Chapter - 1

Skin Aging and Bioactive Compounds from Botanicals

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1.1. Introduction to aging

Aging is a constant, predictable physiological process involves growth and development of living organisms with the passage of time. The growth of tissues, major organ systems of the body ultimately affect our health, behavior, functional capacity, and survival. Aging can't be avoided, but how fast we age depends upon our genes, environmental influences, and lifestyle. Psychological aging processes include changes in personality, mental functioning and sense of self during our middle and older years. Aging involves the steady decline of organ function and body systems like mental illness, wrinkles, loss of muscle tone, hair loss or graying etc. Body changes associated with aging usually make us more vulnerable to various diseases. In spite of tremendous scientific developments, the fact is that aging is the major cause of mortality in developed countries. Although human life is declared to have a basic value in many societies, but there is still no strong awareness of the society to cancel human aging (Stuart-Hamilton, 2006).

Although etiology of aging is important to understand, but it is equally important to differentiate the normal physiological changes from those associated with diseases (premature aging). The physical aging process can be influenced in a variety of ways that take place over the years can be strongly affected by exercise levels and other lifestyle modifications: Dietary and nutritional factors, moderate consumption of alcohol, physical activity throughout life, sexual activity continues in later years, social involvement, and physical environment (Balcombe and Sinclair, 2001). Various physiological aging includes (Laura, 2005):

- **Cardio-vascular system**: left ventricular atrophy, calcification of the heart valves, loss of elasticity inside artery walls, decreased cardiac output, baroreceptor sensitivity and SA node automaticity.
- **Respiratory system**: reduced elasticity of airways and lung tissue with cilia activity.
- **Musculo-skeletal system**: muscular atrophy and loss of muscle tone and strength.
- **Skin**: reduced elasticity, pigmentation and wrinkle.
- **Gastrointestinal system**: reduction in the secretion of gastric HCL, digestive enzymes and saliva may result in gastrointestinal distress.
- **Sexuality**: sexual desire and performance may be reduced due to ovarian, vaginal and uterine tissues atrophy.
- **Changes in sensory organs**: changes in vision, hearing, taste and smell.
- **Cognitive dysfunction with aging**: reduced efficiency of nerve transmission which affect response time and coordination, decrease the length of total sleep time and REM sleep, impairment of intellectual property, learning and memory problem.
- **Changes in personality**: associated with greater attention to personal feelings and experiences and reduced extraversion.
The science of aging explains different theories related to human body's cellular and biochemical reaction such as:

- **Neuro-endocrine theory:** reduced secretion of hormone leading to decline in body's ability to repair and regulate itself.
- **Genetic control theory:** genetic inheritance has a great deal for enormous variation in metabolic function.
- **Free radical theory:** attack the structure of our cell membranes, creating metabolic waste products like lipofuscins to disrupt cellular metabolism.
- **Mitochondrial theory:** electrons leaking from the electron transfer chain (ETC) to reduce molecular oxygen to form $O_2^-$ (superoxide anion radicals) which can cause the generation of other reactive oxygen species (ROS) to damage the mitochondrial DNA.

It is believed that some of these theories of aging may be interlinked to the biological processes of the body and the many factors affecting the progress in aging. Most of these theories have been disputed as the age related changes do not occur uniformly. Anti-aging research eventually discovered medicine by understanding the molecular mechanisms underlying the physiological aging process to prevent age-related problems and diseases of human body (Giacomoni, 2005).

### 1.2. Skin aging and wrinkles

#### 1.2.1. Anatomy of skin

The skin is the largest organ of human body covering the entire outer surface to protect against heat, light, injury, and infection, and also regulates body temperature, stores water and fat, acts as sensory organ, prevents water loss, plays an active role in the immune system etc. The skin is consists of three major layers epidermis, dermis, and subcutaneous tissue. The epidermis is the outer layer of skin and its thickness varies in different parts of body. Thinnest (0.05 mm) on the eyelids and thickest (1.5 mm) on the palms and soles. 5 layers of epidermis from bottom to top are stratum basale, stratum spinosum, stratum granulosum, stratum licidum and stratum corneum. The stratum corneum, is made of dead, flat skin cells that shed about every 2 weeks. Epidermis consists of specialized cells known as ‘melanocyte’ produces pigment melanin, ‘Langerhans’ cell give the frontline defense of the immune system, and ‘Merkel’s cell's’. The dermis is composed of three types of tissue such as collagen, elastic tissue, reticular fibers. Collagen fiber forms two layers papillary and reticular. The papillary dermis is thinner, consisting of loose connective tissue containing capillaries, elastic fibers, reticular fibers, and some collagen. The reticular dermis consists of a thicker layer of dense connective tissue containing larger blood vessels, closely interlaced elastic fibers, and coarse bundles of collagen fibers arranged in layers parallel to the surface. Dermis also contains specialized structures like hair follicles, sebaceous (oil) glands and apocrine (scent) glands, eccrine (sweat) glands, blood
vessels and nerves etc. The deep surface of the dermis is highly irregular and borders the subcutaneous layer. The subcutaneous tissue (hypodermis) is a layer of fatty materials, larger blood vessels and nerves to regulate temperature of the skin itself (Cohen, 1969). Dermis contains a special type of cell known as fibroblast, which produce and secrete pro-collagen and elastic fibers. Pro-collagen is derived from proteolytic enzymes into collagen that aggregates to build cross-linking. These tightly cross-linked collagen fibers makes up 70% of the weight of the dermis provide tensile strength and resistance to shear and other mechanical forces. There are two types of collagen, type I (85% of the total collagen) and type III (15% of the total collagen). Elastic fibers constitute less than 1% of the weight of the dermis, but play an enormous functional role by resisting deformational forces and returning the skin to its resting shape. Dermis also contains gel-like ground substance, composed of mucopolysaccharides (primarily hyaluronic acid), chondroitin sulfates, dermatin sulfates, and glycoproteins known as glycosaminoglycans (Holbrook, 1983).

1.2.2. Etiology and symptoms of skin aging

One of the most frequent dermatologic concerns is skin aging. It is a complex evitable process of human life and researchers are revealing many of the possibilities that cause skin aging as the time passes. There are two types of skin aging, one is chronological aging, which is due to the passage of time and another is premature aging (photo-aging), due to environmental aggressors. The detailed mechanisms involved some interesting alleyway in age-dependent decline of cell tissue function to produce harmful effects during proteolytic degradation of fiber network that leaves visible signs on the surface of the skin. Physiological knowledge of premature skin aging has been explained by micro inflammatory models of both internal and external factors of skin aging includes infections, tractions, cigarette smoke, ultraviolet radiation from sunlight, trauma, hormonal imbalance, electromagnetic fields, chronic alcoholism, psychological stress, anoxia and advanced glycation end-products. These factors have the ability to trigger synthesis of intercellular adhesion molecule-1 (ICAM-1) in endothelial cells. Once the ICAM-1 is synthesized, it is transported to the surface of the endothelial cells of dermis to transmit signal to circulating monocytes and macrophages to release pro-oxidants such as hydrogen peroxide and singlet oxygen, and by proteolytic enzymes, which damage the surrounding extracellular matrix. This damage triggers the arachidonic-acid cascade, which releases prostaglandins, leukotrienes, histamine and tumor necrosis factor - α (TNF-α). These molecules have the ability to induce even more ICAM-1, and thus to damage the extracellular matrix of skin (Giacomoni & D’Alessio, 1996; Giacomoni & Rein, 2001, 2004).

