

Novel Drug Approach: Skin - Aging Benefits of Phytotherapeutic Emulsions

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ABSTRACT

The use of herbs in cosmetics and different formulations are observed from centuries. Due to the antioxidant activity, herbs and herbal formulations show great potential. Their potential is used to treat different skin diseases and improve skin appearance is well known. As UV radiation causes, lower immunity against infections, premature aging, sunburns, wrinkles, the best solution is to prevent the UV radiation and avoid side effects. Antioxidants such as vitamin C, vitamin E flavonoids and phenolic acids perform a very important role in fighting against free radical species, which cause numerous negative skin changes. The isolated plant compounds as well as herbs as a whole have a high potential in the skin protection. The main rationale behind formulating the emulsions are new pharmaceutical formulations of some emulsified plant extracts or pure phytochemicals can also prettify the skin as well as reduce a number of degenerative diseases as well as skin conditions such as skin inflammation, skin cancers or skin aging. The ongoing challenge is to determine qualitatively and quantitatively, phytochemicals which are encapsulated into emulsions are very more efficient and safest.

KEYWORDS: Antioxidant, Skin, Novel approach, Phyto therapeutic emulsion

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INTRODUCTION

Skin is the barrier that separates from the outer environment. With the main role as water loss and microorganism infections, they also have an important role in the cosmetics. Aging is one of the important processes and this is seen usually when the person becomes older. Skin shows more visible and obvious signs of aging as it is the more voluminous organ. Cutaneous aging is promoted by both intrinsic and extrinsic factors. Intrinsic aging results in dry, thin skin, fine wrinkles and gradual dermal atrophy. Extrinsic aging is affected by air pollution, poor nutrition, sun exposure, smoking. These ultimately result in loss of elasticity and laxity. The primary factor for extrinsic skin aging is exposure to Ultraviolet radiation. This is termed as photo aging. The population aging is gaining importance from social and economic points of view in the modern society. The aging associated chronic oxidative stress and related systemic inflammation are two pathways

which contribute to aging. The basic aging associated process is shown by three mechanisms: telomere attrition, autophagy and exhaustion of stem cell production. The oxidative stress and its related inflammation have shown its evidence in atherosclerosis, insulin resistance and various neurodegenerative diseases. Currently innovative nanotechnology-based applications are aimed at improving the oral bioavailability and therapeutic effectiveness and also other natural antioxidants are increasing. Skin aging is a complex biological process influenced by a combination of endogenous or intrinsic and exogenous or extrinsic factors. As the skin has very much exposure to the outer environment, skin suffers from both intrinsic and extrinsic factors. The aging process is associated with heightened oxidative stress and related systemic inflammation. Also antioxidant supplementation supports a

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promising therapy to combat aging and associated pathological conditions.

Types of UV radiation

- Ultraviolet
- Ultraviolet A radiation
- Ultraviolet B radiation
- Ultraviolet C radiation

Ultraviolet radiation: They are broadly classified as infra-red radiation, Visible light and UV radiation. Heat is the part of IR radiation; it is not visible to human eye. Visible light is the wavelength range of general illumination. UV radiation is mainly divided into three distinct bands on the basis of decreasing wavelength and increasing energy:

- UVA (320-400 nm)
- UVB (299-320nm)
- UVC (200-290nm)

Ultraviolet A radiation:

UVA show longer wavelength than UVB radiations. It is less effected by altitude or atmosphere conditions. They penetrate deeper through the skin and it is not filtered by window glass. As compared to

UVB, these are efficient in inducing immediate and delayed pigment darkening and delayed tanning than in producing erythema. These rays are beneficial as they increase Vitamin D3 production through irradiation of 7- dihydrocholesterol.

They show adverse effects such as immunosuppression, photoaging, ocular damage and skin cancer.

Ultraviolet B radiation:

The amount of UVA and UVB reaching the earth’s surface is affected by latitude, altitude, season, time of the day, cloudiness and ozone layer.

The irradiance is highest at the equator and higher elevations. At the earth’s surface, ratio of UVA to UVB is 20 :1. These rays are primarily associated with the erythema and sunburns. It can cause immunosuppression and photocarcinogenesis.

Ultraviolet C radiation:

These are the rays which are filtered by ozone layer. It has the highest energy and potential for biological damage. These is not essentially factor considered for solar exposure in human beings.

