



NOVEL DRUG DELIVERY SYSTEM- BASED HERBAL COSMETICS FOR WRINKLES

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Abstract–The skin is constantly exposed to internal and external stimuli that can cause wrinkles, dry skin, and thinning. Skin health and beauty are important for overall well-being and health perception. While many chemical-based anti-wrinkle creams are available, they can irritate human skin. Customers are turning to herbal cosmetics because they are inexpensive, active, and have no side effects. Recently, many cosmetics have been developed based on Indian herbs. Pharmaceutical delivery systems can improve cosmetic ingredient penetration into deeper skin tissue, lengthen the duration of action, increase stability, prevent incompatibility with other ingredients, and prevent unwanted side effects that could manifest locally or systemically. This review explains what causes wrinkles and how drug delivery systems in cosmetics can reduce them. It includes an overview of cosmetics created by researchers and available in the market and discusses the benefits of herbal cosmetics. The article also describes the structure and function of the skin and the three components that have been the focus of anti-wrinkle research: dermis, collagen, elastin, and glycosaminoglycans (GAGs). Factors that contribute to skin wrinkling are divided into endogenous and exogenous categories. The article provides an in-depth analysis of various novel techniques that can be employed to adjust the composition and surface characteristics of vesicles. These techniques can be used to enhance the release and deposition of medication or other substances at the targeted site. The article also highlights the importance of these approaches in the field of drug delivery and their potential benefits in improving therapeutic efficacy and reducing side effects.

Index terms–Wrinkles, Novel Drug Delivery System, Herbs, Cosmetics

INTRODUCTION

The term aging refers to the gradual loss of skin elasticity and collagen fibers. In India, with a population of over 1.486 billion, approximately 18% of individuals fall into the age group of 50 years and above. ¹ One of the main hallmarks of aging is wrinkles. ²

The evident folds or creases in the skin are known as wrinkles. ¹ Skin aging can occur due to various factors, so it is grouped into two factors which are exogenous factors and endogenous. ³ Endogenous factors are also named intrinsic factors which includes genetics, cellular metabolism, hormone, metabolic process, etc.³⁴ Exogenous factors also termed extrinsic factors comprise exposure to wind, harmful chemicals, UV radiation, ionizing radiation, smoking, etc. ⁴³

The dermis, collagen, elastin, and glycosaminoglycans (GAGs) are the 3 structural components of the skin that have been the major subjects of anti-aging research. As aging is a biological predictable process and not a pathological condition it is correlated with various skin and body pathologies, including progressive disorders, and benign and malignant neoplasms. ⁴

Compounds or drugs which is used for the prevention or treatment of skin aging problems that encompasses of orally administered or locally applied on skin are prepared based on their pharmacokinetics characteristics. However, drugs or compounds that are meant for oral administration have low bioavailability and may not be able to reach the skin tissues. Local application on the skin of these compounds or drugs shows some limitations due to their chemical instability and lack of transdermal absorption. All such factors have limited their use in cosmetics fields.³

To get around this restriction, their pharmaceutical preparation has to be improved even further. A brand-new, innovative drug delivery method might also be employed to boost the drug's absorption via the skin and improve its anti-aging properties.³

To change the release rate and deposition of medications or substances at the target site, novel approaches should be used to adjust the composition of vesicles or their surface characteristics.⁵

The cosmetic is made from plant material that has been extracted for use, either whole or in part is termed as herbal cosmetics. If fewer toxic excipients are used in the preparation of the herbal cosmetics, then there is a slight reduction in their harmfulness. Nowadays, people prefer herbal cosmetics because, during the COVID-19 pandemic, people were more drawn to using a variety of plants and their mixtures as natural remedies to treat a wide range of illnesses. Herbal cosmetics, which include creams, powders, body care products, hair care, and skin care, are becoming more and more popular in the cosmetics industry.

The objective of this review is to investigate the primary factors contributing to the development of wrinkles. The focus will be on the advanced drug delivery techniques employed in various cosmetic products to enhance their efficacy in reducing wrinkles. This will encompass an analysis of cosmetics created by different researchers, as well as those currently accessible in the market. Additionally, the advantages of utilizing herbal cosmetic remedies will be explored.

SKIN

The skin is a multifaceted organ with a wide variety of cell types and structures. With a surface area of 1-2 m², the skin is the largest organ in the human body. Its protective barrier role is merely one of its numerous purposes. An additional organ is the skin. Its four principal compartments are the appendages, subcutaneous tissue, dermis, and epidermis.

➤ **Epidermis** – The epidermis, or outermost layer of the skin, has a thickness of about 100 µm. It functions as keratinized stratified squamous epithelium. Its key responsibilities include reducing fluid loss and protecting the organism from damaging outside influences. About 95% of the epidermal cells in this area are keratinocytes, which are the primary cells of the epidermis. The five layers that make up the epidermis are the stratum germinativum, stratum spinosum, stratum granulosum, stratum lucidum (where keratinocytes gradually migrate to the surface and separate in a process known as desquamation), and the stratum corneum.^{6,7}

➤ **Dermis** – The dermis is a layer of connective tissue that is responsible for linking with the epidermis. It is about 1- 2 mm thick and has a pivotal role in thermoregulation and circulatory network support. The two zones, papillary dermis and reticular layer, usually separate the dermis. Fibroblasts are the majority of its cells, and their secretion of extracellular matrix proteins gives the skin its support and elasticity, including fibronectin, elastin, glycosaminoglycans, and proteoglycans. Collagen makes up 70-80% of the dermis weight. It is one of the strongest proteins found in nature, primarily composed of glycine, proline, and hydroxyproline.⁶ Although elastic fibers only make up a small fraction of the dermis' weight (less than 1% to 2%), they are incredibly effective. This is because they help prevent deformation and enable the skin to return to its resting state. Fibrillin and elastin are the two unique proteins that compose elastic fibers, and they are both produced by local fibroblasts. The fibers' central core comprises cross-linked elastin that is amorphous and hydrophobic. Microfibrils rich in fibrillin surround the core of the fibers.⁸

➤ **Appendages** – Epidermal appendages are intricate structures that lie within the skin tissue. They are made up of cells that can divide and differentiate, providing a source of epithelial cells for re-epithelialization. These structures are essential in restoring the epidermis after it has been damaged by burns, abrasions, or skin transplants. The sebaceous glands, sweat glands, apocrine glands, mammary glands, and hair follicles are examples of the epidermal appendages. These kinds of glands are found deep within the dermis, even in the subcutaneous fat of the face. This explains the skin's remarkable ability to recover from severe cutaneous injuries. The subcutaneous tissue is composed of connective tissue, which is highlighted by fat cells. This layer weakly links the skin and underlying fascia. Fat cells provide insulation and energy for the organism.^{9,10}