The process of photo-aging is due to several factors including the industrialization, pollution and global warming in most part of the world. The human kind is directly exposed to the polluted environment thus causing severe damage to the skin resulting in enhancement of the aging
The term “photo-aging” was first coined in 1986 is actually the result of UV irradiation upon chronic sun exposure. As early as the 19th century, researchers observed the thickening and brownish discoloration of light-exposed skin of farmers and sailors as compared to that of indoor workers. There are two types of UV irradiation known as UVA and UVB, which are absorbed into the skin. UVA is longer wavelength 320 - 400 nm and UVB ranges from 290 - 320 nm. Both UVA and UVB, however, penetrate the atmosphere and play an important role in conditions such as premature skin aging, eye damage (including cataracts), and skin cancers (Figure 1.1). Although UVA account for up to 95 percent of the total UV radiation reaching the Earth's surface, but less intense than UVB. UVA can penetrate the deeper layer of skin to play a major part in skin aging and wrinkling (photo-aging). UVA damages the DNA of skin cells called keratinocytes in the basal layer of the epidermis, where most skin cancers occur.

![Figure 1.1. UVA and UVB irradiation](image)

UVB, the chief cause of sunburn, tends to damage more superficial epidermal layers. It plays a key role in the development of skin cancer and contributes in tanning and photo-aging. However, UVB rays can burn and damage skin, especially at high altitudes and on reflective surfaces such as snow or ice, which bounce back up to 80 percent of the rays so that they hit the skin twice. Photo-aging describes the clinical signs including irregular dryness, dark/light pigmentation, sallowness, deep furrows or severe atrophy, telangiectases, premalignant lesions, laxity, and a leathery appearance. Other signs include elastosis (a coarse, yellow, cobblestoned effect of the skin) and actinic purpura (easy bruising related to vascular wall fragility in the dermis). Alterations and disarrangement of collagen during photo-aging have been suggested to be a
cause of the skin wrinkling (Fisher et al., 1997). Photoaged skin is associated with either increased epidermal thickness or pronounced epidermal atrophy with histological changes like accumulation of elastin-containing material just below the dermal-epidermal junction or disorganization of collagen.

Collagen is one of the main building blocks of human skin synthesized from precursor molecules called pro-collagen, which is derived from dermal fibroblasts. There are two important regulators of collagen production; one is transforming growth factor (TGF)-β, a cytokine that promotes collagen production and another is activator protein (AP)-1, a transcription factor that promotes collagen breakdown by up-regulating enzymes called matrix metalloproteinases (MMPs) (Massagué, 1998; Kang at al., 1997). When human skin is exposed to sunlight, UV radiation is absorbed by skin cells including, keratinocytes, fibroblasts, and inflammatory cells are able to generate ROS causes “oxidative damage” to cellular components like cell walls, lipid membranes, mitochondria, and DNA. Irradiation of human skin causes increased generation of
hydrogen peroxide, which leads to decreased TGF-β and increased AP-1 expression to up-regulate collagen degrading MMPs and remains elevated for at least 24 hours following UV irradiation (Figure 1.2) (Kang et al., 2003; Fisher et al., 1996). Within 24 hours of a single dose of UV irradiation, increased collagen breakdown can be demonstrated (Fisher et al., 1997). Both UVA and UVB have found to induce the expression of MMP-1, -3 and -9 by dermal fibroblasts in-vivo, and the expressions of MMP-1, -2, and -3 in cell culture. Each UV insult induces a wound response with subsequent imperfect repair, leaving an invisible “solar scar,” repetitive UV insults over a lifetime eventually lead to development of a visible “solar scar,” manifesting as a visible wrinkle. This loss of tissue fibers, which underlies most of the easily identified morphological alterations of the skin, is degradation of extracellular matrix (ECM) in both the epidermal and dermal layers. Loss of ECM is the result of cell loss, decreased biosynthetic capacity of remaining cells and to a progressive increase of matrix degrading enzymes. (Lavker, 1995; Gilchrest, 1990). Repetitive exposure to UV radiation leads to the formation of peroxyl free radicals, which break down to form malondialdehyde (MDA) subsequently cross-links and polymerizes collagen, leading to loss of skin elasticity and decreasing the capacity of the skin to hold water, which are implicated in formation of the most obvious symptom of aging skin is wrinkling (Figure 1.3) (Kligman et al., 1985).

The early stage of wrinkling initiated by a condensation reaction between oxidative products of ascorbic acid (L-threose) and the free amino groups of proteins (collagen and elastin), produce singlet oxygen radicals causes skin damage by disrupting the natural balance in the skin by stimulating skin cells to synthesize MMPs, which are degrading collagen and elastin (Südel et al., 2003). Another mechanism of skin wrinkling is lysosomal enzyme known as hyaluronidase which regulates the turnover of the hyaluronan a structural constituent of pericellular matrix synthesized by skin fibroblast, upon aging increase secretion of hyaluronidase causes degradation of hyaluronan and thereby decrease hydration and ion transport in the extracellular space (Kim et al., 1995). Elastase, another enzyme that capable of hydrolyzing material like elastin, fibrillin etc. are insoluble elastic fibers of ECM protein in animal connective tissues form a network under the epidermis together with the collagenous fibers (Nar et al., 2001). It was also found that transcriptional activity of nuclear factor kappaB (NF-kappaB) is induced by UV irradiation and greatly contributes to the skin photo-aging process (Tanaka et al., 2007). Depending on the amount and form of the UV radiation as well as on the skin type of the
individual exposed, may cause sunburn, immunosuppression, non-melanoma, melanoma skin cancers and premature aging of the skin so-called photo-aging.

