

WORLD JOURNAL OF PHARMACEUTICAL RESEARCH

SJIF Impact Factor 8.453

Volume 13, Issue 21, 1250-1268.

Review Article

ISSN 2277-7105

A COMPREHENSIVE REVIEW OF POLYHERBAL NIOSOMAL CREAM FOR ANTI-AGING AND SKIN REGENERATION: A SYNERGISTIC APPROACH

Rahul Santosh Sharma¹*, Pranit Jivan Satale¹, Sonali Bhausaheb Sathe¹, Pradnya Naykodi²

¹B. Pharmacy Student, Yash Institute of Pharmacy, Chhatrapati Sambhajinagar, Dr.

Babasaheb Ambedkar Marathwada University, Maharashtra, India.

²Department of Pharmacology, Assistant Professor, Yash Institute of Pharmacy, Chhatrapati

Sambhajinagar 431136, Maharashtra, India.

Article Received on 20 September 2024,

Revised on 11 October 2024, Accepted on 31 October 2024

DOI: 10.20959/wjpr202421-34517



*Corresponding Author Rahul Santosh Sharma

B. Pharmacy Student, Yash Institute of Pharmacy,Chhatrapati Sambhajinagar,Dr. Babasaheb Ambedkar Marathwada University,Maharashtra, India.

ABSTRACT

Skin aging is a complex biological process characterized by exposure to intrinsic and extrinsic factors that lead to damage to the skin, resulting in wrinkles, dryness, and changes in the pigmentation of the skin. This is the major problem in today's world, which leads to an increase in demand for an effective solution. As the demand for effective anti-aging solutions increased, the focus shifted toward novel herbal treatments, including the use of herbal medicines, as they are very effective and have less side effects on skin as compared to allopathic medicines. This review highlights the study of the potential of polyherbal niosomal creams in improving skin repair, rejuvenation, and protection against aging factors that cause aging; the individual profiles of common herbs used in skincare; studying their roles in antiaging and skin regeneration; and comparing traditional herbal creams with niosomal formulations. The advantages of using niosomes for targeted delivery and improved efficacy are demonstrated. This

comprehensive review provides valuable insights into the future potential of polyherbal niosomal creams as a synergistic approach to combating skin aging and promoting youthful skin.

KEYWORDS: Niosome, Synergistic, Polyherbal, Anti-Aging, Skin regeneration, etc.

1. INTRODUCTION

Skin aging is a complex biological process in every living thing. The skin, which is exposed to environmental oxidative material, leads to skin degeneration. Aging can occur due to environmental factors, namely sunlight, humidity temperature, cigarette smoke, and air pollution. [1] Aging means the thinning, sagging, appearance of age spots, and dryness of skin. Anti-aging products are therefore in high demand due to the growing desire to look or at least stay young. Free radicals are extremely reactive oxygen molecules that interact with collagen molecules to cause a loss of tone and elasticity in the skin, which is the first sign of aging. [2] Aging leads to progressive deterioration of skin structure and function which leads to wrinkles, dryness, reduced elasticity, and pigmentation changes. Skin regeneration after aging is the process by which aged or damaged skin attempts to restore its youthful properties. In the recent advances, various therapies have emerged to promote skin rejuvenation. A complex strategy involving biological processes such as stem cell activation, collagen synthesis, and extracellular matrix remodeling is required to regenerate skin after skin aging.^[3] Recent advances in treatments range from topical solutions to advanced therapies like polyherbal antiaging creams and laser treatments. [4] In this review we highlight the potential of combining herbal extracts with niosomal technology to enhance skin repair, rejuvenation, and protection against aging.

1.1. Brief explanation of skin aging process (intrinsic and extrinsic factors)

The skin aging is influenced by two factors based on the cause of aging, namely intrinsic (internal) and extrinsic (external). These factors contribute to both functional and visual changes in the skin over time, leading to signs suchas wrinkles, sagging, and loss of elasticity. The major changes occur in the form of reduced skin barrier function, slowed epidemic cell turnover, and reduced vascularity in the skin layer, so the skin looks atrophic.^[1]

1.1.1. Intrinsic factors

- 1) Genetic predisposition: the aging is largely dependent on the individual genetics. The rate at which collagen and elastin degrade and the capacity for cellular repair are influenced by the genetic factor of the individual person, it also depends on the gender of the individual.^[5]
- 2) Hormonal imbalance: Hormonal imbalances, specifically decrease in testosterone in males lead to changes in the skin of males. Estrogen or other hormones in females during menopause, accelerate the breakdown of collagen and elastin which are essential proteins

- in skin leading to thinning, dryness and wrinkling of the skin. [6]
- 3) **Reduced Cellular Turnover**: due to decrease in skin turnover, As we age, the ability of skin to regenerate reduces. There is a decrease in the production of collagen and elastin, while the breakdown of this protein increases. This results in thinner and more fragile skin.^[7]
- **4) Decreased Moisture Retention**: as we age, the ability of skin to retain moisture decreases due to a reduction in natural moisturizing factors, lipids, and hyaluronic acid. This leads to dry, rough skin.^[8–10]

