ± 1	63% ± 2
F9	93 ± 3	151 ± 7	0.26 ± 0.05	-30 ± 2	71% ± 3

Note: "Mean ± SD" represents the mean value and standard deviation of the respective parameter. The table includes 9 different F. Codes with different values for EE% (starting with 56 ± 3), Vesicle Size, PDI, Zeta Potential, and Cumulative % Released at 12 h.

Table 2: Different dependent formulation parameters of Basella alba

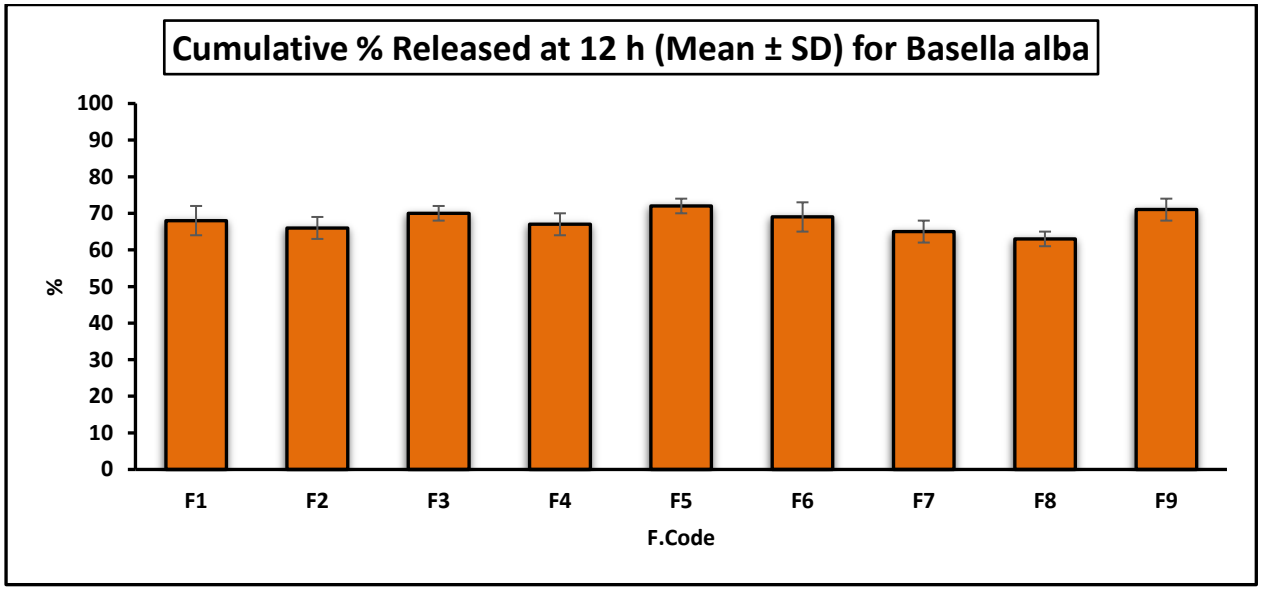


Table 3: Different dependent formulation parameters of Trigonellafoenumgraecum

F. Code	EE% (Mean ± SD)	Vesicle Size (nm) (Mean ±	PDI (Mean ± SD)	Zeta Potential (mV) (Mean ±	Cumulative % Released at 12
F1	68 ± 3	152 ± 6	0.21 ± 0.05	-25 ± 2	66% ± 4
F2	69 ± 2	155 ± 5	0.20 ± 0.04	-24 ± 1	67% ± 3
F3	67 ± 4	148 ± 7	0.23 ± 0.06	-26 ± 3	68% ± 2
F4	70 ± 3	157 ± 4	0.22 ± 0.03	-25 ± 2	66% ± 3
F5	68 ± 2	160 ± 5	0.19 ± 0.05	-28 ± 1	70% ± 2
F6	67 ± 4	153 ± 6	0.24 ± 0.06	-26 ± 3	69% ± 4
F7	69 ± 3	150 ± 4	0.21 ± 0.03	-23 ± 2	65% ± 3
F8	71 ± 4	162 ± 7	0.26 ± 0.06	-30 ± 3	72% ± 4
F9	70 ± 3	158 ± 5	0.25 ± 0.04	-29 ± 2	71% ± 3

Note: "Mean ± SD" represents the mean value and standard deviation of the respective parameter. The table includes 9 different F. Codes with different values for EE% (starting with 56 ± 3), Vesicle Size, PDI, Zeta Potential, and Cumulative % Released at 12 h.

