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Cosmetic Attributes of *Aloe vera* L. Gel

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ABSTRACT

Aloe vera L. (syn. *A. barbadensis* Miller.) is a perennial succulent plant belonging to the Liliaceae family. The plant is known traditionally as the "healing plant" and is claimed to possess wound-healing, burn-healing, immunomodulatory, anti-inflammatory, anti-oxidant, anti-allergic, anti-diabetic, and UV protective properties. Due to these therapeutic properties *A. vera* is being used in a variety of pharmaceutical and cosmetic product formulations. Most of its biological potential has been attributed to the polysaccharides present in its gel. Many attempts have been made to describe the biological potential of *Aloe* gel. This review focuses on the recently explored cosmetic potential of aloe gel in relation to wound healing, anti-oxidant and UV-opacity.

Keywords: antioxidant activity, sun protection factor, UV-opacity, wound healing

INTRODUCTION

Aloe vera L. (syn. *A. barbadensis* Miller.), the 'miracle plant', is a traditionally used medicinal plant belonging to the Liliaceae family, and is grown mostly in tropical areas. The aloe plant was regarded as the 'universal panacea' by Greek scientists 2000 years ago. The Egyptians called the aloe 'the plant of immortality'. The American Indians called aloe 'the wand of heaven' (http://www.amazing-aloevera.com). The plant is often referred to as a 'healing plant' and is a source of two main products from the leaves. The leaves of *A. vera* are surrounded by a thick epidermis with a cuticle. The mesophyll cells are differentiated into chlorenchyma and a thinner-walled parenchyma. The yellow colored exudates from the epidermal part contain a high amount of anthraquinone compounds which have been used as potent cathartics and lacquer agents. The second product is a clear translucent mucilaginous gel which is obtained by removing the epidermal part (Ni *et al.* 2004). This parenchymatous leaf gel possesses a diverse range of pharmacological properties and is commonly referred to as aloe gel (AG; Ni *et al.* 2004; Talmadge 2004).

Over the last decade, the use of AG has gained popularity as a therapeutic botanical and consequently a large industry based on its various products has developed (Eshun and He 2004). Many biological activities including anti-viral, anti-bacterial, laxative, protection against radiation, anti-oxidant, anti-inflammation, anti-cancer, anti-diabetic, anti-allergic and immuno-stimulation have been attributed to this plant gel (Choi and Chung 2003; Park and Lee 2006; Hamman 2008). A large part of these pharmacological properties is due to polysaccharides, which is present in 10% of the dry weight of the gel (Ni *et al*. 2004). Today, AG appears as an ingredient in a myriad of health and cosmetic products that range from skin moisturizers, face and hand creams, cleansers, soaps, suntan lotions, sunscreens, skin whiteners, shampoos and hair tonics, shaving preparations, bath aids, makeup and fragrance preparations to baby lotions and wipes (Eshun and He 2004; Dal'belo *et al.* 2006). The bioavailability of co-administered vitamins in human systems is also improved by the addition of AG (Vinson *et al*. 2005). In a randomized, double-blind, cross-over clinical trial with human Vinson *et al*. (2005) studied the effect of AG on the oral bioavailability of vitamins C and E. Compared to the control, the bioavailability of vitamins C and E was found to be 3 and 3.7 times higher, respectively when administered with AG. The AG also kept the level of vitamin C significantly higher than the baseline. A possible protection effect of AG against the degradation of the vitamins has been attributed for the improved bioavailability of vitamins in the intestinal tract. Binding of the AG polysaccharides to the vitamins may also slow down the rate of absorption. The transport of insulin has been studied in the presence and absence of AG and whole leaf extract solutions using Caco-2 cell monolayers (Chen *et al.* 2009). AG products significantly enhanced the insulin transport. The study indicates the potential of AG as absorption enhancers for drugs with poor bioavailabilities.

As a natural product, AG contains a diverse array of component compounds, including anthraquinones, saccharides, polysaccharides, lignin, and numerous low molecular weight compounds such as vitamins and salicylic acid (Femenia *et al*. 1999; Ni and Tizard 2004); in addition to recently discovered compounds such as bioactive maloyl glucans (Esua and Rauwald 2006), acemannan, a mannose-containing polysaccharide, has been reported as the main active substance present in AG (Ni *et al.* 2004). However, biological activities of AG may not be solely assigned to the polysaccharides. It is believed that the synergistic action of the various components of AG contribute to the occurrence of a wide array of biological functions.

A considerable number of reviews are available on *A. vera* L. including gel chemistry, biological activity and post harvest gel processing (Reynolds and Dweek 1999; Choi and Chung 2003; Boudreau and Beland 2006; Steenkamp and Stewart 2007; Hamman 2008; Josias 2008). The present review summarizes the cosmetic attributes of AG highlighting the recently explored wound healing, antioxidant and UV-opacity potential of the gel.