1.1.2. Extrinsic factors

- 1) Ultraviolet (UV) Radiation: UV exposure is the most significant cause of extrinsic aging. Exposure to UV-B leads to damage to DNA and causes oxidative stress, leading to the degradation of collagen and elastin fibers. This leads in the formation of wrinkles, pigmentation, and leathery texture, known as photoaging.^[9]
- 2) Pollution: Environmental pollutants, particularly in urban areas, can cause oxidative stress in the skin by generating free radicals. Pollutants like particulate matter, ozone, and smoke degrade the skin barrier, leading to inflammation, pigmentation, and accelerated aging.^[11]
- 3) Smoking: Tobacco smoke contains thousands of chemicals that promote oxidative stress, leading to premature wrinkling, loss of elasticity, and reduced skin repair capacity. Smoking also decreases blood flow, impairing the delivery of oxygen and nutrients to the skin. [12]
- 4) Diet and Lifestyle: Poor nutrition, particularly diets lacking in antioxidants, can hasten skin aging. Antioxidants neutralize free radicals that contribute to skin damage, and a diet rich in fruits and vegetables can help slow this process. Additionally, lack of sleep, chronic stress, and excessive alcohol consumption can also negatively impact skin health.^[13]

1.2. Importance of skin regeneration in anti-aging treatments

Skin regeneration is the crucial process for maintaining skin health and reversing the signs of aging. The ability of skin to repair reduces with age, leading to damage to the skin from various factors like sunlight, humidity, etc. In the antiaging treatment, skin regeneration plays a vital role as it enhances the restoration of skin and reduces the damage by enhancing cellular turnover, collagen synthesis, and the overall repair mechanisms. Skin regeneration

also helps to restore the skin rejuvenation, improve texture, and reduce the visible signs of aging.[4,14]

1.3. Importance of Herbal Remedies in Skincare

Herbal plants have been used in skincare products for centuries because they constitute natural ingredients that do not have side effects as shown by synthetic compounds, and they are able to check skin damage and aging. That's why herbal cosmetics have gained immense popularity among the populations in recent years. The inclusion of herbal extracts in cosmetics can minimize skin damage due to oxidative stress, and thus aging process gets delayed. Herbal products improve various functions of skin by boosting collagen growth and thus eradicating harmful effects of free radicals, maintaining the structure of keratin, and keeping skin healthy.^[15]

2. Common Herbs Used in Skincare

There are varieties of herbs, which is used in the skincare in the traditional system of medicine Here's a detailed overview of the Biological classification and chemical constituents, and their physiological actions on the skin:

Table no 1: Individual profile of common herbs used in skin care.

Sr no	Plant	Image	Biological classification	Chemical constituent and Skin benefits	Reference
1	Aloe vera		Kingdom: Plantae Subdivision: Angiosperms Class: Monocots Order: Asparagales Family: Asphodelaceae Scientific name: Aloe barbadensis miller	Chemical constituents: Vitamins (A, C, E), enzymes (Brady kinase carboxypeptidase), amino acids, salicylic acid, cholesterol, campesterol, β- sisosterol, and lupeol, etc. Skin benefits: Increases collagen synthesis, Moisturizing, soothing, anti- inflammatory, wound healing, and anti-aging properties.	[16]
2	Turmeric		Kingdom: Plantae Subdivision: Angiosperms Class: Monocots Order: Zingiberates Family: Zingiberacear Scientific name: Curcurma longa	Chemical constituents: Curcumin, Polyphenol, Turmerone, Curcumol, antioxidants, Arturmerone, etc. Skin benefits: Anti- inflammatory, antioxidant, reduces acne, brightens skin, and combats	[17,18]

				hyperpigmentation.	
			Kingdom: Plantae	Chemical constituents:	
3	Green Tea		Subdivision:	epigallocatechin-3-gallate,	
			Angiosperms	catechin, epicatechin, tannins,	
			Class: Eudicots	flavonoids, etc.	54.03
			Order: Ericales	Skin benefits: Antioxidant,	[19]
				<u> </u>	
			Family: Theaceae Scientific name:	anti-inflammatory, anti-aging,	
				reduces acne, and skin	
			Camelia sinensis	regeneration.	
			Kingdom: Plantae	Chemical constituents:	
			Subdivision:	Nimbidin, nimbin, quercetin,	
		MARIE	Angiosperms	fatty acids, etc.	
4	Neem		Class: Dicots	Skin benefits: Antibacterial,	[20]
	1 (0011)	1911	Order: Sapindales	antifungal, treats acne,	
		-	Family: Maliaceae	reduces dark spots, and	
			Scientific name:	promotes wound healing.	
			Azadirachita indica	promotes would hearing.	
			Kingdom: Plantae	Chemical constituents:	
			Subdivision:	Ginkgolides, Bilobalide,	
			Gymnosperm	Proanthocyanidins,	
_	G: 1		Class: Ginkgopsida	Bilobalide, Carotenoids, etc.	[15,21]
5	Ginkgo		Order: Ginkgoales	Skin benefits: Antioxidant,	[13,21]
			Family: Ginkgoaceare	reduces scars, anti-	
			Scientific name: Ginkgo	inflammatory, skin	
			biloba	regeneration, Wound healing.	
		mla	Kingdom: Plantae	Chemical constituents:	
			Subdivision:	Vitamin C, Gallic Acid,	
			Angiosperms	Ellagic Acid, Phyllembelic	
	Amla		Class: Dicots	Acid, Emblicanin A and B,	1221
6			Order: Geranials	etc.	[22]
			Family: Euphorbiaceae	Skin benefits: Anti-aging,	
			Scientific name:	Antioxidant, prevent, anti-	
			Emblica ofiicinalis		
-				inflammatory, wound healing.	
	Lavender		Kingdom: Plantae	Chemical constituents:	
			Subdivision:	Linalool, linalyl acetate,	
			Angiosperms	terpenoids, etc.	
7			Class: Eudicotcots	Skin benefits: Antibacterial,	[23]
			Order: Lamiales	soothing, promotes skin	
			Family: Lamiaceae	healing, and helps with acne	
			Scientific name:	and irritation.	
<u> </u>			Lavandula augustifolia		
8			Kingdom: Plantae	Chemical constituents:	
			Subdivision:	Rosemaric acid, gallic	
			Angiosperms	acid,eugenol, ursolic acid,	
			Class: Dicots	Caryophyllene, apigenin, etc.	[24]
			Order: Lamiales	Skin benefits: Antioxidant,	
			Family: Lamiaceae	anti-inflammatory, anti-acne,	
			Scientific name:	antiaging.	
			Ocimum sanctum	annaging.	
			1		

