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Anti-aging activity of various topical nano herbal formulations

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Abstract
We utilised a variety of medicinal plants because, as we all know, they are excellent providers of many vitamins and minerals that are used to treat a variety of ailments, including ageing and other disorders. The majority of plants include a combination of elements that work together synergistically to increase a drug's ability to treat problems associated with ageing. Natural herbal plant formulations were created by combining various plant extracts or ingredients in varying proportions to create cream, oil, gel, and lotion. Although helpful in the treatment of ageing issues and a number of ailments, it also has some restrictions when used topically. Some of these restrictions include the potential for localised skin irritation, poor drug permeability through the skin, the difficulty of absorbing drugs with larger particle size and higher molecular weight through the skin, the possibility of toxic reactions following application, or the possibility that drugs may be denatured by the enzymes found in the epidermis. With the advancement of innovative technologies like nanotechnology, we can now get beyond the drawbacks of conventional topical formulations. The typical properties of products created with the aid of nanotechnologies include biocompatibility, biodegradability, a longer duration of action, the ability to perform numerous functions, the ability to modify drug release, potential targeting, and reduced toxicity, among many others. The purpose of the present review is to study different medicinal plants having anti-ageing activity. The review mainly focusses on various nanotechnology based herbal formulations which can be use to enhance the effectiveness in anti-ageing activity. However, nanotechnology has established that it can provide tools to overcome the problem associated with herbal medicine.

INTRODUCTION

The skin, the largest organ in the body, acts as a vital barrier with capacities for protection, sensing, and immunity. Skin is vulnerable to a variety of external elements because of how exposed it is to the outside world, which can lead to numerous sorts of skin damage and suffering.

The skin acts as a shield against the outside environment. Controlling the body's temperature, fluid balance, and defence against harmful microorganisms and UV rays is part of its function. The epidermis, dermis, and subcutaneous tissue are the three layers that make up the skin [1].

Epidermis

The cellular structure of the epidermis is composed of keratinocytes, melanocytes, macrophages, and tactile epithelial cells. Due to its barrier function, keratin, a fibrous protein that protects the skin, plays a significant role in the poor absorption of hydrophilic medications. Keratinocytes are the cells that produce keratin.

Dermis

Under the epidermis, there is a 0.3–0.5 mm thick layer called the dermis. Elastic fibres, sweat glands, and collagen make up the connective tissue. The dermis is a layer that sits 0.3 to 0.5 mm under the epidermis. The connective tissue is made up of sweat glands, elastic fibres, and collagen. This has connective tissue, capillaries, and hair follicles.

Subcutaneous tissue:

The final layer, known as the hypodermis or subcutaneous tissue, contains major blood arteries, areolar and adipose tissue, as well as nerve endings that are pressure-sensitive. The last layer, called the hypodermis or subcutaneous tissue, has major blood vessels, adipose and areolar tissue, and pressure-sensitive nerve endings [1]. Inability to maintain homeostasis and an increased risk of death are prominent features of the ageing process in humans [2]. The main causes of ageing are:

Intrinsic skin aging: The intrinsic ageing of the skin is reflected by functional changes as opposed to morphological changes. Clinical indicators include hair

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loss, increased perspiration, rough, pale skin with fine creases, and numerous benign tumours.

Extrinsic Skin Aging: Extrinsic skin ageing is the term used to explain the morphological and physiological changes that cause premature skin ageing. Its clinical symptoms include coarse wrinkles, pigment irregularities, and solar elastosis, which have twisted, stiffened elastic structures containing elastin and collage particles.

Figure 1: Image of skin aging

Mechanism of skin aging involves

Intrinsic skin aging: Rather than morphological changes, the intrinsic ageing of the skin is represented by functional alterations. Clinical signs include rough, pale skin with fine wrinkles, hair loss, excessive sweating, and various benign tumours. Activated oxygen species (ROS) play a significant part in skin ageing.

Extrinsic skin ageing: Chronic exposure to UV radiation damages the epidermis, causes the stratum corneum layer of skin to thicken, increases dysplasia with cellular atypia and anaplasia, lowers collagen levels, and breaks down elastic fibres.

Mitochondrial damage

By compulsion of oxygen, cellular organelles known as mitochondria make energy (ATP). The UV action on the mitochondrial electron transport chain results in the production of significant amounts of reactive oxygen species (ROS), which can damage mitochondrial DNA (mtDNA).