WRINKLE PROGRESSION

As we age, our skin is constantly exposed to various internal and external factors, which can lead to issues such as wrinkles, dryness, and thinning of the epidermis.¹¹ This is mainly due to the degradation of collagen and elastic fibers in the dermis, which alters the skin's mechanical properties and structural integrity.¹² This gradual loss of structural and functional features of the skin can make it more fragile and susceptible to injuries, increasing the risk of developing age-related illnesses.⁶

The main components of the extracellular matrix in the dermis, namely collagen and elastin, decrease in both density and thickness as we age. This results in less elastic and resilient skin, which may manifest as sagging and wrinkles.¹² Collagen loss also reduces the efficiency of collagen synthesis and the mechanical tension on fibroblasts, leading to less stiff and resilient skin.⁶

At the cellular level, the Hayflick limit describes the aging process when telomeres, which are responsible for maintaining cellular division, can no longer maintain their length due to the replication process. Cellular senescence occurs when cells lose their ability to divide and enter an irreversible cell cycle arrest. Research has shown that human primary fibroblasts have a limited capacity for division, which could explain aging at the cellular level.^{13,14}

TYPES OF SKIN WRINKLES

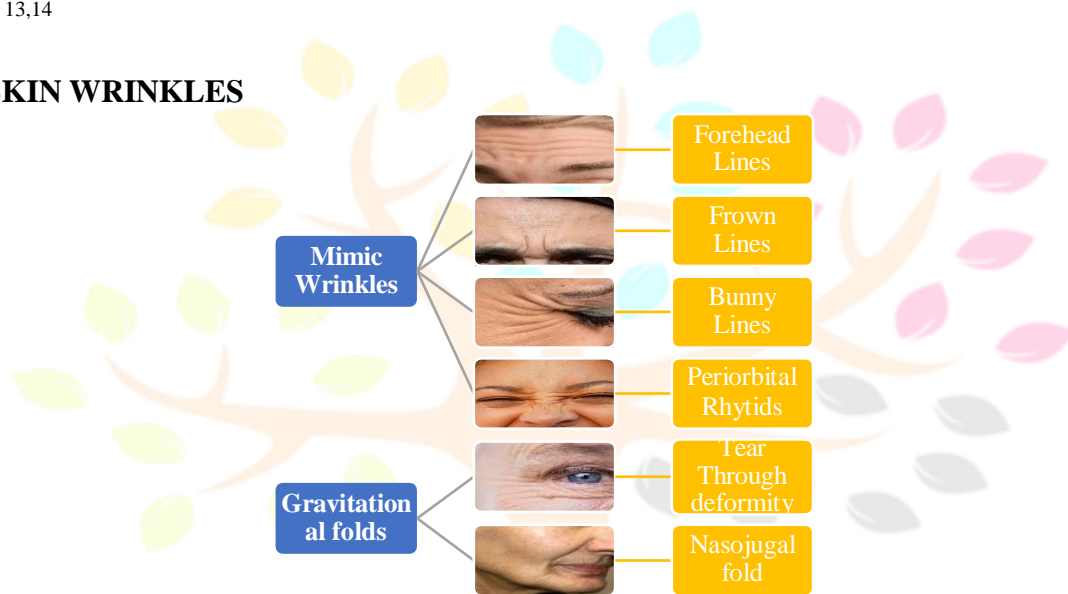


Fig1: Types of Facial Wrinkles Wrinkles have hypothetically been classified into the following:

1. Forehead Wrinkles -

Frequent frown lines are more commonly the result of hyperactivity in the frontalis muscle rather than the natural aging process. The transverse wrinkles that appear on the forehead are caused by the frontalis muscle's simultaneous elevation of the eyebrows and lowering of the scalp.¹⁵

2. Frown Lines -

The suppression of facial muscle contraction causes glabellar frown lines in aging adults. Overstimulation of the muscles beneath the skin in the forehead area, like the corrugator supercilia and procerus muscle, can lead to hyperactivity of the musculature, which results in a loss of elasticity.¹⁶ The two corrugator supercilia muscles draw the eyebrow medially, creating a vertical wrinkle in the glabella.¹⁵

3. Periorbital Rhytids -

Periorbital Rhytids, commonly referred to as wrinkles on the feet. The primary cause of these radial lies is the hyperactivity of the orbital region of the orbicularis oculi. It is also called a crow's feet.

4. Bunny Wrinkles Lines -

The contraction of the transverse section of the nasalis muscle and the lower medial orbicularis muscle results in bunny wrinkle lines, also known as nasalis fanning rhytids.¹⁷

5. Gravitational Folds -

Gravitational folds, as the name suggests, are brought on by gravity pulling loose skin downward. Intrinsic aging, which is caused by the skin's innate loss of elasticity, is a predetermined and inevitable process that exacerbates wrinkles and folds.

6. Tear Trough Deformity -

A significant concern for many seeking periorbital rejuvenation is tear trough deformity. When a patient has a

prominent tear trough deformity, their eye appears sunken and casts a dark shadow over their lower eyelid. This can make them appear tired even when they are getting enough rest, and they are resistant to efforts at cosmetic concealment.¹⁸

7. Naso Jugal fold –

Wybar and Duke-Elder are credited with coining the term "nasojugal fold" back in 1961. This anatomical feature is characterized by a downward and outward extension from the inner canthus, which marks the boundary between the loose tissue of the lower eyelid and the denser cheek structure. It defines the line where the fascia is anchored to the periosteum between the muscles of the upper and lower eyelids.

HOW WRINKLES OCCUR

Endogenous factors are those that come from within, such as hormones, cellular metabolism, genetics, and metabolic processes. Conversely, exogenous factors, also called extrinsic factors, come from outside the body and include things like smoking, exposure to UV and ionizing radiation, hazardous chemicals, wind, and other environmental factors.³⁴ The skin is prone to wrinkles and lines, thinning, loss of elasticity, and fragility due to several factors, including genetic and environmental ones. The environmental factors, such as UV radiation, cause significant changes in the skin's dermis, resembling wounds. While concerns regarding physical appearance might impact one's quality of life, wrinkles are not considered a medical condition requiring treatment. However, worries about appearance can negatively affect self-esteem, professional performance, and interpersonal relationships in certain situations. Age-related anxieties may vary due to cultural differences, geographic location, and personal values. As the population ages, there is a growing need for interventions to reduce the visible signs of aging in countries where maintaining a youthful appearance is highly valued.¹ Moreover, the skin undergoes aging due to environmental damage, which can be attributed to its close proximity with the surroundings. The following elucidates some of the primary factors that contribute to the development of wrinkles.