3. NIOSOMES IN DRUG DELIVERY

3.1. Introduction to Niosomes

Niosomes are non-ionic surfactant vesicles with a bilayer structure. They increase the shelf life of the drug and have the ability to deliver the drug at target site in controlled or sustained manner, which enhances the bioavailability of the drug. Non-ionic surfactants are used due to their ability to enhance the solubility and bioavailability of the poorly water soluble drugs .Mainly, the drugs of BCS class II and Class IV have low solubility and permeability can be given by this method. ^[25] This system is used to increase both permeability and fluidity of the biological membrane, so drug like podophyllotoxins, etopsides, and methotrexate show enhanced bioavailability by transdermal route via niosomes. ^[26,27]

3.2. Structure of Niosomes

Niosomes are made up of non-ionic surfactant vesicles with a bilayer structure. Hydrophilic heads face away from aqueous solutions, while hydrophobic heads face towards organic solutions. The niosome vesicles can be divided into 2 types based on the number of layers that are unilamellar vesicles and multilamellar vesicles. Multilamellar vesicle consist of more than one layer. Niosome can be into 3 types based on size and number of layers. Small unilamellar vesicles (SUV) have particle sizes ranging from approximately 10 to 100 nm, large unilamellar vesicles (LUV) range from 100 to 3000 nm, and multi-lamellar vesicles (MLV) are larger than 5 µm. [29]

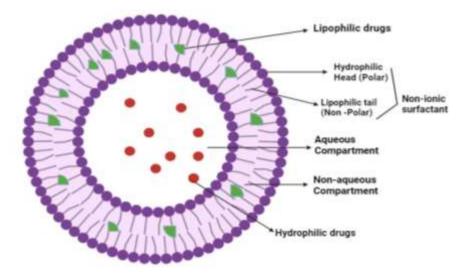


Figure 1: Structure of Niosome.

3.3. Components of Niosomes

The efficacy of a drug delivery system strictly dependent on its components. The basic

component of niosomes include non-ionic surfactant, cholesterol and charged molecules.^[27]

3.3.1. Non-ionic surfactant

Non-ionic surfactants are the basic component of niosomes. Non-ionic surfactants are amphiphilic molecules that have distinct chemical structures, one of which is hydrophilic head and hydrophobic tail. Which, upon hydration form lamellar microscopic and nanoscopic vesicles. Non-ionic surfactants are preferred due to their less irritation power, possessing high interfacial activity, and ability to form stable formulations. Which upon hydration form a bilayer and hence entrap both hydrophilic and hydrophobic drugs. They are stable, compatible and nontoxic; they also function as a solubilizer, wetting agent, and permeability enhancer which makes them to use in the formulation of noisome. The HLB value describes balance between the hydrophilic and lipophilic portion of non-ionic surfactant. The HLB range is from 0 to 20 for non-ionic surfactant. But the surfactant with HLB between 4 and 8 is preferred because of their vesical forming ability. [31]

Table no 2: Non-ionic surfactant used in noisome along with examples.

Non-Ionic surfactant	Examples	
Alkyl Ethers		
1.Alkyl glycerol ethers	Hexadecyl diglycol ether(C16G2)	
2.Polyoxyethylene glycol alkyl ethers	Brij 30, Brij 52, Brij 72, Brij 78	
Alkyl esters 1. Sorbitan fatty acid esters (Spans) 2. Polyethylene sorbitan fatty acids (Tween)	Span 20, Span 40, Span 60, Span 80, Span 65 Tween 20, Tween 40, Tween 60, Tween 80, Tween 65, Tween 85	
Alkyl amides		
1.Glycosides	C-glycoside derivatives surfactant (BRM-BG)	
2.Alkyl polyglycosides	Octyl-decyl polyglycoside (OrCG110)	
Fatty alcohol o fatty acids		
1.Fatty alcohols	Steryl alcohol,cetyl alcohol ,myristyl alcohol	
2.Fatty acids	Steric acid ,palmitic acid ,myristic acid	

3.3.2. Cholesterol

Cholesterol is a steroidal derivative that is mainly used in the formulation of niosomes. It may not show any role in the formulation of bilayer^[32], but In the bilayer structure of niosomes, cholesterol forms hydrogen bonds with the hydrophilic head of a surfactant. Cholesterol content of niosomes thereby influences the structures of niosomes and physical properties such as entrapment efficiency, long term stability, release of payload, and biostability.^[31] Cholesterol improves the rigidity of vesicles, and stabilizes niosomes, decreases the permeability of vesicles for entrapped molecules thus inhibiting leakage. Drug entrapment

efficiency plays an important role in niosomal formulations and it can be altered by varying the content of cholesterol. [27]