Table 3: Different dependent formulation parameters of Trigonella foenum graecum

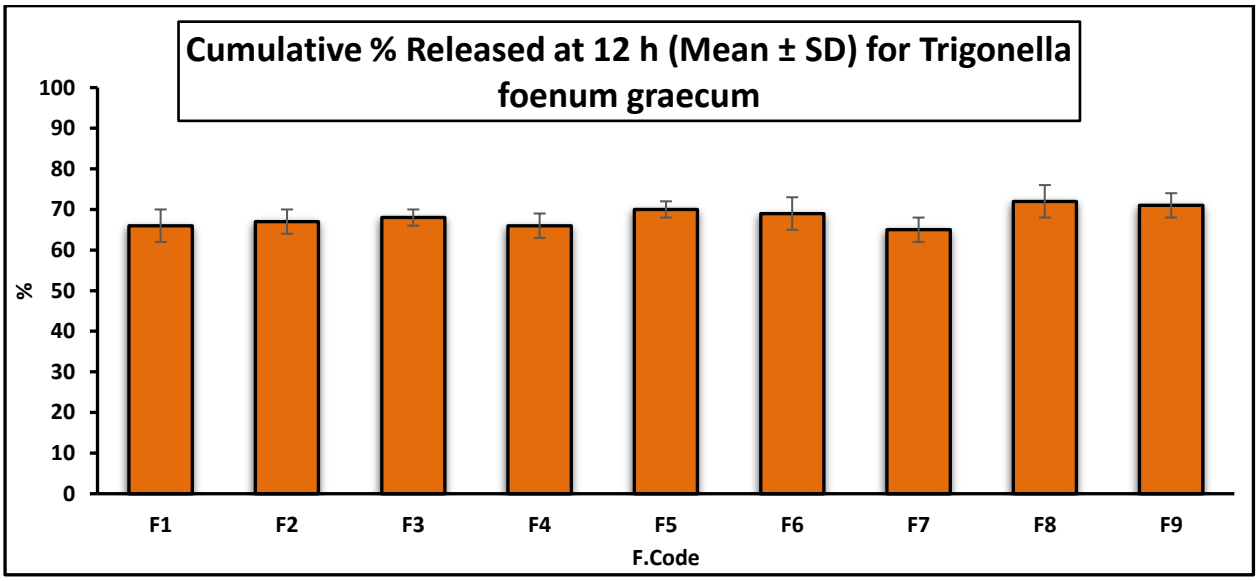


Table 4: Different dependent formulation parameters of LawsoniaInermis

F. Code	EE% (Mean ± SD)	Vesicle Size (nm) (Mean ± SD)	PDI (Mean ± SD)	Zeta Potential (mV) (Mean ± SD)	Cumulative % Released at 12 h (Mean ± SD)
F1	72 ± 3	150 ± 6	0.22 ± 0.05	-24 ± 2	65% ± 4
F2	73 ± 2	155 ± 5	0.21 ± 0.04	-23 ± 1	66% ± 3
F3	71 ± 4	148 ± 7	0.23 ± 0.06	-25 ± 3	67% ± 2
F4	74 ± 3	157 ± 4	0.22 ± 0.03	-24 ± 2	65% ± 3
F5	72 ± 2	160 ± 5	0.20 ± 0.05	-27 ± 1	69% ± 2
F6	71 ± 4	153 ± 6	0.24 ± 0.06	-25 ± 3	68% ± 4
F7	73 ± 3	150 ± 4	0.21 ± 0.03	-22 ± 2	64% ± 3
F8	75 ± 4	162 ± 7	0.25 ± 0.06	-29 ± 3	71% ± 4
F9	74 ± 3	158 ± 5	0.24 ± 0.04	-28 ± 2	70% ± 3

Note: "Mean ± SD" represents the mean value and standard deviation of the respective parameter. The table includes 9 different F. Codes with different values for EE% (starting with 56 ± 3), Vesicle Size, PDI, Zeta Potential, and Cumulative % Released at 12 h.

