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A Review on Ageing and Anti-Ageing Approach

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ABSTRACT

The bulk of the human body is skin, which is also the outermost organ; it serves as our body's first line of protection. The skin suffers from both intrinsic and extrinsic ageing factors as the most voluminous organ of the body that is exposed to the outside world. Ageing is the growing human cycle in which there is incapacity to retain homeostasis and rises in the probability of dying. After a certain period of time, we call ageing the progressive loss of skin elasticity and collagen fibers. There are different symptoms of ageing and skin wrinkling is one of them. Collagen and elastin are our skin's key structural elements, and are actively involved in reducing collagen breakdown to prevent ageing and wrinkling formation. This review overviews both intrinsic and extrinsic mechanism of skin ageing, also the factors which are involved in skin ageing. Though there are various problems which arise due to ageing, there is various anti-ageing treatments which includes, hormone replacement therapy, lifestyle changes, restricted diet, antioxidants, retinoids, anti-progeria strategies, stem cell therapy, telomere modification. There are various natural herbs which can be employed for their therapeutic properties for reduction and prevention of skin ageing. Proper nutrition play major role in this, it has solid potential in preserving youth and vitality. Objective of this review is to focus on various anti-ageing treatment, enlist various natural herbs which are effective for reducing factors responsible of ageing.

INTRODUCTION

As we know that skin is the largest organ of the integumentary system, overall perception of health and well being in human beings depend very much on health and beauty of the skin. There is vital role of skin in protecting the body against pathogens, in immunity, for maintaining water and electrolyte balance and it also play important role in regulating the body temperature[1]. The barrier that segregates body from outer environment is skin. Apart from protecting the body from microbial infection and from water loss, skin has also an important cosmetic role[2]. Being the body's most voluminous organ exposed to outside world, skin is suffering from intrinsic as well as extrinsic factors. The ageing of the skin is marked by features such as wrinkling, laxity, loss of elasticity and rough texture[3]. An intrinsic ageing is an inevitable physiological phenomenon resulting in thin, dry skin, fine wrinkles and progressive dermal atrophy, whereas extrinsicageing is caused by external environmental factors such as smoking, air pollution, exposure to sun and poor nutrition resulting in coarse wrinkles laxity, rough appearance and loss of elasticity[4,5].

Figure No. 1: Exposome factor that have been identified to potentiate skin ageing

The study of ageing skin issues can be categorized according to cellular, biochemical and molecular changes. Ageing is defined as genetic physiological process associated with functional and morphological changes in cellular and extracellular components exacerbated by life-long injury and resulting in a progressive imbalance of organism's regulatory control systems, including hormonal, autocrine, neuroendocrine and immune homeostatic

mechanisms. It is the process of getting older; it involves a decline in energy, stamina, reaction speed, hearing, sexual activity, mobility and basal metabolism. The bones are more brittle, the skin more rigid and less elastic and the teeth shed[6].

Collagen is one of the skin's main building blocks, responsible for the skin's elasticity and strength, and maintaining its versatility. Hyaluronic acid plays a part in maintaining the skin's moisture, structure and elasticity intact, it also promotes the exchange of nutrients and waste materials and is involved in rapid growth. With ageing, the level of collagen, elastin and hyaluronic acid decreases, resulting in a loss of strength and flexibility in the skin resulting in visible wrinkles associated with the thickened epidermis, mottled discoloration, laxity, dullness and skin ruggedness[7]. Hence, there are many anti-ageing approaches used for the treatment of ageing or slow down the ageing process, eg., Stem cell therapy, Hormone replacement Therapy, Retinoids, Antioxidants, Telomere modification, diet restriction, etc[3]. In the last decade, the use of herbal extracts in cosmetics has been growing to reduce the ageing cycle. Owing to their skin beneficial properties, the extract from Aloe vera, Ginseng, Honey, Amla, Turmeric, Wheat, Cucumber, Arjuna, Liquorice, Jatamansi are commonly used in herbal cosmetic industries[8]. There are various factors which causes skin ageing, some of them are list in Figure 2[9].