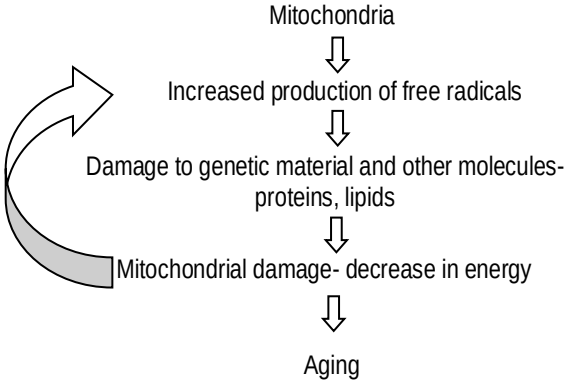

Fig 2: Mitochondrial damage

Protein oxidation:

Oxidative damage can also destroy proteins and photodamaged skin. The effects of oxidative protein damage include changes in enzyme activity, loss of structural protein function, and changes in susceptibility to disintegration.[4] Because of the popular belief that "natural medicines" are kinder, safer, and have less side effects and unpleasant drug reactions than their synthetic counterparts, people are becoming more enthusiastic about using herbal pharmaceuticals. An increasing quantity of clinical data also supports the therapeutic use of herbal treatments for a number of illnesses. Among the medicinal plants used to slow down the ageing process are aloe vera, turmeric, amla, honey, and other ones. Also becoming more and more popular is the topical application of herbal plants. New phytochemical delivery methods have already been created using an emerging idea known as nanoformulation, and the results are rather exciting. The well-known plant curcuma longa is an example of how nanoformulations have been used to help curcumin's poor water solubility and constrained systemic absorption. The goal of the current review is to examine various medicinal plants with anti-aging properties. The review primarily focuses on various herbal formulations based on nanotechnology that can be used to increase the potency of anti-ageing activities.

NANOTECHNOLOGY

The term "nanotechnology" refers to the creation and application of materials with physicochemical characteristics distinct from those of their bulk equivalents at the nanoscale. These novel materials have had particular internal structural reorganisations that give them a bigger surface area and alter how they interact with biological systems. By creating nanoproducts, the loading of active pharmaceutical ingredients (APIs) into nano-sized medication delivery systems is currently being used to encourage product innovation. As a number of products are already on the market for the treatment of skin injuries (such as atopic dermatitis, skin cancer, skin burns, wound healing, and protection from ultraviolet (UV) radiations), nanoproducts used for the delivery of APIs to the skin (e.g., nanopharmaceuticals, nanocosmeceuticals) have already demonstrated their effectiveness [6].

ROLE OF NANOTECHNOLOGY IN PROMOTING ANTI-AGING: The distribution of coenzyme Q10 [CoQ10], which has anti-aging properties, is made possible through nanotechnology. Co Q10 has low levels of permeability due to the fact that it is an insoluble antioxidant. Excellent anti-wrinkle qualities are possessed by CoQ10. In light of this, an O/W nanoemulsion formulation containing CoQ10 was created, and its penetration into the stratum corneum was

examined [7]. Both in vitro and in vivo studies have consistently demonstrated the potential of nanotechnological applications in the treatment of age-related metabolic diseases. The ability of phytobioactive compound-loaded nanodelivery devices to control inflammation and oxidative stress, two factors known to play significant roles in pathological disorders linked to ageing, has been repeatedly demonstrated. There has been strong evidence in recent years that phytochemical-loaded nanocarriers can be very efficient at preventing diseases associated with ageing [8].

Table 1: List of herbal plant showing anti-aging effect [5]

Species	Used parts	Active ingredients	Activities	Product form
Cocos nucifera 	Oil,fruits, seeds	Fatty acid	Moisturizing, softening, and helpful for rashes and irritation.	goods for the bathroom, makeup for the eyes, hair, shaving creams, etc.
Helianthus annuus 	Oil,flower, leaves, seeds	Lecithin, tocopherols, carotenoids, waxes	Smoothing	Creams, creams for the skin, and creams for the hair.
Daucus carota 	Fruits, seeds, flowers, leaves, roots	Vitamin A	Smoothing for Anti-Aging, Revitalizing, and Rejuvenating	Skin care products

Advantage of nanoformulation over topical formulation

1. Enhanced in vitro transcutaneous penetration.
2. Higher rates of transdermal absorption.
3. Improved skin pigmentation.
4. A higher rate of transdermal absorption.
5. Increase solubility, delivery, and dissolution rates.
6. Boost water solubility, amorphous nature, and dissolving profiles
7. Withaferin A's irritative effects are reduced.