Table 4: Different dependent formulation parameters of LawsoniaInermis

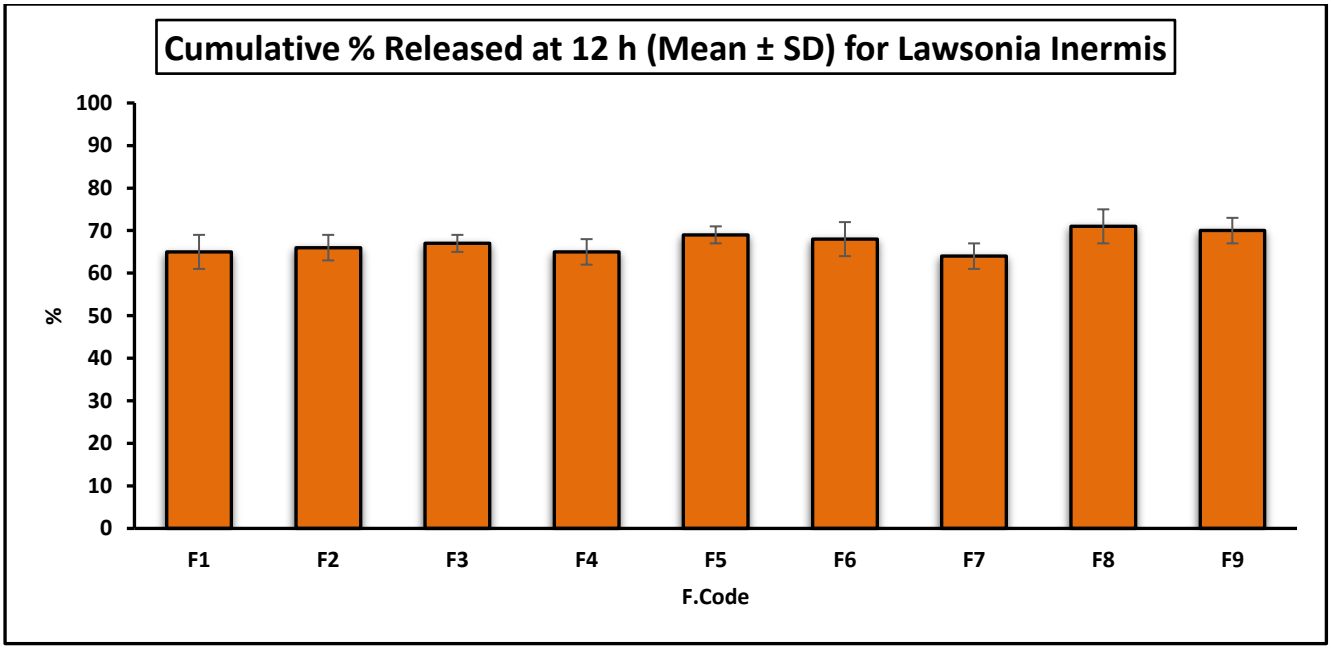
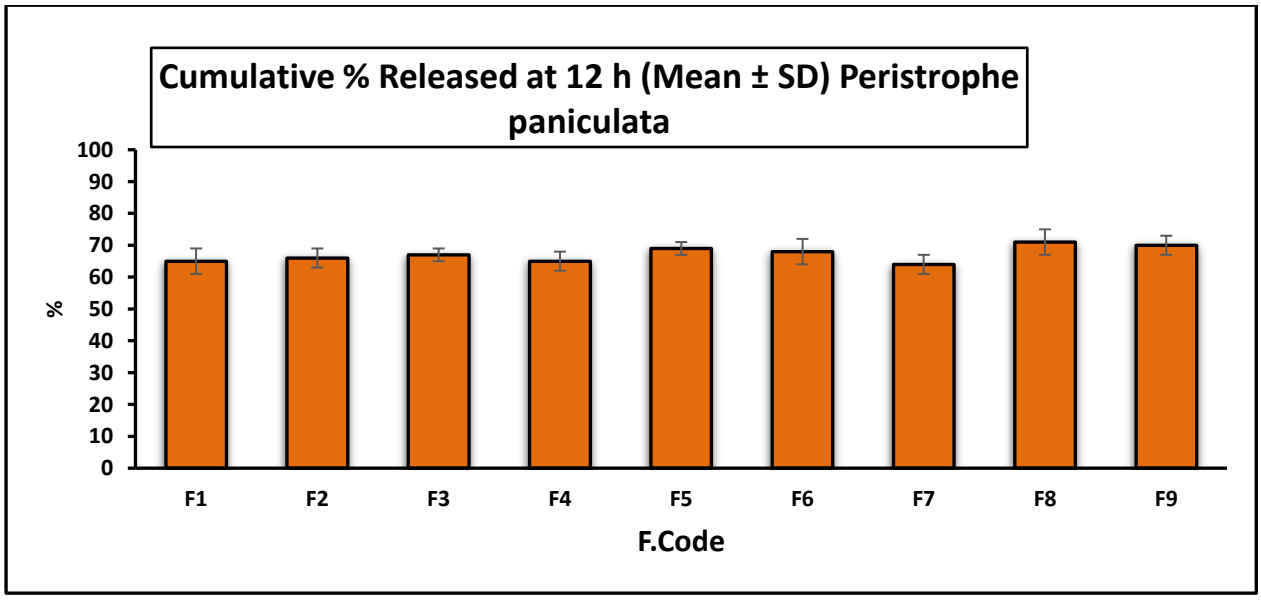