COSMETIC POTENTIAL OF *ALOE VERA* GEL

The varied nature of therapeutic properties of AG may be manifested due to the presence of more than 200 bioactive compounds that work together in a finely tuned system network. There may be some synergetic action between the polysaccharide moiety and other components in AG (Leung *et al.* 2004). Davis (1997) proposed the "Conductor-Orches-

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Review

Table 1 Summary on wound-healing potential of *Aloe vera* L. gel.

Wound incised in mice and rats	Decolorized extract more effective in stimulating wound healing	Davis *et al.* 1987
Oral and topical applications of extracts on wound healing	Wound diameter reduced in both conditions	Davis *et al.* 1987
Burn wound healing and comparison with AgSD	AgSD treated wounds showed higher epithelization rates	Kaufman *et al.* 1988
Effect of acemannan on wound healing	Acemannan showed wound healing when administered topically and systemically	Tizard *et al.* 1994
Influence on collagen characteristics in healing dermal wounds	Increased collagen content and characteristics of granulation tissue; increased degree of cross linking; enhanced level of type-III collagen	Chithra *et al.* 1997
Testing a glycoprotein fraction to stimulate wound healing	Glycoprotein fraction G1G1M1D12 showed wound healing via cell proliferation and migration of keratinocytes	Choi *et al.* 2001
Testing the effect of silver sulfadiazone and *Aloe* on full thickness excised wounds	Retardation of wound healing by silver sulfadiazine is reversed by *Aloe vera* L. and nystatin	Muller *et al.* 2003
Skin permeation enhancer of drugs using porcine ear skin	For colchicine, oxybutynin and quinine the presence of *Aloe vera* L. within the formulation provided enhancements	Cole and Heard 2007
Wound burn in humans	Average percent of healing with *Aloe vera* L. on day 10 was 90.6% compared with silver sulfadiazine which was only 29.8%	Moghbel *et al.* 2007
Mice, MTT and *in vitro* scratch assay	Aloe extracts from five Indian germplasms significantly stimulated the migration and proliferation of fibroblasts	Manoj *et al.* 2009

Abbreviations: AgSD: silver sulfadiazine, MTT : 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide

tra concept" to explain the inter-relationship among more than 200 biologically active compounds within *A. vera*. According to him the polysaccharide molecule acts as conductor and keeps working in a proper way synergistically with other compounds that leads various biological activities. However, the proteins and polysaccharides are fundamental components in the study of biological activity of AG (Kostalova *et al.* 2004).

Wound healing activity

Wound healing is the process of repair and regeneration of dermis and epidermis that follows injury to the skin and other tissues of the body. Skin regeneration involves inflammation, cell proliferation and contraction of collagen lattice formation (Kumar *et al.* 2007; Reddy *et al.* 2008).

The wound healing activities of AG have been demonstrated using both *in vivo* and *in vitro* models (**Table 1**). The most commonly used model systems are excision, incision and dead space where higher breaking strength and higher hydroxyproline content are obtained in the treated groups with a decrease in surface area of wound.

The experiment conducted by Davis *et al*. (1987) to determine the effects of *A. vera* on wounds incised in mice and rats showed stimulating effects in wound healing. Decolorized *A. vera* (with anthraquinone removed) and whole *A. vera* extract was injected subcutaneously into animals. It was observed that the decolorized extract was more effective in stimulating wound healing than whole extract. However, the study raises doubt about its validity in human system as the study was limited to 7-12 days only. In another set of experiments, oral and topical activity of *A. vera* on wound healing was investigated. The experiment was conducted with three groups. One group received *A. vera* in their drinking water for consecutive two months before inflicting wound on them and the second group received 25% decolorized *A. vera* topically on wounds. The third group was made a control without any treatment. The wound diameter was significantly reduced in both the *A. vera*-treated groups compared to the untreated group. AG-mediated stimulation and enhancement of vascularity around the wound site as well as reduction in the amount of dead tissue at the wound site were also observed using *in vivo* models. The most commonly used model systems were excision, incision and dead space where higher breaking strength and higher hydroxyproline content were obtained in the treated groups with a decrease in surface area of wound (Heggers *et al.* 1996; Yagi *et al.* 1997; Thomas *et al.* 1998).

In contrast, Kaufman *et al.* (1988) failed to demonstrate that AG has the ability to hinder burn wound healing. Kaufman *et al.* (1988) tested the effectiveness of *A. vera* on burn wound healing and compared its efficiency with silver sulfadiazine (AgSD). AgSD-treated wounds showed higher epithelization rates than aloe-treated wounds although the latter had a higher wound contraction. There have been contradictory reports on the wound-healing effects of AG components. Acemannan isolated from aloe did not show a significant would-healing effect, whereas mannose 6-phosphate and a glycoprotein fraction stimulated proliferation in mice fibroblasts and human keratinocytes, respectively (Davis *et al.* 1994; Choi *et al.* 2001).