Exposure To UV Radiation –

The aging of human skin is affected primarily by environmental factors, with UV radiation from the sun being the most significant contributor. Photoaging, which refers to sun-induced aging of the skin, is a gradual process that occurs over time. Unlike chronological aging, which is a function of time, photoaging is primarily influenced by skin pigment and the extent of sun exposure. Individuals with light skin tones and those who reside in sunny areas and engage in outdoor activities exhibit the fastest rates of aging.¹⁰

Mechanism –

1. By Activation of Cell Surface Growth Factor and Cytokine Receptors

UV radiation triggers the activation of growth factor receptors and cytokines present on the surface of cells. In human skin, this exposure leads to the activation of several receptors, such as those for epidermal growth factor (EGF), interleukin (IL) 1, and tumor necrosis factor α (TNF- α), within 15 minutes, when twice the minimal erythema dose is applied. For these receptors to function, certain tyrosine kinase activities must be stimulated.¹⁹ The initial biochemical step for activating receptors is to add phosphate groups to the tyrosine residues on both the receptors and the adaptor proteins that bind to them. As a result, specific docking sites are created for molecules that facilitate signal propagation within the cell.²⁰

2. By production of ROS

UV irradiation triggers molecular reactions in human skin by producing ROS photochemically. ROS, such as superoxide anion, peroxide, and singlet oxygen, play a crucial role in this process. However, it is still unclear how UV radiation activates receptors. According to indirect experimental data, a possible explanation is that certain protein-tyrosine phosphatases are inhibited by the photochemical production of ROS. These enzymes counteract receptor-activated protein-tyrosine kinases by removing phosphate groups from receptors or the adaptor proteins linked with them.²¹ Multiple studies have provided evidence for the process through which cell surface receptors get activated by UV light. As a result, an increase in receptor phosphorylation, which is indicative of activation, is expected. There isn't enough conclusive proof to indicate that cell surface receptors activation state is regulated by protein tyrosine phosphatases.^{22,23}

3. By inducing metalloproteinase (matrix-degrading enzymes) which degrades skin collagen

When the skin is exposed to ultraviolet light, it triggers the production of MMP-1, also known as collagenase. This enzyme works by cleaving fibrillar collagen, specifically type I and III, at a single location within its central triple helix. However, MMP-1 is not the only responsible for breaking down collagen in the skin. Elevated levels of MMP-3, also called stromelysin-1, and MMP-9, also known as 92-kDa gelatinase, can further degrade collagen after it has been cleaved by MMP-1.²⁴ Research has shown that when human skin is exposed to UV light, the dermis coexists with the actions of metalloproteinase 1, MMP-3, and MMP-9. Additionally, covalent cross-linking between molecules stabilizes type I collagen.²⁵ Collagen that has been partially degraded may or may not remain cross-linked within the insoluble collagen matrix, depending on the extent of degradation. These fragments of insoluble collagen can be broken down through proteolytic cleavage by broad-specific proteases such as chymotrypsin when tested in vitro. Consequently, skin collagen that is weakened by UV-induced MMPs can compromise the structural integrity of the dermis.¹⁰

4. Lifestyle Influence

Changes in temperature and humidity can affect the skin in various ways. For instance, the amount of water that evaporates from the skin doubles when the skin temperature rises by 7-8 degrees Celsius. In contrast, despite high humidity, low temperatures can make skin more rigid. This happens because the proper arrangement of skin lipids and structural proteins is closely linked to temperature, which can reduce evaporative water loss.²⁶ Some medicines, particularly those prescribed for hypocholesterolemia, can have adverse effects on the skin and result in an excessive shedding of skin cells.²⁷

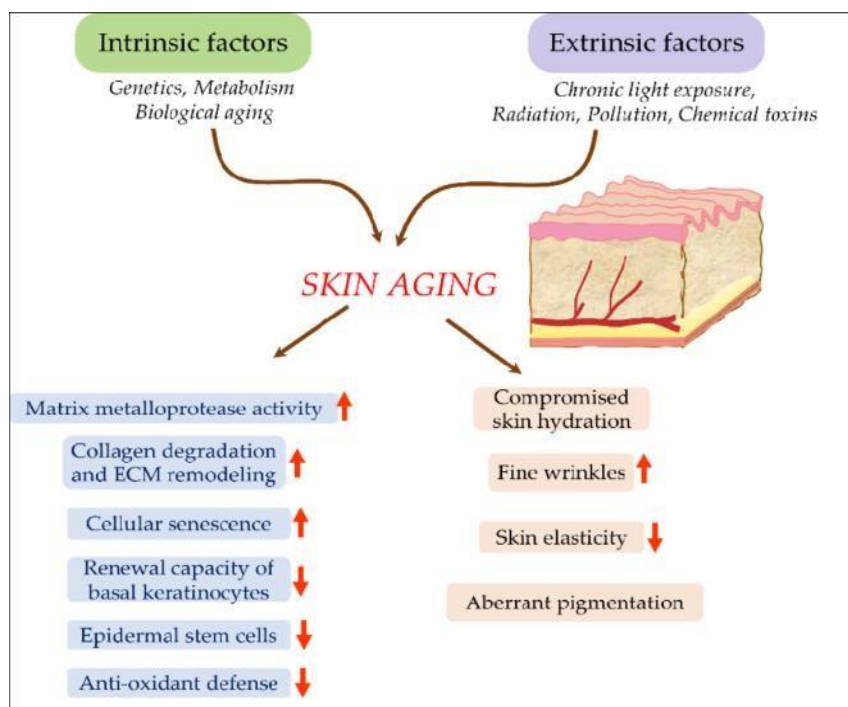
5. Effect of Smoking

Men who smoke cigarettes are at a high risk of developing telangiectasia, which are red spots on the skin. Additionally, both men and women who smoke are susceptible to elastosis, which is a condition that causes the skin to lose its elasticity.²⁸ Smoking harms the skin by decreasing blood flow to it. This deprivation of oxygen and nutrients leads to a reduction in collagen and elastin fibers in the dermis. As a result, skin becomes less elastic and more rigid. Smoking also damages the elastin and collagen in lung tissue, which can be harmful to the skin.²⁸

Smoking can cause the skin to become rough and also lead to the development of keratinocyte dysplasia.²⁹ Research has demonstrated that smoking is more strongly associated with wrinkles in a dose-dependent manner^{30,28}, with smoking contributing more to wrinkles on the face than even sun exposure. Research has demonstrated that smoking presents a distinct hazard for the early onset of wrinkles, even when age, sun exposure, and pigmentation are factored in.²⁸ Despite the fact that hormone replacement therapy could potentially reverse wrinkles, it was observed that the skin of long-term smokers did not improve. Moreover, smoking not only increases the production of free radicals but also poses a significant risk for cutaneous squamous cell carcinoma.²⁸

6. Air Pollution

When our skin comes in contact with air pollutants such as particulate matter, volatile organic compounds, and nitrogen dioxide, they can generate harmful molecules known as free radicals. These highly reactive molecules have the potential to cause damage to crucial proteins in the skin like collagen and elastin, which are responsible for keeping the skin firm and youthful.^{31,32} The breakdown of structural proteins is a major contributor to the formation of wrinkles. Air pollution, particularly ozone, can damage the skin's natural moisture content and lipid barrier, making it more prone to dehydration and fine lines. Therefore, it is important to keep the skin hydrated to maintain its plumpness and prevent wrinkles.^{33,34}

Fig2: Causes of Wrinkles³⁵

ANTI-WRINKLE

Anti-wrinkle medications are becoming increasingly popular as they can extend life span and reduce the signs of aging. There are various skin anti-aging techniques designed to improve the dermal and epidermal signs of aging, which can be grouped into five categories: cosmetic procedures, topical substances or medications, invasive methods, systemic agents, and modifying one's lifestyle and habits to avoid external factors that contribute to aging.