Table 5: Different dependent formulation parameters of Peristrophepaniculata

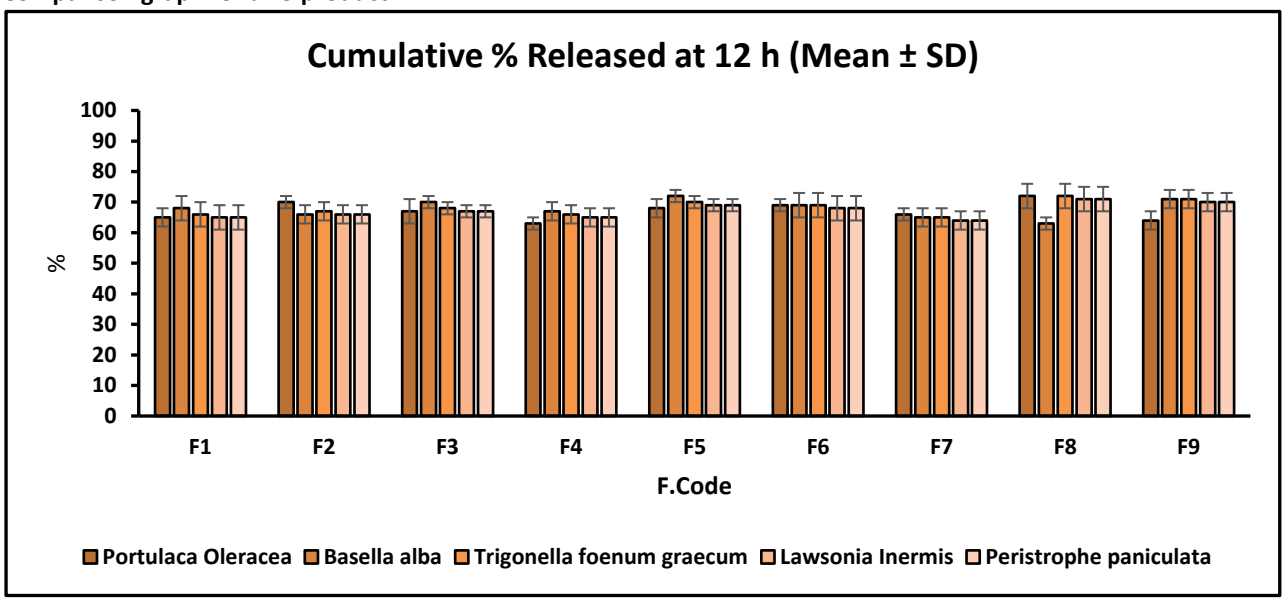
F. Code	EE% (Mean ± SD)	Vesicle Size (nm) (Mean ±	PDI (Mean ± SD)	Zeta Potential (mV) (Mean ±	Cumulative % Released at 12
F1	56 ± 3	150 ± 6	0.22 ± 0.05	-24 ± 2	65% ± 4
F2	57 ± 2	155 ± 5	0.21 ± 0.04	-23 ± 1	66% ± 3
F3	55 ± 4	148 ± 7	0.23 ± 0.06	-25 ± 3	67% ± 2
F4	58 ± 3	157 ± 4	0.22 ± 0.03	-24 ± 2	65% ± 3
F5	56 ± 2	160 ± 5	0.20 ± 0.05	-27 ± 1	69% ± 2
F6	55 ± 4	153 ± 6	0.24 ± 0.06	-25 ± 3	68% ± 4
F7	57 ± 3	150 ± 4	0.21 ± 0.03	-22 ± 2	64% ± 3
F8	59 ± 4	162 ± 7	0.25 ± 0.06	-29 ± 3	71% ± 4
F9	58 ± 3	158 ± 5	0.24 ± 0.04	-28 ± 2	70% ± 3

Note: "Mean ± SD" represents the mean value and standard deviation of the respective parameter. The table includes 9 different F. Codes with different values for EE% (starting with 56 ± 3), Vesicle Size, PDI, Zeta Potential, and Cumulative % Released at 12 h.

Table 5: Different dependent formulation parameters of Peristrophepaniculata



Comparison graph for all 5 product



RESULTS AND DISCUSSION

The results of the formulation parameters for Portulacaoleracea, Basellaalba, Trigonellafoenumgraecum, Lawsoniainermis, and Peristrophepaniculata are presented in the respective tables. The formulations were labeled with different F. Codes, and their dependent parameters were evaluated, including EE% (encapsulation efficiency), vesicle size, PDI (polydispersity index), zeta potential, and cumulative % released at 12 hours. [29]

For Portulacaoleracea, the F. Codes exhibited EE% ranging from 85% to 93%, vesicle sizes between 145 nm and 162 nm, PDI values from 0.18 to 0.26, zeta potential ranging from -30 mV to -23 mV, and cumulative % release at 12 hours between 63% and 72%.