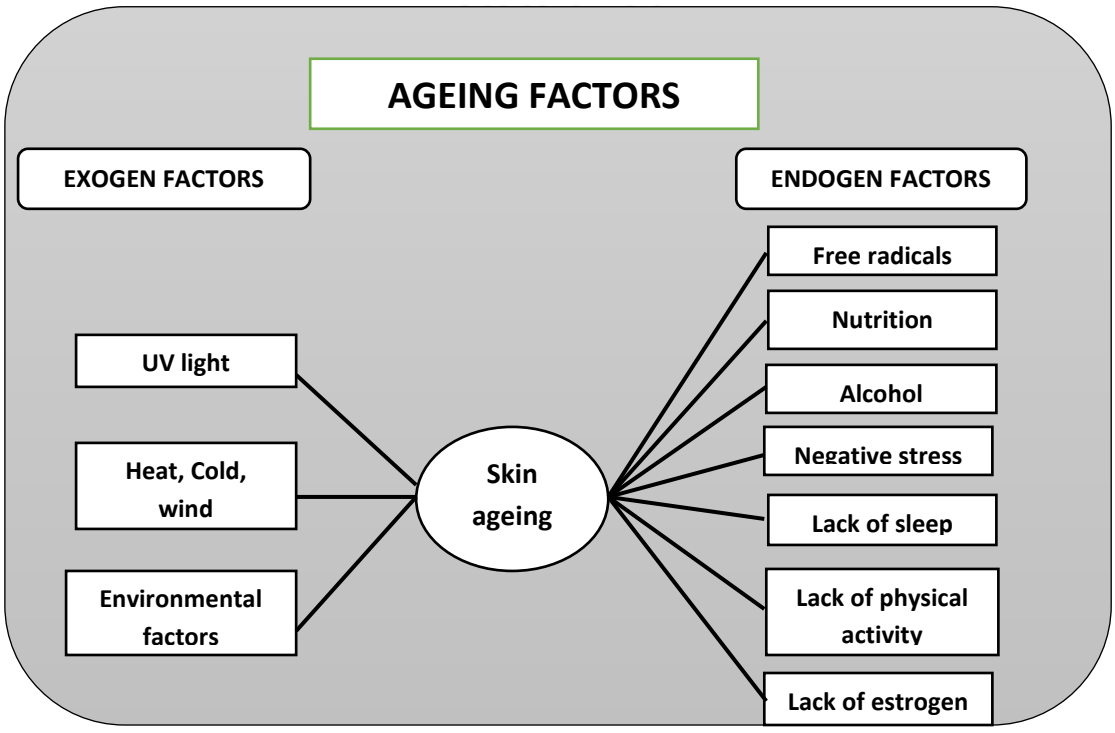

Figure No. 2: Factors causing skin ageing

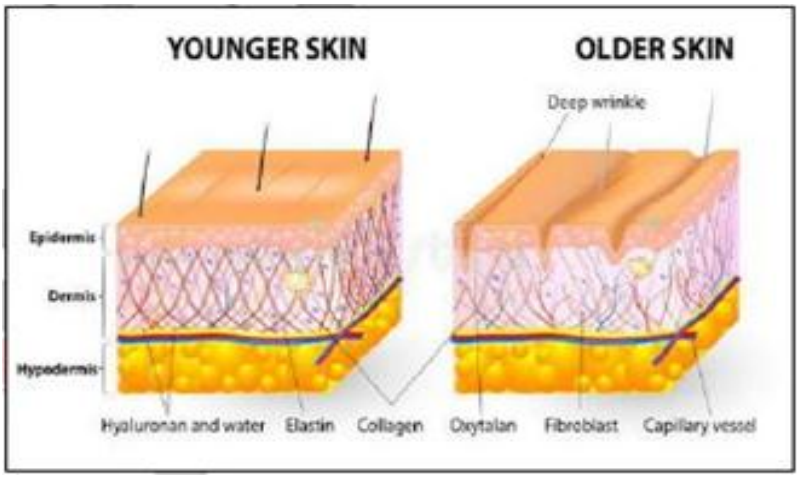

Figure No. 3: Collagen changes during ageing process

There is imbalance between the collagen production and its degradation during ageing, level of production of collagen decreases while collagen degrading enzyme level increases. Important feature of ageing of the human skin is wrinkling, but exact mechanism of its formation is still unknown. One of the major factor in skin health is skin elasticity; low skin tensile strength, excessive stress, unsuitable hormone balance and mutation often contribute to skin tension and wrinkle. Dryness of the epidermal layer induces wrinkling of the skin, so that adequate hydration should be preserved to minimize wrinkles[9,10].

FACTORS INVOLVED IN SKIN AGEING

Photo-ageing:

Chronic repeated exposure of human skin to solar UV rays induces marked changes in morphology, histology, biochemistry and biophysics identified as photo-ageing. Small and coarse lines, actinic keratoses, solar elastosis, pigmentation disorders yellowing premalignant lesions, senile purpura, skin atropy, frenkles, telangiectasia, laxity, ruggedness and extreme dryness are the clinical symptoms of photo-ageing.

UV radiations induces activator protein-1(AP-1) through ROS formation over expression along with the upregulation of collagen degrading enzymes like matrix metalloproteinases (MMPs). It usually induces collagen degradation and inhibits biosynthesis of procollagen resulting in the loss of collagen content and the development of wrinkles, thus inducing skin photo-ageing[11]. Photo-ageing which is induced by UV, can be viewed as a premature skin

ageing. Inflammageing in the skin and other tissues and the roles of complement system and macrophage is shown Figure 4[12].

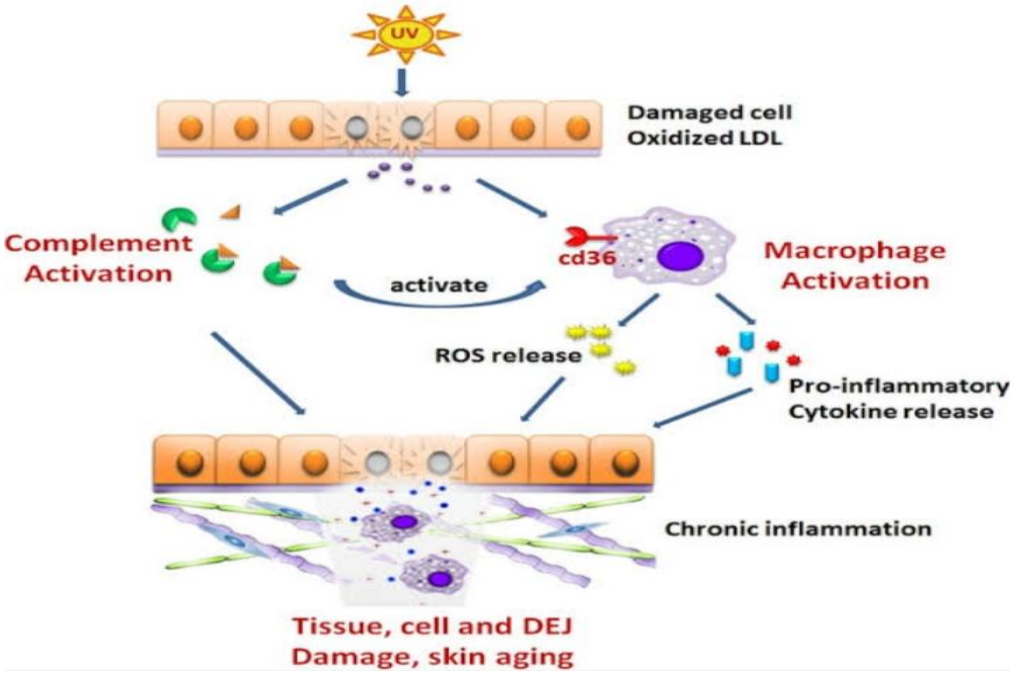

Figure No. 4: Inflammageing in skin and other tissues/ skin matrix damage

Effects of UVR on the Dermal white adipose tissue (dWAT) *in vitro*: UV radiation is able to profoundly modulate the subcutaneous white adipose tissue (sWAT) metabolism. This effect can be observed not only in human skin damaged by chronic sun but also after UV exposure to a single non-damaged skin. In sWAT, the free fatty acid and triglyceride content of sun-exposed skin (forearm) is significantly lower than in the buttocks (sun-protected area) of the same subject. Furthermore, both single UVR and chronic exposure significantly decreases master adipogenic factors like peroxisome proliferator activated receptor γ (PPARγ); this decrease was rapid and remained stable after acute UVR exposure for at least 72 h. From this point of view dWAT content correlates with a much more pronounced extrinsic ageing process in the dorsal hand comparing to the palm area[13].