There are numerous treatments for damaged skin that include skin care products, fillers, microbeam radiation therapy, and energy-based therapies like lasers and light sources. In recent years, medical professionals have developed innovative soft tissue augmentation techniques to treat aging.

Cosmetic wrinkle treatments are gaining popularity, and this review will focus on herbal cosmetic treatments for wrinkles. We will discuss various cosmetic formulations available for people to use, research studies that have been conducted to improve their efficiency, and numerous plants or active ingredients that can cure wrinkles.

HERBAL COSMETIC

Cosmetics and beauty have been popular since the beginning of civilization. Natural cosmetics are also known as herbal cosmetics. These use a base of various cosmetic ingredients to which one or more herbal ingredients are added to treat skin issues. Plants are widely used in the creation of new pharmaceutical and cosmeceutical products. Herbal cosmetics use herbs in their raw or extracted form.³⁶

Herbal cosmetics, also known as herbal-based products, are created by combining permissible cosmetic ingredients with one or more herbal ingredients aimed at providing specific cosmetic benefits. Unlike chemical-based products, herbal cosmetics take some time to deliver the desired outcomes. However, they offer a means for the body to reconnect with nature and promote natural healing.³⁷ In recent times, there has been a significant surge in the usage of Indian herbs in toiletry and cosmetic products. Researchers and manufacturers have been exploring the potential of these herbs for personal care formulations, in addition to their traditional applications. This trend is driven by the increasing popularity of herbal medicines, which are known for being gentle on the skin and having no adverse side effects.³⁸

Herbal extracts are derived from herbs, as the name suggests. This technique is ancient, with references in the Unani and Vedas scriptures. These extracts are processed to treat various ailments and provide additional health benefits. The method involves crushing the herbs to extract the juice, which is then blended with the necessary ingredients to create the extract. Fresh herbs and medicinal plants can be obtained by foraging in the wild, cultivating them in your garden, or purchasing them from other gardeners and health food stores. Although

antibiotics have been developed to treat various illnesses, it is becoming increasingly evident that chemical medications are not always "magic cures" and can have negative side effects. This realization has led to a resurgence in herbalism and traditional medicines. Our goal is to ensure that important botanicals remain widely available for future generations. These plants are referred to as infusions and are made by steeping them in boiling water to make tea. The best thing about herbal cosmetics is that they are made entirely of herbs and shrubs, meaning they have no negative side effects. The natural ingredients in the herbs provide the body with nutrients and other beneficial minerals without any adverse effects. Raymond Reed, a founding member of the US Society of Cosmetics Chemists, coined the term "cosmeceutical" to refer to products that combine cosmetics and pharmaceuticals.³⁹ In 1984, Dr. Albert Kligman further expanded the meaning of the term to include substances that offer both medicinal and cosmetic benefits.⁴⁰ Cosmeceuticals are a class of cosmetic products that contain biologically active ingredients. They are formulated to enhance the health and appearance of the skin by interacting with its biological texture and function. Cosmeceuticals can help improve skin hydration, reduce the appearance of fine lines and wrinkles, and protect the skin from environmental damage. They are often used as a complementary treatment alongside traditional skincare products to provide additional benefits to the skin.⁴¹

Advantages

Herbal cosmetics are the latest trend in fashion and beauty. These products have gained immense popularity among women who prefer natural solutions for personal care to enhance their appearance. The primary reason for this shift towards natural products is that they provide essential nutrients to the body and promote overall health. Unlike synthetic cosmetics, herbal cosmetics don't contain any harmful chemicals and have fewer side effects, making them a safer option for personal care.

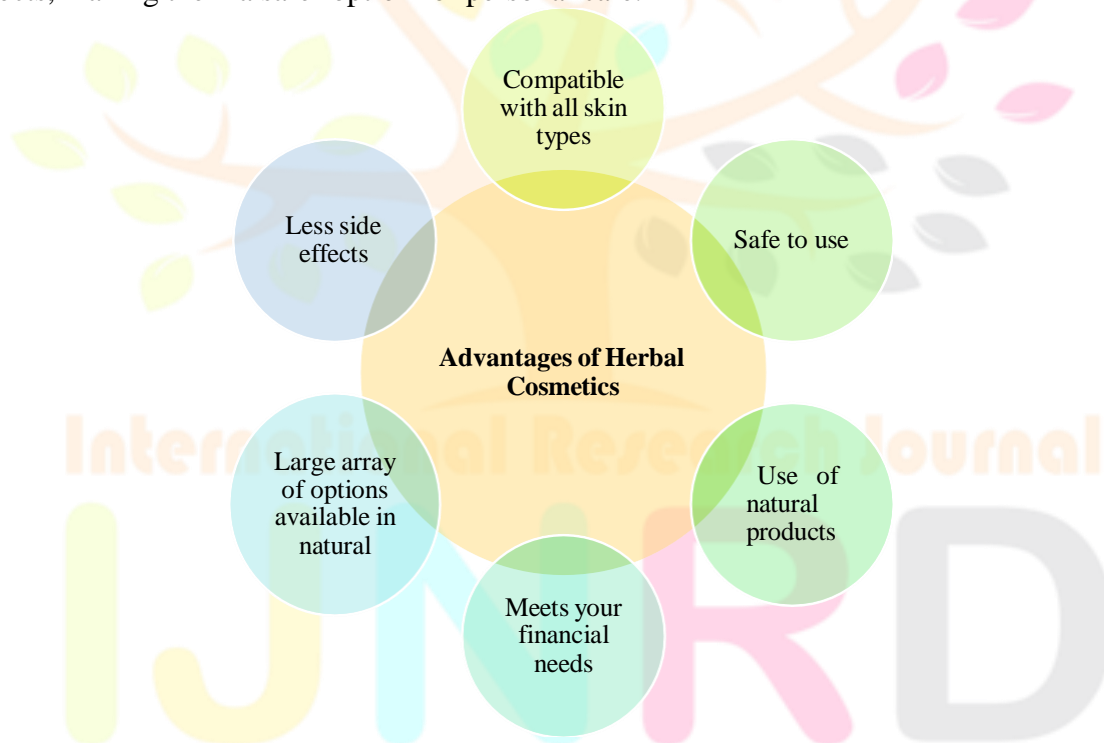


Fig3: Advantages of Herbal Cosmetic

The benefits of using natural cosmetics over synthetic ones are as follows, which make them a preferable option:

Compatible with all skin types – It is a well-known fact that natural cosmetics can benefit people with any skin type. Whether you have fair or dark skin, you can find natural cosmetics like lipstick, eye shadow, and foundation that work well on all skin tones. Moreover, they are safe for use by individuals with sensitive or oily skin and do not worsen their skin's condition. While coal tar is considered to be carcinogenic to humans, it is still widely used in the production of coal tar-derived colours used in cosmetics. The main concern with these colours, whether they are made from coal tar or synthetic sources, is their potential to cause cancer. However, there are safer alternatives available that are made from natural colours derived from herbs.⁴²

Safe to use – Did you know that natural cosmetics are considered to be safer than conventional beauty products? Dermatologists have tested and confirmed that these products are hypo-allergenic and can be safely

used at any time or location. Unlike conventional products, natural cosmetics are composed of natural ingredients which reduce the chances of developing skin rashes or experiencing itching on the skin. For instance, synthetic antioxidants like BHA (butylated hydroxy anisole) and BHT (butylated hydroxytoluene) are commonly used as preservatives in moisturizers and lipsticks, but these chemicals can pose a risk to our health. By choosing natural cosmetics, you can ensure that you are not exposing yourself to unnecessary health risks.⁴³ It's important to be aware that certain synthetic preservatives like BHA and BHT can cause allergic reactions on the skin. Additionally, BHA has been classified as a potential human carcinogen by the International Agency for Research on Cancer. In contrast, herbal cosmetics containing natural antioxidants like vitamin C can be a safer alternative for those seeking to avoid synthetic preservatives and potentially harmful chemicals.⁴⁴

Use of natural products – Herbal cosmetics are all-natural and free of synthetic ingredients. They utilize plant extracts like coconut oil and aloe vera, which contain organic nutrients like vitamin E to maintain skin health. Consumers are increasingly demanding natural products that are free of harmful chemicals and emphasize the benefits of botanicals.⁴⁵ **Meets your financial needs** – Natural cosmetics are affordable and some of them are cheaper than synthetic ones. You can find them on sale for even lower prices if you do some research. Traditional herbal remedies are widely available and relatively safe, which is why the World Health Organization supports and encourages their use in natural health care programs. In fact, about 80% of the world's population uses natural products for their medical care due to the negative effects and high cost of modern medicine.⁴⁶

A large array of options available in Natural – Although natural cosmetics are still relatively new to the beauty industry, they offer a wide range of products for all makeup enthusiasts. You can find numerous naturally formulated options for foundation, eye shadow, lipstick, blush, mascara, concealer, and much more. Moreover, you can easily find natural cosmetics produced locally or created by internationally renowned designers.

Less side effects – Many people are concerned about synthetic cosmetics and their potential to irritate the skin, causing breakouts and clogging pores. They can leave the skin feeling greasy or dry, which is not ideal. In contrast, natural cosmetics offer a safer solution. You can use them anytime and anywhere without worrying about negative effects. For example, herbal cosmetics are free of parabens, the most common preservative in cosmetics. Parabens can penetrate the skin and disrupt hormone function, but herbal cosmetics remove this risk and provide a healthier alternative.⁴³

COSMECEUTICALS

Cosmetics are the fastest growing category in the beauty business. Cosmeceuticals are pharmaceutical-cosmetic products that aim to enhance skin health and appearance, lying between pure cosmetics and pure drugs. According to Dr. Albert Klingman's theory, cosmeceuticals provide specific results such as sun protection or acne control.³⁹

The classification of a product as a drug or a cosmetic depends on its intended use, as per the law. However, the distinction between the two categories is not always clear, and different regulations apply to different types of products.

According to the Drugs and Cosmetics Act of 1940, a substance is classified as a drug if it is used internally or externally by humans or animals, and if it is intended to diagnose, treat, prevent, or mitigate a disease or disorder. Conversely, cosmetics are defined as items that are applied to any part of the human body for the purpose of cleansing, beautifying, enhancing attractiveness, or altering appearance.

These definitions may overlap, but the intended use of each product ultimately determines its classification under the law.

HERBS USED IN TREATMENT OF WRINKLES

Aloe Vera -

Aloe vera, also known as *Aloe barbadensis*, is a plant that has the potential to heal skin. The development of wrinkles in the skin is tied to the production of collagen and the expression of matrix metalloproteinase. Aoin A and B, which are found in aloe vera, have been shown to possess the ability to obstruct collagenase activity, which is responsible for the degradation of collagen fibers, and the expression of matrix metalloproteinases (MMPs). Thus, they can be utilized to combat aging and wrinkles.⁴⁷ It belongs to the Liliaceae family and is often used to treat issues such as acne, wrinkles, dark or white patches, and stretch marks. An experiment has shown that the extract from baby aloe shoots (BAE) has more potential to treat UV-damaged skin than the extract from adult aloe shoots (AE).²

Triticum aestivum -

The *Poaceae* family includes wheat (*Triticum aestivum*). Wheat grains include carbohydrates, phytochemicals, and phenolic compounds. It causes the dermis to produce more collagen fibers.⁴⁸ Wheat proteins improve the skin's suppleness and collagen fiber synthesis.²

Cucumis sativus -

The *Cucurbitaceae* family includes the cucumber (*Cucumis sativus*), which is used for its fruits and seeds. Cucumber is a very beneficial herb for the skin. Its fruits and seeds are used as a main ingredient in many cosmetic products that treat sunburn and wrinkles on the skin. Cucumbers also could keep skin supple and slow down the aging process.³⁸ Cucumbers can also be used as moisturizers and to lighten our skin by blocking the enzyme tyrosinase.²

Camellia sinensis -

Camellia sinensis (black tea) is a member of the *Theaceae* family. In an in-vitro experiment, it was discovered that anti-hyaluronidase activity is dose-dependent.⁴⁹ Because of this activity, it is a safe and effective ingredient for use in anti-aging and anti-wrinkle cosmetics for the skin. Tea is also simple to use, has a pleasant flavor, and is non-toxic even when consumed in large quantities.²

Panax ginseng -

The chemical components present in various ginseng varieties are called ginsenosides. Ginsenosides exhibit a variety of therapeutic qualities; most recently, an in-vitro model study revealed that ginsenosides had antiaging and antiwrinkle effects⁵⁰. Ginseng's antiaging properties account for a large portion of its usage in skin care products.²

Citrus sinensis -

This particular thing is packed with a good amount of vitamin C, which, in turn, has the potential to halt the expression of metalloproteinase. The presence of matrix metalloproteinase and the loss of collagen fibers are responsible for the onset of wrinkles in the skin.²

Piper betel -

Piper betel, an herb belonging to the *Piperaceae* family, is a great source of antioxidants and has remarkable neuroprotective and anticancer properties. It helps eliminate free radicals in the body, making it an effective antiaging agent. Piper Betel is also known to be useful in treating wrinkles, diabetes mellitus, kidney problems, and cancer. The leaves of this herb contain allyl pyrocatechol, a phenolic component that has antioxidant activity and helps fight against oral bacteria that can cause bad breath.²

Rosmarinus officinalis -

Rosa (*Rosmarinus officinalis*) is a member of the *Lamiaceae* family. Our body contains a variety of enzymes that react with different types of free radicals and neutralize them; one such enzyme is superoxide dismutase, which converts free radicals into oxygen and hydrogen peroxide. The next step is the conversion of hydrogen peroxide (H₂O₂) into oxygen and water.⁴² Rosemary extract is used to prevent wrinkles and aging by imitating the action of superoxide dismutase, which neutralizes free radicals.