Skin anti-aging approaches

Cosmetological care	Daily skin care Correct sun protection Aesthetic non- invasive procedures
Topical medical agents or Topical agents	Antioxidants Cell regulators
Invasive procedures	Chemical peelings Visible light devices Intense pulse light Radiofrequency Prevention of dynamic wrinkles
Systemic agents	Hormone replacement therapy Antioxidants
Avoiding of exogenous factors of aging,	Smoking Population Solar UV radiation Stress Nutrition, diet restriction, alimentary supplementation Physical health Control of general health

Skin Aging Prevention and Therapy

➤ **Skin Care:**

Healthy and functioning skin barrier is important protector against dehydration, penetration of various microorganisms, allergens, reactants reactive oxygen species and radiations. They are specifically adjusted for allowance of penetration. The factors which affect the skin conditions are elasticity, smoothness and it also increases the skin regeneration. The main step for formation of wrinkles is degradation of primary structural constituents such as collagen, elastin. The other approach for prevention of formation of wrinkles are to promote natural synthesis of substances exception case in elastin enhancing. Another approach is reduction in inflammation by topical or systemic antioxidants. It is used in the combination with sunscreen products and retinoids for enhancing protective effects.

➤ **Photoprotection and Systemic Antioxidants:**

The extrinsic aging is mainly affected by chronic photodamage. The recent approach is the DNA photodamage and UV generated reactive oxygen species (ROS). These strategies include sun protection includes blockage of UV rays and retinoids in order to inhibit collagenase synthesis and to promote collagen production anti-oxidants to reduce and neutralize free radicals. The Nutritional anti-oxidants mainly include FR scavengers: i) by directly reducing FR scavengers. ii) reduction of peroxide concentrations and repair oxidised membranes. Iii) Quenching of iron to decrease ROS production. Iv) lipid metabolism, fatty acids and cholesteryl esters neutralize ROS production.

➤ **Topical Pharmacological Agents:**

These includes the anti-aging cream components which contain two groups: antioxidants and cell regulators. Antioxidants contains vitamins, polyphenols and flavonoids. They act by reduction in collagen degradation, thereby reducing the collagen degradation. The cell regulators such as retinols, peptides and Growth factors have direct effect on collagen production and influence collagen production. The important antioxidants are Vitamin C, Vitamin B3 and Vitamin E shows ability to penetrate through the skin. Also, bit has proven that topical application of green tea polyphenols before UV exposure leads to an increase in the minimal erythema dose, reduction in number of Langerhans cells and also reduces DNA damage to skin. Other botanical topical application includes isoflavones from soya. Cell regulators such as vitamin A derivatives, polypeptides and botanicals directly acts on the village metabolism, thereby stimulating production of elastic and collagen fibres. Tretinoin, nonaromatic retinoids so approved for application in anti-aging treatment in concentration of 0.05 %. Polypeptides stimulate active dermal metabolism.

➤ **Invasive Procedures:**

The main application is to resurface of epidermis, to remove the damaged epidermis and replace the tissue with remoulded skin layers. It also enhance the formation of new collagen. Recent approach includes tissue engineering and gene therapy.

➤ **Chemical Peels:**

These methods cause chemical ablation of defined skin layers to induce an even tight skin as a result of regeneration and repair mechanisms after the inflammation of epidermis and dermis. These are classified into three categories: Superficial Peels, trichloroacetic acid, medium – depth peels. Medium- depth peels reach the upper reticular epidermis; Superficial peels exfoliate epidermal layer without penetrating the basal layer. The depth of peeling depends not on the substance, but ultimately on its concentration. Superficial peels target the corneosomes, increase epidermal activity of enzymes. These conditions are called as epidermolysis and exploitation. Medium- depth peels cause coagulation of membrane proteins, destroy living cells of epidermis and dermis. Deep peels coagulate proteins and produce complete epidermolysis These also follows restoration of dermal architecture.

➤ **Visible Light devices: IPL, Lasers, RF for the Skin Rejuvenation, Resurfacing and Tightening**

Rejuvenation is controlled form of skin wounding which achieves wounding aiming youthful appearance after the wound heals.

Skin rejuvenation or “sub surfacing” shows low risk while it improves aging structural changes without changing cutaneous integrity. The mechanism of action is heat- induced denaturalization of dermal collagen that leads to reactive synthesis. Laser resurfacing has shown effectiveness in photo aging through entire epidermal collagen shrinkage, stimulation of neocollagenesis, extensive remodelling, regeneration of cellular organelles and intercellular attachments. It results in long recovery time and long-lasting side effects such as erythema, hypopigmentation and hyperpigmentation, infections or scarring.

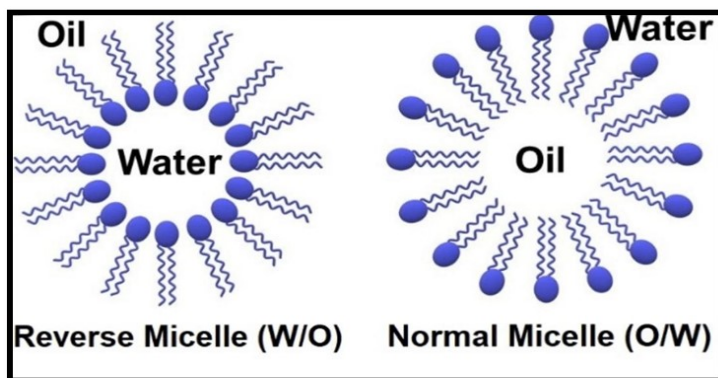
➤ **Hormone replacement therapy**

There is progressive decrease of hormone synthesis with increase in age. The levels of growth hormone and insulin-like growth factor- I, melatonin, TSH, thyroid hormones, estrogen and testosterone are progressively decreasing. The main hormonal defects are menopause, andropause and partial androgen deficiency of the aging male

DHEA substitution has been proven to an improvement of sexual activity, bone density and well- being. HRT with estrogen and progesterone has been long considered to have anti- aging effects.