Would healing potential of AG has also been studied at the cellular level (Kumar *et al.* 2009). Fibroblasts are the major source of extracellular connective tissue matrix and migration of fibroblasts are considered to be vital in rapid and effective repair of damaged skin. Fibroblasts produce collagen (protein) to strengthen the new tissue formations which heal wounds. Chen *et al.* (2005) investigated the influence of polysaccharides from *A. vera* on the proliferation of human epithelial cells cultured *in vitro*. Aloe polysaccharides effectively protected epithelial cells by elevating cell proliferation by inducing the progression of epidermal cells from phase G0/G1 into G2/M and S phases.

Acemannan has been identified as one of the main compounds responsible for wound healing. It is capable of wound healing and the possible mechanism might be through macrophage activation (Zhang and Tizard 1996). There are various mechanisms by which *A. vera* can promote wound healing e.g. a glycoprotein fraction G1G1M1D12 has been shown to stimulate wound healing by increasing keratinocyte proliferation and migration (Choi *et al.* 2001). Wound healing is a fundamental response to tissue injury that results in restoration of tissue integrity. This is achieved mainly by the synthesis of the connective tissue matrix. Collagen is the major protein of the extracellular matrix, and is the component which ultimately contributes to wound strength. AG influences collagen content of the granulation tissue and the degree of cross linking, thus promoting wound healing (Chithra *et al.* 1998). In their work, the ratio of type I/type III collagen of treated groups were found to be lower than that of the untreated controls indicating enhanced levels of type III collagen. Furthermore, AG can inhibit matrix metalloproteinase in a dose-dependent manner (Barrantes and Guinea 2003). Activity-guided fractionation led to an active fraction enriched in phenolics and aloins. Aloins have been shown to bind and inhibit *Clostridium histolyticum* collagenase (ChC) reversibly and non-competitively. AG and aloins are also effective inhibitors of stimulated granulocyte matrix metalloproteinases (MMPs). The remarkable structural resemblances between aloins and the pharmacophore structure of inhibitory tetracyclines, suggest that the inhibitory effects of aloins are via an interaction between the carbonyl group at C9 and an adjacent hydroxyl group of anthrone (C1 or C8) at the secondary binding site of enzyme, destabilizing the structure of granulocyte MMPs (Barrantes

and Guinea 2003).

The effects of acemannan on gingival fibroblasts proliferation, keratinocyte growth factor-1 (KGF-1), vascular endothelial growth factor, type I collagen production and oral wound healing was investigated in murine model (Jettanacheawchankit *et al.* 2009). [^{3}H]-Thymidine incorporation assay and ELISA test were employed in the experimental procedures. Punch biopsy wounds were created at the hard palate of male Sprague Dawley rats. Histological features and wounded areas were observed at the 7th day after treatment. Acemannan at 2-16 mg/ml significantly stimulated keratinocyte growth factor 1, vascular endothelial growth factor, and type 1 collagen expressions. Wound healing of animals treated with Carbopol® containing 0.5% acemannan (w/w) was significantly higher than that of the other groups. The findings indicate the role of acemannan in oral wound healing process.

Manoj *et al.* (2009) documented the AG-induced stimulation of fibroblast cells using [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] (MTT) and *in vitro* scratch assay (Liang *et al.* 2007), which is based on the observation that, upon creation of an artificial gap or scratch, on a confluent cell monolayer, the cells on the edge will move toward the opening and close the gap gradually by cell-to-cell contacts.

Proliferation and migration of fibroblasts was evident in all the tested *Aloe* germplasms in a dose-independent manner. The germplasm TN showed the maximum potential, while the minimum potential was evident with RJN. The description of aloe germplasms along with their place of collection and agroclimatic zones has been detailed in our previous work on wound healing potential of AG (Manoj *et al.* 2009). Among the aloe germplasms, a positive relationship was observed in proliferation and migration of cells. The migration of fibroblasts in the scratch area may be attributed to the combined effect of absolute cellular migration, proliferation and cell death (Ozturk *et al.* 2007). The *in vitro* scratch assay appeared to be an easy and low-cost method to measure fibroblast migration *in vitro* and could be employed to evaluate the wound-healing potential of medicinal plants.

AG-induced stimulation of fibroblasts could be explained by the notion that either AG directly stimulates fibroblasts (Davis *et al.* 1994) or it first stimulates macrophages; these macrophages then release chemical messengers that stimulate fibroblasts (Tizard *et al.* 1989). It might be that the components of AG contain mannose-6-phosphate that fits into growth receptors present on fibroblast cells and stimulates them (Davis *et al.* 1994). This type of receptor is also found on macrophages and other immune cells (Winters 1993). This very mechanism has been referred to above, showing a route to the stimulation of fibroblasts. Inherent to this idea is the concept that fibroblast cells – which are key cells in forming the structure of connective tissue – possess special receptors, which are sensitive to mannose-6-phosphate and hence to mannose-containing polysaccharides, mannose-containing glycoproteins, and breakdown products derived from these large mannose-rich molecules (Munier-Lehmann *et al.* 1996). Danof *et al.* (1983) observed that the fractions prepared from AG contain lectin-like glycoprotein substances. Presumably, these substances promote the growth of human fibroblasts. The aloe glycoproteins, mainly lectin, were reported to have wound-healing activity (Heggers *et al.* 1996; Utsunomiyal 1998) however, the mannose-binding lectin shows improved wound healing, hemagglutination (agglutination of red blood cells) and mitogenic (agent that triggers mitosis) activity.