Disadvantage: [9]

(1) Significant funding for research and development.
(2) A lack of qualified workers and researchers in the area.
(3) Lack of information about new business potential based on nanotechnology among business groups and entrepreneurs.
(4) Concern for negative health impacts from using products based on nanotechnology.
(5) Pricey in terms of modern technologies.

Various nanocarrieers use for anti-aging [10]

Nanomaterials are used as medicinal drug delivery systems. These nanoparticles serve as a vehicle to demonstrate the anti-aging impact.

1. Nanoemulsion: Nanoemulsions are transparent, thermodynamically stable substances with distinct rheological characteristics. Oil droplets kept their lightness and clarity while being stabilised in an aqueous dispersion by a mixture of surfactants and co-surfactants. For nutraceuticals and APIs that need to be released gradually into deeper epidermal layers, nanoemulsions are a frequent delivery method.[11]

2. Solid lipid nanoparticles and nanostructured lipid carriers

The first generation of lipid-based NPs, known as solid lipid nanoparticles (SLNs), have regulated release and a lower risk of skin damage since they transfer a smaller amount of the active ingredient to the skin at once. The solid nature of the used lipids helps to encapsulate and release the active ingredients. The production process and the physicochemical characteristics of the active ingredient, particularly its lipophilicity, have a significant impact on the effectiveness of SLNs. Storage of SLNs causes the crystalline structure to reorganise into a more ordered and stable form, minimise matrix flaws, and reduce the amount of space available to hold the desired active ingredient, which leads to its loss or reduction. includes plant oils and extracts with anti-inflammatory and anti-scaling properties

that aid in skin regeneration. One example is Phyto NLC Active Cell Repair

3. Liposomes: Since lipid bilayers are the building blocks of liposomes, cream capture, a product created by the Dior Company in 1986, was built from them. Despite its instability and antioxidant addition, liposomes would be used in cosmetics. The first nano-carriers for drug administration were liposomes, which were created in the early 1970s. When used to carry both hydrophobic and hydrophilic molecules, liposomes are flexible vesicles that are biocompatible, biodegradable, non-toxic, and easily encapsulate active compounds. By enhancing their skin absorption, liposomes can increase the concentration of active ingredients.

4. Niosomes: By directing the medicine to the targeted treatment location, niosomes—vesicles made of non-ionic surfactants—which are biodegradable and quite safe—help to accomplish site-specific delivery. Although it resembles liposomes and is stable, it also has hydrophilic and hydrophobic ends. Consequently, L'Oreal's first product, Lancôme, was released in 1987. Drugs that are amphiphilic and lipophilic are transported via niosomes.

5. Metal Nanoparticles: In the fight against bacterial resistance, broad-spectrum antibacterial medicines known as metal nanoparticles have been proposed as an alternative to conventional antibiotics. Silver, zinc oxide, gold, or copper are the most popular materials used to make metal nanoparticles. Since they can be used as preservatives and have antifungal and antibacterial properties, they are popular as cosmetic ingredients. Additionally, these particles have a high physicochemical stability, are non-toxic, biocompatible, and chemically inert.

6. Nano-gold and Nano-silver: Antibacterial and antifungal characteristics are shared by nano-gold and nano-silver. They are frequently used in cosmeceutical goods including deodorant, face packs, and anti-aging lotion. They have been utilised in facial masks and moisturising cream.

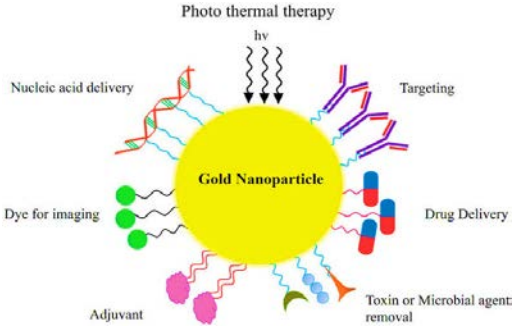

Figure 3: Gold nanoparticle

7. Cubosomes: Cubosomes are classified as discrete nanoparticles of the continuous cubic liquid crystalline phase with a significantly higher specific surface area than the parent cubic phase. It may also hydrate the skin and has high heat stability.