➤ **Emulsion System for Skin Care:**

Topical application of cosmetics in the form of emulsions, used in lotions and creams contribute to retrieve certain rejuvenation and delay psychopathological aging process. Due to their anti-oxidants such as polyphenols, vitamin C and vitamin E.



Emulsions are defined as the dispersed system which consists of small globules of dispersed phase of liquid that are distributed into an immiscible vehicle. An emulsifying agent is known to possess hydrophobic and hydrophilic parts. When surfactant is adsorbed on the water and oil interface reduces the interfacial tension and helps in distribution of small globules in dispersion medium. The two types of emulsions are commonly used in cosmetics, the oil-in-water (O/W) type emulsion which is used in general cosmetics and hydrophilic drug bases. ii) water-in-oil (W/O) type of emulsion is used for the dry skin as emollient. O/W emulsions consist of an oily internal phase (upto 55%) and an aqueous external phase. The emulsifier agent needs to be hydrophilic and may be ionic or non-ionic. W/O emulsions system consists of an aqueous internal phase (up to 45%) and an oily external phase. The emulsifier agent needs to be lipophilic in nature.

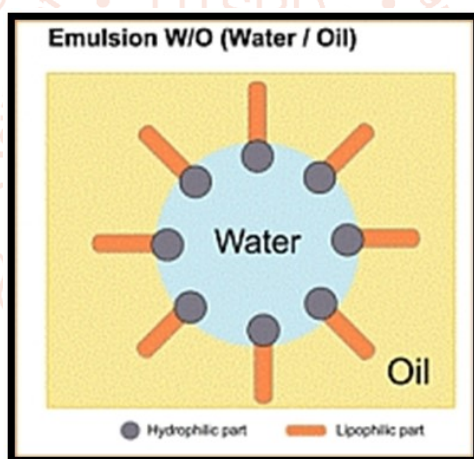


Fig: Water/Oil (W/O) emulsion.

Another type of emulsion, it is due to complexity in nature and instability issues, it is termed as multiple emulsions. In these systems, water-in-oil-in-water (W/O/W) emulsion or oil-in-water-in-oil emulsion can be produced. The macro emulsions are also known as conventional emulsions / colloids are depending on the density of dispersed phase and dispersion medium, droplets sediment or float. The adsorption of solids onto their surface is called as Pickering emulsions. Nano-emulsions systems have been used as a vehicle for drug delivery of NSAIDs and targeted drug delivery for anti-cancer drugs and cosmetics. The recent nanoemulsions system constitute to the promising vehicles for the development of theranostics and cosmetics.

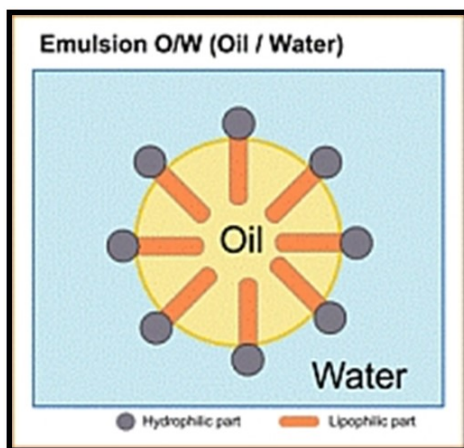


Fig: O/W (Oil/ Water) Emulsion

➤ Therapeutic Nanodelivery Systems:

The efficiency of oral administration route is most acceptable way for drug delivery due to simplicity of administration, pain avoidance, patient compliance and self administration. However, the disadvantage for this delivery substantially reduces the efficacy due to chemical and enzymatic barriers, therefore the therapeutic compounds loaded into nanocarriers has gained importance. Another purpose is to develop novel multifunctional nanomaterials possessing properties for transfer of particular therapeutics across various biological barriers and having ability to target specific cell types. These contain two type of nanodelivery systems:

- Solid (nanocrystals, lipid and polymeric nanoparticles)
- Liquids (Nanoliposomes, nanoemulsions and nanopolymerosomes)

Nanocrystals:

These are the sub- micron colloidal dispersion systems consisting of pure drug nanoparticles. These usually range from 10-800nm. These can be achieved by mechanical or physical methods. The advantage of these system include reducing particle size to nanoscale range, increase in surface area which is in contact with the dissolution medium. These have potential therapeutic effect as compared to conventional pharmaceutical application. These shows improve saturation solubility and high drug loading.

