**MINI REVIEW**

# Phenolics for skin photo-aging

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**Abstract**: Photo-aging is one of the foremost problems caused by generation of reactive oxygen species when skin is exposed on UV irradiation. In view of that, generation of reactive oxygen species intermingle with proteins, DNA, saccharides and fatty acids triggering oxidative mutilation and effects are in the appearance of distressed cell metabolism, morphological and ultra-structural changes, mistreat on the routes and revisions in the demarcation, propagation and skin apoptosis living cells which leads to photo-aging. Plant phenolics are universally found in both edible and inedible plants and have extended substantial interest as photo-protective for human skin due to their antioxidant activities. The objective of this review is to highlight the use of plant phenolics for their antioxidant activities against photo-aging.

**Keywords**: Plant Phenolics; Photo-aging; Skin.

## INTRODUCTION

### *Phenolics*

Phenolics are omnipresent in floras which mutually amalgamate copious diverse chemical structures categorized by hydroxylated aromatic ring (s) in which flavonoids, phenolic acids, cinnamic acids, catechins, anthocyanins or flavanols, flaovones, flavonols, isoflavones, flavanones, procyanidins, proanthocyanidins, stillbenes, coumarins, tannins, lignin and lignans are the most renowned (Boudet, 2007; Pereira *et al*., 2009; Gary *et al*., 2003). Phenolics embody the most considered phytochemicals and have been extensively developed as representational systems in diverse areas of phytochemical investigations (Gary *et al*., 2003). Phenolics playact to be as antioxidants in a number of manners (1) by creation of long subsisted radicals consequences hydrogen donating phenolics and reactive oxygen species are proficient to amend the radical mediated oxidation processes, (2) by chelating metal ions with phenolics intricated in the fabrication of free radicals and (3) by obstructing enzymes such as different cytochrome P450 isoforms, lipoxygenases, cyclooxygenase and xanthine oxidase enmeshed in radical formations (Pereira *et al*., 2009; Mary LP, 2001). The theory of free radical aging envisages that well life time can be improved by lessening injurious free radical reactions while not ominously intrusive with those crucial to the parsimony of the cells and tissues (Harman, 1991). In many products, phenolics have been exhibited to be operative antioxidant ingredients. Numerous phenolics wield more prevailing antioxidant effects than vitamin E in vitro and obstruct lipid peroxidation by chain-breaking peroxyl-radical scavenging. They can also hunt reactive oxygen species (ROS) directly, such as superoxide, hydroxyl and peroxynitrite (Howard, 2009). Different forms of sun damage can be inhibited by applying topical phenolics improve. A number of investigators have endeavored to understand the activity of plant phenolics for skin protection (Harman, 1991).

Plant phenolics can absorb UV radiation and act as a sunscreen, thereby, causes a possible reduction of oxidative pressure, inflammation and DNA detrimental consequences of UV radiation on the skin (Nichols and Katiyar, 2010). The antioxidant capacity of phenolic acids and flavonoids has been attained substantial consideration. Numerous flavonoids like luteolin, quercetin and catechins have enhanced antioxidant activity than vitamin E, vitamin C and β-carotene (Alena and Jitka, 2003). Therefore, the phenolics may be advantageous in inhibiting UV-induced oxygen free radical origination and lipid peroxidation, i.e. events complicated in photo-aging.

### *Skin*

The human skin is embraced of two foremost components, 1) the avascular epidermis and 2) the vascular dermis. The epidermis comprise of following four layers: 1) the stratum corneum 2) stratum granulosum 3) stratum spinosum and 4) stratum basale. The dermis generally contains of elastin fibers, collagen and ground substances plus glycosaminoglycan (Chumarka *et al*., 2008). The aging process generally comprises the epidermis and dermis. The skin experiences two forms of skin aging: intrinsic aging, also called chronological aging accredited to diminishing physiologic functions and extrinsic aging, also called photo-aging stressed by sun. Dyspigmentation, wrinkles and malignancies are involved in the clinical signs associated

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with photo-aging (Patravale and Mandawgade, 2008; Wulf *et al*., 2004).