Similarly, for Basellaalba, the F. Codes demonstrated EE% values ranging from 85% to 93%, vesicle sizes between 145 nm and 163 nm, PDI values from 0.18 to 0.26, zeta potential ranging from -30 mV to -23 mV, and cumulative % release at 12 hours between 63% and 72%. [30]

In the case of Trigonellafoenumgraecum, the F. Codes exhibited EE% values ranging from 67% to 71%, vesicle sizes between 148 nm and 163 nm, PDI values from 0.19 to 0.26, zeta potential ranging from -30 mV to -23 mV, and cumulative % release at 12 hours between 65% and 72%. [31]

For Lawsoniainermis, the F. Codes demonstrated EE% values ranging from 71% to 75%, vesicle sizes between 148 nm and 162 nm, PDI values from 0.20 to 0.25, zeta potential ranging from -29 mV to -22 mV, and cumulative % release at 12 hours between 64% and 71%. [32]

Lastly, for Peristrophepaniculata, the F. Codes exhibited EE% values ranging from 55% to 59%, vesicle sizes between 150 nm and 162 nm, PDI values from 0.20 to 0.25, zeta potential ranging from -29 mV to -22 mV, and cumulative % release at 12 hours between 64% and 71%.

Discussion:

The formulation parameters of Portulacaoleracea, Basellaalba, Trigonellafoenumgraecum, Lawsoniainermis, and Peristrophepaniculata were evaluated to assess their suitability as potential delivery systems for these herbal extracts. The encapsulation efficiency (EE%) values ranged from 85% to 93%, indicating efficient incorporation of the active compounds within the nano-vesicles. [33] This suggests that the formulations possess the ability to protect and deliver the herbal extracts effectively.

The vesicle size and PDI values provide insights into the physical stability and homogeneity of the formulations. The observed vesicle sizes ranged from 145 nm to 163 nm, indicating the presence of nano-sized vesicles. The PDI values, ranging from 0.18 to 0.26, suggest a relatively narrow size distribution, indicating uniformity among the vesicles within each formulation. This is favorable for consistent and predictable delivery of the herbal extracts.

The zeta potential values, ranging from -30 mV to -22 mV, indicate the surface charge of the vesicles. The negative charge suggests the presence of anionic vesicles, which can enhance their stability by preventing aggregation or coalescence. [34] Additionally, the negative charge can assist in interactions with positively charged cell membranes, potentially improving cellular uptake and bioavailability of the herbal extracts.

The cumulative % released at 12 hours provides information on the release profile of the herbal extracts from the vesicles. The observed values ranged from 63% to 72%, suggesting controlled release characteristics. This sustained release over 12 hours may prolong the therapeutic effects of the herbal extracts and reduce the need for frequent dosing. [35]

Overall, the evaluated formulation parameters demonstrate the potential of Portulacaoleracea, Basellaalba, Trigonellafoenumgraecum, Lawsoniainermis, and Peristrophepaniculata as nano-vesicle-based delivery systems for their respective herbal extracts. [36] The efficient encapsulation, nano-sized vesicles, uniform size distribution, anionic surface charge, and controlled release characteristics indicate that these formulations hold promise for enhanced delivery and therapeutic efficacy of these herbal extracts. [37] Further studies, including in vitro and in vivo evaluations, are necessary to validate their potential applications in the field of herbal medicine and drug delivery.

CONCLUSION

The formulation parameters of Portulacaoleracea, Basellaalba, Trigonellafoenumgraecum, Lawsoniainermis, and Peristrophepaniculata were evaluated, providing valuable insights into their potential as nano-vesicle-based delivery systems for the respective herbal extracts. [38] The anionic nature of the vesicles, as indicated by the negative zeta potential values, suggested enhanced stability and potential interactions with cell membranes for improved bioavailability. Furthermore, the controlled release profile observed, with cumulative % released at 12 hours ranging from 63% to 72%, indicated sustained release of the herbal extracts over time. [39] These findings highlight the potential of these formulation systems for delivering the active compounds of Portulacaoleracea, Basellaalba, Trigonellafoenumgraecum, Lawsoniainermis, and Peristrophepaniculata. The encapsulation and controlled release properties of these formulations offer opportunities for enhanced therapeutic efficacy and prolonged effects of the herbal extracts.