The glycoprotein molecule in AG has cell proliferation boosting activity. Yagi *et al.* (1997) described the presence of a 29 kDa glycoprotein in AG responsible for cell proliferating activity. Choi *et al.* (2001) isolated another 5.5 kDa glycoprotein having the same type of biological activities. The carbohydrate molecules present in these biologically active glycoproteins are mainly mannose (70%). In 1994, Davis *et al*. studied the potency of mannose-6 phosphate and glycoproteins in *A. vera* for wound healing. Mannose-6-phosphate promoted wound healing in a dose-dependent manner but increased wound healing effects were noted with mannose-6-phosphate linked to a insulin-like growth factor 11 receptor protein (Morgan *et al.* 1987).

It is not surprising that the processes of immune stimulation and healing have something in common and that they should also be linked in another way. Both seem to reside, at least in part, in the high molecular weight carbohydrate-rich fraction of aloe. It appears that the "final common pathway" for initiating both the immune-stimulatory effect and the tissue-healing effect of aloe is the stimulation of predominantly mannose-sensitive cell-surface receptors. It is also believed that the intact leaves anthraquinones and their derivatives may also take part in wound healing. Anthraquinones in the leaves diffuse into the gel from the bundle sheath cells, this possibly confirms the conclusion of that the healing agent is passed from the rind into gel on standing (Yen *et al.* 2000; Mackay and Miller 2003; Rajendran *et al*. 2007). The presence of Vitamin D in gel also acts as the healing agent (Mackee 1938). Apart from vitamin D, vitamin C, vitamin B complex and the minerals such as zinc are very important in wound healing activity of AG.

Antioxidant activity

In recent years, there has been increasing interest in natural antioxidants to prevent the deleterious effects of free radicals. Any imbalance in the cellular metabolism can lead reactive oxygen species (ROS) to do oxidative damage to cellular membranes or intracellular molecules. These ROS can also induce peroxidation of membrane lipids leading to increased accumulation of lipid peroxides and hydroperoxides. Antioxidative defense mechanisms protect cells from the

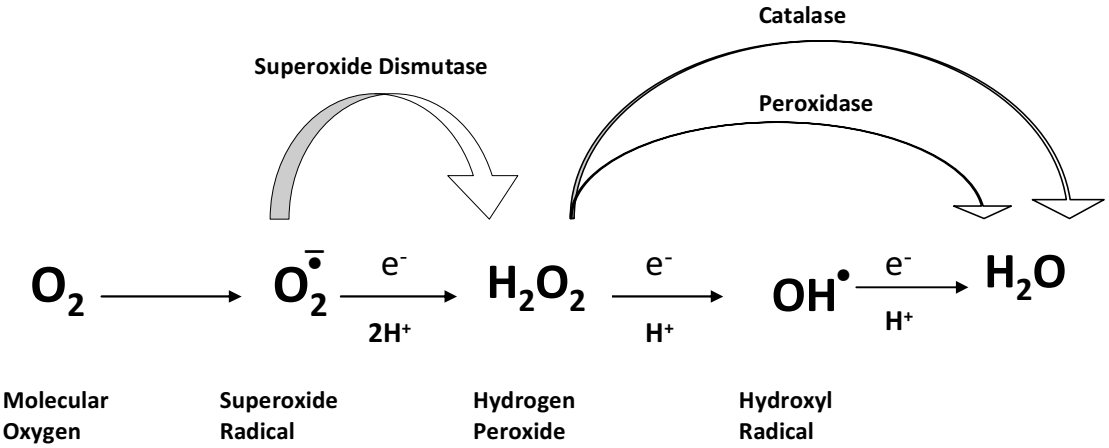

Fig. 1 Enzymatic pathway for detoxification of reactive oxygen species.

Table 2 An overview of antioxidant potential of *Aloe vera* L.