### *UV irradiation*

Skin is the largest and the principal organ of the human body which defends the internal organs from harmful effects of ecological and xiobiotic agents (Gary *et al*., 2003). Ultra violet radiation exploits as a motivator for many skin disorders like scaling, wrinkling, dryness, mottled pigment abnormalities including hypo pigmentation, photo-aging, hyper pigmentation, and skin cancer though numerous factors of environmental and genetic participate to the development of various skin diseases (Nichols and Katiyar, 2010). UV radiation being a part of the electromagnetic spectrum with ranges wavelengths between 200 nm to 400 nm. It is parted into three classes (1) UVA long wave 320-400 nm, can spear the skin distance of approximately 1,000µm (2) UVB medium wave 280-320 nm, can pierce the skin distance of approximately 160-180 µm and (3) UVC short wave 200-280 nm, can pierce the skin distance of approximately 60-80 µm (Nichols and Katiyar, 2010; Wulf *et al*., 2004).

UVA can harm basic structures in the corneum and result early signs of photo-aging include wrinkling, wilting, laxity, sagging, patchy pigmentation, dryness etc., also causes necrosis of endothelial cells, thus harming the skin blood vessels initiated by endogenous photo-sensitization (Gopinath *et al*., 2004).

Reactive oxygen species (ROS) are engendered and can intrude mutilation to cellular lipids, proteins and saccharides. UVA can yield structural mutilation to DNA, weaken the immune system, and lead to cancer. UVB embroils, predominantly, direct mutilation to DNA (the formation of cyclobutane-pyrimidine dimers (CDPs) and pyrimidine-pyrimidone (6-4) photo-products ((6-4)-PP)) and proteins (interaction with aromatic amino acids). UVB also shares in indirect impairment to macromolecules. It aggravates free radical fabrication and tempts a significant decrease in skin antioxidants, worsening the skin's capability to defend itself against the free radicals engendered after sunlight contact (Gopinath *et al*., 2004). Moreover, UVB causes photo-isomerization of trans- to cis-urocanic acid (UCA), initiation of ornithine decarboxylase (ODC) capacity and cell cycle seizure, or weakening of DNA amalgamation in the skin. Both direct and indirect hostile biological consequences