Figure 1.3. Molecular mechanism of premature skin aging [+ = Induction; ── = Inhibition]

1.2.3. Role of enzymes in skin aging

1.2.3.1. Hyaluronidase

Hyaluronidase is an enzymes belong to the family of endolytic glycoside hydrolases that depolymerize the $\beta_1-4$ linkages between N-acetylglucosamine and glucuronic acid of hyaluronan, also known as hyaluronic acid in the ECM of connective tissue (Figure 1.3). It is found in organs such as testis, spleen skin, eye, liver kidney, uterus, placenta and in body fluids like tears, blood, sperm etc. Hyaluronic acid is one of the major components of the skin, especially in dermis, but it is also present in high concentration in the epidermis, where it is synthesized by keratinocytes. Skin contains about half of the total amount of hyaluronan of the human body, estimated to about 5 g. Most reports agree about an age-dependent decrease of hyaluronan content of the skin. Hyaluronidase isoforms expressed in the skin are Hyal-1, Hyal-2 and Hyal-3. Hyal-1 is the major hyaluronidase involved in hyaluronic acid degradation. Upon UV-B exposure the expression of mRNA levels of these isoforms are increased by a dose-dependent manner. It has been found that fragments of low molecular weight hyaluronic acid
accumulate in the epidermis in response to UV-B irradiation. These evidences suggested that hyaluronidase synthesis/degradation balance of hyaluronan in the irradiated epidermis might be strongly altered in favor of hyaluronan degradation. Therefore, increased hyaluronic acid catabolism induced by UV-B stimulation of hyaluronidase activity might be one of the main factors involved in skin photo-aging (Kurdykowski et al., 2011).

1.2.3.2. Elastase

Elastase belongs to the family chymotrypsin. It is a protease capable of degrading elastin, which is the fiber material found within the ECM. Elastin has the ubiquitous nature of elastic recoil to provide elasticity to arteries, lungs, ligaments and skin. Elastases can utilize elastin as substrate as well as having a broad substrate range including collagen, fibronectin and other fiber materials of ECM. During phagocytosis by neutrophils under normal conditions elastase activity is necessary to degrade foreign proteins within the ECM and to enable tissue repair. The secretion and activation of elastase from dermal fibroblasts in response to UV irradiation and/or to cytokines released by keratinocytes are responsible for the degeneration of the three-dimensional structure of elastic fibers during the formation of wrinkles. Skin elasticity is remarkably reduced in the early stage of photo-aging as a result of the degeneration of elastic fiber by at least two types of elastases is neutrophil elastase and fibroblast elastase. These elastases have significant impact in the metabolism of elastic fibers in skin tissues during photo-aging (Tsuji et al., 2001).

1.2.3.3. Matrix metalloproteinase-1

Matrix metalloproteinases (MMPs) are calcium (Ca) dependent zinc (Zn) containing endopeptidases belongs to the ‘Metzincins’ superfamily. It consists of 28 members sharing a regular catalytic core or domain with a Zn metal in their active site. They are excreted by a variety of cells including fibroblasts, osteoblasts, endothelial cells, macrophages, neutrophils, lymphocytes etc. MMPs play a crucial role in several normal or abnormal physiological processes such as the degradation of ECM including collagens, elastins, gelatin, matrix glycoproteins, proteoglycan, intercellular communication, atherosclerosis, embryonic development, organ morphogenesis, cartilage remodeling, bone growth, corneal repair, wound healing, cell migration, invasion, angiogenesis and tumor progression (Verma and Hansch, 2007). According to structure and substrate specificities the MMPs are classified into five broad groups, such as: collagenases, gelatinases, stromelysins, matrilysins, MT-MMPs (membrane-type MMPs). These endopeptidases are secreted as inactive zymogen or pro-MMPs and are activated by serine proteases (plasminogen activator and kallikriens), mast cell proteases, plasma membrane MMPs etc (McIntush and Smith, 1998). MMPs production, transcription, pro-MMP activation, regulation and inhibition are dynamic equilibrium process which helps to make
homeostasis in the ECM through tissue formation and breakdown of different proteins. MMPs (Figure 1.5) are organized into basic domain like structure consisting of an N-terminal pre-peptide signal sequence directs their secretion in the extracellular environment; followed by an N-terminal pro-peptide domain contains a conserved cysteine which chelates the catalytic Zn$^{2+}$ maintains their zymogenic form (inactive). During the activation, the pro-peptide will be removed by proteases. It also contains a catalytic domain and a C-terminal haemopexin (Hpx) like domain (Nelson et al., 2000). MMPs are considered as a leading target for a number of therapies and there is an emerging trend in design and synthesis of MMPs inhibitors (MMPIs). A large number of synthetic MMPIs have been identified to undergo clinical trials. MMPIs have been designed depending on the ZBG (zinc-binding group) in the MMPI molecule which is essential for chelating the catalytic Zn$^{2+}$ ions of MMPs. These are hydroxamic acid, carboxylate, organoborate and dithiolate derivatives as zinc chelators (Hoekstra et al., 2001).

Collagenase, MMP-1 (fibroblast collagenase) is the key collagenase, which is involved in the physiological and pathological turnover of ECM of skin. Its synthesis is significantly increased at inflammation sites due to the stimulation of pro-inflammatory cytokines. The MMP-1 is capable of degrading triple-helical fibrillar collagens into distinctive ¾ and ¼ fragments which are the major components of ECM (Alaaaho and Kahari, 2005). Collagenase cleaves the X-glycine bond of collagen and also synthetic peptides that contain the sequence: Proline-X-Glycine-Proline where X is an amino acid provided that the amino terminus is blocked (Van Wart and Steinbrink, 1981). MMP-1 preferably degrades type III collagen (Balbi’n et al., 2001). Collagenase from the bacteria *Clostridium histolyticum* hydrolyses triple-helical collagen in both physiological conditions and *in-vitro* conditions using synthetic peptides as substrates (Kim et al., 2004). As the age increases, collagen synthesis are reduced and collagenase level becomes higher, causing changes such as skin wrinkling and loss of elasticity (Varani et al., 2000). There is increasing evidence that UV irradiation from sun light induces extensive generation of ROS, which activates the mitogen-activated protein kinase (MAPK) signal transduction pathway, which further induces the expression of AP-1 driven genes including collagenase in the exposed skin (Kang et al., 2003). Therefore, control of collagen metabolism and control of oxidative stress.
would be functional for a variety of therapeutic and cosmetic applications. Phytoconstituents and also crude extracts from natural resources have been widely explored and found to have anti-collagenase activity. Plants contain a huge variety of compounds including polyphenols such as flavonoids, terpinoids, glycosides, vitamin E, vitamin C, phenolic acids and tannins which have been found to provide collagenase inhibitory activity.

1.3. Anti-aging and anti-wrinkle agents

1.3.1. Treatment of skin aging

It has been found that a wide variety of cosmeceuticals and formulas can facilitate the skin to repair wrinkles, leading to a younger healthy looking face, glowing skin and fight against skin aging, accelerate the synthesis of collagen, leading to a younger-looking face and healthy skin.