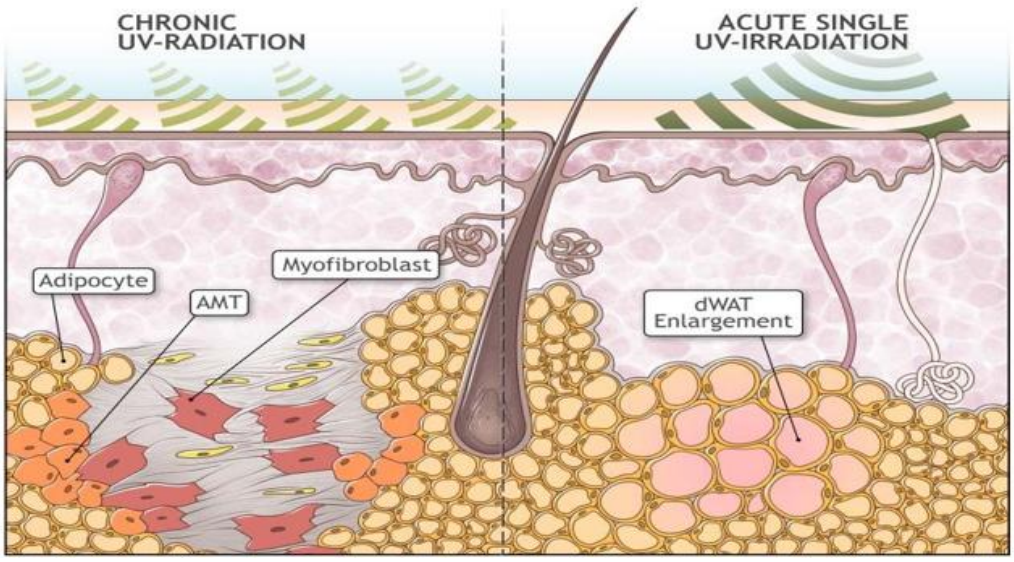

Figure No. 5: Role of Adipocyte myofibroblast transition in the extrinsic ageing

Environmental factors beyond UV radiations

Infrared radiation and heat: IR thermogenic radiation will enter the dermis (65%) and hypodermis (10%), and its ability to induce expression of metalloproteinase in the dermis is well established along with its oxidative role[4]. Chronic IR and heat exposure both induces skin angiogenesis of the skin and inflammatory cell filtration, interferes with the dermal extracellular matrix by inducing metalloproteinases and alterations[14].

Pollution: Damaging effects of the skin exposure to pollutants can lead to skin disorders and pathologies, allergic skin, including xerotic skin, premature skin ageing and accelerated ageing symptoms such as wrinkle development, skin dryness and abnormal pigmentation. Pollutantscan also cause acne, skin rashes, eczema and skin cancers. Particulate matter, Ozone (O_3) and cigarette smoke are one which are most noxious pollutants to which humans are exposed[15].

Lifestyle related factors-

Smoking: It is established that smoking has an aggravating effect on the skin ageing. Even external exposure to the cigarette smoke prematurely ages skin.[16] Smoking has a negative impact on the dermal microvascular particularly due to nicotine and hinders the healing process. This also has a toxic effect on the keratinocytes and fibroblasts by increasing the metalloprotein and tropoelastin expression.[11]

Sleep: Restricted sleep negatively affects the facial appearance and diminishes the ability of others to socialize with the sleep-restricted adult[17]. An estimated 50-70 million US adults are suffering from one or other sleep disorder. Sleep is essential for the multiple physiological system to develop and renew[18].

Diet and Nutrition: Skin sagging, rhytides and loss of elasticity are all associated with changes in the skin's collagen and elastic fibres of the skin which are affected by the diet itself. These signs of ageing can be aggravated particularly by ingestion of sugar, as it promotes cross-linking of collagen fibres. Cooking methods resulting in increased AGE levels include grilling, frying and roasting. Herbs and spices like oregano, cloves, ginger, cinnamon, garlic and substances considered to be naturally uncertain fruits and vegetables, like lipoic acid inhibit AGE production. Frequently studied antioxidants such as carotenoids, flavonoids and tocopherols and vitamins (A, C, D and E) necessary omega-3 fatty acids, other proteins and lactobacilli were preferred as agents capable to promoting fewer wrinkles throughout the skin[19].

Hormone and metabolic processes

The global ageing cycle is impacting all endocrine glands. They are also related to the decreased function of the pituitary gland, adrenal glands, ovaries and testes[20]. Vitamin D, which is a normal metabolism for calcium, is the most important endocrine compounds in the skin and also exhibits many systemic effects. Vitamin D3 and its analogs control many skin physiological processes like differentiation and apoptosis, keratinocytes and skin-related wrinkles associated with chronological ageing or skin ageing[21 .

MECHANISM OF SKIN AGEING

Extrinsic skin ageing:

It is caused by environmental factors like exposure to the sun rays, repeated facial expressions, sleeping positions, gravity and smoking. Extrinsic ageing is caused by prolonged exposure to UV radiation and it is often called as photo-aging.

Membrane/ nuclear signaling: UV irradiation induces reactive oxygen species (ROS) that inhibits the enzyme protein phosphatase tyrosine activity. This enzyme preserves skin cell surface receptors, including receptor factor (EGF), in active (hypophosphorylated) state for

epidermal interleukin growth (IL)-1, keratinocyte growth factor, and tumor necrosis factor (TNF)-α[22]. The activated receptors impel the intracellular signaling by stimulating the kinases p38 and c-Jun amino terminal kinase (JNK) of stress associated protein coordinated with mitrogen (MAP). Activation of kinase stimulates the transcription of MMPs (matric metalloproteinase) and decreases the expression of procollagen I and III and TGF-β receptors, thus reducing the production of collagen.

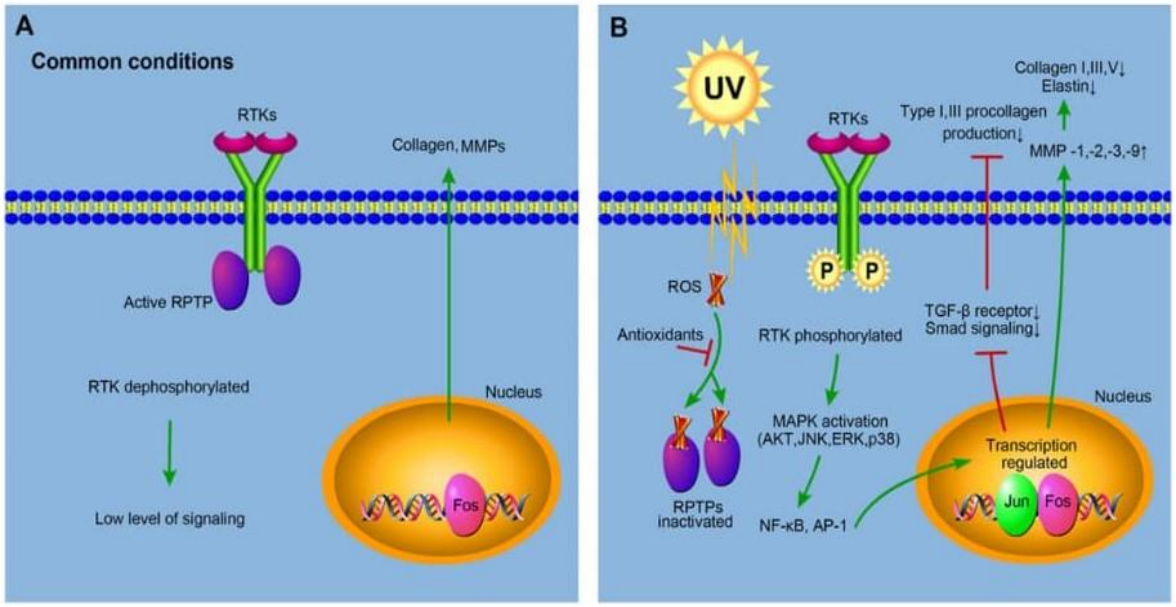

Figure No. 6: Molecular mechanism of reactive oxygen species (ROS) in skin ageing

(A)-Under specific conditions i.e., without the ligands, function of the receptor tyrosine kinases i.e., RTKs on the cell surface is inhibited by the receptor protein tyrosine phosphatases (RPTPs), which then dephosphorylates the RTKs and alsohold low signaling rates, in effect generating normal amount of the collagen and matrix metalloproteinases (MMPs).