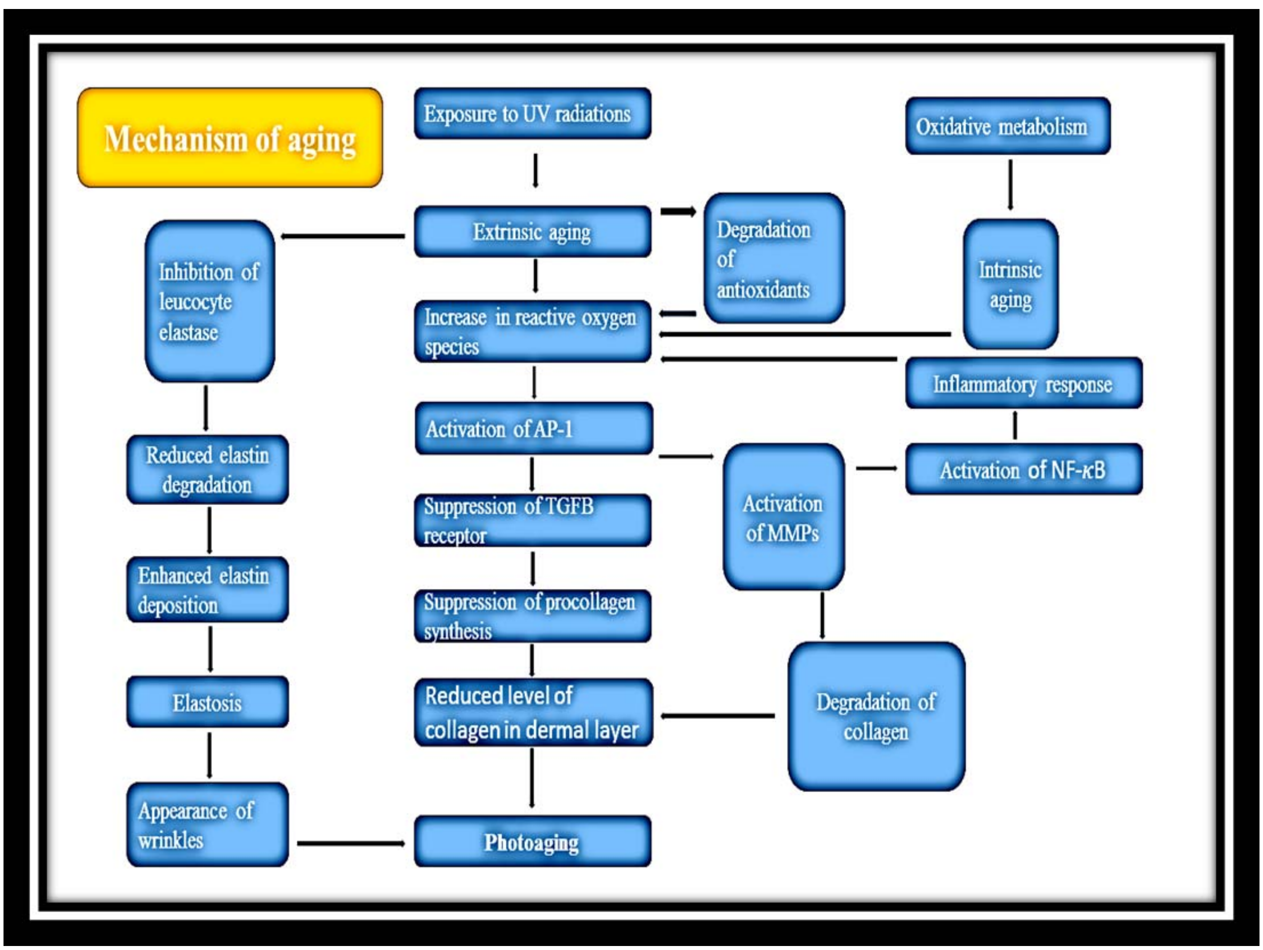


**Fig. 1**: Mechanism of skin aging.

of UVB may cause in photo-aging. UVB is deliberated to be prone for encouraging BCC and SCC due to DNA mutilation. It is also alleged of lowering the skin's immune defense system. The UVC light is the furthermost vigorous and has the extreme potential for biological damage to all kinds of life, even with only very tiny exposures. It is highly mutagenic and lethal. It is enthralled by proteins and nucleic acids and is particularly injurious to the skin (Alena and Daniela, 2006).

UV irradiation summons a multifaceted movement of specific molecular retorts that harm skin connective tissue. These molecular activities draw from the capability of UV irradiation to foster highly grown cellular machinery that intercedes UV damage to human skin connective tissue embraces (1) UV irradiation stimulates cell surface growth factor and cytokine receptors (2) UV irradiation stimulates NADPH oxidase, which breeds hydrogen peroxide (3) UV irradiation stimulates signaling pathways (4) UV-induced MMPs vitiate skin collagen (5) UV irradiation encumbers production of type I and type III procollagen (Gary *et al*., 2002; Gopinath *et al*., 2004).

***Quercetin***

The chemical formula of quercetin is 3, 5, 7, 3', 4'-pentahydroxyflavon, a natural flavonoid act as influential antioxidant and metal ion chelator adept of foiling the injurious effects of UV light or at least of lessening the mutilation (Mimica-Dukic *et al*., 2008). Quercetin reported as protected skin antioxidant in various systems of glutathione reductase, glutathione peroxidase, super oxide dismutase and catalase activities against UVA exposing mutilation to a significant degree. Quercetin taken orally inhibits UVB-induced immunosuppression in SKH-1 hairless mice. Quercetin and its semisynthetic derivatives, particularly, quercetin 3-O-acetate, quercetin 3-O-propionate, quercetin 3-O-palmitate were narrated to prevent UVC radiation-induced peroxidation in liposomal membranes in vitro (Pittella *et al*., 2009).