A rational approach to wrinkle free skin care would focus on the application of skin cosmetics that provide moisture and include a sunscreen with a sun protection factor (SPF) of 15 or higher to minimize the UV rays that penetrate skin cells. The most promising topical treatments incorporate antioxidants, hormone estrogen, vitamins and minerals that scavenge free radicals from skin cells known to contribute to physiological aging by permanently damaging cell structure and function. Lot of skin care product including anti aging creams, ointments is available for protecting and restoring the skin damage. In spite of their good antioxidant property or skin care property they have several disadvantages like side effects, allergic reactions, high cost, contact time during cleansing is too little to ensure any anti wrinkle effect etc. Consumers are progressively more proactive about their health as they pass through middle and old age, and a heightened awareness of a variety of herbal extracts (plus a full pipeline of innovative plant-derived chemicals) is expected to spur robust gains. Natural vitamins and antioxidants supplement have been accepted widely as anti aging nutrients, and most promising topical treatments of herbal extracts that remove damaging free radicals from skin cells to restore skin damage, such as loss of elasticity, wrinkling and premature aging. Preliminary experiments have revealed that topically used antioxidants ameliorate long-term damage from environmental influences and also promote self-repair (Dreher & Maibach, 2000).

Botulinum toxin from Clostridium botulinum has the stretching effects over wrinkle skin. It works by blocking neurotransmission that can paralyze the muscles, which results in non constriction of the muscle for a period of 3-4 months. This inability prevents the skin to fold, thus eliminating possibility of wrinkling (Ramos-e-Silva and da Silva Carneiro, 2007). But, the major risks of using botulinum toxin over skin are; allergic reaction, muscle weakness, double vision, hoarseness of voice, blurred vision, drowsiness, headache, dry mouth, fatigue, and flu-like symptoms (Baizabal-Carvallo et al., 2011). However, the “modern” botulinum treatment for skin stretching has great risks. Cosmetic formulations based on botanical ingredients have been used since
from ancient times, and botanical and natural extracts plays a major role in contemporary cosmetics. Present era of treating aging skin has become technologically more invasive; but, herbal products including botanicals are still relevant and can be highly efficacious. Scientific researches continue to corroborate traditional uses of many plants for skin benefits to elucidate biochemical mechanisms of action for a growing number of phytochemicals. Additional clinical trials is mandatory to optimize the application of natural ingredients for cosmetics, but scientific validation for the safety and efficacy of a host of botanical extracts and compounds for treating aging skin is evident, with the continued potential of many more.

1.3.2. Antioxidant nutrients

Anti-aging treatment today often includes skin care products contain vitamin and mineral supplements, which so-called ant-aging vitamins and antioxidants slow down the process of aging (Glaser, 2004). Antioxidants scavenge free radicals; remove by-products of metabolism from cells to protect against aging and disease. Some foods are being identified as potent antioxidants such as blueberries and chocolates. Vitamins such as A, C, E and minerals like selenium included in the antioxidant group. It supports integrity of the skin and mucous membranes, which serve as our barrier and protection against the environmental exposures. Vitamin A can significantly reduce the incidence of erythema, scaling, burning/pruritus over skin and increase epidermal thickness and induce of 4-hydroxylase activity. Vitamin A plays a critical role in the maintenance of the epithelial cells of the glands, ducts, and organs of our bodies. Vitamin A is one of the most important antioxidants, which modulate the immune system and anti-cancer nutrient (Cordero, 1983). Topical application improved the appearance of skin wrinkles and hyper-pigmentation (Bisset et al., 2002).

Vitamin C (ascorbic acid) is the most important water-soluble antioxidant benefits every cell in the body to provide antiaging protection. A considerable amount of data has been reported on vitamin C in enhancing the immune system and helping to prevent many common diseases like aging. Topical vitamin C stimulates the collagen-producing activity of the dermis (Humbert et al., 2003). The active form L-ascorbic acid acts as an antioxidant by neutralizing reactive oxygen molecules created by UV radiation. The use of a topical preparation for the prevention and treatment of photo-aging is useful as antioxidant and collagen stimulating properties of vitamin C, because the cutaneous tissues receive approximately 8% out of total systemically absorbed amount (Darr et al., 1992). L-ascorbic acid in combination with zinc, and tyrosine showed greater skin penetration, collagen remodeling, significant improvement of wrinkles/rhytids, roughness, color, and overall features (Moy et al., 1999).

Vitamin E is a primary fat-soluble antioxidant found inside the fatty membranes surrounding every cell in the body. Vitamin E helps prevent formation of potent free radicals called lipid
peroxides that attack cell membranes and enzymes, negatively impacting tissues, organ systems, and the brain in the process of free radical induced aging. The biologically active form of vitamin E is $\alpha$-tocopherol, which inhibits protein kinase C activity in fibroblasts and collagenase production to protect against aging. Topical application of vitamin E significantly reduces the erythema and edema in UV-B-induced mice whereas, oral administration of vitamin E do not have significant effect in the prevention of UV-induced skin damage (Werninghaus et al., 1994).

Co-enzyme-Q10 (CoQ10) protects cumulative damage of DNA from free radical during aging process. Its Antioxidant properties and ability to significantly reduce fibroblast expression of UV-A induced mRNA collagenase, CoQ10 protects cultured keratinocytes from UV-A induced oxidative stress and DNA damage may be helpful in protecting the dermal matrix from UV radiation as well (Hoppe et al., 1999). n- Acetyl cysteine is an amino acid has value as anti-aging nutrient. Also, know as (NAC) it helps the body produce glutathione which is one of our most important internal antioxidants. The liver uses glutathione to convert toxins into harmless substances that can be quickly eliminated from the body. Topical N-acetyl cysteine prevents UV-induced signaling that leads to photo-aging in human skin in-vivo (Kang et al., 2003). $\alpha$-lipoic acid is another antioxidant compound nutrient available as a dietary supplement. It is neutralizing free radicals and improves nerve function, helps insulin to carry out its blood sugar regulating functions, and prevent cataracts. In addition $\alpha$-lipoic acid recycles other antioxidants such as vitamin C and vitamin E (Farris, 2003). Alpha hydroxy acids includes Glycolic acid, Lactic acid, Mandelic acid, Malic acid, Tartaric acid, Citric acid, Pyruvic acid, Benzylic acid, Tropic acid etc., which are a group of organic carboxylic acids that have a hydroxy group in the alpha position. These compounds are found naturally in many foods popular as skin rejuvenators and used in many moisturizers, cleansers, and cosmetic products (Draelos. 1998).