(B)- Under UV radiation, ROS is developed which then inhibits the activity of the RPTPs by binding to RPTPs catalytic sites, increasing the level of phosphorylated RTKs and also activating downstream signaling pathways also including activation of the mitogen activated protein kinase i.e., MAPK and subsequent nuclear factor-Kb(NF- κB) and transcription of the MMP gene while AP-1 down regulates the expression of the transforming growth factor-β (TGF-β) type II receptor, leading to decreased phosphorylation of the transcription factor Smads and subsequent repression of collagen development. Hence, the complete amount of collagen content in the photoaged skin reduces.

Mitochondrial damage: Mitochondria are the cellular organelles that generate energy (ATP) by making oxygen compelling. Abundant ROS is provided by the electron transport chain of mitochondria on the effect of UV which can damage the mitochondrial DNA (mtDNA). Mitochondrial genome encoded 13 components of electron transportation chain and oxidative damage may be primarily due to deletion or rearrangement of the DNA**,** most likelydue to double-strand breaks that may impair the mitochondrial capacity to produce energy for the cell. (Figure 7).

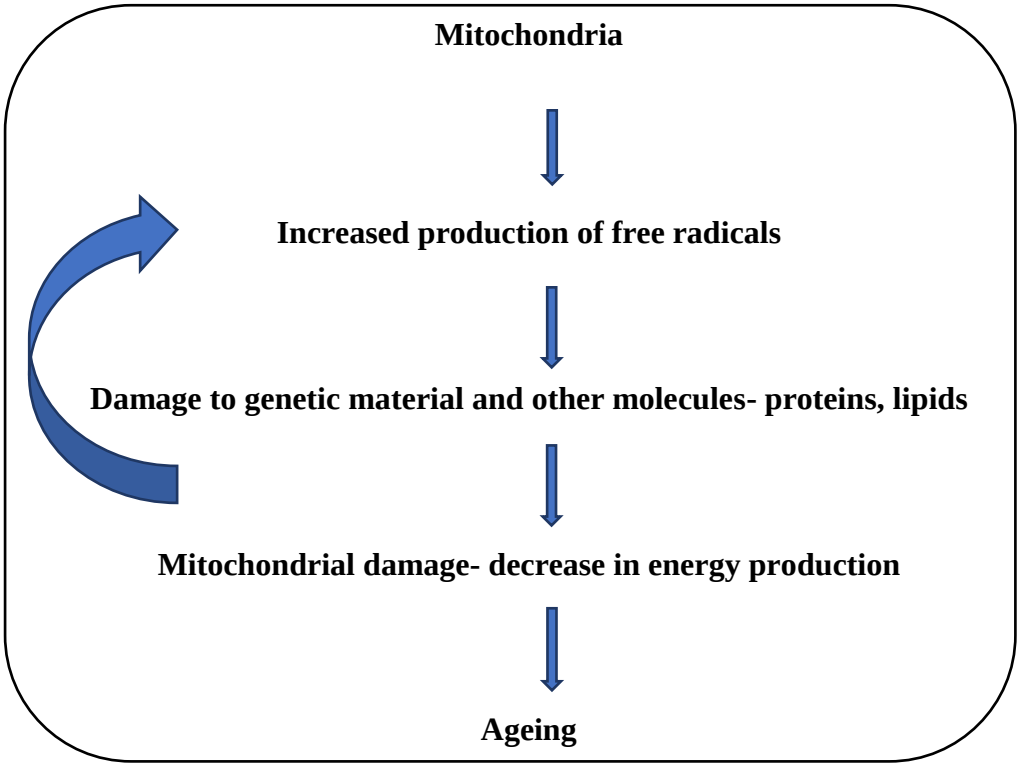

Figure No. 7: Mitochondrial damage

Protein oxidation: Oxidative damage can also affect the photo-damaged skin and proteins. Oxidative protein deficiency may lead to loss or activity gain (i.e., enzymes), increased/reduced degradation susceptibility and loss of structural protein function.

Telomeres: Telomeres are tandem repetitions of short TTAGGG chain, which occurs in a loop of configuration. If these loops are interrupted by cell divisions or UV irradiation, telomeres become critically small. The telomeres cap (the terminal part of chromosomes, preventing the fusion of telomeres with each other) cannot be repeated during cell division, meaning that the telomeres cap bases are lost with each cell division and ultimately enter a state of apoptosis or senescence. When telomeres are weakened by UV irradiation, the loop

structure is exposed and the protein interactionactivates the tumor suppressor proteins p^{53} and other proteins that are responsible for DNA damage and also causes apoptosis or senescence.