3.3.3. Charged molecules

Charged molecules improves the stability of noisome by preventing vesicles aggregation by increasing surface charge density. Dicetyl phosphate (DCP) and phosphatidic acid are the commonly used negatively charged molecules for niosome preparation, and similarly, stearylamine (STR), and stearyl pyridinium chloride are well-known positively charged molecules used in niosomal preparations.^[33] Normally, the charged molecule is added in niosomal formulation in an amount of 2.5–5 mol%. However, increasing the amount of charged molecules can inhibit niosome formation.^[31] It forms the zeta potential, which is necessary for electrostatic stabilization.^[29]

3.4. Method of preparation of Niosomes

3.4.1. Hand shaking (Thin film hydration techniques)

In the hand shaking method, non-ionic surfactant is dissolved in a volatile organic solvent such as diethyl ether or chloroform with cholesterol in a rotatory evaporator, then the organic solvent evaporates and the thin film of the solid mixture is deposited on the wall of the flask.^[26] Then the film is rehydrated with an aqueous phase containing drug at room temperature with agitation. Multilamellar vesicles are formed by this method.^[31]

3.4.2. Transmembrane pH gradient

Surfactant and cholesterol are dissolved in volatile organic solvent. The solvent is then evaporated, and a thin film is formed on the round bottom flask using a rotatory evaporator. Then the film is hydrated with citric acid (pH 3.0 or 4.0) by vertex mixing. Then sonicated three times and then the aqueous solution containing drug is added to the niosomal suspension. Then the pH of the sample is raised to 7.0 with phosphate buffer. This mixture is then heated at 60°C for 10 minutes to produce multilamellar vesicles. [31,34]

3.4.3. Reverse phase evaporation technique

Surfactant and cholesterol are dissolved in the mixture of ether and chloroform. The aqueous phase containing drug is added and then sonicated at 4-5°C. The clear gel is formed after sonication and then a small amount of phosphate buffer saline (PBS) is added. The organic phase is evaporated at 40°C under low pressure. The obtained viscous niosomal suspension was then diluted with PBS and heated in the water bath at 60°C for 10 min to yield large

unilamellar vesicles.[31]

3.4.4. Ether injection method

The ether injection method is based on the rate of injection of a solution of surfactant in diethyl ether through a 14-gauge needle. The aqueous solution containing the drug is maintained at 60°C, then the organic phase is added, if the speed of injection is slow (0.25 ml/min) into aqueous phase then there is the formation of large unilamellar vesicles, if the speed of injection is fast into aqueous phase then there is the formation of small unilamellar vesicles. The only disadvantage of this method is that a small amount of ether is frequently present in the vesicle suspension, which is difficult to remove. [31,35]

3.4.5. Sonication

The aqueous phase containing drug is added to the mixture of surfactant and cholesterol in the scintillation vial. then the mixture is homogenized using a sonicator at 60°C for 3 minutes. The small unilamellar vesicles are formed with uniform size.^[31]

3.4.6. The bubble method

Surfactant and cholesterol are added into the three necked flask .niosomal components are dispersed at 70°C, and then this dispersion is mixed with homogenizer for 15 seconds, and immediately afterwards it is bubbles using nitrogen gas to yield large unilamellar vesicles.^[29]

4. SYNERGISTIC EFFECTS OF POLYHERBAL FORMULATIONS

4.1. Concept of synergy in herbal medicine

The concept of synergy in herbal medicine is rooted in the traditional system of medicine, that combining multiple herbs can enhance the therapeutic effect, leading to the effect that are greater than the sum of the individual action of the drugs. the interaction between various bioactive compounds, which may lead to improved efficacy, reduced toxicity, or broader therapeutic coverage. The use of more than one plant extract to treat disease or disorder is called polyherbism. This concept was since the Ayurveda was effective in ayurvedic products for mankind are developed with the numbers of natural sources in a single formulation by getting synergism, which resulted in a better therapeutic effect than a single herb. The pharmacokinetic parameters like absorption, distribution, metabolism, and elimination will ease the drug to be effective and active metabolite with similar pharmacodynamics targeted by diverse mechanism of action will present in synergism effect. [37]

4.2. How combining multiple herbs leads to enhanced therapeutic effects

Synergism occur when mixture of two or more drugs produce greater action than expected which is greater than the sum of their individual effect of the drug. Synergy in polyherbal formulations enhance the therapeutic effect by several mechanisms:

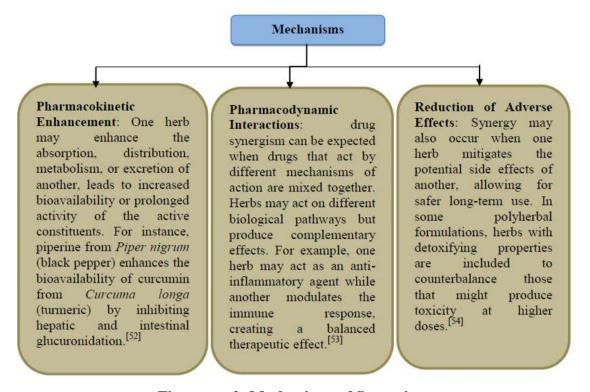


Figure no. 2: Mechanisms of Synergism.