Assay procedures	Significant findings	References
Compound isolation by Amberlite XAD-2 column, TLC, HPLC; TBARS in rat brain homogenate and free radical reactivity	Antioxidant activity similar to that of α-tocopherol	Lee *et al.* 2000
Lipid peroxidation, DPPH and superoxide anion scavenging activity	Isorabaichrome showed potent antioxidative activity; isorabaichrome with feruloylalosein and coumaroylalosein showed potent DPPH and superoxide anion scavenging activity	Yagi *et al.* 1999
Radical scavenging by DPPH and linoleic acid system (FTC method)	Three year old aloe plants exhibited greater radical scavenging activity	Hu *et al.* 2003
Lipid peroxidation and enzymatic assays in STZ-induced diabetic rats	Oral administration at 300 mg/kg significantly decreased blood glucose, glycosylated hemoglobin and lipid peroxidation, Reduction in the levels of reduced glutathione, SOD, glutathione peroxidase and glutathione transferase; activities with aloe extracts	Rajasekaran *et al*. 2004
FRAP, Fe^{3+} reduction, TBARS, protein carbonyl content assays	Oxidative damage in hippocampus and cerebral cortex was reduced as marked by decline in lipid peroxidation and protein carbonyls	Parihar *et al*. 2004
ABTS and DPPH radical scavenging activity	Free radical scavenging activities of 33.5% and 39.7% for supercritical carbon dioxide extraction and solvent extracts	Hu *et al.* 2005
Superoxide and hydroxyl radicals scavenging activity	Isolated derivatives of dihydrocoumarins showed antioxidant activity	Zhang *et al*. 2006
Superoxide, site-specific and non-site-specific hydroxyl radicals scavenging activity, peroxidation of LDL, MDA, LDH, GSHpx, CAT and SOD activities	Separated polysaccharide, APS-1 was demonstrated to scavenge free radicals	Wu *et al.* 2006
TEAC assay	The presence of Aloe-emodin and aloresin B in the dried aloe flower might be responsible for antioxidant activity	Keyhanian and Stahl-Biskup 2007
β-carotene bleaching method, DPPH radical scavenging assay and reducing power	The chloroform-ethanol fraction showed the highest radical scavenging activity and reducing power, whereas hexane fraction resulted in maximum antioxidant activity with β-carotene bleaching method	Miladi and Damak 2008
Antioxidant enzyme assay in Ehrlich ascite carcinoma cell model	A significant elevation of antioxidant enzyme activity was observed with active principles of AG such as aloesin, aloe-emodin and barbaloin	El-Shemy *et al.* 2010

Abbreviations: ABTS: 2,2'-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid), APS-1: aloe polysachharide 1, CAT: catalase, DPPH: 2,2-diphenyl-1-picrylhydrazyl, FRAP: ferric reducing antioxidant power, FTC: ferric thiocyanate, GSHpx: glutathione peroxidase, HPLC: high-performance liquid chromatography, LDH: lactate dehydrogenase, LDL: Low density lipoprotein, MDA: malondialdehyde, SOD: superoxide dismutase, STZ: streptozotocin, TBARS: thiobarbituric acid reactive substances, TEAC assay: trolox equivalent antioxidant capacity assay, TLC: thin layer chromatography

damages induced by ROS.

Biological antioxidants irrespective of whether they are enzymatic or non enzymatic inhibit reactions promoted by oxygen free radicals and reactive oxygen species (**Fig. 1**). Numerous traditional medicinal plants are now being investigated in search of natural antioxidants. In particular, antioxidant effects of aloe have been demonstrated by several authors utilizing various assay procedures from different fractions of AG as well as unfractionated crude gel (**Table 2**). Various components of AG possess anti-oxidative activity. Phenolic anthraquinones such as aloin, aloe-emodin, barbaloin, and emodin are capable of scavenging ROS (Malterud *et al.* 1993; Yen *et al.* 2000).

Phenolic compounds separated from lyophilized AG showed antioxidant activity comparable to α-tocopherol. The compound has been identified as 8-C-β-D-[2-O-(E)-coumaroyl]glucopyraosyl1-2-[2-hydroxyl]-propyl-7-methoxy-5-methylchromone (Lee *et al.* 2000). Yagi *et al.* (1997, 1999) investigated the antioxidant and free radical scavenging effects of aloesin derivatives of *A. vera*. The antioxidant components were examined for lipid peroxidation using rat liver mitochondrial and microsomal enzymes. Among the aloesin derivatives, isorabaichrome showed a potent antioxidadative activity. Isorabaichrome together with feruloylalosein and *p*-coumaroylaloesin also showed potent DPPH radical and superoxide scavenging activities. Electron spin resonance (ESR) using the spin trapping method suggested that the potent superoxide anion scavenging activity of isorabaichrome may be due to its caffeoyl group.

An active glycoprotein fraction containing 58% protein isolated from *A. vera* gel by precipitation with 55% ammonium sulfate followed by gel filtration showed a radical scavenging activity against a superoxide anion generated by xanthine-xanthine oxidase system as well as inhibition of cyclooxygenase-2 (COX-2) and reduction of thromboxane A2 synthase (Tx A2 synthase) level *in vitro*. The ability of aloe-emodin to inhibit free radical and ROS was tested using isoluminol and luminal enhanced chemiluminescence and electron absorption spectra in a cell free system (Vargas *et al.* 2004). The compound was capable of trapping the singlet oxygen generated by rose Bengal and showed an efficient ROS scavenging activity.