1.3.3. Bioactive compounds from natural resources

Ayurveda is one of the most ancient systems of traditional medicine and has over 200 herbs, minerals and several formulations for management of aging and enhance the health and beauty of the skin. The whole range of cosmetic usage and its practice as conceived by the ancient Indians was based on natural resources and there has been great upsurge in recent years (Mukherjee et al., 2010). Ayurveda is one of the ancient systems of medicine in India, where the concept of skin aging have been discussed in several aspects. In this age old Indian medicine system several concerns about aging has been discussed in Sanskrit like Vayasthapana (age defying), Varniya (brighten skin glow, Sandhaniya (cell regeneration), Vranaropana (healing), Tvachya (nurturing), Shotahara (anti-inflammatory), Tavachahnivardhani (strengthening skin metabolism) and Tvagrasayana (retarding aging) (Datta and Paramesh, 2010). Natural skin care products are quickly absorbed by the superficial layers of the skin when applied topically such as
in lotions or ointments or cream. They are a hypo-allergenic character, no additives or preservatives and therefore they are very safe and reliable products that are properly formulated to match a specific skin care need often don’t cost any more than their synthetic opponents. They are naturally derived, providing long-lasting results because they contain ingredients the body recognizes and can readily breakdown. The largest groups of these anti aging natural ingredients are the ones that contain antioxidants clear away free radicals and byproducts of metabolism are always being produced in our body damage cells and contribute to aging and disease. Many herbs, particularly fruits, vegetables, and whole grains contain antioxidants, polyphenols can also be used together to design a diet that is both healthy for the body in general and helpful for avoiding the typical signs of aging, while a few are astonishingly high in these beneficial anti-aging food molecules. Review on these plants and their constituents are being described in later section to highlight the potentials of medicinal plants useful in skin aging from natural resources.

*Aesculus hippocastanum* L. (Family: Hippocastanaceae)

*A. hippocastanum* is able to generate contraction forces by non-muscle (fibroblast) cells using fibroblast populated collagen gels. It plays an important role in determining cell morphology, vasoconstriction, and wound healing (Fujimura et al., 2006).

*Aloe vera* L. (Family: Liliaceae)

Aloin A (1) and B have been shown to inhibit *Clostridium histolyticum* collagenase reversibly and non-competitively. Both aloe gel & aloin are also effective inhibitors of stimulated granulocyte MMPs (Barrantes and Guinea, 2003). Aloesin [2-acetonyl-8-beta-d-glucopyranosyl-7-hydroxy-5-methylchromone] isolated from the *A. vera* have been reported to modulate melanogenesis via competitive inhibition of tyrosinase. Tyrosine hydroxylase and 3, 4-dihydroxyphenylalanine oxidase activities of tyrosinase from normal human melanocyte cell lysates were inhibited by aloesin in a dose dependent manner (Jones et al., 2002).
**Astragalus membranaceus** (Fisch.) Bunge (Family: Fabaceae)

It is perennial herb, indigenous to China, Republic of Korea, Mongolia, and Siberia. Primarily, the active constituents of *A. membranaceus* consist of polysaccharides and flavonoids (Xia et al., 2002). *A. membranaceus* have been found to increase the content of hyaluronic acid in cultures of keratinocytes and fibroblasts by elevating the hyaluronan synthase-3 and hyaluronan synthase-2 mRNA expressions (Hsu and Chiang, 2009). Therefore, it’s a promising candidate for preventing the age-dependent loss of hyaluronic acid content.

**Berberis aristata** DC. (Family: Berberidaceae)

*B. aristata* has a prominent role in Ayurveda for the treatment of liver and gallbladder ailments. Russian healers used it for inflammations, high blood pressure, and abnormal uterine bleeding (Kirtikar and Basu, 1984). Decoction of roots of *B. aristata* has been claimed for skin troubles and in blood purification. *B. aristata* mixed with honey is useful in the treatment of aphthous sores abrasions and ulcerations of the skin (Nadkarni, 1976). Topical formulation containing *B. aristata* has been reported to prevent acne vulgaris with the patients suffering skin disorders (Mamgain, 2000). The plant is native to India and also found throughout South East Asia. Berberine (2) isolated from *B. aristata* have been reported to inhibit basal and TPA-induced expression and activity of MMP-9, and also suppressed TPA-induced IL-6 expression, ERK activation and AP-1 DNA binding activity in UV-induced skin inflammation, aging process and degradation of extracellular matrix proteins (Kim et al., 2008b). The MMP-1 and type I procollagen expression in human dermal fibroblasts regulated by berberine has been reported by Kim and Chung, (2008a).

**Calendula officinalis** L. (Family: Asteraceae)

*C. officinalis* flowers have long been employed in folk therapy. The main uses are as remedies for burns (including sunburns), bruises, cutaneous and internal inflammatory diseases of several origins. Oral treatment of hairless mice maintained glutathione levels close to non-irradiated control mice and affects the activity/secretion of MMP-2 and MMP-9 stimulated by exposure to UVB irradiation (Yris et al., 2010).

**Camellia japonica** L. (Family: Theaceae)

Anti skin aging property of *Camellia japonica* oil has been reported by Jung et al., (2007), in human dermal fibroblast cells by human COL1A2 promoter luciferase assay in a concentration dependent manner. It has been found that human type-I pro-collagen synthesis is induced by *C. japonica* oil while MMP-1 activity has been inhibited. *C. japonica* oil also can hold trans-epidermal water loss (TEWL) without interrupting any adverse reactions.
Camellia sinensis L. (Family: Theaceae)

Originally cultivated in East Asia, this plant grows as large as a shrub. Sunscreen formulated with 2-5% green tea extract has been reported to protect UV irradiation induced photo-aging, photo immunosuppression, cutaneous erythema, thickening of the epidermis, over expression of CK5/6, CK16, MMP-2, MMP-9 etc. (Li et al., 2009). A double-blinde, placebo-controlled trial have been executed with moderate photo-aging treated with either a combination regimen of 10% green tea cream and 300 mg twice-daily green tea oral supplementation or a placebo regimen for 8 weeks to monitor the clinical and histologic appearance of photo-aging skin (Chiu et al., 2005). It has been found that patients treated with a combination regimen of topical as well as oral showed histological improvement in tissue elastic content, but clinically significant changes have not been observed and it may require longer supplementation for clinically observable improvements. Nichols and Katiyar, (2010) reported that green tea polyphenols catechin (3), epiglactocatechin (4), epiglactocatechin-3-gallate etc. favorably sunscreens supplement to protect the skin from the adverse effects of UV radiation induced inflammation, oxidative stress and DNA damage including the risk of skin cancers.