4.3. Examples of Synergistic Polyherbal Formulations

Products	Composition of polyherbal formulation	Description and use	Reference	
		It is a classical ayurvedic		
		formulation composed of three		
	Emblica officinalis (Amla),	fruits. Triphala is known for its		
Triphala	Terminalia bellirica, and	antioxidant, digestive, and anti-	[38,39]	
-	Terminalia chebula	inflammatory properties. which		
		synergistically work to enhance the		
		gastrointestinal health.		
		It is an ayurvedic formulation,		
Amruthotha	Terminalia chebula (fruit),	which is also known for its		
ram	Tinospora cordifolia (stem), and	synergistic effect in the treatment	[40]	
kashayam	Zingiber officinale (rhizome)	of fever, digestion, and other		
-		health issues like infections.		
	Jasminum officinale,	It is an ayurvedic formulation		
Loti Irolmo	Azadirachta indica,	which is gives synergistic effect in		
Jati kalpa	Stereospermum suaveolens,	the treatment of diabetic, chronic	[41]	
ghrita	Hemidesmus indicus, Pongamia	wounds, fistula, fissure, eczema,		
	pinnata, Vetiveria zizanioides,	and burn management.		

	Glycyrrhiza glabra, etc		
Bihat ashwagandh a Ghrita	Ashwagandha, sarpi (goghrta), ksira (godugdha), chagamamsa, kakoli, honey.	It is an ayurvedic formulation. It is used in the treatment of wrinkling on skin, in aging, in graying of hairs, infertility, fever.	[42]
Agastya Haritaki Rasayana	Aegle marmelos Linn, Oroxylum indicum, Gmelina arborea, Stereospermum suaveolens, Premna mucronta, Desmodium gangeticum, Solanum indicum linn, Solanum surattense, Tribulus terrestis Linn.	It is an ayurvedic formulation known for its antioxidant, antimutagenic, anticarcinogenic, antiaging, antibacterial, antiviral, antifungal, antidiabetic, cardioprotective, antiulcer, and wound healing properties.	[43]
Polyherbal formulation	Ageratum conyzoides, Culcasia scandens, and Mitracarpus villosus	It is a polyherbal formulation. it shows the Antimicrobial activity, wound healing, antiaging properties.	[44]
Poly herbal cream	Malva Sylvestris, and Solanum nigrum	It is a polyherbal formulation it shows Antimicrobial activity and wound healing properties.	[45]

5. POLYHERBAL NIOSOMAL CREAM FORMULATION

The polyherbal niosomal cream is the cream that consists of multiple herbs that show synergistic effect, and that are encapsulated in the vesicular structure, which is made up of niosomes, and this structure is made into a cream formulation. The formulation of polyherbal niosomal creams involves several steps which are as follows:

5.1. Selection of herbs and active compounds

The selection of herbs is the crucial process in the formulation of polyherbal cream. The herbs which are compatible with each other and show the synergistic effect in the cream or enhance the action of cream are selected. The extraction of this plant is done in which separation of medicinally active portions of the plant using selective solvents through standard procedures given in the traditional system.^[46]

5.2. Preparation of Niosomes

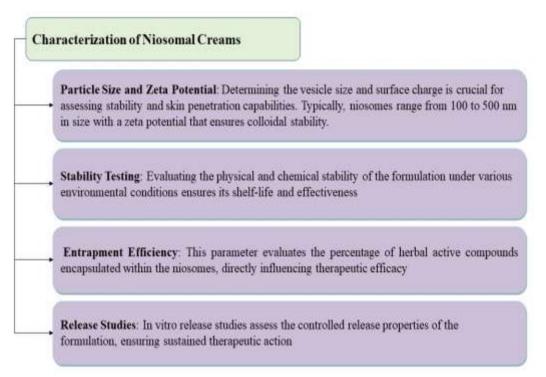
The next step of this formulation is the encapsulation of the extract in the niosomes. Niosomes are typically prepared using the thin-film hydration method or ether injection method. Where the drug is encapsulated, the non-ionic surfactants like Span 60 or Tween 80 are dissolved with cholesterol, followed by hydration and sonication to form niosomal vesicles.^[47]

5.3. Incorporation into Cream Base

This is the final step in which the prepared niosomal vesicles are incorporated in the suitable base, often containing emulsifier, stabilizer, and preservative. The cream is prepared by the standard method to ensure consistency and shelf life of the formulation.^[48]

5.4. Characterization of Niosomal Creams

Characterization of niosomal cream is essential to ensure the efficacy and stability if polyherbal niosomal cream. The characterization is as follows:



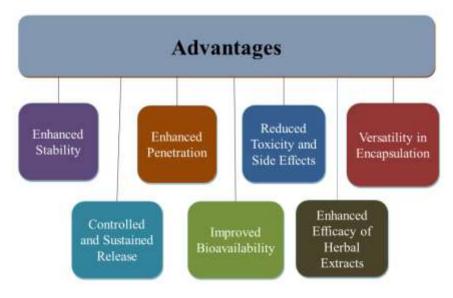


Figure no 3: Advantages of Niosomal creams.

5.5. Overview of Polyherbal Ingredients Used in Anti-aging and Skin Regeneration

Sr No	Ingredients	Description and use	REFERENCE
1	Aloe Vera (Aloe barbadensis Mill.), Neem (Azadirachta indica), Turmeric (Curcuma longa Linn.), Mint (Mentha piperata Linn.).	The polyherbal face cream which is prepared by using ethanolic extract of Aloe Vera gel, Neem, Turmeric, and Mint showing multipurpose effect such as whitening, anti-aging, antioxidant, antimicrobial effect.	[46]
2	Moringa oleifera, Ocimum sanctum.	the extract of moringa oleifera, and Ocimum sanctum are formulated using traditional knowledge. Which has synergistic effect and possess antiaging, antioxidant, antimicrobial, anti- inflammatory, antibacterial properties.	[49]
3	Moringa oleifera, Juglans regia, Vitis vinifera, Camellia sinensis, Punia granatum, and rosa grandiflora.	It provides excellent antioxidant, Anticollagenase activity, antiaging property, and shows skin rejuvenating effects. It also reduce fine lines, wrinkles, and also increase the collagen synthesis.	[2]
4	Turmeric (Curcuma domestica Val.), tamarind (Tamarindus indica L.), and mineral oil.	This formulation shows synergistic activity and used for its Anti-acne activity, anti-aging, skin regeneration property and beautifying property.	[50]
5	Lawsonia inermis, Ficus carica, Carica papaya and Pisidium guajava.	This formulation is used for its antimicrobial, antioxidant, anti-inflammatory, antidermatitic, wound healing, and in the treatment psoriasis.	[51]
6	Cucumber, Aloe Vera, Coconut oil.	It gives cooling effect, detoxes the whole skin and provide nourishment to skin. It act as a anti-dark spot, anti-aging, and provide hydration to the skin.	[10]