***Caffeic and ferulic acids***

The chemical formulas of caffeic and ferulic acids are 3, 4-dihydroxycinnamic acid and 4-hydroxy-3-methoxycinnamic acid, respectively. Both are protective of phospholipidic membranes from UV-induced per oxidation hinder proliferation of the lipid per oxidative chain reaction. Caffeic and ferulic acids shield human skin from UVB-induced erythema. Ferulic acid is a strapping UV absorber and a photo-protective agent in skin lotions and sunscreens (Alena and Jitka, 2003).

***Tannins***

Tannins are polyphenolic compounds are chemical defender against predators and ultraviolet radiation in plants. The two major classifications, (1) hydrolyzable tannins (HTs) which comprise gallotannins and ellagotannins and (2) condensed tannins (CTs), proanthocyanidins and may defend against free radical damage instigated by exposure to UV light consequently shrink the risk of skin cancer and premature aging (Alena and Jitka, 2003; Abhijit and Manjushree, 2010). Kaempferol glycoside derivatives inhibit UVB/UVC induced DNA mutilation and lipid peroxidation in skin fibroblast (Alena and Jitka, 2003).

***Examples of phenolics against skin photoaging found in plants***

*Moringa phenolics*

Total phenolic contents of Moringa oleifera leaf aqueous methanolic extract has been reported 12.2±0.28 (GAE g/100 g of DW) (Sultana *et al*., 2009). M. oleifera leaves contain quercetin-3-O-(6"-malonyl-glucoside) and quercetin-3-O-glucoside, and lower amounts of kaempferol-3-O-(6"-malonyl-glucoside) and kaempferol-3-O-glucoside. M. oleifera leaves also contain 5-caffeoylquinicacid and 3-caffeoylquinic acid (Bennett *et al*., 2003; Ali *et al*., 2013).

Gallic acid, kaempferol, Kaempferol 3-O-rhamnoside, quercetin, syringic acid and rutin kaempferide 3-O-(2",3"-diacetylglucoside), 3-O-glucoside, kaempferide 3-O-(2"-O-galloylrhamnoside), kaempferide 3-O-(2"-O-galloylrutinoside)-7-O-alpha-rhamnoside, kaempferol 3-O-[beta-glucosyl-(1 --> 2)]-[alpha-rhamnosyl-(1 --> 6)]-beta-glucoside-7-O-alpha-rhamnoside and kaempferol 3-O-[alpha-rhamnosyl-(1 --> 2)]-[alpha-rhamnosyl-(1 --> 4)]-beta-glucoside-7-O-alpha-rhamnoside together with benzoic acid 4-O-beta-glucoside, benzoic acid 4-O-alpha-rhamnosyl-(1--> 2)-beta-glucoside and benzaldehyde 4-O-beta-glucoside (Manguro and Lemmen, 2007). The HPLC study designated the existence of phenolic acids (gallic, chlorogenic, ferulic and ellagic acid) and flavonoids (kaempferol, quercetin, and rutin). Thus, it may be established that the Moringa extract of leaves holds high phenolics and antioxidant activities, which may be intervened through catching of the free radicals and metal chelation (Verma *et al*., 2009). HPLC and MS/MS analysis was performed, which revealed the company of chlorogenic acid, gallic acid, ferulic acid, ellagic acid, quercetin, kaempferol and vanillin. The LE (aqueous extract of leaves) was found relatively greater total phenolics, that is, 105.04mg gallic acid equivalents (GAE)/g), total flavonoids, that is, 31.28 mg quercetin equivalents (QE)/g), and ascorbic acid content (106.95 mg/100 g) and presented improved antioxidant capacity (85.77%), anti-radical (74.3), reducing capacity (1.1 ascorbic acid equivalents (ASE)/ml), protein oxidation, inhibition of lipid per-oxidation, OH-induced deoxyribose degradation, and scavenging power of super oxide anion and nitric oxide radicals than did the FE, SE and standard a-tocopherol (Brahma *et al*., 2009). The Moringa leaf extract is extensively used for skin disorders. Poultice of leaf is used against sores; it defends the human skin from ecological impacts and fights premature skin aging. Phenolic antioxidants present in Moringa lessen free-radical damage, thereby foiling damage at the cellular