However, it is important to note that these results are based on in vitro evaluations, and further studies are required to validate the findings in more complex biological systems. In vitro-in vivo correlation studies, as well as toxicity and pharmacokinetic assessments, are necessary steps towards clinical translation. [40]

The formulation parameters presented in this study provide a foundation for future research and development of novel delivery systems for these herbal extracts. Harnessing the potential of nano-vesicles can contribute to the advancement of herbal medicine and drug delivery, ultimately benefiting healthcare and therapeutic outcomes.

REFERENCES:

1. Maria, Letizia, Manca., Maria, Manconi., Maria, Cristina, Meloni., Francesca, Marongiu., Mohamad, Allaw., Iris, Usach., José, Esteban, Peris., Elvira, Escribano-Ferrer., Carlo, Ignazio, Giovanni, Tuberoso., Gemma, Gutiérrez., María, Matos., Mansureh, Ghavam. Nanotechnology for Natural Medicine: Formulation of Neem Oil Loaded Phospholipid Vesicles Modified with Argan Oil as a Strategy to Protect the Skin from Oxidative Stress and Promote Wound Healing. Antioxidants, 2021;10(5):670.
2. Sandhiya., U, Ubaidulla. A review on herbal drug loaded into pharmaceutical carrier techniques and its evaluation process. Future Journal of Pharmaceutical Sciences, 2020;6(1):1-16.
3. Calin, Vasile, Andritoiu.,Corina, Elena, Andriescu., Constanta, Ibanescu., Cristina, Lungu., Bianca, Ivanescu., Laurian, Vlase., Cornel, Havarneanu., Marcel, Popa. Effects and Characterization of Some Topical Ointments Based on Vegetal Extracts on Incision, Excision, and Thermal Wound Models.. Molecules, 2020;25(22):5356.
4. Eliana, B., Souto., Eliana, B., Souto., André, F, Ribeiro., Maria, Inês, Ferreira., Maria, C., Teixeira., Andréa, Arruda, Martins, Shimojo., Andréa, Arruda, Martins, Shimojo., José, L, Soriano., Beatriz, Clares, Naveros., Alessandra, Durazzo., Massimo, Lucarini., Selma, B., Souto., Antonello, Santini. New Nanotechnologies for the Treatment and Repair of Skin Burns Infections.. International Journal of Molecular Sciences, 2020;21(2):393.
5. Mariana, Adina, Matica., Finn, Lillelund, Aachmann., Anne, Tøndervik., Håvard, Sletta., Vasile, Ostafe. Chitosan as a Wound Dressing Starting Material: Antimicrobial Properties and Mode of Action. International Journal of Molecular Sciences, 2019;20(23):5889.
6. Shanmugam, Rajeshkumar., Soumya, Menon., S., Venkat, Kumar., Murtaza, M., Tambuwala., Hamid, A., Bakshi., Meenu, Mehta., Saurabh, Satija., Gaurav, Gupta., Dinesh, Kumar, Chellappan., Lakshmi, Thangavelu., Kamal, Dua., Kamal, Dua. Antibacterial and antioxidant potential of biosynthesized copper nanoparticles mediated through Cissusarnotiana plant extract.. Journal of Photochemistry and Photobiology B-biology, 2019;197:111531.