Dihydrocoumarin derivatives isolated from *A. vera* L. showed antioxidant activity against superoxide and hydroxyl radicals (Zhang *et al.* 2006). Among the two compounds isolated, compound 1 with a molecular formula of C22H18O7 obtained by combined HR-FAB-MS and 13 NMR spectrums appears to be more effective in regulating the ROS levels by directly scavenging ROS and promoting the oxygen respiratory burst than compound 2.

Attempts have also been made to isolate phyto-polysaccharides having antioxidant activities. Glycan extract of *A. vera* var. *chinensis* was found to be highly antioxidative (Wu *et al.* 2006). A polysaccharide named as APS-1, was isolated using a combination of anion-exchange and repeated gel chromatographes. APS-1 is composed of mannose and glucose in a proportion of 18:5 with a molecular weight of 2.1X10 5 Da and is effective in scavenging superoxide and hydroxyl radicals. The polysaccharide was also found to inhibit significantly lipid peroxidation in human low density lipoprotein (LDL) in a dose dependent manner. Liu *et al.* (2007) isolated two polysaccharide enriched fractions from the gel and the skin of *A. barbadensis* Miller following ion-exchange chromatography and gel chromatographic techniques. The plants were irrigated with sea water for 3.5 years. The polysaccharide fractions isolated from parenchymatous gel and from the leaf skin were designated as GAPS-1 and SAPS-1 respectively. Both SAPS-1 and GAPS-1 were composed of Man: Glc: Gal but in a ratio of 296: 36: 1 and 120: 2: 3. GAPS-1 and SAPS-1 exhibited strong scavenging activities against superoxide radical, moderate ferrous chelating effect, moderate scavenging activities of hydroxyl radical, moderate reductive power and moderate inhibition of lipid peroxidation in a dose dependent manner. GAPS-1 showed higher antioxidant potential

than SAPS-1. It has been suggested that the more number of acetyl groups present in GAPS-1 may be responsible for better activity.

The growth stage of aloe plants (*A. vera* L.) has found to play an important role in displaying antioxidative properties (Hu *et al.* 2003). The polysaccharide and flavonoid concentrations of two-, three-, and four-year-old *A. vera* were determined, and their antioxidant activities were evaluated compared to BHT and α-tocopherol employing the DPPH radical scavenging method and the linoleic acid system. Three-year-old plants contained significantly higher levels of polysaccharides and flavonoids than two- and four-year-old plants. The antioxidant activity of aloe extracts and reference compounds followed the order: three-year-old aloe > BHT > four-year-old *A. vera* > α-tocopherol >Two-year-old aloe. The three-year-old extract exhibited the strongest radical scavenging activity of 72.19%, which was significantly higher than that of BHT (70.52%) and α-tocopherol (65.20%).

The presence of antioxidant property in the alcoholic extract of *A. vera* leaf gel was also demonstrated in streptozotocin (STZ) induced diabetic rats (Rajasekran *et al.* 2005). Oral administration of AG extract significantly decreased the levels of blood glucose and glycosylated hemoglobin in the diabetic rats. The findings suggest ameliorative role of aloe extract during oxidative stress caused by hyperglycemia. Antioxidative potential of ethanolic extract of aloe was demonstrated by a significant increase in the activities of the antioxidant enzymes (SOD, CAT, GPx and GST) in the liver and kidney of diabetic rats. The treatment with gel extract also resulted in a significant increase in the reduced glutathione (GSH).

The dried flowers of *A. vera* were analyzed by HPLC-DAD and HPLC-MS/MS and the flower extracts were found to contain aloe-emodin as well as the glycosylchromone aloresin B with antioxidative capacity measured to 85.7-94.9 μmol TEAC/g dried flower. The antioxidative activity was directly correlated with the polyphenol and flavonoid contents (Keyhanian and Stahl-Biskup 2007).

The free radical-scavenging activities of extracts of *Aloe barbadensis* Miller obtained by different extraction procedures were studied by Hu *et al.* (2005). The AG extracts derived from supercritical carbon dioxide extraction and solvent extraction methods yielded significantly higher free radical scavenging activities of 33.5 and 39.7%, respectively than samples of AG extracted by ethanol with a free radical-scavenging activity of 14.2%. The effects of extraction techniques (shaking and reflux) and various extraction solvents such as absolute ethanol, absolute methanol, aqueous ethanol and aqueous methanol on the antioxidant activity were investigated by Sultana *et al.* (2009). A decrease in the content of total phenol and antioxidant activities was observed with extracts prepared by reflux technique. Among the solvents, higher extract yield, phenol content and antioxidant activity were obtained with aqueous organic solvents. Various fractions of ethanolic extracts of *A. vera* leaf skin were subjected to antioxidant assay following β-carotene bleaching method, radical scavenging activity using DPPH and reducing power (Miladi and Damak 2008). The chloroform-ethanol fraction showed the highest radical scavenging activity and reducing power, whereas hexane fraction resulted in maximum antioxidant activity with β-carotene bleaching method. Active principles of *A vera* such as aloesin, aloe-emodin, barbaloin and the N-terminal octapeptide verectin extracted by supercritical fluid extraction were investigated for modulation of antioxidant enzymes in EACC (Ehrlich ascite carcinoma cell) model. A significant elevation of antioxidant enzymes was observed in EACC tumors treated with active principles indicating the chemopreventive effect of aloe (El-Shemy *et al.* 2010).