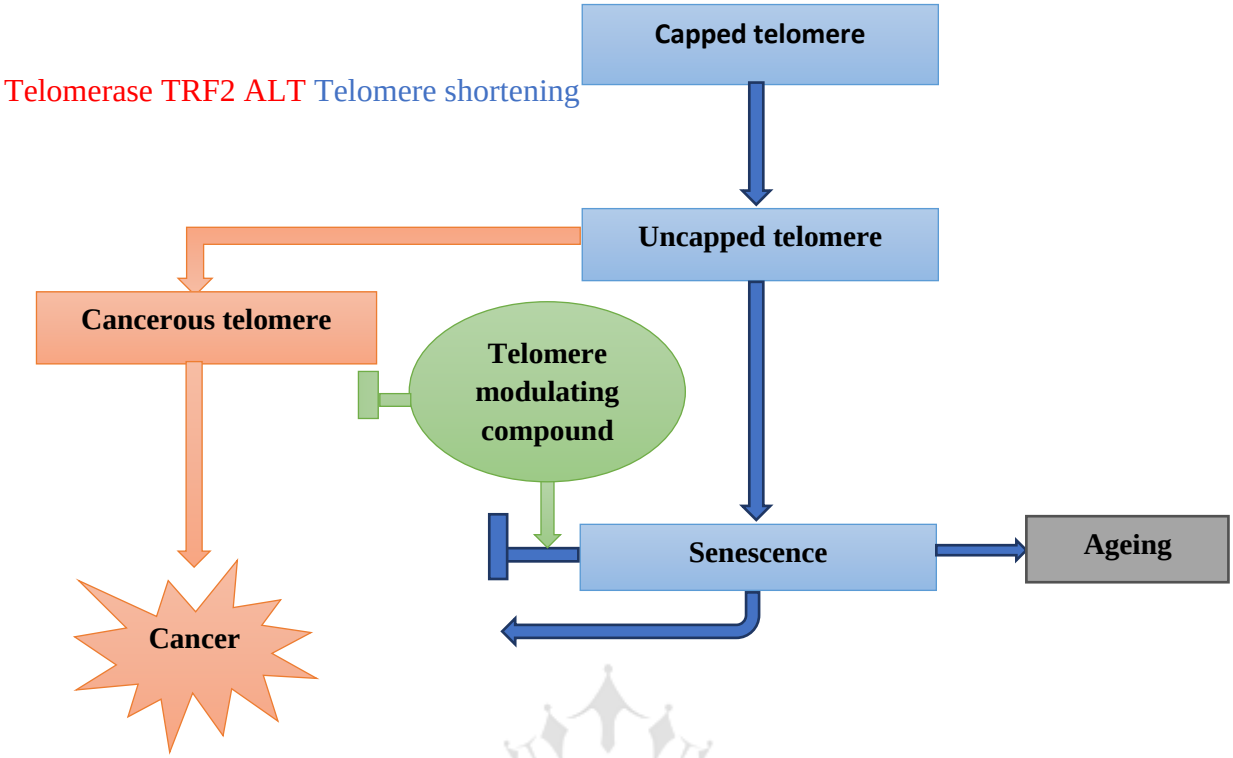

Figure No. 8: Telomere shortening

Intrinsic skin ageing:-

Intrinsic skin ageing, which is also known as natural ageing, is seen mainly in protected area of the sun. This is caused by the passing of time or by the inherited gene, thus also called chronological ageing. Generally the molecular mechanisms in both the form in skin ageing (intrinsic as well as extrinsic) are identical, such as telomeres shortening, genetic mutations, oxidative stress, mitochondrial DNA changes and other hormone levels decreasing. ROS, which begins primarily from oxidative cell metabolism, plays a prominent role in both sequential ageing and photoageing, according to free radical theory of ageing. ROS affects transcription factor c-Jun through MAPK (mitrogen activated protein kinase).

Intrinsic skin ageing is the same as extrinsic ageing, and collagen is damaged close to photoaged skin found in intrinsically aged skin. Intrinsic skin ageing can also be altered by hormonal changes. In the mid-20s, the display of sex hormones in the gonads, the pituitary and adrenal glands already decreased slowly. During menopause the hormone oestrogen and

progesterone continue to decrease. The imperfection of oestrogen and androgens in particular causes atropy of epidermis, wrinkling, dryness, collagen breakdown and loss of elasticity[3].

Inflammageing:-

Low-grade, chronic inflammation is often recognized as an important part of ageing process, this process is termed as "inflammageing". This plays a part in initiation and development of age related diseases like frailty, sarcopenia, Alzheimer's disease, type II diabetes, osteoporosis and skin ageing. In 2014 a model is being proposed based on pervious data to clarify its incidence in the skin[23,24]. In short, UV radiation causes oxidative stress in the epidermal cells, resulting in oxidized lipid cells that are impaired. Oxidation specific epitopes on the damaged cells and oxidized lipids are recognized as inducing inflammation by the complement system.

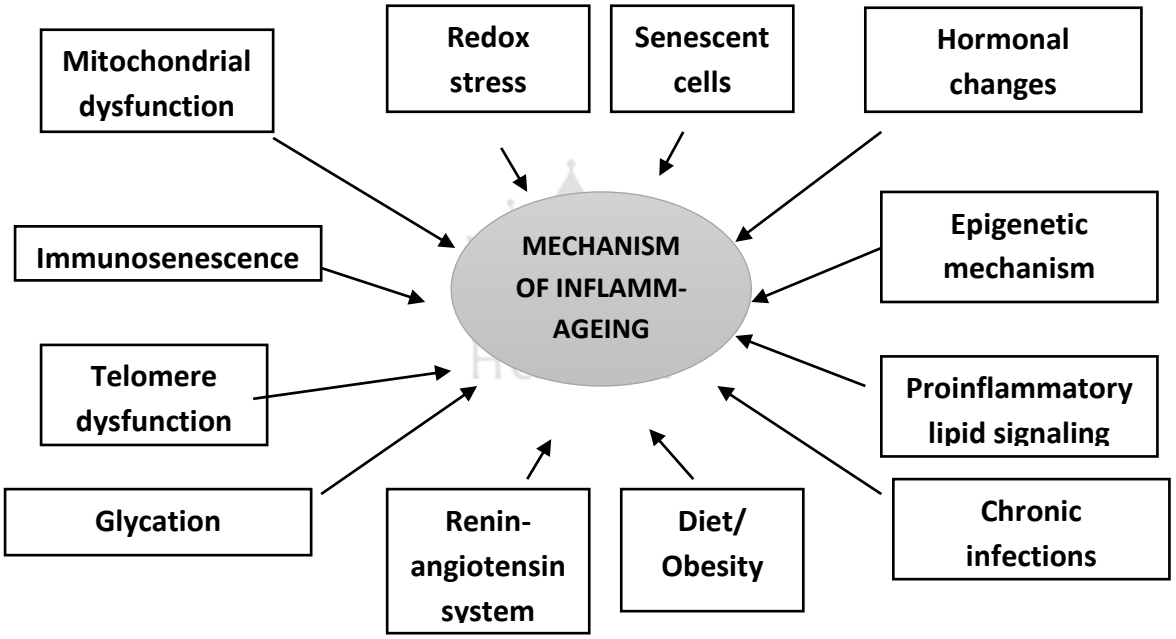

Figure No. 9: Mechanism contributing to age-related inflammation

TREATMENT FOR SKIN AGEING (ANTI-AGEING)

Stem Cell Therapy:

Transplantation of the stem cells is a promising therapy for skin ageing diagnosis. In addition to increasing the skin volume, adipose tissue transplantation may improve skin quality at the recipient site. Additional studies show that adipose derived stem cells (ADSCs) contribute to skin regeneration during ageing. Autologous fat grafting rejuvenates aged skin in recent clinical studies and raises the amount of periocular and perioral skin in recipients with an

average age of 50 years.

Data shows that ADSCs generate a variety of growth factors such as a vascular endothelial growth factor (VEGF), basic fibroblast growth factor (Bfgf), a transforming growth factor (TGF)-b1, TGF-b2, hepatocyte growth factor (HGF), keratinocyte growth factor (KGF), platelet growth factor AA (PDGF-AA), and placental growth factor (PGF) 80, reminding us that ADSC also seemed to be able to transdifferentiate into epithelial stem cells, expressing the epithelial stem cell marker p63 after fat grafting [3].

Antioxidants:

To prevent symptoms which are related to the photo-induced ageing in skin, antioxidants can be effectively used. Antioxidants as a reducing agents can relieve skin ageing by neutralizing already developed ROS[25]. Antioxidants like vitamin C and E, or antioxidant enzymes such as superoxide dismutase, catalase, glutathione peroxidase and co-enzyme Q10 may avoid this. Some herbs like green tea and aloe vera, can also be used as a natural source of antioxidants. Epigallocatechingallate (EGCG), which is a recent example of a kind of green tea catechin, prevents skin ageing in an ageing mouse model through the epidermal growth factor receptor (EGFR) pathway, leading to improved skin structure than the control [26].