Boerhavia diffusa -

It belongs to the rasayana category of plants, according to Ayurveda. It has antiaging properties and is an antioxidant in nature.²

Glycine max -

Hyaluronic acid can be found in large amounts in soybeans (*Glycine max*), during a demonstration of the filling effect of a cosmetic procedure. It has six different kinds of hyaluronic acid made from soybeans. It has been noted that the volume and depth of wrinkles reduced after the treatment.² The mechanism of action was that hyaluronic acid keeps the stratum corneum hydrated, and wrinkle development is significantly influenced by the stratum corneum's dryness.

Coriandrum sativum -

Exposure to UV radiation can cause damage to the skin, which results in the breakdown of the extracellular matrix in the dermis. A noteworthy constituent of coriander leaves, linolenic acid, has been found to possess anti-aging and anti-wrinkle properties. This compound has the ability to enhance the synthesis of collagen in normal human dermal fibroblasts (NHDF), while also reducing the expression of matrix metalloproteinases.²

Tamarindus indicus -

Aging and wrinkles are skin-damaging effects caused by harmful UV rays. Alcohol was used to prepare a tamarind seed coat extract, which demonstrated higher antioxidant activity.⁵¹ When skin is damaged, the expression of matrix metalloproteinases by fibroblasts increases, and it has been observed that the damage rate of skin cells caused by UV radiation decreases from 25% to 10% in the presence of tamarind extract.²

***Terminalia arjuna* -**

Reduced collagen production is the cause of aging. Pentacyclic triterpenoids from *Terminalia arjuna* enhance the production of collagen and the function of the epidermal barrier. It also reduces scaliness and moisturizes the skin more.

2

***Thymus vulgaris* -**

Thyme oil can help to prevent fine lines and wrinkles caused by free radicals⁵². The antioxidant activity of thymus species may be due to a variety of mechanisms, including chain initiation prevention, peroxide decomposition, continued hydrogen abstraction prevention, free-radical scavenging, reducing capacity, and binding of transition metal ion catalysts.

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***Punica granatum* -**

Pomegranate extract, derived from *Punica granatum*, could potentially benefit skincare supplements. The extract provides protection against UVB-induced oxidative stress and photoaging. The active ingredient in *Punica granatum*, catechin, has been shown to prevent skin aging caused by UVB exposure.^{54,55}

***Labisia pumila* -**

The extract from *Labisia pumila* has a strong potential for photoprotection and may find application as a treatment for extrinsic aging. In addition, *L. pumila* may increase the production of collagen in human dermal fibroblast cells. Additionally, the herbal extract can shield human skin from reactive oxygen species (ROS) attacks caused by prolonged UVB exposure. This is mostly because plant extracts include phenolic acids and bioflavonoids.⁵⁶

***Emblica officinalis* -**

Did you know that the fruit extract derived from *Emblica officinalis* plant has been found to possess antioxidant properties that are believed to provide protection against UV radiation? Recent studies have shown that this natural extract could be beneficial in protecting the skin from harmful UV rays, which are known to cause premature aging, wrinkles, and skin cancer. So, if you want to keep skin healthy and youthful, incorporating *Emblica officinalis* fruit extract in skincare routine could be a great idea.⁵⁷

***Areca catechu* -**

Areca catechu contains a phenolic substance that has anti-aging properties by safeguarding connective tissue proteins. Scientists were able to identify this substance, known as CC-517, using specific methods. The remarkable inhibition of elastase by CC-517 may protect the major proteins of the extracellular matrix, activate its reconstruction, and indirectly improve capillary wall tone.⁵⁸

***Dioscorea villosa* -**

The anti-inflammatory properties of wild yam (*Dioscorea villosa*) make it suitable for dermatologic products used to treat irritated or aged skin. The extract also exhibits anti-collagenase activity, implying a potential application in anti-aging products and, more broadly, in the treatment of skin degenerative syndromes.⁵⁹ In addition to the beneficial effects of Diosgenin on aging skin, it has been proposed that Diosgenin may be a good and safe health food for the elderly, particularly to alleviate the effects of climacteric issues.⁶⁰ The effects of Diosgenin, on the other hand, may vary depending on endogenous estrogen levels, tissue or cell types, route of administration, time, and level of exposure.⁶⁰

***Diospyros kaki* -**

The extract of the Persimmon leaf, scientifically known as *Diospyros kaki*, has been found to have an effect on the skin comparable to hydroquinone, without any of the detrimental side effects. The extract has been shown to have both anti-wrinkle and skin-lightening properties, making it a promising ingredient for skin care products.

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***Peucedanum graveolens* -**

Research has shown that the use of Dill (*Peucedanum graveolens*) extract in skin care treatments can lead to improvement in skin elasticity, resulting in smoother appearance of wrinkles and remodeled face contours. Many people report that their skin feels more elastic after treatment with this extract.⁶²

***Rhodiola rosea* -**

The plant known as *Rhodiola rosea* has several names and belongs to the family *Crassulaceae*. *R. rosea* is a plant that contains high levels of phenolic compounds, which are known to have powerful antioxidant properties. This makes *R. rosea* a popular choice for those seeking natural sources of antioxidants to support their health and well-being. It grows in chilly climates and is primarily found in arctic regions of Europe and Asia. It has been used in traditional folk medicine to treat various health conditions such as fatigue, depression, anaemia, impotence, gastrointestinal problems, infections, and nervous system disorders. It is also believed to

increase physical endurance, longevity, and resistance to high-altitude sickness. ⁶³

***Daucus carota* –**

Carrot seed oil is obtained from the *Apiaceae* family plant *Daucus carota* and has been highly valued for centuries due to its rich content of vitamin A and other essential vitamins. It is often used as a revitalizing, rejuvenating, and anti-aging agent. The distinctive and vivid orange color of carrots is due to the presence of carotenes (β -carotene) and smaller amounts of α - and γ -carotene. These carotenes are partially metabolized into vitamin A by humans. ⁶⁴

Vitamin C –

One nutrient required for many biological processes is vitamin C. It can stop lipid peroxidation and is a scavenger of reactive oxygen species. ⁶⁵ A 20% vitamin C cosmetic was used to test fifty randomly chosen female participants. Every day, the vitamin C was applied to their faces. The fourth and eighth weeks were used to measure the skin's melanin index, elasticity, gloss, moisture, smoothness, roughness, scaliness, and wrinkles. The outcomes demonstrated that vitamin C could enhance the skin's elasticity, color, and luster. ⁶⁶ This implies that vitamin C may have an anti-aging effect on the skin.