Centella asiatica L. Urban. (Family: Umbelliferae)

Centella asiatica is a perennial herb found in India, Sri Lanka, Madagascar, South Africa, Australia, China, and Japan. It contains several active triterpenoids, saponins, including madecassoside (5), asiaticoside (6), centelloside, and asiatic acid, which has been reported to increase cellular hyperplasia, collagen production, granulation tissue levels of DNA, protein, total collagen, hexosamine, rapid maturation and cross-linking of collagen etc. (Suguna et al., 1996; Shetty et al., 2006). Madecassoside isolated from C. asiatica, known to induce collagen expression and modulate inflammatory mediators.
To justify this statement Haftek et al., (2008) have performed a randomized double-blind clinical trial and found significant improvement of the clinical score for wrinkles, suppleness, firmness, roughness and skin hydration. Asiaticoside is another active saponin, which induced type I collagen synthesis in human dermal fibroblast cells. The molecular mechanism behind this has been partially assumed that SB431542, an inhibitor of the TGF-β receptor I (TβRI) kinase, which is known to be an activator of the Smad pathway (Lee et al., 2006). Topical formulation of aqueous extract of C. asiatica showed increased cellular proliferation and collagen synthesis on the skin wound of rats, which is an evidence of increasing collagen content and tensile strength. The treated wounds epithelialised faster and the rate of wound contraction was higher (Kumar et al., 1998). Triterpines including asiatic acid, madecassic acid and asiaticoside extracted from C. asiatica were screened on human foreskin fibroblast monolayer cultures and observed that collagen synthesis was increased in a dose-dependent manner whereas the specific activity of neosynthesized collagen was decreased (Maquart et al., 1990). Tenni et al., (1988) has reported that triterpinoid fraction can influence the biosynthesis of collagen, fibronectin and proteoglycans in human skin fibroblast cultures.

**Citrus sinensis** L. (Family: Rutaceae)

Cimino et al., (2007) have accounted that phenolic compounds such as anthocyanins, flavanones, hydroxycinnamic acids (7) and ascorbic acid is responsible for the anti photo-aging activity of three different varieties of C. sinensis in modulating cellular responses such as NF-kB and AP-1 translocation and procaspase-3 cleavage to UV-B in human keratinocytes (HaCaT). Thus, C. sinensis has been proposed as a useful natural standardized extract in skin photo protection with promising applications in the field of dermatology.
Curculigo orchioides Gaertn. (Family: Hypoxidaceae)
Curculigoside (8) isolated from rhizomes of *C. orchioides* have been reported to possess strong inhibitory activity against MMP-1 in cultured human skin fibroblasts suggest its skin improvement property (Lee et al., 2009b).

Curcuma longa L. (Family: Zingiberaceae)
The effect of a *C. longa* extract have been found to do potential changes in skin thickness, increased elasticity, decreased pigmentation and wrinkling caused by long term, low-dose UV-B irradiation in melanin-possessing hairless mice (Sumiyoshi and Kimura, 2009). It prevents the formation of wrinkles and melanin as well as increases in the diameter and length of skin blood vessels and decrease expression of matrix metalloproteinase-2 (MMP-2). Therefore, skin wrinkling can be minimized by curcumin (9).

Curcuma xanthorrhiza Roxb. (Family: Zingiberaceae)
Xanthorrhizol (10) isolated from *C. xanthorrhiza* was investigated on the expression of MMP-1 and type-I pro-collagen in UV-irradiated human skin fibroblasts (Oh et al., 2009). Xanthorrhizol and *C. xanthorrhiza* extract (0.01-0.5 μg/ml) induced a significant, dose-dependent decrease in the expression of MMP-1 protein and increased the expression of type-1 pro-collagen.
Dioscorea coomposita or Dioscorea villosa L. (Family: Dioscoreaceae)

Extracts of *D. coomposita* or *D. villosa* are consumed as supplemental health foods containing large amounts of the plant steroid, diosgenin etc. Efficacy of diosgenin (11) against skin aging has been established with *in vitro* human 3D skin equivalent model. It showed enhanced DNA synthesis and increased bromodeoxyuridine uptake and intracellular cAMP level in adult human keratinocytes (Tada et al., 2009). These results suggest that for restoration of keratinocyte proliferation in aged skin, diosgenin have a potential effect.

Emblica officinalis L. (Family: Euphorbiaceae)

*E. officinalis*, shows significant type-I collagen promotion and anti-collagenase effects on primary mouse fibroblast cells at a concentration of 0.1 mg/ml, determined by immuno-cytochemistry and Western blot analysis (Chanvorachote et al., 2009). Fruit extract has been reported to stimulate the proliferation of fibroblasts and induced production of pro-collagen in a concentration and time dependent manner. On the contrary, MMP-1 production from fibroblasts was dramatically decreased whereas TIMP-1 was significantly increased (Takashi et al., 2008).

Fraxinus chinensis Roxb. (Family: Oleaceae)

Study reveals that five major compounds have been isolated from *F. chinensis* extract; among them esculetin (12) has been found to have potent free radical scavenging activity with dose-dependently decreases the expression levels of MMP-1 mRNA and protein in UVB-irradiated human dermal fibroblasts (HDFs) (Lee et al., 2007).

Glycine max L. Merr (Family: Fabaceae)

Anthocyanin (13) isolated from black soybean [*G. max* (L.) Merr] seed responsible for down regulation of *in vitro* and *in vivo* UVB induced reactive oxygen species levels and apoptotic cell death through the prevention of caspase-3 pathway activation and reduction of pro-apoptotic Bax protein levels (Tsoyi et al., 2008). This finding highlights that anthocyanin from the seed coat of black soybean is useful compounds to modulate UVB-induced photo-aging.
**Hamamelis virginiana** L. (Family: Hamamelidaceae)

*Hamamelis virginiana* is also known as *Witch-hazel* is a well known plant has long been used as cosmetics. The oil isolated from fresh leaves and twigs by steam distillation is used as mild astringent, and has also been recommended for certain skin conditions, such as boils, ulcers, itching eczema, bruises etc. (Harry, 1963). Decoction from the twigs is accounted for its use to treat swellings, inflammations and tumors. Both bark and leaves contain volatile oil, hamamelitannin, catechins, gallic acid etc. (Engel et al., 1998; Wang et al., 2003). Its astringent action may be attributed for it relatively high tannin content, which has great value in the treatment of varicose veins due to haemostatic property. It’s soothing and anti-couperose effects are useful for mucosa, skin and minor capillary problems. It has also been used in treating atopic dermatitis with Hamamelis ointment, sun protection, facial toning lotion for oily skin, control minor pimple formation, and reduces the pain of sprains or athletic injuries (Swoboda and Meurer, 1992). Masaki et al., (1995) have evaluated the anti skin aging activity of *Witch-hazel* on a murine dermal fibroblast culture system using both ESR spin-trapping and malondialdehyde generation methods. Polymeric pro-anthocyanidins and polysaccharides have been isolated from the bark. It showed increased the proliferation of the cells and reduced the transepidermal water loss and erythema formation, while screened on cultured human keratinocytes (Deters et al., 2001). Anti-inflammatory effect of hamamelis lotion has been evaluated on 30 healthy volunteers using a modified UVB erythema test model. It was found that erythema was suppressed with in the range of 20 – 27 % within 48 hours compared to other formulation significantly (Hughes-Formella et al., 1998). Anti-inflammatory efficacy of the topical preparations with 10% hamamelis distillate was screened on 40 human volunteers in a modified UV erythema test with three UV dosages. Even though the effect was less, but the UV erythema was reduced significantly (Hughes-Formella et al., 2002).