8. Phytosome: By releasing a photo reactivating enzyme from a marine plant called Anacystinidulans, they are utilised in sun care products to protect skin that has been exposed to the sun[13].

These are some of the carrier that maninly help to carry the drug and are use as drug delivery system. Below the carrier system we have discuss about some of the various nanoherbal formulation that are use for anti-aging purpose and also shows antioxidant properties.

Brief discussion on some of nanoherbal formulation use for anti-aging

Canola oil (*Brassia napus L)*:

Canola oil is made from a type of rapeseed and is a member of the Brassicaceae family. Canola's scientific name is Brassica napus L. Vitamin E, which is abundant in canola oil and beneficial for skin care. Vitamin E is a powerful antioxidant that shields our skin from free radical damage, maintains skin suppleness, evenness, eliminates blemishes, fades acne scars, and delays the ageing process of the skin developed a canola oil nano cream and evaluated if it had a stronger anti-aging impact than the canola oil cream. They used a high-energy emulsification technique (high-shear stirring) to prepare the nanocream. The DPPH [2, 2-Diphenyl-1-picrylhydrazil] technique is used to measure antioxidant activity, and the pH of the nanocream formulation was calibrated with a standard buffer solution and found to range from 5.7 to 6.3. It was decided that the canola nanocream preparation is safe for usage after tests were conducted on 12 human volunteers to determine the irritant test.

The formulation was applied behind the ear and left for 24 hours. In addition, they discovered that it improves the moisturising effect since it contains vitamin E, a moisturiser, and restores dehydration to normal. So, compared to cream preparations, nanocream preparations with canola oil have better antiaging efficacy. This is demonstrated by a higher percentage of recovery from many ageing indices, including as hydration, pores, spots, and wrinkles, in nanocreams as compared to creams[14].

Annona squamosa leaf:

The biological actions of flavonoids, which are organic molecules, have been linked to the antioxidant process in

a number of ways. Rutin and hyperoside are two flavonoids found in abundance in the leaves of A. squamosa. One of the significant therapeutic plants is Annona squamosa, sometimes known as "custard apple" and a member of the Annonaceae family. In A. squamosa leaves, acetogenins and polyphenols are thought to function as FR scavengers. The antioxidant capacity of a herbal anti-aging cream made with Annona squamosa leaf extract was assessed by Mahawar, et al. in 2019.

A. squamosa aqueous exhibits more inhibition than ascorbic acid when tested for free radical scavenging activity using the 2, 2-diphenylpicrylhydrazyl (DPPH) method. A qualitative phytochemical examination of A. squamosa (custard apple) leaf extract reveals the presence of flavonoids, tannins, alkaloids, and phenols, however terpenoids and steroids are not present. An anti-aging lotion can be created using an aqueous extract of A. squamosa leaf thanks to the plant's high antioxidant content. A. squamosa formulation is furthermore shown in research to be stable for 3 months. The formulations demonstrated high spreadability, no sign of phase separation, and satisfactory consistency throughout the trial period. They were also homogenous, emollient, non-greasy, and easily removed after application. The formulation displays the appropriate pH range, indicating that it is compatible with skin secretions. Due to the high antioxidant qualities of custard apple leaf extract, it is feasible to make anti-aging creams that contain it. These creams will aid in minimising oxidative damage and provide our skin with an antioxidant impact [15].

Curcuma longa

The dried rhizomes of C. longa were used because they contain the three majors pharmacologically significant curcuminoids curcumin, demethoxycurcumin, and bisdemethoxycurcumin, as well as antioxidant properties. Using a Soxhlet apparatus and ethyl alcohol (90% vol/vol), continuous hot extraction of alcohol was performed. Utilizing the Folin-Ciocalteu colorimetric method to estimate total phenolic content and the reducing power estimation method to measure antioxidant activity, photoprotective activity was measured.

The liposomal formulations were created using a rotary evaporator and the lipid film hydration approach with soy phosphatidylcholine and cholesterol (7:3% w/w). The ultra-centrifugation technique was used to measure the entrapment effectiveness of the vesicles. Cream formulations were tested for pH, viscosity, smoothness, stickiness, spreadability, microbiological count, stability at 4 2 C for three months, and stability of the encapsulated curcumin of C. longa extract using high-performance liquid chromatography at 425 nm. Human volunteers (age 25–30) with dry, UV-irradiated skin were given 0.2 g of the formulations twice daily at the volar forearm (for skin hydration) and at the forehead (for sebum content); measurements were taken three times after 1, 2, and 6 weeks of application.