Hyaluronic Acid –

Wrinkles are the most visible sign of photoaging, caused by the loss of collagen fibers and aberrant elastin accumulation. Hyaluronic acid degradation may occur before the breakdown of fibril components. ⁶⁷ In clinical trials, 60 women with aging skin took 200mg of hyaluronic acid orally every day for 28 days. After the trial, their skin's moisture content and wrinkle depth were measured, showing that hyaluronic acid can improve skin elasticity, strength, and moisture content, suggesting its efficacy in reducing signs of aging.

Protocatechuic acid –

Protocatechuic acid has anti-inflammatory and antioxidant properties. It helps reduce wrinkles and crow's feet on the skin. This is because it regulates the primary pathway in keratinocytes. In a study, twenty-two female subjects used a 0.02% protocatechuic acid solution topically for eight weeks to treat MMP-1 secretions, radiation-induced MMP-1 production and other facial wrinkles. The findings showed that protocatechuic acid can reduce the percentage of wrinkles on the skin and inhibit MMP-1. Therefore, protocatechuic acid has anti-aging or anti-wrinkle properties for the skin. ⁶⁸



Fig3: Various kinds of herbs with anti-wrinkle properties

ACCESSIBLE MARKET FORMULATION

Name	Type	Route of administration	Effects
Phytoceramide ⁶⁹	Herbal agent	Topical application. Depending on severity	causes the skin's aging process to lose more procollagen-1 and fibrillin-rich microfibrils.
Hyaluronic acid ⁶⁹	Natural chemical	Topical application Depending on the type of formulation	It increases the hydration and mechanical damage resistance of tissues.
Green tea polyphenols ⁶⁹	Herbal agent	Topical application Varies according to severity	reduces DNA damage in the skin and the quantity of Langerhans cells.
Garlic extract (caffeic acid, S-allyl cysteine, and uracil ⁶⁹	Herbal agent	Topical application Varies according to severity	inhibits the expression of MMIPs and the breakdown of type I procollagen.
Retinol ⁶⁹	Vitamin-A	Topical application 5% concentration	Increase collagen biosynthesis while decreasing MMPI (collagenase) expression
Niacinamide ⁶⁹	Vitamin-B3	Topical application 5% concentration	controls the renewal and metabolism of cells
Tocopherol ⁶⁹	Vitamin-E	Topical application 5% concentration	regulates cell metabolism and renewal

I-ascorbic acid ⁶⁹	Vitamin-C	Topical application 5% concentration	enhances elasticity, lowers inflammation, and produces collagen to plump up the skin
Nifedipine ⁶⁹	Synthetic chemical	Topical application Varies with patients	increases the skin's elasticity and pigmentation
Alpha-hydroxy acid ⁶⁹	Chemical agent	Topical application not more than 8% concentration	gentle exfoliators that dissolve the "glue" that holds surface skin cells together,
Palmitoyl peptide ⁶⁹	Polypeptide	Topical application	boost the production of collagen and turn on the skin's metabolism
Botulin-um toxins ⁶⁹	Synthetic chemicals	Dermal injections Varies with the type of neurotoxins used	Botulinum toxin works at the neuromuscular plate and other cholinergic synapses.
Chemical peels ⁶⁹	Synthetic chemicals	Topical administration Varies with the type of chemicals used	increase in collagen fiber content water in the dermis has been reported to improve skin elasticity
Mixture of <i>Panax ginseng</i> and <i>Crataegus pinnatifid</i> ⁶⁹	Human dermal fibroblast	Dermal injections Varies with the severity	human dermal fibroblast.

Activation of TGF- β /SMAD and P38 MAPK signalling pathway ⁶⁹	Dermal multipotent stem cells.	Dermal fillers Varies with the patients	activating TGF- β /SMAD and P38 MAPK signaling pathway and then stimulating
DHEA (Dehydroepiandrosterone) ⁶⁹	Chemical agent	Topical administration Depends on patient	fibroblast to secrete and synthesize collagen
Gene silencing ⁶⁹	Chemical agent	Dermal injections · Varies with the patients	DNA demethylation agents and histone
Paracrine cytokine linkage ⁶⁹	PCL between keratinocytes and fibroblasts	Dermal injections Depending on the severity	diacylation inhibitors genes
Quercetin ⁶⁹	Herbal agent	Topical administration Varies with the patient	maintaining the elasticity and firmness of the skin
Rice-wine ⁶⁹	Cultured in human fibroblast and keratinocytes	Topical application No fixed dose	reduces the expression of UV-induced matrix metalloproteinase-se-
Pogostone ⁶⁹	Chemical constituent of patchouli oil	Topical application No fixed dose	Inhibited the wrinkle formation and skin laxity mainly by repairing collagen and elastic

mesenchymal stem cells ⁶⁹	Medium from human bone marrow	Dermal injections No fixed dose	fiber.
Cyclopia ⁶⁹	Fermented and non-fermented	Topical application 2-5% concentration	procollagen synthesis
Coca pod extract ⁶⁹	Herbal agent	Topical application Not more than 5% concentration	collagen tissue breakdown reactions
A mixture of human growth factor and hyaluronic acid serum ⁶⁹	Semi-synthetic	Topical application Varies with the patients.	HGF and HA serum are beneficial in reducing peri-orbital
Retinyl retinoate ⁶⁹	Micro sphere	Topical application No fixed dose	Wrinkles
Autologous platelet-rich plasma ⁶⁹	Whole blood plasma	Dermal injection No fixed dose	synthesis of collagen and other matrix component by stimulating the activation of fibroblast

NOVEL DRUG DELIVERY SYSTEM IN COSMETIC INDUSTRY

Pharmaceutical delivery systems are capable of improving the penetration of cosmetic ingredients into deeper skin tissues, extending their duration of action, enhancing stability, preventing incompatibilities with other ingredients in formulations, and averting the manifestation of unwanted side effects, both locally and systemically. By utilizing such delivery systems, cosmetic formulations can achieve better efficacy and safety profiles, thereby meeting the diverse needs and expectations of consumers. The application of pharmaceutical delivery systems in cosmetic formulations represents a promising avenue for research and development and holds great potential for advancing the cosmetic industry.⁷⁰ Below are some examples of preferred delivery systems for medications: vesicular systems such as liposomes, niosomes, nanosomes, phytosomes, herbosomes, marinosomes, oleosomes, aquasomes, ultrasomes, photozomes, ethosomes, transferosomes, sphingosomes, and colloidosomes; multilayered carriers; silicon carriers and matrices; emulsified systems, such as microemulsions, multiple emulsions, and nanoemulsions; microgel, nanogel, liquid crystals; specific systems, such as microparticles, nanoparticles, solid lipid nanoparticles, nano-structured lipid carriers, microcapsules, nanocapsules, microspheres, nanocrystals, and cyclodextrins.⁷¹⁷²⁷³⁷⁴ Herbal cosmetics and personal care

products use liposomes to encapsulate natural extracts, vitamins, and antioxidants. This helps increase efficacy, stability, and bioavailability while decreasing toxicity and allergic potential.⁷¹⁷⁵ Skin acts as a barrier that prevents high molecular weight and hydrophilic substances from passing through. This makes it difficult to apply dermatological cosmetics that require high concentrations of active ingredients to the skin. The skin's brick-and-mortar structure makes it hard for drugs to be deposited. Vitamins can lose their effectiveness when exposed to UV light and may not be very stable. To ensure that the drug is deposited and protected from photodegradation, it's vital to choose the right carrier.⁷⁶