A selection of *Aloe* species other than *A. vera* L. was subjected to tests for possible inhibition of lipid peroxidation and free-radical scavenging effects (Lindsey *et al.* 2002). Most of the *Aloe* species tested contained chromone glycoside compounds with radical scavenging activity in the DPPH-TLC assay. *Aloe claviflora*, *A. tharskii* and *A. maculata* had moderate activity in the lipid peroxidation assay, whereas the other species tested did not show inhibition of lipid peroxidation. *Aloe ferox* and *A. greatheadii* lyophilized gel shows antioxidant activity as analysed by oxygen radical absorbance capacity (ORAC) and ferric reducing antioxidant power (FRAP) analyses (Loots *et al.* 2007; Botes *et al* 2008). However, *A. vera* L. seems to be the most promising candidate for natural antioxidants along with other associated biological potentials.

UV-Opacity

Sunlight is indispensable for organisms living on earth. Apart from its beneficial effects the exposure to sunlight can causes a number of hazards to the human skin. The major short-term hazard of prolonged exposure to sunlight is erythema, which is popularly known as sunburn (redness of the skin resulting from inflammation). Sunburn primarily results from the over exposure of ultraviolet (UV) radiation. There are three sub-bands of UV radiation UVA (380-315 nm), UVB (315-280 nm) and UVC (280-180 nm). Low frequency of UVB radiation near the 320 nm transition to UVA is responsible for severe sunburn.

Long-term exposure to UV, often lead to malignant

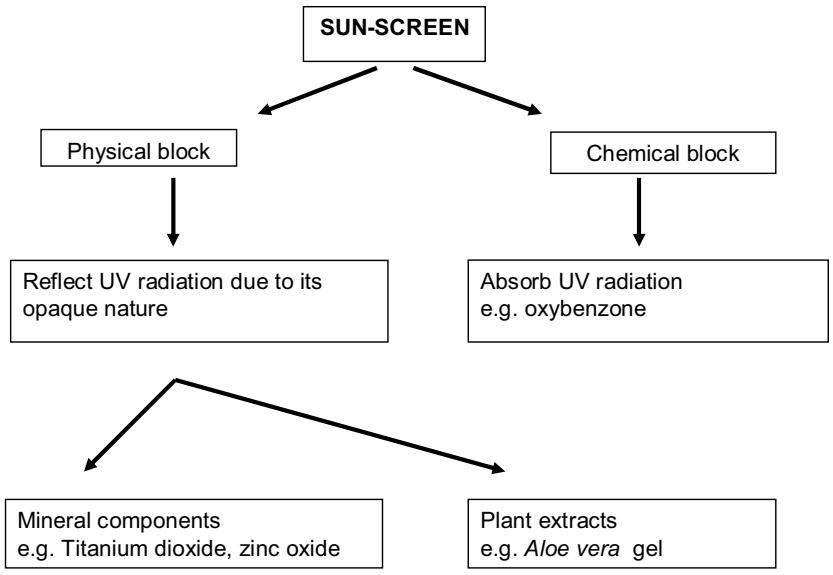

Fig. 2 Schematic illustration for the components of sunscreen.

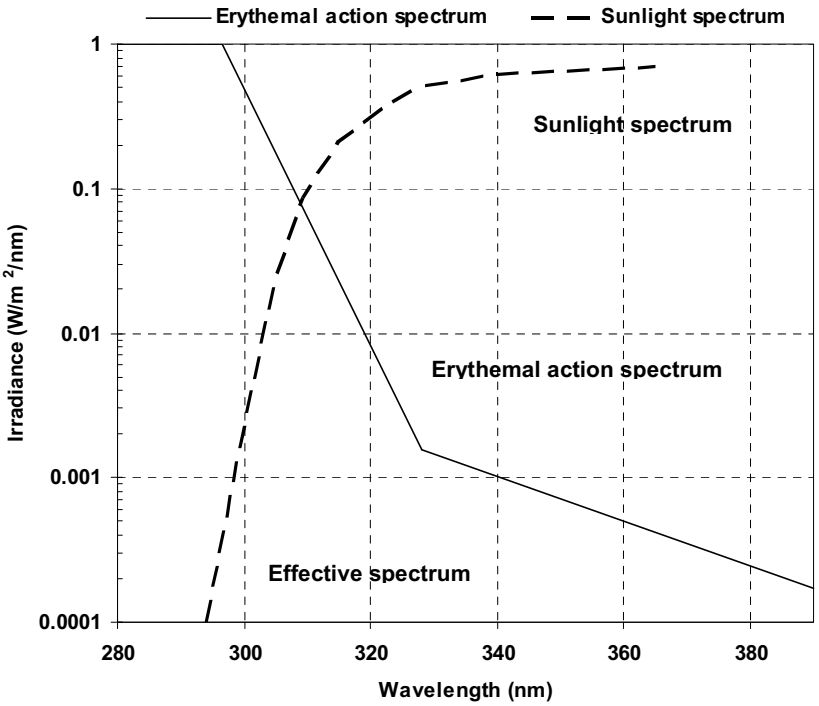

Fig. 3 UVB sunlight spectrum (on a summer day), along with the erythemal action spectrum. (Source: Wikipedia)