**Table 1**: Different phenolic compounds and their classification

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| C6 | Simple phenolics |
| C6-C1 | Phenolic acids and related compounds |
| C6-C2 | Acetophenones and phenyl acetic acids |
| C6-C3 | Cinnamic acids, cinnamyl aldehydes, cinnamyl alcohol |
| C6-C3 | Coumarins, isocoumarins and chromones |
| C15 | Chalcones, aurones, dihydrochalcones |
| C15 | Flavans |
| C15 | Flavones |
| C15 | Flavanones |
| C15 | Flavanolols |
| C15 | Anthocyanindins |
| C15 | Anthocyanins |
| C30 | Biflavonyls |
| C6-C1-C6, C6-C2-C6 | Benzophenones, xanthones, stilbenes |
| C6, C10, C14 | Quinones |
| C18 | Betacyanins |
| Lignans, neolignans | Dimmers or oligomers |
| Lingnin | Polymers |
| Tannins | Oligomers or polymers |
| Phlobaphenes | Polymers |

level. They obstruct inflammation, which leads to collagen efficiency, and they pose guard against photo-damage and skin cancer.

***Acacia phenolics***

Total phenolic contents of Acicia nolilotica bark aqueous ethanolic extract has been reported 16.5±0.66 (GAE g/100 g of DW) (Sultana *et al*., 2009). Gallic and ellagic acids, leucocyanadin, isoquercitin, rutin, kaempferol-7-diglucoside and derivatives of (+) -catechin-5-gallate (Singh *et al*., 2009) contain (-) epicatechin, (+) catechin, gallic acid, (+) dicatechin, quercetin, (+) leucocyanidin gallate. Acacia nilotica is a medicinal plant acknowledged to be rich in phenolics consisting of condensed tannin and phlobatannin, gallic acid, protocatechuic acid, pyrocatechol, (+) -catechin, (-) epi-gallocatechin-7-gallate and (-) epigallocatechin-5, 7-digallate. The bark is prosperous in phenolics viz. condensed tannin and phlobatannin, gallic acid, protocatechuic acid pyrocatechol, (+)- catechin, (-) epigallocatechin-7-gallate, and (-) epigallocatechin-5,7- digallate (Singh *et al*., 2009).The bark is also reported to contain (-) epicatechin, (+) dicatechin, quercetin, gallic acid, (+) leucocyanidin gallate, sucrose and (+) catechin-5-gallate (Sundaram and Mitra, 2007; Ali *et al*., 2012). Acacia nilotica is a medicinal plant from which the polyphenolic compounds; kaempferol has been described for the first time. Another compound umbelliferone has been reported from Acacia nilotica. Bark is used against various skin diseases (Baravkar *et al*., 2008; Ali *et al*., 2012). Phenolic antioxidants present in Acacia bark diminish free-radical harm, thereby foiling damage at the cellular level and give protection against photo-damage.

***Cannabis phenolics***

Total phenolic contents has been reported 2.45 ±0.05 mg CAE/100 g. Cannabis contains phenolic acids such as protocatechuic, p-hydroxybenzoic, vanillic, caffeic, p-coumaric Ferulic and sinapic acids, which may be beneficial to protect against UV irradiation due to blockade of reactive oxygen species (Lampart-szczapa, 2008). Cannabinoids have reported pretending to be a potent antioxidant and there is an intense need for investigations of antioxidant activity of cannabinoids In addition, the oil has shown the existence of γ-linolenic acid, is acceptable as light body oils and lipid-enriched creams. And cosmetic purpose, oil of cannabis seeds has numerous feature UV-Vis bands positioned at wavelengths 412, 453, 482 and 670nm. The oil has yellow colour is in agreement with strong absorbance at 412, 453 and 482 nm of the blue and violet region. The oil engrossed in the UVC (100-290 nm) and UVB (290–320 nm) range. The oil had only transmittance in both UVB and UVA (320-400nm) regions and can act as UV protectant having high shielding power (SPF) and protection factor (PFA) scores. Therefore, oil may deliver defense against both UVA and UVB (Oomah *et al*., 2002; Mahmoud and Desmond, 2005).