The goal of antioxidant treatment is to restore homeostasis of oxygen, instead of removing all oxidants completely because they have their physiological functions.

Retinoids:

Retinoids are chemically identical to vitamin A and tretinoin is first clinically approved retinoid. Topical tretinoin application inhibits AP-1, thereby suppressing MMP expression and preventing collagen degradation. There is an improvement in epidermal thickness and anchoring fibrils, and intrinsically aged skin may also be benefit from topical use of retinoids[27,3].

Hormone Replacement Therapy:

In addition to being used in treatment of menopause-caused symptoms, to reverse the process of skin ageing hormone replacement therapy (HRT) is used. HRT increases skin thickness, collagen content and elasticity and improves hydration. There are research however which indicate that HRT raises the risk of breast cancer.

Telomere modification:

Telomere shortening is mechanism which is underlying replicative ageing in the fibroblasts. While the activation of telomerase seems to be an ideal approach to reverse skin ageing, and indeed high level expression of telomerase reverse transcriptase (TERT) in skin fibroblasts and keratinocytes, it results in significantly increased proliferative ability, but risks of epidermal carcinogenesis meanwhile increase. Further research is therefore required to determine the protection of the enhanced proliferation brought about by the lengthened telomere[28,3].

Diet Restriction:

Since glycated proteins are still potentially infeasible to return to their original state, at present the primary strategy remains on shielding proteins from glycation. But the issue is that diet not only offers sugars such as glucose and fructose but also preformed AGEs, and the latter have a significant amount of grilled, fried or roasted food but rather low content in foods prepared by water based cooking such as boiling and steaming. Hence the consumption of preformed exogenous AGEs and endogenous development of physiologically glycated proteins will be decreased by low sugar food cooked with water.

In addition, as the relation between diet and ageing is more clearly defined, a host of dietary compounds have emerged as potential therapeutic candidates in the inhibition of the AGE-mediated changes. Some scientists claim that some culinary herbs and spices like cinnamon, oregano, cloves and all spice, can inhibit fructose induced glycation, and some compounds including ginger, garlic, carnitine, alipoic acid, carnosine, taurine, flavonoids (eg., green tea, catechins), benfotiamine, tocopherol, pyridoxal, sodium selenite, niacinamide,, selenium yeast, zinc, riboflavin and manga [29,30].

Anti-progeria Strategies:

The original therapies are designed to inhibit farnesylation process, because the fatrnesyl group was considered the predominant deleterious and toxic component in the mutant protein progerin. In a clinical trial, the lonafarnib farnesyl transferase inhibitor was used for 2 year treatment of 25 patients with HGPS (Hutchinson-Gilford progeria syndrome), resulting in improved vascular integrity, bone structure and audiology[31]. Another technique using the combination of 2 drugs, statin and amino-bisphosphonate, effectively blocked both

farnesylation and geranylgeranylation of progerin and prelamin A and significantly enhanced the ageing-like phenotypes of Zmpste 24-deficient progeria mice model like growth retardation, weight loss, lipodystrophy, hair loss, and bone deficiencies [32].

Anti-inflammageing

Given that the mechanism of skin inflammation is far from being completely understood, no progress has been made in developing targeted therapies. Suh et al. reported that treatment with UV-absorbing compound mycosporine like amino acids (MAAs) in the human fibroblast cell line suprresd the gene expression cyclooxygenase-2 (COX-2), which is normally increased in response to skin inflammation. Moreover, after UV irradiation, the expressions of skin-related proteins elastin and procollagen C-proteinase enhancer, which is an significant determinant of procollagen production in the regulation of collagen deposition in the skin, are strongly suppressed but restored to normal levels after MAA treatment as in the control[33].

NATURAL ANTI-AGEING HERBS

Herbal cosmetics are important in preventing and reversing skin ageing. Ingredients used in herbal cosmetics have an effect on the skin's biological functions and also provide nutrition needed for healthy skin. More than 50 % of all drugs in worldwide are believed to be natural products and their derivatives, and plant based remedies are promising. The mechanism of action of various herbs in anti-ageing is shown in Figure 10[1].

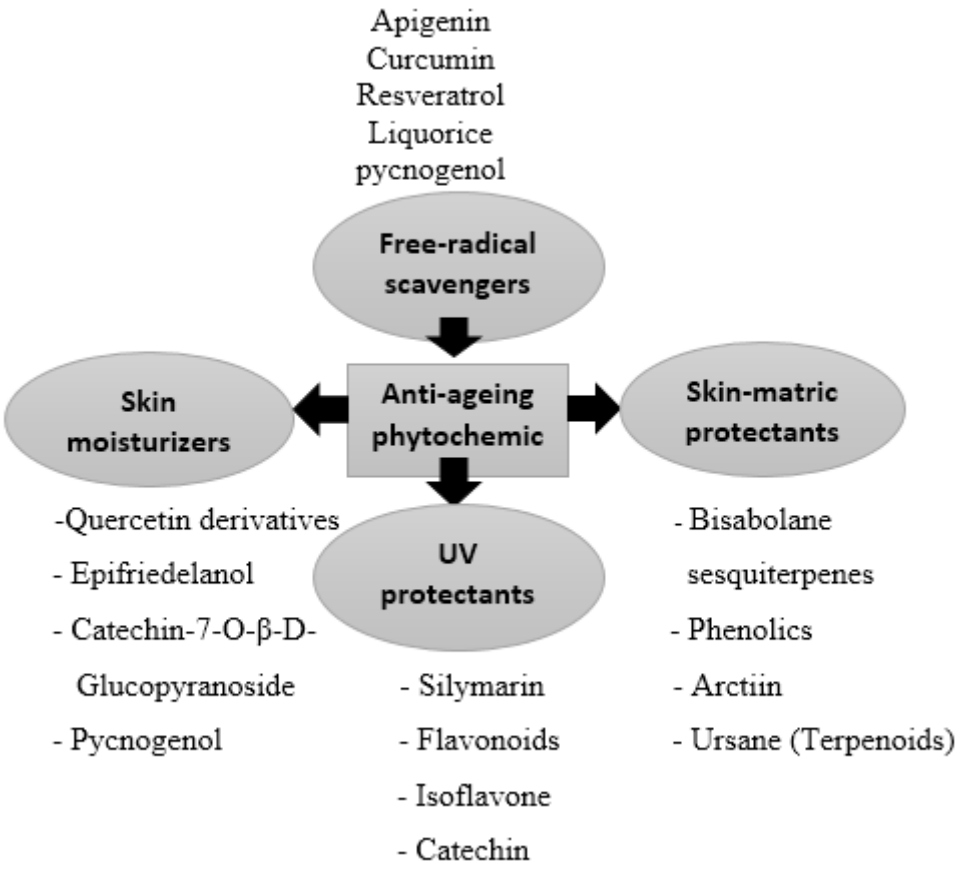

Figure No. 10: Mechanism of action of herbs in anti-ageing

Natural anti-ageing herbs:

There are many natural herbs which are used as anti-ageing, few of them are listed below,