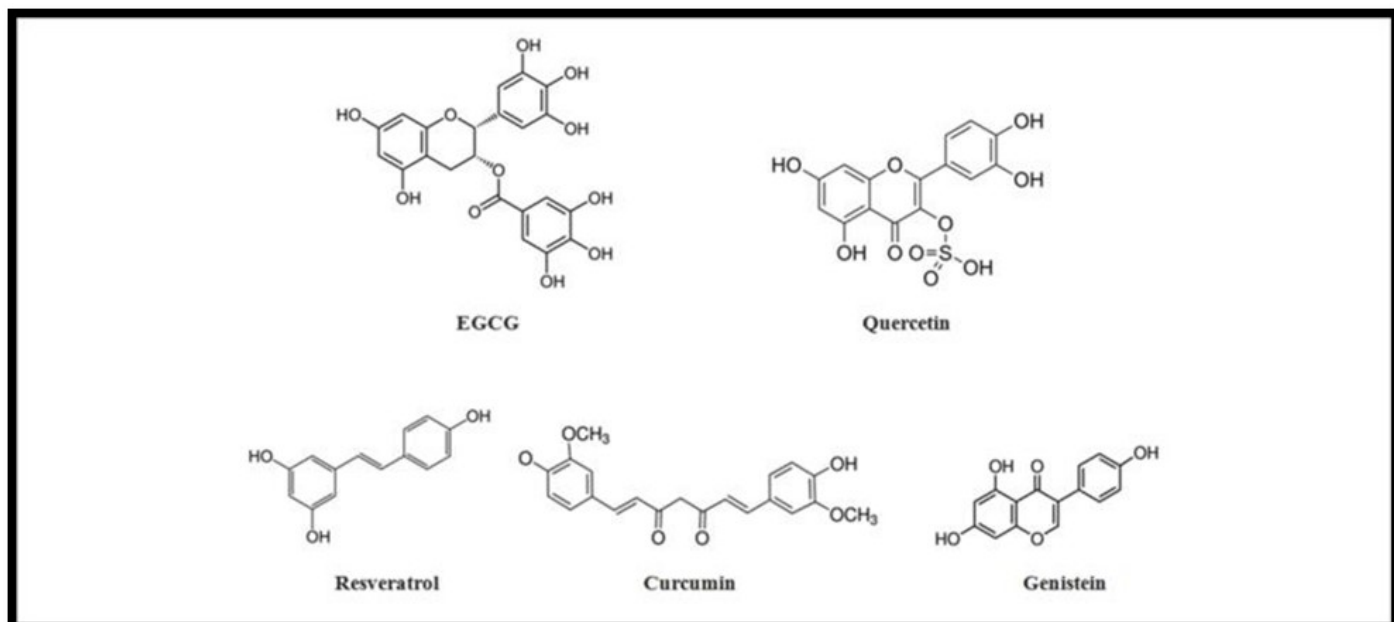
Solid lipid nanoparticles:

Solid lipid nanoparticles are similar to nanoemulsions, except they contain lipid in solid phase. These sub-micron colloidal nanocarriers range from 50-1,000 nm. SLP are produced by high energy methods such as microfluidization and ultrasonification. The advantage includes small size, large surface area, high drug loading capacity and interaction of phases at the surface. The loading of therapeutic agents takes place in two ways: They can be attached to surface of nanoparticle and integration in the core matrix. One of the important advantages is that it allows entrapment of lipophilic molecules in stable particles without applying organic solvents.

Polymeric nanoparticles:

Polymeric nanoparticles include solid colloidal nanoparticles sized from 10-1,000 nm consisting of natural and synthetic polymers. These show modification such as bulk conducting, high electrical conductivity, high electrochemical activity, large surface area and short chain lengths for transport of ions. The methods for preparation of polymeric nanoparticles are nanoprecipitation, solvent evaporation, salting -out, dialysis and supercritical fluid technology. These can be directly synthesized by the polymerization of polymers such as mini and micro – emulsion, interfacial polymerization and controlled living polymerization methods. Drug- loaded polymer nanoparticle synthesis is carried using biodegradable and biocompatible polymers or copolymers, in which therapeutic agents are encapsulated within the carriers physically adsorbed or chemically linked to the nanoparticle surface. Polymeric nanoparticles fall into two categories:

- Nanospheres where loaded agents are uniformly distributed
- Nanocapsules where therapeutics are confined into oily cavities surrounded by polymeric membrane.



Metallic nanoparticles:

Metallic nanoparticles with diameters ranging from 1-100 nm such as silver, gold, copper, magnesium, aluminium, titanium and zinc ones are increasing being applied for active or passive drug delivery in different biomedical applications. The important advantage for metallic nanoparticles is they can be synthesized and modified using various functional groups to target certain cells and tissues.