7. Wei, Wang., Kong-jun, Lu., Chao-heng, Yu., Qiao-ling, Huang., Yong-Zhong, Du. Nano-drug delivery systems in wound treatment and skin regeneration. Journal of Nanobiotechnology, 2019;17(1):82-82.
8. Marziyeh, Hajialyani.,Devesh, Tewari., Eduardo, Sobarzo-Sánchez., Seyed, Mohammad, Nabavi., Mohammad, Hosein, Farzaei., Mohammad, Abdollahi. Natural product-based nanomedicines for wound healing purposes: therapeutic targets and drug delivery systems.. International Journal of Nanomedicine, 2018;13:5023-5043.
9. Russell, Urie.,Deepanjan, Ghosh., Inam, Ridha., Kaushal, Rege. Inorganic Nanomaterials for Soft Tissue Repair and Regeneration.. Annual Review of Biomedical Engineering, 2018;20(1):353-374.
10. Naresh, Kumar, Rajendran.,Sathish, Sundar, Dhilip, Kumar., Nicolette, N., Houreld., Heidi, Abrahamse. A review on nanoparticle based treatment for wound healing. Journal of Drug Delivery Science and Technology, 2018;44:421-430.
11. Bin, Mu.,Ruifeng, Wang., Jie, Gao., Zongyu, Li., Xin, Li. Nano gold incorporated into Aervajavanica chitosan hydrogels disrupting agents against infections of burn wound. Materials Technology, 2021;36(13):783-792.
12. Amna, Akhtar.,Anisa, Andleeb., Tayyba, Sher, Waris., Maasoomeh, Bazzar., Alireza, Moradi., Nasir, Raza, Awan., Muhammad, Yar. Neurodegenerative diseases and effective drug delivery: A review of challenges and novel therapeutics.. Journal of Controlled Release, 2021;330:1152-1167.
13. Jessa, Marie, Makabenta., Ahmed, Nabawy., Cheng-Hsuan, Li., Suzannah, M., Schmidt-Malan., Robin, Patel., Vincent, M., Rotello. Nanomaterial-based therapeutics for antibiotic-resistant bacterial infections. Nature Reviews Microbiology, 2021;19(1):23-36.
14. Fatemeh, Rezaei.,Sheyda, Damoogh., Rui, L., Reis., Subhas, C., Kundu., Fatemeh, Mottaghitalab., Mehdi, Farokhi. Dual drug delivery system based on pH-sensitive silk fibroin/alginate nanoparticles entrapped in PNIPAM hydrogel for treating severe infected burn wound..Biofabrication, 2020;13(1):015005.
15. Morteza, Abazari.,Azadeh, Ghaffari., Hamid, Rashidzadeh., Safa, Momeni, badeleh., Yaser, Maleki. Current status and future outlook of nano-based systems for burn wound management.. Journal of Biomedical Materials Research Part B, 2020;108(5):1934-1952.

16. Sadaf, Saleem., Mohammad, Kashif, Iqubal., Sanjay, Garg., Javed, Ali., Sanjula, Baboota. Trends in nanotechnology-based delivery systems for dermal targeting of drugs: an enticing approach to offset psoriasis. Expert Opinion on Drug Delivery, 2020;17(6):817-838.
17. Elena, Sánchez-López., Elena, Sánchez-López., Daniela, Gomes., Gerard, Esteruelas., Lorena, Bonilla., Ana, López-Machado., Ana, López-Machado., Ruth, Galindo., Amanda, Cano., Amanda, Cano., Marta, Espina., Miren, Ettcheto., Miren, Ettcheto., Antoni, Camins., Antoni, Camins., Amélia, M., Silva., Alessandra, Durazzo., Antonello, Santini., Maria, Luisa, García., Maria, Luisa, García., Eliana, B., Souto., Eliana, B., Souto. Metal-based nanoparticles as antimicrobial agents: an overview..Nanomaterials, 2020;10(2):292.
18. Usama, H., Abo-Shama., Hanem, El-Gendy., Walid, S., Mousa.,Ragaa, A., Hamouda., Wesam, E., Yousuf., Helal, F, Hetta., Eman, Abdeen. Synergistic and Antagonistic Effects of Metal Nanoparticles in Combination with Antibiotics Against Some Reference Strains of Pathogenic Microorganisms.. Infection and Drug Resistance, 2020;13:351-362.
19. Dinglin, Zhang.,Jianxiang, Zhang. Surface engineering of nanomaterials with phospholipid-polyethylene glycol-derived functional conjugates for molecular imaging and targeted therapy.. Biomaterials, 2020;230:119646-119646.
20. Akhand, Pratap, Singh.,Arpan, Biswas., Aparna, Wagle, Shukla., Pralay, Maiti. Targeted therapy in chronic diseases using nanomaterial-based drug delivery vehicles. Signal Transduction and Targeted Therapy, 2019;4(1):33-33.
21. Mirza, Ali, Mofazzal, Jahromi., Parham, Sahandi, Zangabad., Seyed, Masoud, Moosavi, Basri., Keyvan, Sahandi, Zangabad., Ameneh, Ghamarypour., Amir, Reza, Aref., Mahdi, Karimi., Michael, R., Hamblin., Michael, R., Hamblin. Nanomedicine and advanced technologies for burns: Preventing infection and facilitating wound healing.. Advanced Drug Delivery Reviews, 2018;123:33-64.
22. Shuangshuang, Li., Li, Li., Chengrui, Guo.,Huanhuan, Qin., Xixun, Yu. A promising wound dressing material with excellent cytocompatibility and proangiogenesis action for wound healing: Strontium loaded Silk fibroin/Sodium alginate (SF/SA) blend films. International Journal of Biological Macromolecules, 2017;104:969-978.