6. Traditional Herbal Creams vs. Niosomal Creams

Aspects	Traditional Herbal creams	Niosomal Creams	
Topical formulation in which Herbal extract is dispersed in cream base, which comprising od oils, waters, emulsifiers, and other excipients.		Topical formulation in which herbal extracts are encapsulated within noisome which is incorporated in suitable base containing excipients.	
Stability	High chances of degradation from environmental factors like light, heat and oxidation, which can reduce the efficacy of active compound overtime.	Enhanced stability as niosomes protect herbal extracts from degradation, extending shelf life and maintaining potency.	
Bioavailability	Limited by the cream's ability to deliver active ingredients through the skin barrier, often resulting in	Improved bioavailability due to the encapsulation of herbal extracts in niosomes, which enhance penetration	

	lower absorption and efficacy.	and absorption through the skin.
Controlled Release	Typically provides immediate release of active ingredients, which may lead to rapid depletion and the need for frequent reapplication.	Provides controlled and sustained release of herbal extracts, maintaining therapeutic levels over extended periods and reducing the frequency of application.
Compatibility with Multiple Ingredients	Potential for ingredient interactions within the cream base, which may affect the stability and efficacy of herbal extracts.	Niosomes can encapsulate multiple herbal extracts simultaneously, preserving their synergistic interactions and ensuring compatibility.
Shelf Life	Shorter shelf life due to the instability of certain herbal extracts and potential for microbial growth if preservatives are inadequate.	Longer shelf life as niosomes enhance the stability of encapsulated herbal extracts and can incorporate effective preservatives within the vesicles.

7. Challenges and Future Perspectives

Polyherbal niosomal creams offer a synergistic and novel application for anti-aging and skin regeneration by enhancing the drug delivery, stability, and efficacy of multiple herbal extracts. But there are some challenges, such as formulation complexity, encapsulation efficiency, and stable consistency. Advancements in nanotechnology, growing consumer demand for natural skincare products, and increased research into novel herbal combinations offer opportunities in the current world to make formulations like this. Future studies should focus on improving encapsulation technologies, and conducting detailed clinical studies to speed up the development and market acceptance of these innovative polyherbal niosomal formulations.

8. CONCLUSION

Polyherbal niosomal cream holds significant effect as a novel drug delivery system for antiaging and skin regeneration formulations, offering enhanced bioavailability and synergistic effect of the multiple herbal extracts. The niosomal creams have many challenges like formulation complexity, encapsulation efficiency, clinical validation, and rigrous regulatory approval. In the current scenario, the advancement in nanotechnology and rising demand for natural skin care products in the world, polyherbal niosomal cream, have a strong foundation for the future. Further research in the novel herbal combination is essential for establishing the safety and efficacy. Polyherbal niosomal cream is seen as very effective as it enhances the drug delivery and therapeutic use of herbal extracts makes the drug very effective. Niosomal formulations have the potential to revolutionize the skincare market.

REFERENCE

- 1. Ramadhani S, Lister IN, Fachrial E, Nasution I. Antiaging Cream Formula From Lemongrass Leaf Extract (Chymbopogon Citratus). International Journal of Health and Pharmaceutical (IJHP), 2024; 4: 225–30.
- 2. Damle M, Mallya R. Development and Evaluation of a Novel Delivery System Containing Phytophospholipid Complex for Skin Aging. AAPS PharmSciTech, Jun. 2016; 17(3): 607–17.
- 3. Neves J, Sousa-Victor P, Jasper H. Rejuvenating Strategies for Stem Cell-Based Therapies in Aging. Cell Stem Cell., Feb. 2017; 20(2): 161–75.
- 4. Shimizu Y, Ntege EH, Sunami H. Current regenerative medicine-based approaches for skin regeneration: A review of literature and a report on clinical applications in Japan. Regenerative therapy, Dec. 2022; 21: 73–80.
- 5. Makrantonaki E, Bekou V, Zouboulis CC. Genetics and skin aging. Dermato-endocrinology, Jul. 2012; 4(3): 280–4.
- 6. Thornton MJ. Estrogens and aging skin. Dermato-endocrinology, Apr. 2013; 5(2): 264–70.
- 7. Farage MA, Miller KW, Elsner P, Maibach HI. Characteristics of the Aging Skin. Vol. 2, Advances in wound care. United States, 2013; 5–10.
- 8. Guo J, Huang X, Dou L, Yan M, Shen T, Tang W, et al. Aging and aging-related diseases: from molecular mechanisms to interventions and treatments. Signal Transduction Targeted Therapy, 2022; 7(1): 391.
- 9. Khyade VB, Bajolge R V, Yamanaka S. Antiaging Influence of Cream Derived from Black Soldier Fly (BSF) on Human Skin. Journal of Biochemical Technology, 2024.
- 10. SRS, PRK, AVT, NBA. Research On formulation and Evaluation of Polyherbal Acne Cream. International Journal for Multidisciplinary Research, Jun. 20, 2024; 6(3).
- 11. Gu X, Li Z, Su J. Air pollution and skin diseases: A comprehensive evaluation of the associated mechanism. Ecotoxicology Environmental Safety, 2024; 278: 116429.
- 12. Morita A. Tobacco smoke causes premature skin aging. Journal of Dermatological Science, Dec. 2007; 48(3): 169–75.
- 13. Schagen SK, Zampeli VA, Makrantonaki E, Zouboulis CC. Discovering the link between nutrition and skin aging. Dermato-endocrinology, Jul. 2012; 4(3): 298–307.
- 14. Pleguezuelos-Beltrán P, Herráiz-Gil S, Martínez-Moreno D, Medraño-Fernandez I, León C, Guerrero-Aspizua S. Regenerative Cosmetics: Skin Tissue Engineering for Anti-Aging, Repair, and Hair Restoration. Cosmetics, 2024; 11(4).