To reduce variances, all processes were carried out at a constant room temperature of 20 to 5 degrees Celsius and a relative humidity of 45 to 5 percent. The order of C. longa extract loaded creams, C. longa extract loaded ethosomal creams, C. longa extract loaded liposomal creams, C. longa extract loaded creams, empty transfersome loaded cream, empty ethosome loaded cream, empty liposome loaded cream, and base cream determined the effectiveness.

The emollient, moisturising lipid components of nano vesicles and the photoprotective qualities of C. longa extract's active ingredients led to improved skin properties like hydration and sebum production. The cream's nano vesicles that are filled with herbal extract could be used to create photoprotective formulations [16]

Coriandrum. sativum and rose hip

The herb coriander (Coriandrum sativum L.), which belongs to the Apiaceae (Umbelliferae) family fats and essential oils make up the majority of it. The fruit of Rosa species like Rosa canina, Rosa rubiginosa, and Rosa moschata, all of which are members of the Rosaceae family, is where rosehip seed oil (RHO) is derived from. It includes vitamin C as well as polyunsaturated fatty acids including oleic acid (16%), linoleic acid (54%), and linolenic acid (17%).

A cream containing coriander oil and rose hip oil in various concentrations was created after the fruits of the Coriandrum sativum plant were extracted using the soxhlet technique and water. Following the trial, the cream's pH was measured, and it was discovered to be in the healthy range for skin pH of 5.6 to 6.8. The formulation's viscosity, which was measured by a Brookfield viscometer and ranged from 500 to 1500 cps, shows that the cream is readily spreadable with only a modest amount of shear. On laboratory animals (mice with their backs shaved), the cream's safety was assessed using a basic skin irritation test. They conducted a skin irritation test but discovered no redness, edoema, inflammation, or irritation. These compositions were found to be skin-safe, and it was determined that natural creams with antioxidant properties might be utilised to provide a barrier to shield the skin and prevent ageing[17].

Table 2: Some of the herbal nano formulation used in anti-aging

MEDICINAL PLANT	FAMILY	PART USE	FORMULATION TYPE	REFERENCE
Acasia hispida	*Mimosaceae*	Bark	Cream	[18]
Benincasa hispida	*Cucurbitaceae*	Fruit	Cream	(Jadoon et al., 2015)
Calendula officinalis	*Compositae*	Flower	Cream	(Jadoon et al., 2015)
Sclalerocarya birrea	*Anacardiaceae*	Fruits	Cream, oil	[19]
Phyllanthus emblica	*phyllanthaceae*	Fruits and bark	Gel	[20]

Some of the marketed product use in anti-aging formulation: [6]

Table 3: Anti-aging products available

Brand –product	Characteristics and uses
Agera®-Nano Eye Lift	Skin care for aged skin. Soften the skin around your eyes.
Bionova-Nano Skin Tech Tennis Player Sun and Wind Protection	Boost the level of sun radiation defence. Widespread use for dry skin.
Chantecaille-Nano Gold Energizing Cream	Reduce the appearance of lines, wrinkle, dullness, and dryness substantially. Anti-aging and antioxidant properties.
StriVectinTM-Specialised Hand Care System	Provides specialised hand care for the treatment of sun damage, age spots, ageing skin, fine lines, and wrinkles.
Rosactive® Phytoceutical Skin care-Biomixyl	Several anti-aging treatments in this category are intended to increase collagen formation and hence minimise wrinkles and lines.

CONCLUSION

The current work has demonstrated how innovative drug delivery technologies and the quickly evolving field of nanomedicine are addressing the pharmacological drawbacks of commonly prescribed herbal medicine formats. In addition to dealing with issues like low bioavailability and stability of phytochemical elements, nanoformulations are also used to get past the strong barrier of the skin in dermal and transdermal applications. Even though research in this area is still in its relative infancy, it already shows very promising possibilities for topical nanoformulations to distribute herbal ingredients successfully and strategically in order to have both local and systemic benefits. The study examined a number of herbal plants that exhibit ageing effects as well as antioxidant effects that aid in reducing human ageing. Combining herbal and nanotechnology has demonstrated excellent results in anti-aging and has a promising future. Therefore, increasing and improving target efficiency should be the main focus of topical treatment for greater effectiveness. Because of this, researcher must focus on creating nanomaterial that can have an impact on the healing process at every stage while also being biocompatible and biodegradable.

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