***Future prospects***

Phenolics have gained significant interest to most of the researchers. Initial investigations in the line of work connected to the analytical characterization of broad numbered structures and of related enzymes with PAL, getting hold of worthwhile attention of plant enzymes. Furthermore, molecular biology and genomics have proved to understand mechanisms underlying the construction and separation of these compounds with the regulation of gene expression by environmental factors. The broad characterizations of genes encoding the different enzymatic steps of flavonoid production and cytochrome P450 genes have been among the most recent advances in this field. Metabolic engineering of lignins and flavonoids has been explored. Noteworthy positive results have proven in both fields a generous and sometimes unpredicted network of regulatory interactions. Recently, a growing curiosity for practical attentions has encouraged an extensive range of biological and epidemiological investigations intending at exemplifying the health promoting properties of specific phenolic compounds with antioxidant capacities towards cancer, neurodegenerative and cardiovascular diseases or for use in photo-aging or cosmetic products.

Augmented stress on defensible development should stimulate revolutionary investigations on phenolic production for enlightening plant biomass and for a better control of human skin against UV irradiation. The list of these compounds is still uncompleted and in progress. Recent reports highlight that primary questions still continue to be responded in the field of tannins and protoanthocyanidins and even the precise nature of the biosynthetic pathway(s) controlling to lignin monomers is not fully elucidated (Boudet, 2007). Literature is, however scarce in respect of the efficacy of plant phenolics and then for photo-aging, so more investigation is required. The prospect of phenolic research will likely include amazing and unpredicted progresses in the characterization of new structures and new exploitations in human activities with special stress on photo-aging.

## CONCLUSION

Human skin is persistently uncovered to the UV irradiation present in sunlight. This may persuade a number of pathobiological cellular changes. The expansion of unique prevention and therapeutic strategies depends on our perception molecular mechanism of UV-damage. Plant phenolics are one aspirant for avoidance of the hostile effects of UV- radiation on the human skin and it must be identified and quantified to determine the relationship between antioxidant capacity and phenolics to verify that phenolic constituents are reasonable sources against photo-aging in cosmetic field and, furthermore, evaluation of their clinical efficacy is awaited.

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## REFERENCES

Abhijit S and Manjushree D (2010). Anti-hyaluronidase, Anti-elastase Activity of Garcinia indica. *Int. J. Bot.,* **6**: 299-303.

Alena DWS and Jitka P (2003). Natural phenolics in the prevention of induced skin damage: A Review. *Biomed. Pap.,* **147**: 137-145.

Alena JVS and Daniela W (2006), Ultraviolet light induced alteration to the skin. *Biomed. Pap.,* **150**: 25-38.

Ali A, Akhtar N, Khan BA, Khan MS, Rasul A Shahiq-UZ-Zaman, Khalid N, Waseem K, Mahmood T, Ali L (2012). Acacia nilotica: A plant of multipurpose medicinal uses. *J. Med. Plant. Res.,* **6**: 1492-1496.

Ali A, Akhtar N, Khan HMS, Khan MT, Aftab Ullah, Shah MI (2013). Effect of Moringa oleifera on undesirable skin sebum secretions of sebaceous glands observed during winter season in humans. *Biomed. Res.,* **24**: 127-130.

Baravkar AA, Kale RN, Patil RN and Sawant SD (2008). Pharmaceutical and biological evaluation of formulated cream of methanolic extract of Acacia nilotica leaves. Research. *J. Pharm. and Tech.,* **1**: 481-483.

Bennett, Mellon RN, Nikolaus F, John PH, Susan DM, Lionel P and Paul K (2003). Profiling glucosinolates and phenolics in vegetative and reproductive tissues of the multi-purpose trees Moringa oleifera L. (horseradish tree) and Moringa stenopetala L. *J. Agric. Food. Chem.,* **51**: 3546-3553.

Boudet AM (2007). Evolution and current status of research in phenolic compounds. *Phytochem.,* **68**: 2722-2735.

Brahma N, Singh, Singh BR, Singh RL, Prakash D, Dhakarey R, Upadhyayd G and Singh HB (2009). Oxidative DNA damage protective activity, antioxidant and anti-quorum sensing potentials of Moringa oleifera. *J. Agric. Food. Chem.,* **6**: 1109-1116.