**Kaempferia pandurata** Roxb. (Family: Zingiberaceae)

In a dose-dependent manner (0.01-0.5µg/ml) *K. pandurata* extract have been reported significantly to reduce the expression of MMP-1 and increased the expression of type-1 pro-collagen at the protein and mRNA levels through the inhibition of UV induced phosphorylations of MAPKs such as ERK (extracellular-regulated kinase), JNK (Jun N-Terminal kinase) and p38 kinase, respectively. It also led to the inhibition of AP-1 DNA binding activity in human skin fibroblasts (Shim et al., 2009).
**Labisia pumila** Blume. (Family: Myrsinaceae)

*L. pumila* also known as "Kacip Fatimah," showed free radical scavenging activity. Its extract markedly inhibited the TNF-α production. Extract of *L. pumila* down regulated the enhanced MMP-1& MMP-9 expression in keratinocytes dose-dependently (Choi et al., 2010) which suggest potential of its extract as an anti-photoaging cosmetic ingredient.

**Machilus thunbergii** Sieb et Zucc (Family: Lauraceae)

Meso-dihydroguaiaretic acid (14) obtained from the stem bark of *M. thunbergii* have been reported for its strong inhibitory effect on MMP-1 in primary human fibroblasts by heat shock induced premature skin aging (Moon and Jung, 2006).

![Meso-dihydroguaiaretic acid (14)](image)

**Magnolia obovata** Thunb. (Family: Magnoliaceae)

*M. oovata* extract has been found to inhibit NF-κB-mediated gene expression and prevents photo-aging processes through keratinocyte hyperproliferation and diminish degradation of collagen fibers in mice skin. Magnolol (15) is the compound responsible for the protective activity without hampering other inducible transcription factors such as AP-1 and cyclic-AMP responsive element-binding protein (CREB) (Tanaka et al., 2007). Magnolol inhibited matrix metalloprotease-1 (MMP-1) from the cells over expressing p65. These findings suggest that magnolol has potential effect against photo-aging via inhibiting NF-κB by external topical application.
**Melothria heterophylla** (Lour.) Cogn. (Family: Cucurbitaceae)
1,2,4,6-tetra-O-galloyl-\(\beta\)-glucopyranose and gallic acid (16) isolated from *M. heterophylla* known to play an important role over MMPs expression in photo-aging by mediating the degradation of extracellular matrix proteins, but no inhibition of MMP-1 mRNA expression (Cho et al., 2006). Both these compounds significantly inhibited MMP-1 expression at the protein level and have a potent antioxidant activity suggesting the usefulness as an anti-photo-aging agent.

**Panax ginseng** L. (Family: Araliaceae)
Bioactive constituents, ginsenoside (17) believed to have anti-skin aging activities. A randomized, double-blind, placebo-controlled study revealed that red ginseng extract improved type-I procollagen gene and protein expression, prevent MMP-9 gene induction and elongated the fibrillin-1 fiber length, thereby reduces facial wrinkles (Cho et al., 2009). Red Ginseng extract inhibited the increases of epidermal thickness and skin TGF-β1 content induced by UVB irradiation, which may be due to partial inhibition of the increase of skin TGF-β1 (Lee et al., 2009a). These results substantiate the alleged beneficial effects of red ginseng on photo-aging and support its use as an effective "beauty food."
**Piper betle** L. (Family: Piperaceae)

Allylpyrocatechol (18) and chavibetol (19) isolated from *P. betel* have been established to protect photosensitization-mediated lipid peroxidation of rat liver mitochondria effectively. Allylpyrocatechol has been found to be significantly more potent (Mula et al., 2008). Allylpyrocatechol also prevented the unfavorable effects of the type-II photosensitization-induced toxicity to mouse fibroblast L929 cells. The results suggested that allylpyrocatechol have an important role in protecting biological systems against damage, by eliminating $^{1}\text{O}_2$ generated from certain endogenous photosensitizers.

![Chavibetol (19)](image)

**Prunus dulcis** Mill. (Family: Rosaceae)

The role of almond oil in reducing the degenerative changes induced in skin upon exposure to UV radiation has been proposed by Sultana et al., (2007) illustrated that biochemical parameters, glutathione, and lipid peroxidation have been ameliorated by almond oil.

**Tagetes erecta** L. (Family: Asteraceous)

Small bushy plants widely cultivated in India, Mexico and Central America. The flowers are popularly known as *Marigold* contains pro-vitamin A ‘$\beta$-carotene’ (20) responsible for photo-protection (Del et al., 2010).

![$\beta$-carotene (20)](image)

**Terminalia chebula** Retz. (Family: Combretaceae)

*In vitro* skin cell protective activity of *T. chebula* have been evaluated through anti-oxidative and tyrosinase inhibition activity as well as the anti-proliferative and MMP-2 inhibition activity on early aged human skin fibroblasts (Manosroi et al., 2010). The plant showed 1.37 times more potent MMP-2 inhibition than ascorbic acid on fibroblasts determined by zymography. Isolated compound 1, 2, 3, 4, 6-penta-O-galloyl-$\beta$-D-glucose (21) from this plant showed anti-elastase...
and anti-hyaluronidase inhibitory activity with significant induction of type II collagen expression in rabbit articular chondrocytes (Kim et al., 2010).

Theobroma cacao L. and Cola acuminate Schott & Endl. (Family: Sterculiaceae)
Cacao bean and cola nut are popular edible plants that contain polyphenols and xanthine derivatives, which protective effects against UV-induced erythema when topically applied to the dorsal skin of hairless mice. The desired mechanism behind this has been highlighted by Mitani et al., (2007) which suggested that the total hydroxyproline and pepsin-resistant hydroxyproline content down regulated markedly increased after UV irradiation.

Vaccinium uliginosum L. (Family: Ericaceae)
Fruits of bog blueberry (V. uliginosum) are rich in anthocyanins like cyanidin-3-glucoside (22), petunidin-3-glucoside, malvidin-3-glucoside, and delphinidin3-glucoside which have been documented for pigmentation and attenuation of photo-aging through removal of reactive oxygen species (ROS) production and the resultant DNA damage responsible for activation of p53 and Bad in UV-B-irradiated human dermal fibroblasts (Bae et al., 2009).