Nano-phytoantioxidants: -New promise in Anti-aging research

Many nanodelivery systems loaded with plant -based bioactive compounds have been formulated to be efficacious modulating oxidative stress and related chronic inflammation which prevents most of the anti- aging disorder

Nano-Resveratrol:

Resveratrol (3,5,4'- trans – trihydroxystilbene) is a polyphenol compound found in grapes skin and seeds and in lesser amounts in other plant sources. The main role in plants it acts as a phytoalexin, protecting them from pathogens such as fungi and bacteria. The antioxidant capacity of resveratrol depends on redox properties of phenolic hydroxyl groups and has potential for electron delocalization in the chemical structure. Antioxidant properties of resveratrol are believed to be responsible for health promoting effects. It acts as an anti-inflammatory, cardioprotective, neuroprotective and anti- cancer properties. It acts as a calorie restriction mimetic. It is used to treat metallic syndrome, obesity, cardiovascular disorders, chronic kidney and inflammatory diseases, breast and colorectal cancers. The therapeutic applicability of resveratrol is substantially reduced through extensive hepatic and presystemic metabolism.

Nano- Curcumin:

Curcumin is a polyphenol extracted from rhizome of turmeric plant, *Curcuma longa*. It is used traditionally in herbal treatment. These contain three chemical components one diketone moiety and two phenolic groups. The active functional groups of curcumin undergo oxidation via electron transfer and hydrogen abstract process. Some of these complex exhibit antioxidants by enzyme mimetic activities. The polyphenol compound exhibit anti-inflammatory, anti- neurodegenerative and anti- cancer activities. The conditions which are treated with curcumin are oxidative stress, inflammation, atherosclerosis, cardiovascular and neurodegenerative diseases, type 2 diabetes, osteoporosis, rheumatoid arthritis.

Nano- Quercetin:

Quercetin is a bioactive flavonoid with strong antioxidant properties., including its effect in ROS levels. It also has its effect on cellular signal transduction pathways and activities of antioxidant enzymes. The antioxidant activity of this polyphenolic flavonoid is mainly attributed to metal ion complex and complex ions.

When quercetin reacts with a free radical, it donates a proton and becomes radical itself. Quercetin loaded solid lipid nanoparticles have been recently developed which improves bioavailability as compared to quercetin powders. Quercetin- loaded nanoparticles also improve antioxidant defence mechanisms in animal models. quercetin loaded silica nanoparticles treats inflammatory conditions in different cell lines.

Nano- Genistein:

Genistein is a soy phytoestrogenic isoflavone possessing potent antioxidant activity. These antioxidant properties ability to induce the expression of genes encoding antioxidant enzymes including SOD and CAT. The clinical use of these compound is less due to low bioavailability. When applied in high doses, they show endocrine – disrupting and toxic effects. The oral bioavailability was found to be improved in genistein loaded in polymeric nanomicelles as compared to bulk or suspension powders. PEGylated silica nanoparticles may potentiate it's antioxidant effects. It has demonstrated to be efficient in treatment of age related disorders, neurodegenerative diseases, osteoporosis, type 2 diabetes and cancer.

Nano- Epigallocatechin -3- Gallate:

Epigallocatechin -3- gallate is one of the major polyphenol found in the green tea. The molecules of EGCG is a complex structure. It consists of gallic acid group and a gallate ester linked to flavanol core structure. The gallic acid rings determines its antioxidant properties because they directly capture free radicals. The evidence proved that these compounds show stronger antioxidant properties than other green tea catechins. It is also more effective in ROS scavenging than vitamins C and E. Two- fold higher bioavailability of pH – sensitive EGCG- loaded nanoparticles as compared to EGCG have been demonstrated. This optimized nanotransfersomal formulation was found to reduce the lipid peroxidation and intracellular ROS levels.

**Molecular Mechanisms in Skin Aging:**

- Oxidative stress
- DNA Damage
- Telomere Shortening
- MicroRNA (miRNA) regulation
- Genetic Mutation
- Inflammaging
- Advanced Glycation End Product Accumulation

➤ Oxidative Stress:

It is regarded as the reactive oxygen species (ROS) plays an important role in the dermal extracellular matrix alterations of both intrinsic and photoaging. The sources for producing ROS are mitochondrial electron transport chain, peroxisomal and endoplasmic reticulum (ER), localized proteins, the Fenton reaction and enzymes such as cyclooxygenases, lipoxygenases, xanthine oxidases and nicotinamide – adenine dinucleotide phosphate oxidases.