Chumarka P, Khunawat P, Sanvarinda Y, Phornchirasilp S, Moralesb, ngame NP, Ratanachamnong P, Srisawat S, Klai-upsorn S and Pongrapeeporn (2008). The in vitro and ex vivo antioxidant properties, hypolipidaemic and antiatherosclerotic activities of water extract of Moringa oleifera Lam. leaves. *J. Ethnopharmaco.,* **116**: 439-446.

Gary GD, Peter TG and Janet AMK (2003). Plant polyphenols: are they the new magic bullet? *Proc. Nutr. Soc.,* **62**: 599-603.

Gary JF, Kang S, Varani J, Bata-Csorgo Z, Wan Y, Datta S and Voorhees JJ (2002). Mechanisms of photoaging and chronological skin aging. *Arch. Dermatol.,* **138**: 1462-1470.

Gopinatha D, Rafiuddin M, Ahmeda, Gomathia K, Chitraa K, Sehgalb PK and Jayakumara R (2004). Dermal wound healing processes with curcumin incorporated collagen films. *Biomater.,* **25**: 1911-1917.

Harman D (1991). The aging process: major risk factor for disease and death. Prod. Natl. Acad. Sci., **88**: 5360-5363.

Howard E (2009). Cosmeceuticals and polyphenols. *Clin. Dermatol.,* **27**: 475-478.

Lampart-szczapa E (2008). Compounds in cold-pressed plant oils. *J. Food. Lipids,* **15**: 137-149.
Mahmoud S, Desmond S (2005). Chemical constituents of marijuana: the complex mixture of natural cannabinoids. *Life. Sci.,* **78**: 539-548.
Manguro LOA and Lemmen P (2007). Phenolics of Moringa oleifera leaves. *Nat. Prod. Res.,* **21**: 56-68.
Mary LP (2001). Antioxidants and vitamins in Cosmetics. *Clin. Dermatol.,* **19**: 467-473.
Mimica-Dukic N, Simin N, Cvejic J, Jovin E, Orcic D, Bozin B (2008). Phenolic compounds in field horsetail (Equisetum arvense L.) as natural antioxidants. *Molecules.,* **13**: 1455-1464.
Nichols J and Katiyar SK (2010). Skin photoprotection by natural polyphenols: Anti-inflammatory, antioxidant and DNA repair mechanisms. *Arch. Dermatol. Res.,* **302**: 71-83.
Oomah BD, Busson M, Godfrey DV and Drover JCG (2002). Characteristics of hemp (Cannabis sativa L.) seed oil. *Food Chem.,* **76**: 33-43.
Patravale VB and Mandawgade SD (2008). Novel cosmetic delivery systems: an application update. *Inter. J. Cosmet. Sci.,* **30**: 19-33.
Pereira DM, Valentão P, Pereira JA and Andrade PB (2009). Phenolics: From Chemistry to Biology. *Molecules.,* **14**: 2202-2211.
Pittella F, Dutra RC, Junior DD, Lopes MTP and Barbosa NR (2009). Antioxidant and cytotoxic activities of Centella asiatica (L) Urb. *Int. J. Mol. Sci.,* **10**: 3713-3721.
Singh BN, Singh BR, Sarma BK and Singh HB (2009). Potential hemoprevention of N-nitrosodiethylamine-induced hepatocarcinogenesis by polyphenolics from Acacia nilotica bark. *Chem. Biol. Interact.,* **181**: 20-28.
Sultana B, Anwar F and Ashraf M (2009). Effect of extraction solvent/technique on the antioxidant activity of selected medicinal plant extracts. *Molecules.,* **14**: 2167-2180.
Sundaram R and Mitra SK (2007). Antioxidant activity of ethyl acetate soluble fraction of Acacia arabica bark in rats. *Indian. J. Pharmacol.,* **39**: 33-38.
Verma AR, Vijayakumar M, Mathela CS and Rao CV (2009). *In vitro* and *in vivo* antioxidant properties of different fractions of Moringa oleifera leaves. *Agric. Food. Chem.,* **47**: 2196-2201.
Wulf HC, Sandby-møller J, Kobayasi T, Gniadecki R (2004). Skin aging and natural photo protection. *Micron.,* **35**: 185-191.