- 15. Sharma RR, Deep A, Abdullah ST. Herbal products as skincare therapeutic agents against ultraviolet radiation-induced skin disorders. Journal of Ayurveda and Integrative medicine, 2022; 13(1): 100500.
- 16. Surjushe A, Vasani R, Saple DG. Aloe vera: a short review. Indian Journal of dermatology, 2008; 53(4): 163–6.
- 17. Vaughn AR, Branum A, Sivamani RK. Effects of Turmeric (Curcuma longa) on Skin Health: A Systematic Review of the Clinical Evidence. Phytotherapy research: PTR, Aug. 2016; 30(8): 1243–64.
- 18. Soleimani V, Sahebkar A, Hosseinzadeh H. Turmeric (Curcuma longa) and its major constituent (curcumin) as nontoxic and safe substances: Review. Phytotherapy research :PTR, Jun. 2018; 32(6): 985–95.
- 19. Di Sotto A, Gullì M, Percaccio E, Vitalone A, Mazzanti G, Di Giacomo S. Efficacy and Safety of Oral Green Tea Preparations in Skin Ailments: A Systematic Review of Clinical Studies. Nutrients, Jul. 2022; 14(15).
- 20. Baby A, Freire T, Marques G, Rijo P, Lima F, Carvalho JC, et al. Azadirachta indica (Neem) as a Potential Natural Active for Dermocosmetic and Topical Products: A Narrative Review. Cosmetics, 2022; 9: 58.
- 21. Abdellatif AAH, Mohammed H, Al-Khalaf A, Khan O, Mostafa M, Al Haidari R, et al. Ginkgo biloba Leaves Extract's Cosmeceutical Evaluation: A Preliminary Assessment of Human Volunteers towards Achieving Improved Skin Conditions and Rejuvenation. Drug development and industrial pharmacy, 2023; 49: 1–28.
- 22. Das D, Bhadra P. A Review on Antimicrobial and Phytochemical Effects of Amla in Skin Care (Anti-Aging), 2020.
- 23. Cavanagh H, Wilkinson J. Lavender essential oil: A review. Healthcare infection, 2005; 10.
- 24. Chaiyana W, Anuchapreeda S, Punyoyai C, Neimkhum W, Lee KH, Lin WC, et al. Ocimum sanctum Linn. as a natural source of skin anti-ageing compounds. Industrial Crops and Products, 2019; 127: 217–24.
- 25. SAWANT G, BHAGWAT G. NIOSOMES AS AN APPROACH TO IMPROVE THE SOLUBILITY AND BIOAVAILABILITY OF BCS CLASS II DRUGS. International journal of Applied Pharmaceutics, 2021; 13(2): 94–101.
- 26. Mahale NB, Thakkar PD, Mali RG, Walunj DR, Chaudhari SR. Niosomes: Novel sustained release nonionic stable vesicular systems An overview. Advance in Colloid and Interface Science, 2012; 183–184: 46–54.

- 27. Marianecci C, Di Marzio L, Rinaldi F, Celia C, Paolino D, Alhaique F, et al. Niosomes from 80s to present: The state of the art. Advances in Colloid and Interface Science, 2014; 205: 187–206.
- 28. Rajera R, Nagpal K, Singh SK, Mishra DN. Niosomes: a controlled and novel drug delivery system. Biological & Pharmaceutical bulletin, 2011; 34(7): 945–53.
- 29. Ge X, Wei M, He S, Yuan WE. Advances of Non-Ionic Surfactant Vesicles (Niosomes) and Their Application in Drug Delivery. Pharmaceutics, Jan. 2019; 11(2).
- 30. Uchegbu IF, Vyas SP. Non-ionic surfactant based vesicles (niosomes) in drug delivery. International Journal of Pharmaceutics, 1998; 172(1): 33–70.
- 31. Ag Seleci D, Seleci M, Walter JG, Stahl F, Scheper T. Niosomes as Nanoparticular Drug Carriers: Fundamentals and Recent Applications. Journal of Nanomaterials, 2016; 2016(1): 7372306.
- 32. Liga S, Paul C, Moacă EA, Péter F. Niosomes: Composition, Formulation Techniques, and Recent Progress as Delivery Systems in Cancer Therapy. Pharmaceutics, Feb. 2024; 16(2).
- 33. Junyaprasert VB, Teeranachaideekul V, Supaperm T. Effect of charged and non-ionic membrane additives on physicochemical properties and stability of niosomes. AAPS PharmSciTech, 2008; 9(3): 851–9.
- 34. Kazi KM, Mandal AS, Biswas N, Guha A, Chatterjee S, Behera M, et al. Niosome: A future of targeted drug delivery systems. Journal of advanced pharmaceutical technology & research, Oct. 2010; 1(4): 374–80.
- 35. Witika BA, Bassey KE, Demana PH, Siwe-Noundou X, Poka MS. Current Advances in Specialised Niosomal Drug Delivery: Manufacture, Characterization and Drug Delivery Applications. International journal of molecular sciences, Aug. 2022; 23(17).
- 36. Nutmakul T, Chewchinda S. Synergistic effect of Trikatuk, a traditional Thai formulation, on antioxidant and alpha-glucosidase inhibitory activities. Heliyon, Jan. 2023; 9(1): e13063.
- 37. Somavanshi DB, Kamble PR, Jadhav KR. Development and Evaluation of Polyherbal Based Novel Antiaging Synergistic Formulation. Journal of Pharmaceutical Research International, 2021; 33(44A): 278–291.
- 38. Peterson CT, Denniston K, Chopra D. Therapeutic Uses of Triphala in Ayurvedic Medicine. Journal of alternative and complementary medicine (New York, NY), Aug. 2017; 23(8): 607–14.
- 39. Belapurkar P, Goyal P, Tiwari-Barua P. Immunomodulatory effects of triphala and its