➤ **DNA damage:**

When skin is exposed to UV radiation increases DNA damage and mutations and leads to premature aging or carcinogenesis. When DNA absorbs photons from UV- B, structural rearrangement of nucleotide occurs, resulting in defects of DNA strands. Once the deficiency of protein occur, damage of DNA and premature skin aging occurs. The use of sunscreen products prevents DNA damage in vivo and protects the skin from squamous cell carcinoma and melanoma

➤ **Telomere shortening:**

Telomeres are the repetitive nucleotide sequences that cap and save the ends of chromosomes from degradation and abnormal recombination. These become shorter on every cell division and results in cellular senescence and limited cell division. Telomerase is a enzyme that add telomere repetition to ends and prevents telomere from shortening. Telomerase defecient nice exhibited accelerated telomere shortening resulting in defective tissue regeneration. Also the plorification capacity of epidermal stem cells with short telomeres were suppressed. On exposure to UV radiation, further there is excessive ROS production, resulting in telomere mutation, and further cell death or senescence.

➤ **MicroRNA Regulation:**

miRNAs are a class of conserved noncoding RNAs that bind to the 3' untranslated region of target m RNA to promote their degradation or inhibit their translation. miRNA dysregulation is found to occur in cellular senescence and organisamal aging. Hyaluronam is a kind of polysaccharide in extracellular matrix. Both aged and senescent fibroblasts showed increase in miR-23a-3p expression and secrete significantly lower amounts of HA as compared to young and nonsenescent fibroblasts.

➤ **Genetic Mutation**

Genetic mutation causes progeroid synthesis, such as Hutchinson- Guilford progeria syndrome (HGPS), Werner Syndrome, Rothmund – Thomson syndrome, Cockayne syndrome, ataxia – telangiectasia, and Down syndrome. Gene Mutation is inherited and causes progeria, type of premature aging, accelerated skin aging phenotype, skin atrophy and sclerosis, thinning and graying of hair. HGPS is caused by mutation of gene LMNA, which produces progerin, a mutant protein that supports many important cellular process.

➤ **Inflammaging:**

The chronic, low-grade inflammation is major characteristics of aging process. This phenomenon is termed as “inflammaging”. It plays and important role in the initiation and progression of age related disease, cardiovascular diseases, frailty, sarcopenia, osteoporosis and skin aging

UV radiation induces oxidative stress in epidermal cells, resulting in damaged cells with oxidised lipids.

➤ **Advanced Glycation End Product Accumulation:**

Advanced glycation end products are formed by nonenzymatic process called glycation during which proteins, lipids or nucleic acids are covalently bound by sugar molecule such as glucose and fructose resulting in Inhibition in normal function of target molecules. Glycation is involved in both intrinsic and extrinsic aging. Long- lived proteins in dermal matrix and cytoskeleton are particularly susceptible to glycation resulting in tissue stiffening and reduced elasticity. Among extracellular proteins, glycated elastic fibres abnormally aggregate and unusually interact with lysozyme in skin of solar elastosis but avoiding sub- protective sites, indicating that glycation is involved in photo aging.

Rationale of Skin- Aging Benefits:

There is emerging evidence that topical application of some emulsified plant extracts or pure phytochemicals can improve the skin appearance and also reduce number of degenerative diseases as well as skin conditions such as skin inflammation, skin cancers or skin Aging. The ongoing challenge is that to determine qualitatively and quantitatively from the psychopathological view through which phytochemicals are encapsulated into emulsions is an efficient and safest method. Recent advances in biotechnology have demonstrated the feasibility of encapsulating plant extracts or derived pure phytochemicals into various types of carriers in order to specifically target the damaged tissue while enhancing the bioavailability and reducing their cytotoxicity. Topical or local application of phyto-agents appears to be suitable for skin aging prevention and skin therapy.

Nano-Phytoantioxidants: New Promise in Anti – aging research:

➤ Nanodelivery systems loaded with plant- based bioactive compounds have been efficiaous in modulating oxidative stress and related chronic inflammation which mediates most aging- associated disorders. Accumulating evidence indicates that nano- phytoantioxidants have a potential in preventing and tea wide

range of aging- associated pathological conditions. In several animal models, orally administered nano-phytoantioxidants demonstrated a powerful potential in combating cardio- metabolic disorders than raw forms. Treatment with curcumin loaded nanoparticles led to attenuation of palmitate – induced cardiomyocyte apoptosis in H9C2 embryonic rat heart- derived cells. Nano- phytoantioxidants therapy has also shown promising solution in treating rheumatoid arthritis, caused by chronic inflammatory process. Innovative nanobiotechnology have been recently developed in anti- cancer therapy. These approaches helps drug directly to tumour sites without damaging the nearby healthy tissues. The effectiveness of nanobiotechnology has shown in combating neurodegenerative disorders such as Alzheimers and Parkinson’s disease. These approaches are also important in treating disorders of therapeutic area because blood brain barrier plays an important role in delivering pharmaceuticals to the brain. Curcumin loaded solid lipid nanoparticles and resveratrol loaded N – trimethyl chitosan -g- palmitic acid and surface modified solid lipid nanoparticles. Various nanocomposites administered by intranasal and intravenous route shows improved bioavailability to the brain as comparison to free drug administration. Quercetin loaded solid lipid nanoparticles provided enhance quercetin delivery to the brain along with improved antioxidant effect to the brain cells compared to those of pure quercetin It also improves mental retention in Alzheimers disease.