Liposomes –

Liposome compositions can contain phospholipids from either natural or artificial sources. These bilayers may also include other components such as surfactants or cholesterol. In most cases, cholesterol is utilized to bolster the bilayer properties of liposomes. It decreases the permeability of molecules soluble in water through the membrane, while promoting bilayer stability and fluidity.⁷⁷⁷⁸

The topical liposomes' occlusive effect has been demonstrated, although the exact mechanism by which they function is still up for debate. The skin gets rough and flaky and loses its elasticity when dehydrated. One of the most significant and expansive categories of skin care products is that of moisturizing products.⁷⁷ Because lipids are well-hydrated and can lessen skin dryness, which is a major factor in skin aging, liposomes as carriers themselves have benefits.

While the rate of penetration is slowed, liposomes promote the distribution of encapsulated active ingredients in the dermis and epidermis. In cosmetic products, this aids in fixing active ingredients to the outermost layers of skin as desired. To make sun care products that, for instance, contain liposome-encapsulated UV filters water resistant, the washing out may be postponed concurrently.⁷⁹⁸⁰

Niosomes –

Niosomes represent a novel vesicular drug delivery system that can be employed for targeted, controlled, and sustained drug delivery. Synthetic non-ionic surfactants are hydrated to form multilamellar vesicles called niosomes, which may or may not include sterols like cholesterol or other lipids. Niosomes, which range in size from 10 to 1000 nm, are small lamellar structures composed of biodegradable, non-immunogenic, and biocompatible surfactants.⁸¹ Niosomes contain non-ionic surfactant vesicles called amphiphiles, which are stabilized by the addition of cholesterol and a small amount of anionic surfactant, like diacetyl phosphate, which helps to stabilize the vesicles.⁸² Niosomes are preferred over liposomes, it is because niosomes exhibit better chemical stability and economy.⁸³ Niosomes are tiny particles used in the cosmetic industry to improve skin care. They were first developed and patented by L'Oréal, a cosmetics company. In 1987, Lancôme introduced their first cosmetic product, called "Niosome," to the public. Later, they created an anti-aging cream called "Niosome Plus." The benefits of niosomes include improved penetration of poorly absorbed ingredients and increased stability of entrapped drugs. This makes them useful for skin care products.⁸⁴

Phytosomes –

Standardized extracts or purified fractions combined with phospholipids are called phytosomes, and they have been shown to have improved activities and bioavailability. Because of their lipophilic nature, they enhance the topical absorption of complex molecules, resulting in improved specific activity in the functions of the skin, including hydration, collagen structure, enzyme balance, and so on. Biologically active phytoconstituents can be applied locally at the required site through topical absorption. Through better absorption, increased bioavailability, and improved tissue delivery, the phytosome process intensifies herbal compounds.⁸⁵⁷⁹

Because phosphatidylcholine is a necessary component of cell membranes, it not only serves as a carrier during the phytosome process but also nourishes the skin.⁷⁹

Nanoparticles –

Due to their great stability and affinity for the stratum corneum, nanoparticles enhance the bioavailability of the material they encapsulate for the skin. The nanoparticles enter the stratum corneum's upper layers. The active ingredients are released when they combine with the lipids in the skin. The occlusive effect of ultrafine particles creates an adhesive film on the skin that facilitates the penetration of active ingredients. Nanoparticles containing active ingredients such as vitamins, sunscreens, fragrances, and essential oils are commonly utilized.⁷⁹

The novel antiaging compound alpha lipoic acid is chemically labile and when it degrades, it smells bad. To

solve this issue, the active was encapsulated in solid lipid nanoparticles.

Nanoemulsions –

Small droplet emulsions (20–300 nm) are known as nanoemulsions. They could be applied to compounds with improved bioavailability that are hydrophilic or lipophilic. Droplets larger than 100 nm in nanoemulsions appear white, while dispersions between 70 and 100 nm appear opaque, and less than that becomes transparent. Coenzyme Q10, sometimes referred to as ubiquinone, is a special cosmetic ingredient that guards against premature aging, wrinkle development, and loss of cell activity; it has a very low topical bioavailability and is highly lipophilic. When ubiquinone is encapsulated in a nanoemulsion, its concentration in the dermis is increased relative to traditional formulations. Likewise, it may be possible to boost the bioavailability of herbal cosmetic extracts.⁷⁹

Table1: Formulations using nanotechnology are currently available for purchase to treat anti-wrinkles.

PRODUCT	COMPANY	USES	REFER-ENCE
Cutanova Cream Nano Repair Q 10	Dr. Rimpler	Fragrance-free and comedogenic anti-wrinkle face cream for delicate skin types minimizes the appearance of fine lines.	11
Intensive Serum Nano Repair Q 10	Dr. Rimpler	Richly concentrated, creamy serum with anti-aging properties that are both reconstructive and protective.	11
Cutanova Cream Nano Vital Q 10 SUMMER	Dr. Rimpler	It's a mild anti-aging product that gives your face instant, noticeable contour toning.	11
SUMMER Crème Legere Nano-Protection	Isabelle Lancray	Used as a deeply hydrating day or nighttime care cream	11
SURMER Crème Riche Nano-Restructurante	Isabelle Lancray	hydrating lotion with a blend of unusual plant extracts	11

CONCLUSION

In India, over 1.5 billion people aged 50 and above struggle with wrinkles. As we dug deeper into the topic and scoured various articles, it became clear that there are numerous alternative methods for treating different types of wrinkles. In recent years, several dosage forms have been developed, including anti-wrinkle lotions, serums, creams, tablets, capsules, and gels. These forms are more potent in improving skin care and have better therapeutic efficacy. Researchers are also exploring the use of herbal ingredients that exhibit anti-wrinkle activity in their formulations. The goal is to achieve faster recovery times with less toxicity and adverse effects. Some herbs with anti-wrinkle properties include ginseng, aloe vera, cucumber, carrot, and others. In addition, herbal cosmetics use less harmful excipients, which will lead to an increase in customer base. Novel drug delivery systems are also gaining popularity due to their numerous benefits, such as better penetration of cosmetic ingredients into deeper skin tissues, longer duration of action, increased stability, avoidance of incompatibilities with other ingredients in formulations, and prevention of unwanted side effects that could manifest locally or systemically.

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