- individual constituents: a review. Indian journal of pharmaceutical Sciences, 2014; 76(6): 467–75.
- 40. Sulaiman CT, Anju K, Anandan EM, Balachandran I. Synergistic Interactions of Phytochemicals in Polyherbal Formulation Enhance the Chemical Transformations of Active Constituents. Journal of Applied Spectroscopy, 2021; 88(1): 181–6.
- 41. Karole S, Shrivastava S, Thomas S, Soni B, Khan S, Dubey J, et al. Polyherbal Formulation Concept for Synergic Action: A Review. Journal of Drug Delivery and Therapeutics, Feb. 15, 2019; 9(1-s SE-Review).
- 42. THE AYURVEDIC PHARMACOPOEIA OF INDIA. Pharmacopoeia Commission for Indian Medicine & Homoeopathy, 2003; 2: 758.
- 43. Poudel S, Yadav MP. Agastya Haritaki Rasayana: A Critical Review. Journal of Drug Delivery and Therapeutics, Feb. 15, 2019; 9(1-s SE-Review).
- 44. Ee, Ilodigwe et al. Evaluation of the Wound Healing Activity of a Polyherbal Remedy. Scholars Research Library Annals of Biological Research, 2012; 11: 5393–5398.
- 45. Fahimi S, Abdollahi M, Mortazavi SA, Hajimehdipoor H, Abdolghaffari AH, Rezvanfar MA. Wound Healing Activity of a Traditionally Used Poly Herbal Product in a Burn Wound Model in Rats. Iranian Red Crescent medical journal, Sep. 2015; 17(9): e19960.
- 46. SHIVATHAYA N, SURVE R, SAWANT R, KHOT S, BIRADAR K, VERMA R, et al. FORMULATION AND IN VITRO EVALUATION OF ETHANOLIC EXTRACT OF POLYHERBAL FACE CREAM. International Journal of Current Pharmaceutical Research, 2022; 14(2): 41–47.
- 47. CHAUDHARI PD, DESAI US. FORMULATION AND EVALUATION OF NIOSOMAL IN SITU GEL OF PREDNISOLONE SODIUM PHOSPHATE FOR OCULAR DRUG DELIVERY. International Journal of Applied Pharmaceutics, 2019; 11(2): 97–116.
- 48. P.S. Salve.Development and Evaluation of Topical Drug Delivery System for Terbinafine Hydrochloride using Niosomes. Research Journal of Topical and Cosmetic Science, 2011; 2(2): 52–63.
- 49. Yadav A, Mishra DK, Paliwal P, Farooqui NA, Gawshinde A. Formulation and Evaluation of Polyherbal Antiaging Cream. Asian Journal of Pharmacy and Technology, 2021.
- 50. Bambang Admadi Harsojuwono, I Ketut Satriawan, Sri Mulyani. The antiaging cream characteristics from extract of turmeric (Curcuma domestica Val.) rhizome and tamarind (Tamarindus indica L.) leaves. International Journal of Scholarly Research in Engineering

- and Technology, Jan. 30, 2023; 2(1): 020–30.
- 51. Umbreen S. FORMULATION OF POLYHERBAL CREAM BASED ON PRESENCE OF SECONDARY METABOLITES, ITS ORGANOLEPTIC ASSESSMENT AND THERAPEUTIC EFFECT ON DERMATITIS PATIENTS. Journal of Population Therapeutics and Clinical Pharmacology, Jan. 25, 2024; 1525–35.
- 52. Shoba G, Joy D, Joseph T, Majeed M, Rajendran R, Srinivas PS. Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. Planta Medica, May 1998; 64(4): 353–6.
- 53. Muir WW, Sams RA. 7 Pharmacologic Principles and Pain: Pharmacokinetics and Pharmacodynamics. In: Gaynor JS, Muir WW, editors. Handbook of Veterinary Pain Management (Second Edition). Saint Louis: Mosby, 2009; 113–40.
- 54. Borse SP, Singh DP, Nivsarkar M. Understanding the relevance of herb–drug interaction studies with special focus on interplays: a prerequisite for integrative medicine. Porto Biomedical Journal, 2019; 4(2).