Table No. 1: Natural Anti-ageing herbs

Sr. No.	Herbs	Role in anti-ageing	Image
1	**Ginseng** (*Panax ginseng*)	• Chief constituent of ginseng is Ginsenoside • It is responsible for the anti-ageing activity of ginseng • Improves blood circulation and skin tone	

		• Synthesis of type 1 collagen are induced by Ginsenosides	
2	**Aloe vera** (*Aloe barbedensis*)	• Constituents like aloin A, B shows the property to inhibit the activity of the collagenase (enzyme causing degradation of collagen fibres), which acts as anti-ageing and anti-wrinkles.	
3	**Arjuna** (*Terminalia arjuna*)	• Pentacyclictriterpenoids present in *Terminalia arjuna* enhance collagen synthesis and the epidermal barrier function.	
4	**Liquorice (***Glycyrrhiza glabra*)	• Anti-ageing liquorice activity is induced by the existence of phenyl flavonoids (dehhydroglyasperin C, D and isoangustone A that function as a superoxide scavenger which prevents wrinkles.	
5	**Turmeric** (*Curcuma longa*)	• Curcumin (major constituent of Turmeric) acts as a superoxide scavenger & singlet oxygen quencher.	

6	**Amla (***Emblica officinalis*)	• As amla is a very good source of vitamin C, it is considered to be important for slowing down the process of ageing and improving skin health. • Tannins, ellagic acid and gallic acid shows free radicle scavenging activity.	
7	**Honey** (*Apis mellifera*)	• Honey's antioxidant property is due to the phenolic compounds (i.e., cinnamic acid and benzoic acid) and flavonoids found in it, which helps to avoid skin wrinkles.[1]	
8	**Milk thistle** (*Silybum marianum*)	• Adds skin protection preferably. Silymarin has carcinogenic anti-inflammatory properties as well as anti-photo.	
9	**Japanese Anise** (*Illicium anisatum*)	• Proto-catechuic acid refers to the free radical anise scavenging activity.	

10	**Kasip Fatimah** (*Labisia plumila*)	• The human fibroblast collagen synthesis restores to normal when the extract is applied.	
11	**Nevvari** (*Ixora parviflora*)	• Ixora polyphenols influence the reduction of UVB-induced intracellular reactive agents species of oxygen.	
12	**Dill leaves** (Anethumgraveolens)	• It is found that the dill extract increases skin elasticity, firmness and also reduces wrinkles.	
13	**Cassia** (*Cassia fistula*)	• It plays a potentially important role in increasing the synthesis of collagen and also hyluronidase acid.[9]	
14	**Green tea** (*Camellia sinensis*)	• Epigallo-catechin and the other catechins which are present in green tea prevents adverse effects that are caused by UV radiations[34]	
15	**Pomegranate** (*Punica granatum*)	• Flavonoids, Anthocynincatechins from the peels, seeds and nuts demonstrate antioxidant activity, peels being the more in	

		character[35]	
16	**Coffee** (*Coffea arabica*)	• Caffeine, chlorogenic acid and melanoidin serve as anti-inflammatory agents and resist ageing.[36]	
17	**Soybean** (*Glycine max*)	• Skin cell prevents isoflavones apoptosis and erythema reactions to inflammation.[37]	
18	**Wild yam** (*Dioscorea villosa*)	• Leaf extract of leaves of the wild yam combats the skin inflammation.[38]	
19	**Grapes** (Vitisvinifera)	• Flavonoid astringin (anthocyanins, catechins) and the non-flavonoids (stilbenes) have anti-oxidant properties.[39]	
20	**Oregano** (*Origanum vulgare*)	• Vanillic acid exhibits greater antioxidant activity than orgeno vanillin.[40]	

HOW DOES NUTRITION SLOW DOWN RATE OF AGEING?

One solution is to maintain a safe and well balanced diet, and the good thing is that there are certain foods that are thought to give us extra ammunition when it comes to battling the signs of ageing. Special foods contains special nutrients which:

- Combat muscle fatigue
- Reduced DNA damage
- Neutralize free radicle
- Naturally detoxify

Avocado: It is a good source of safe monounsaturated fate which can help raising the amount of bad body cholesterol form. It is also a good source of vitamin E which can help to maintain healthy skin which avoid skin ageing (vitamin E can also help relieve hot flushes from the menopause).

Dark chocolates: Cocoa beans, which make chocolate, have a higher antioxidant potential than any other food and high concentration of antioxidants flavanols in cocoa beans helps to minimize inflammation of the skin induced by exposure to UV light. In fact, eating dark chocolate will improve the skin's circulation and boost its ability to maintain moisture, which can minimize wrinkle appearance and make you look younger.

Berries: Both black and blue berries like blueberries, blackberries, blackcurrants and black grapes contain phytochemicals which is known as flavonoids and anthocyanins; strong antioxidants that help protect the body from damage caused by free radicals and ageing, delay the growth of some cancers and diabetes and also improves brain function, muscle tone and balance. Vitamin C has been shown to decrease skin redness and to help the skin heal from sunburns.

Cruciferous vegetables: The Cruciferous vegetables family includes cauliflower, kale, cabbage, broccoli, radish, turnip, radish and watercress. They help the body to fight against toxins and cancer. Broccoli can help to protect the skin from damage caused by sun. It is also rich in vitamins like C and A in the skin. Help to prevent problems associated with ageing. Nuts: Most varieties of nuts, especially walnuts and brazi nuts are good sources of mineral.

They can enhance functioning of immune system and improve skin control, and help in reducing cholesterol.

Fish: Fish provide omega-3 fatty acids which help fight body inflammation. People who eat multiple portions of fish a week have lower risk of Alzheimer's disease and stroke. Omega-3 fatty acids are known to avoid premature ageing.

Oatmeal: Non-instant oatmeal is high in B vitamins, and also gradually increases blood sugar. This prevents you from being hungry right after you eat. Oatmeal is also a great source of magnesium which is also essential foe healthy skin.

Yogurt: Yogurt is an excellent source of calcium, phosphorous and vitamin D. All of these are essential to skin. Additionally, plain yogurt also contains healthy bacteria which make digestion easier than milk. Yogurts also contain probiotics that can reduce the inflammation your skin may have and raise the levels of oxygen your skin receives.[6]

Table No. 2: Skin anti-ageing approaches

Cosmetological care	Correct sun protection, daily skin care, aesthetic non-invasive procedures, visible light devices, chemical peelings, intense pulsed light (IPL), radiofrequency.
Topical medical agents or topical agents	Antioxidants, cell regulators
Invasive procedures	Injectable skin bio-stimulation and rejuvenation, correction of static, prevention of dynamic wrinkles, anatomical wrinkles, skin augmentation and contouring, restoration (redistribution) of fat and volume loss
Systemic agents	Hormone Replacement Therapy (HRT)
Avoiding of exogenous factors of ageing, correction of habits and lifestyle	Pollution, smoking, solar UV irradiation, nutrition, stress, diet, physical activity, restriction and alimentary supplementation, control of general health.[41]

TOPICAL ANTI-AGEING PREPARATIONS

Ascorbic Acid (AA): It was used as a skin lightener. AA also serves as an important co-factor for the enzymes lysyl hydroxylase and prolyl hydroxylase, both of which are necessary for post-translational collagen biosynthesis (Types I and III). Therefore, ascorbic acid can increase the production of collagen by stimulating these biosynthetic steps, leading to a reduction in wrinkles.