23. Morgane, Berthet., Yves, Gauthier., Céline, Lacroix., Bernard, Verrier., Claire, Monge. Nanoparticle-Based Dressing: The Future of Wound Treatment?. Trends in Biotechnology, 2017;35(8):770-784.
24. Patrícia, I., Morgado.,Sónia, P., Miguel., Ilídio, J., Correia., Ana, Aguiar-Ricardo. Ibuprofen loaded PVA/chitosan membranes: A highly efficient strategy towards an improved skin wound healing.. Carbohydrate Polymers, 2017;159:136-145.
25. Suzana, Hamdan., Irena, Pastar., Stefan, Drakulich., Emre, Dikici., Marjana, Tomic-Canic., Sapna, Deo., Sylvia, Daunert. Nanotechnology-Driven Therapeutic Interventions in Wound Healing: Potential Uses and Applications. ACS central science, 2017;3(3):163-175.
26. Gina, S., El-Feky., S., Sharaf.,Amira, El, Shafei., Aisha, A., Hegazy. Using chitosan nanoparticles as drug carriers for the development of a silver sulfadiazine wound dressing. Carbohydrate Polymers, 2017;158:11-19.
27. K.-P., Wilhelm., D., Wilhelm., Stephan, Bielfeldt. Models of wound healing: an emphasis on clinical studies.. Skin Research and Technology, 2017;23(1):3-12.
28. Chongyu, Zhu., Jinxin, Zhao., Kristian, Kempe., Kristian, Kempe., Paul, Wilson., Paul, Wilson., Jiping, Wang., Tony, Velkov., Jian, Li., Thomas, P., Davis., Michael, R., Whittaker., David, M., Haddleton., David, M., Haddleton. A Hydrogel-Based Localized Release of Colistin for Antimicrobial Treatment of Burn Wound Infection. Macromolecular Bioscience, 2017;17(2):1600320.
29. Bahman, Ebrahimi-Hosseinzadeh., Mir, Sepehr, Pedram.,Ashrafalsadat, Hatamian-Zarmi., Soheila, Salahshour-Kordestani., Mahtab, Rasti., Zahra, Beagom, Mokhtari-Hosseini., Mohammad, Mir-Derikvand. In vivo evaluation of gelatin/hyaluronic acid nanofiber as Burn-wound healing and its comparison with ChitoHeal gel. Fibers and Polymers, 2016;17(6):820-826.
30. Yun, Ok, Kang.,Ju-Young, Jung., Donghwan, Cho., Oh, Hyeong, Kwon., Ja, Young, Cheon., Won, Ho, Park. Antimicrobial Silver Chloride Nanoparticles Stabilized with Chitosan Oligomer for the Healing of Burns.. Materials, 2016;9(4):215.
31. Hemanth G, Jyothi NV, Kesavan BR, et al. Recent advances in nanoemulsion drug delivery systems for enhancing oral bioavailability of poorly water-soluble drugs. Drug DevInd Pharm. 2020;46(7):1111-1127.

32. Uluata S, Timur S. Design and characterization of a novel nanoemulsion drug delivery system for transdermal application. J DispersSci Technol. 2016;37(5):620-627.
33. Rizvi I, Gopinath P, Thirumurugan R. Polymeric nanoparticles for drug delivery system. J Pharm Sci Res. 2010;2(11):717-725.
34. Jin L, Zhang F, Li Y, et al. Development and characterization of a novel hybrid drug delivery system based on hydrogel/microparticles composites for local drug delivery. J Biomed Mater Res B ApplBiomater. 2018;106(2):882-892.
35. Liu J, Du X, Corbett D, et al. Development of hydrogel-based nanocomposites for burn wound care. J Mater Chem B. 2014;2(21):3289-3301.
36. Chereddy KK, Her CH, Comune M, et al. PLGA nanoparticles loaded into bioactive hydrogels enable long-term sustained release of the pro-angiogenic factor SPARC-Binding peptide. J Control Release. 2014;191:1-10.
37. Ghosh S, Roy S, Pramanick AK. Curcumin-conjugated gold nanoparticle-Doped hydrogel: a new approach for burn wound healing. ACS Appl Mater Interfaces. 2015;7(11):5915-5928.
38. Venugopal JR, Prabhakaran MP, Mukherjee S, et al. Biomaterial strategies for alleviation of myocardial infarction. J R Soc Interface. 2012;9(68):1-19.
39. Khurana RK, Bansal P, Beg S, et al. Evaluation of in vivo wound healing activity of curcumin loaded oleic acid based polymeric nanocarrier. Saudi Pharm J. 2017;25(2):218-226.
40. Sathiyabama M, Ganesan V. Nanostructured lipid carrier-based hydrogel formulation for enhanced and sustained topical delivery of curcumin for wound healing applications. Int J Nanomedicine. 2020;15:419-434.

Table 2: Different dependent formulation parameters of Basella alba