Applications of Phytoantioxidants:

- Anthocyanins and their derivatives found in foods protect against a variety of Future prospects of using Emulgel:
- The nano emulgel drug delivery system is a formulation to improve the systemic delivery and therapeutic profile of lipophilic drugs. Nanoemulgel is a mixture of two different systems in which nanoemulsions drugs are incorporated into gel base. Lipophilic drugs can be easily formulated and enhancement of skin permeability by several folds of droplets due to nanoemulsions phase. Also the pharmacokinetics and pharmacodynamic are significantly increased.
- Patent Ability of Emulgel:
- An increasing trend in topical nanoemulgel use in recent years has been noticed due to their better acceptability due to their invasive delivery, avoidance of gastrointestinal side effects, easier applicability and good therapeutic profile. Nanoemulgel has considered as a promising formulation and great potential for drug delivery. The hydrophobic drugs are also formulated using emulgel as a novel drug delivery. through a number of mechanisms. Cyanidins found in most fruit sources of anthocyanin have been” function as a potent antioxidant in vivo”. Cyanidins protect cell membrane lipid from oxidation by a variety if harmful substances.
- Proanthocyanidins (OPC) works as a DNA mutation inhibitor. OPC blocks elastase, maintain the integrity of elastin in the skin acts as a synergistically with both vitamin C and E,protect and replenish them.
- Grape seed Proanthocyanidins (GSP) are potent antioxidants and free radical scavengers. GSP inhibit skin tumour formation.
- Apigenin is a widely distributed plant flavonoid are effective against prevention of UVA/UVB induced skin carcinogenesis.
- Dieatory carotenoids from a healthy unsupplement diet accumulate in the skin and their level significantly correlates with sun protection.
- Tea (camellia sinesis is a common home remedy for sunburn. The Chinese recommended applying cool black tea to the skin to soothe sunburn. The tannic acid and theobromine in tea help to remove heat from sunburns. Other compounds in tea catechins helps to prevent skin damage and helps to prevent chemical and radiation induced skin cancers.
- The reputable Aloe Vera or Aloe barbadensis has been scientifically proven to treat all forms of radiation, include radiation, thermal or solar. It also show prophylactic effect used before, during or after skin damaging events. The plants is mainly used for soothing and cooling effect. It also improves the collagen production process.

- Walnut extract is made from fresh green shells of English Walnut *Juglans regia*. It is used in self-tanning sunscreen agent. These are the coloured compounds and have UV protection properties. Juglone is known to react with the keratin proteins present in the skin to form sclerojuglonic compounds.
- Borage (*Borago officianilis*) oil stimulates skin cell activity and encourages skin regeneration. It contains high levels of gamma – linolenic acid useful in treating allergies, dermatitis, inflammation and irritation.
- Evening promise oil (*Oenothera biennis*) oil has a high GLA content that promotes healthy skin and skin repair. It soothes skin problems and inflammation. It also used as a good choice for eczema, psoriasis or any type of dermatitis.
- High-quality, natural suntan and after-sun products are found in Avocado (*Persa Americana*) oil is rich in vitamin E, vitamin D, protein, lecithin and fatty acids.
- The Antioxidant vitamin E tocopherol may protect both animal and plant cell membranes from light – induced damage. Topical application of these anti-oxidants to the skin has shown reduce acute and chronic photodamage. Alpha – tocopherol and tocotrienol reduce skin roughness, length of facial lines and depth of wrinkles. Topically applied vitamin E increases the hydration of stratum corneum and increases water-binding capacity.

Herbal source of extract	Effects
Green tea, black tea (<i>Camellia sinensis</i>)	Soothe sunburn and remove heat from sunburns Repair Skin damage Anti-inflammatory and anti-ageing effects Protect epidermal Langerhans cells
Aloe vera (<i>Aloe barbadensis</i>)	Prophylactic effect during, before and after skin damage. Soothing and cooling effect Self-tanning sunscreen Accelerate collagen production process
Rhatany (<i>Krameria triandra</i>) root extract	Anti-oxidants Photoprotective Cytoprotective effect Radial scavenger
Borage (<i>Borago officianilis</i>) oil	Encourage skin regeneration Stimulate skin cell activity
Evening primrose (<i>Oenothera biennis</i>) oil	Soothe skin inflammations
Avocado (<i>Persea americana</i>) oil	Natural suntan Soothe and protect skin
Tea tree (<i>Melaleuca alternifolia</i>)	Antiseptic Fungicide Relieve sunburn Provides nutrients to damage skin