Ceramide: Ceramide prevalent moisturizers have become a standard in skin disease care. Moisturizing treatment requires a four-step process: a) repairing the skin barrier; b) increasing water content; c) decreasing TEWL; and d) restoring the capacity of lipid barriers to absorb, retain and redistribute water. Ceramide cream improves skin hydration and enhances barrier function that can make it ideal for dry skin use[11].

α-lipoic acid: α-lipoic acid (ALA) is a naturally occurring sulfhydryl compound present in nearly all plant and animal species and in both prokaryotic and eukaryotic cells. This is bound to lysine residues in the human body, and functions as a cofactor in various complexes of multienzymes. Topical application of 3 percent lipoic acid has shown its ability to minimize erythema caused by UVB, demonstrating its photoprotective and anti-inflammatory properties[42].

Retinoids: Retinoids play a significant role in development of the skin and control keratinocyte growth and differentiation. Retinol, retinyl esters (eg., retinyl propionate, retinyl acetate and retinyl palmitate) and retinaldehyde are the most commonly used ones. All of these are ultimately converted to trans-retinoic acid (trans-RA), which is the active form of vitamin A in the skin, through endogenous enzymatic reactions. In particular, the retinyl esters are converted through esterases to retinol. Then, retinol dehydrogenase is converted to retinaldehyde by retinol (ROL). Lastly, retinaldehyde gets oxidized to RA by retinaldehyde oxidase. Retinol and retinal have to be metabolized to the active trans-retinoic acid in the blood. Topical natural precursors of retinoic acid, like retinaldehyde or ROL, are less irritant than acidic retinoids.

β-glucans: β-Glucan is a dietary fiber which is present in many natural sources and effectively controls chronic metabolic diseases. In the epidermis, where macrophage-derived cells include keratinocytes as well as Langerhans cells, β-Glucans serve as our first line of defence to activate the defensive qualities of these cells. Topical β- Glucans can improve

wound healing by enhancing macrophage-mediated phagocytosis and increase infection resistance. β-Glucans are extremely soothing and relaxing to the skin by strengthening the skin macrophages.

Nicotinamide: There are two possible sources of niacin (vitamin B3) that can be used in cosmeceuticals: niacinamide (nicotinamide) and nicotinic acid. Topical nicotinamide (the active source of vitamin-B3) has been shown to enhance hyperpigmented spots of the fine lines and wrinkles, red blotchiness and sallowness (yellowing) and elasticity. Furthermore, nicotinamide has been shown to increase collagen and ceramides development in the skin, and to promote keratinocyte differentiation, resulting in improved barrier function and skin appearance.

β-Hydroxy Acids (BHAs): BHAs like salicylic acid, are very similar to AHAs except for their solubility variations. In addition to showing the anti-inflammatory effect of BHAs (eg., salicylic acid), they have also been shown to be the skin irritant effect than AHAs. A topical mixture of 2% salicylic acid, 10.4% L-lactic acid, and alpha-hydroxy acid/ retinoate conjugate (ethyl lactyl retinoate) was used in the topical treatment of females aged 20-58 years. Improvement was achieved after 4 weeks, which stayed steady and cumulative in the 8th week[42,11].

α-Hydroxy Acids (AHAs): Hydroxy acids, which is also called as fruit acids, are among the non-organic acids that have been used for about 50 years in the treatment of skin disorders. These are some of the skin care chemicals most commonly used and researched for anti-ageing. The pH and concentration levels of the effects of AHAs are calculated.AHAs function on epidermal as well as dermal levels. By interfering with the ionic bonding between these cells, AHAs stimulate the exfoliation of epidermal cells in the stratum corneum when applied to the skin. This results in dry and raw skin sloughing off and encourages cellular regeneration[42,43].

Coenzyme Q10 (CoQ10): It has been reported as powerful anti-oxidant in the plasma. Coenzyme Q10 (a ubiquinone) is a potent free radical inhibitor which inhibits the formation of lipid peroxides in plasma membranes. Q10 plays a very important role in the production of cellular energy, and functions in the cell's energy-producing mitochondrial ATP pathway. Q10 scavenges ROS, shielding the cells from oxidative stress. Q10 is an insoluble, poorly permeable antioxidant with a high biological value that acts as an anti-ageing and anti-wrinkle agent[42,44].

Zinc: The skin is the body's third most concentrated of zinc (Zn) tissues. Zinc acts to preserve many homeostatic functions, including immune system performance, serving as a structural and regulatory catalyst for the biological activity of many enzymes, proteins and signal transcription. Zn is a cofactor for more than 1000 enzymatic reactions and needed for more than 2000 transcription factors. Zn-finger proteins function for interaction with DNA, RNA packaging, transcription activation, apoptosis control, protein folding and assembly, and lipid binding. Zn also functions as an intracellular signalling agent, such as calcium, by converting extracellular stimuli into intracellular signalling[45,11].

CONCLUSION

There is a paradox between skin ageing irreversibility and people's desire for an everlasting youthful look. Skin ageing is a complex, multifactorial phenomenon that is best characterized and interpreted in dichotomous expression: intrinsic or normal ageing is defined cellularly as a function of inheritance, is unavoidable and results in cutaneous alterations; extrinsic ageing which often occurs in cutaneous alterations, originates from exogenous sources and is preventable. Skin ageing is marked by characteristics such as wrinkling, loss of elasticity, laxity and the appearance of rough-textures.

The main perceived risk factors are poor eating habits, less exercise, stress, fatigue, diseased conditions and sleeping habits, while UVR is the principle factor responsible for extrinsic ageing. The predominant cause of extrinsic skin ageing is exposure to UVR, which accounts for around 80% of offal ageing. Sleep deficiency is associated with increased signs of skin ageing (fine lines, irregular pigmentation, diminished elasticity), with much reduced recovery rate. A stronger skin ageing appearance is associated with higher intakes of vitamin C and linoleic acid and lower intakes of fats and carbohydrates.

The recent advancement in the field of cosmetics and pharmacy have played very influential role in providing the therapeutic effects for the skin and providing preventive factors which are contributing to the ageing factors. Hence, for the treatment for ageing various approaches are applied such as, stem cell therapy, antioxidants, retinoids, diet restriction, etc. Plant derived phytochemicals have many beneficial skin properties related to UV defence, antioxidant action, defensive matrix and skin hydration. Natural herbs are widely used as anti-ageing. Proper nutrition is also one of the major factors to slow down the rate of ageing, it is important for well balanced diet. There are also many recent anti-ageing drugs which are

used for the treatment of ageing.

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