Viola hondoensis W. Becker et H. Boissieu (Family: Violaceae)
Moon et al., (2005) isolated quercetin-3-O-β-d-(6″-feruloyl)-galactopyranoside an isoflavonoid from the stems of Viola hondoensis which reduced UV-irradiated human skin fibroblasts MMP-1 expression at the protein levels in dose-dependent manner.

Vitis vinifera L. (Family: Vitaceae)
V. vinifera shoot extract has stronger in vitro antioxidant capacity than vitamin C or vitamin E on cultured normal human keratinocytes and also in vivo photo-aging activity of a serum based formulation of this extract in combination with a biotechnological extract (Ronacare Hydroine) (Cornacchione et al., 2007). The dermatologic evaluation showed that a 4-week twice daily application of a serum containing the combination improved the main clinical signs of photoaged skin.
Zingiber officinale L. (Family: Zingiberaceae)

Topical application of Z. officinale extract to hairless mouse skin significantly inhibited the wrinkle formation induced by chronic UV-B irradiation at a sub-erythemal dose accompanied by a significant prevention of the decrease in skin elasticity (Tsukahara et al., 2006).

Miscellaneous

Tamsyn et al., (2009) have screened 21 plants for their anti-collagenase, anti elastase and antioxidant activity. Triterpenoids known as boswellic acids (23) isolated from frankincense (Boswellia spp.) (Family: Burseraceae) resin showed anti-elastase activity (Melzig et al., 2001). Rosemary extracts from Rosmarinus officinalis L. (Family: Lamiaceae) have also been reported to have good anti-elastase activity (Baylac and Racine, 2004). Acevedo et al., (2005) isolated two compounds known as linarin (24) and verbascoside (25) from Buddleja scordioides H.B.K. (Family: Buddlejaceae) to determine the photo-protective properties and verbascoside showed the largest SPF measurement. A quinazolinedione alkaloid isolated from the fruits of Evodia officinalis (Dode) Huang (Family: Rutaceae) have been reported to have MMP-1 inhibitory activity (Jin et al., 2008). Aucubin (26) isolated from Eucommia ulmoides Oliv. (Family: Eucommiaceae) has been found to inhibit MMP-1 and also decrease the senescence associated β-galactosidase activity, which indicates it as an antiphoto-induced aging compound (Jin et al., 2005).
1.4. Conclusion

Natural vitamins and antioxidants supplement have been accepted widely as anti aging nutrients, and most promising topical treatments of herbal extracts that remove damaging free radicals from skin cells to restore skin damage, such as loss of elasticity, wrinkling and premature aging. Preliminary experiments have revealed that topically used antioxidants ameliorate long-term damage from environmental influences and also promote self-repair (Dreher & Maibach, 2000).

Recently natural antioxidants including vitamins A and E, squalene, co-enzyme Q10, ferulic acid, idebenone, pycnogenol and silymarin are being used into topical skin care formulations which donate electrons and neutralize the ROS and thereby protects skin from aging (Pinnell, 2003). Vitamin C, alpha-hydroxy acids, and penta-peptides have been the most comprehensively researched compounds, and their anti aging capabilities have been replicated in the literature (Van Scott et al., 1996; Chiu and Kimball, 2003). Various plants are being used in anti-aging cosmeceuticals contain these compounds. However, phyto-pharmaceuticals, which have become popular over the last few years, require significantly more researches to formulate any positive conclusions for their topical application. Many botanical antioxidants are available and they are generally classified into one of three categories: carotenoids, flavonoids, and polyphenols (Draelos, 2003a). The carotenoids are related to vitamin A and encompass the naturally occurring retinols. Polyphenols are accountable for the inherent antioxidant are reported to provide UV protection and metal chelation in addition to antioxidant properties can be divided into several classes of chemicals: anthocyanins, bioflavonoids, proanthocyanidins, catechins, hydroxycinnamic acids, and hydroxybenzoic acids (Manach et al., 2005). Botanicals such as rosmarinic acid (rosemary), hypericin (Saint John’s wort) and oleuropein (olive leaf) have already been used to various skin care products. Some of these possess anti-inflammatory agents help to block the inflammatory changes that may result in cutaneous aging and thus are purported to reverse the signs of aging. Allantoin is a popular botanical anti-inflammatory additive promote photo-damage repair, induce cell proliferation, and used in skin care products also reduce the amount of inflammation induced by UV radiation (Draelos, 2003b). Green tea polyphenols have been shown to decrease the formation of cyclobutane pyrimidine dimers play an important role in initiating UV-induced mutagenesis and carcinogenesis and thereby protect against UV-induced edema and erythema when applied to the skin (Draelos, 2003b). Aloe vera is possibly the best known botanical anti-inflammatory agent used in the powdered form which may not be the same as the juice that is extracted from a broken leaf (Draelos, 2003b). Ginkgo biloba used in some skincare products promoting the antioxidant properties along with promoters of collagen synthesis (Draelos, 2003b). Soybeans are rich in isoflavones affects may be linked to its estrogenic effect, especially aging associated with postmenopausal women. Another isoflavone genistein found to increase collagen gene expression in cell culture (Draelos, 2003a).
Anti wrinkling effects of the mixture of vitamin C, vitamin E, pycnogenol and evening primrose oil, and molecular mechanisms on hairless mouse skin caused by chronic ultraviolet B irradiation by Cho et al., 2007, had proved that oral administration of the antioxidant mixture significantly inhibited wrinkle formation caused by chronic UV-B irradiation through significant inhibition of MMPs activity accompanied by enhancement of collagen synthesis. Anti-Wrinkle Activity of Ziyuglycoside I Isolated from a Sanguisorba officinalis Root Extract and Its Application as a Cosmeceutical Ingredient by Young et al., 2008, have measured that Sanguisorba officinalis root extract has potent free radical scavenging activity, elastase and expression of MMP-1 inhibitory activity in vitro, and type I collagen synthesis in normal human fibroblast cells. Richard, 2008 has been reported to have a potent anti aging properties of resveratrol in skin care formulation. Indeed, anti wrinkle or anti aging formulations slow down or reverse the effects of skin aging and help people to live longer, healthier, happier lives. Consumers are progressively more proactive about their health as they pass through middle and old age, and a heightened awareness of a variety of herbal extracts (plus a full pipeline of innovative plant-derived chemicals) is expected to spur robust gains. Topical agents can be an important treatment and preventative step in the photo-aging process with many of the mechanisms outlined throughout this chapter will help to maximize results and maintain the desired benefits of cosmetic formulations based on botanical ingredients.

1.5. Publications