Natural Substances for skin protection

Active agent	Natural sources	Effects
Anthocyanins	Strawberry, banana, red radish, potato	Antioxidant, protect cell lipid from oxidation, neutralization of enzymes that destroys connective tissue, anti-inflammatory, repair damaged proteins
Pelargonidin	Strawberry, banana, red radish, potato	Antioxidant, protect cell lipid from oxidation, neutralization of enzymes that destroys connective tissue, anti-inflammatory, repair damaged proteins
Cyanidin	Apple, blackberry, elderberry, peach, pear, fig, cherry	Antioxidant, protect cell lipid from oxidation, neutralization of enzymes that destroys connective tissue, anti-inflammatory, repair damaged proteins
Proanthocyanidins (OPC)	Grape seeds (<i>Vitis vinifera</i>) White pine (<i>Pinus maritima</i>) Blackjack oak (<i>Quercus</i>	DNA mutation inhibitor, block elastase antioxidant, free radical scavengers

	marilandica)	
Resveratrol	Grapes, wine, grape juice, peanuts, berries of Vaccinium species	Antioxidant, antimutagenic, anti-inflammatory, inhibited tumorigenesis
Quercetin	Evening primrose, mayapple, onion, tea, neem, sunflower, apple	Anti-inflammatory, anti-oxidants, immunomodulator, inhibit skin tumour formation, potential topical sunscreen
Apigenin	Citrus fruit, peppermint, lemon, marigold, Artemisia	Prevention of UVA/UVB – induced skin carcinogenesis, anti-inflammatory
Silymarin	Milk thistle (Silybum marianum)	Antitumour, reduce UV – induced sunburn cell formation, antioxidant
Curcumin	Turmeric (Curcuma lounga)	Anti-inflammatory, antitumoural, antioxidative, free radical scavenger

Future Prospects of Phytoantioxidants in Skin-Anti-aging:

The growing awareness of dangers of the sun has influenced the cosmetic industry an sun care segment. Human skin is constantly exposed to UV irradiation present in the sunlight. The need of sunscreen products for a longer period of time is also the recent need. Most the products are targeted at a specific market and nearly every manufacturer has complete range of products. The most recent introductions are focused on children, athletes, one who wants UV protection. In the past two years, most of the cosmetic companies have launched products containing sunscreen, moisturizers, antioxidants and also the combination of all three. The development of novel preventive and therapeutic strategies depends on molecular mechanisms of UV- damage. The newest trend will be stay continuously cool, while remaining in the sun. Cooling is achieved through evaporating water, alcohol, or any low- density vapour producing solvents or materials that leave a cooling effect on the skin. The encapsulation technology that can deliver cooling agent or water through rub mechanism. The other forms are intermittent spray/water based thin emulsion, containing sunscreen, menthols and cooling esters with SPF number and hydroalcohol based systems with silicone and cooling esters in a thin light gel vehicle and fragrance note. It is also important to increase the effectiveness of sunscreen by increasing the skin accumulation of UV absorbance with minimal permeation to the systemic circulation. An ideal products with cosmetic appeal can be constructed in the form of thin sprayable gel with a flim forming polymers combined with cooling ingredients. Number of conventional and novel herbal cosmetics are useful to treat damaged skin. Herbal sunscreens are rapidly replacing the modern sunscreen containing UV filters due to associated side effects of UV filters.

Patent Ability:

The use of Phytoantioxidants in the various UV drug has proved to be a novel drug delivery approach in recent development. These formulations use the natural sources and various natural products which in the end reduce the harmful side effects. The various types of emulsions from macro nanoparticles to Nanoemulsions. Another type of emulsion is the complex type which are the multiple emulsions. Depending on the size, there is development of two novel methods Macroemulsions and microemulsions. These macroemulsions are termed as the conventional or colloidal type of emulsions as they are unstable, sediments floats depending on the density of dispersed phase and dispersion medium. These are also termed as the Pickering stabilization. Microemulsions are the transparent, homogeneous in size, show higher thermodynamic stability and higher bioavailability. The Nanoemulsions are transparent, translucent and stable. These nano emulsions are used as a promising vehicle for non- steroidal and anti-inflammatory drugs. The use of natural components in various cosmetics is termed to be the main guide for scientists and researchers to develop the various novel formulations.

Conclusion:

Radiation causes skin damage. Everybody needs protection from harmful UV lights. There are different ways to protect skin. Skin damage mainly causes by Intrinsic as well as extrinsic factors. The main approach is to avoid direct skin exposure. It was concluded that using single component is not suitable for skin protection. On the contrary, the combination of several natural substances may be considered as a suitable solution. The ideal need is to make the product with natural components, avoiding side effects. It is also necessary to study which combination is stable and show the best effects. There is no such product which can accomplish all requests of consumers. This is the main direction for product development. Consumers prefer the product which show all in one effect. It means that protection from

SUV radiation, anti-ageing and wrinkles reduction, moisturizing and cooling effects on the skin. This request is the main guide for scientists and researchers. The chemical components in various products show harmful effects on the skin. For this reason, there is the recent need to use more and more natural products.

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