changes in the skin surface. Numerous epidemiologic studies demonstrate a strong relationship between sunlight exposure, human skin type and human skin cancer (Ichihashi *et al.* 2003; Melnikova and Ananthaswamy 2005; Reichrath 2006). Aging of the skin is an another long-term hazard of ultraviolet radiation, and is primarily caused by UV-A (315 nm to about 400 nm) radiation. This condition is characterized by wrinkling and pigment changes of the skin, along with other physical changes such as cracking, telangiectasis, solar dermatoses, ecchymoses, and loss of elasticity.

Strategies aimed at reducing overexposure to sunlight include the use of topical sunscreens. Many agents affect the transmission of ultra-violet light to human skin these are called as sunscreen. In contrast, agents act as opposite to sunscreens are suntans. The term suntan refers to lotion designed to maximize UV exposure rather than to block it. Sunscreen is a lotion, spray or other topical product, that helps protect the skin from the sun's ultraviolet (UV) radiation, and which reduces sunburn and other skin damage, ultimately leading to a lower risk of skin cancer. The most effective sunscreens protect against both UVB and UVA. UVC is almost filtered out by the ozone in the earth's atmosphere. Most Sunscreens can be categorized either as a chemical blocks or a physical blocks or a combination of both (**Fig. 2**). Chemical blocks absorb UV radiation and physical blocks reflect UV radiation due to its opaquenature. UV opacity is related with these lastly mentioned physical blocks. UV-opacity of a sunscreen product is the property by which UV radiations are blocked thereby preventing skin diseases.

The protective ability of sunscreen to block the UV radiation is measured by sun protection factor (SPF). The SPF is defined as the ratio of the ultraviolet energy required to produce minimal erythema on protected skin to that required to produce the same minimal erythema on unprotected skin in the same individual. The SPF test provides a clinically relevant *in vivo* measure of sunscreen product efficacy (Toyoshima *et al.* 2004). Higher SPF rating indicates greater protection.

SPF provides an index of protection against erythemally effective solar UV, largely confined to the UVB (290-320 nm) and short wavelength UVA (320-340 nm) region (Diffey *et al.* 2000). The transmittance of the sunscreen is measured over all wavelengths in the UVB and short wavelength of UVA region, along with a table of how effective various wavelengths are in causing sunburn (the *erythemal action spectrum*) and the actual intensity spectrum of sunlight (**Fig. 3**).

SPF is expressed as (Springsteen *et al.* 1999):

$$SPF = \frac{\int A(\lambda) E(\lambda) d\lambda}{\int A(\lambda) E(\lambda) / MPF(\lambda) d\lambda}$$

where $E(\lambda)$ is the solar irradiance spectrum, $A(\lambda)$ the erythemal action spectrum, and MPF(λ) the monochromatic protection factor, all functions of the wavelength λ. The MPF is roughly the inverse of the transmittance at a given wavelength.

The widespread use of sunscreens has its limitation. Certain ingredients in sunscreen, particularly the chemical benzophenone may cause allergic reactions to individuals.It is not clear how much of benzophenone is absorbed into the bloodstream, but trace amounts can be found in urinalysis after use. The risk of skin cancer is also associated with these sunscreens. Use of plants extracts having the ability to reflect UV radiation may ameliorate the negative effects of conventional sunscreen. Thus, evaluation of UV opacity property of medicinal plants known to cure skin ailment is essential.

Natural substances with photoprotective properties extracted from plants are being explored widely and find applications in cosmetic formulations. Root extract of *Pothomorphe umbellata* were investigated for its photostability properties as well as the chemical and the *in vitro* SPF (Silva *et al.* 2005). Extracts from lichens and boldo tree were tested *in vivo* and *in vitro* as possible UV-light filters. Usnic acid resulted to be the best UVB filter (Rancana *et al.* 2002). The protection factors as well as the good UV-light absorption of their photo-products suggest natural substances may be useful as new filters in sun-screen preparations.

A. vera is commonly used to treat a number of skin complaints, such as dry skin and irritant contact dermatitis, and for the healing of burns. The use of *A. vera* in the treatment of radiation-induced dermatitis has been reported. The topical applications of *A. vera* gel were found not to alter the development of either erythema or increased blood flow in human skin exposed to UVB radiation (Reynolds and Dweek 1999). A detailed study of the interactions of UVB and AG on mouse skin demonstrated that the gel prevents immune suppression by UV. No sunscreen activity was

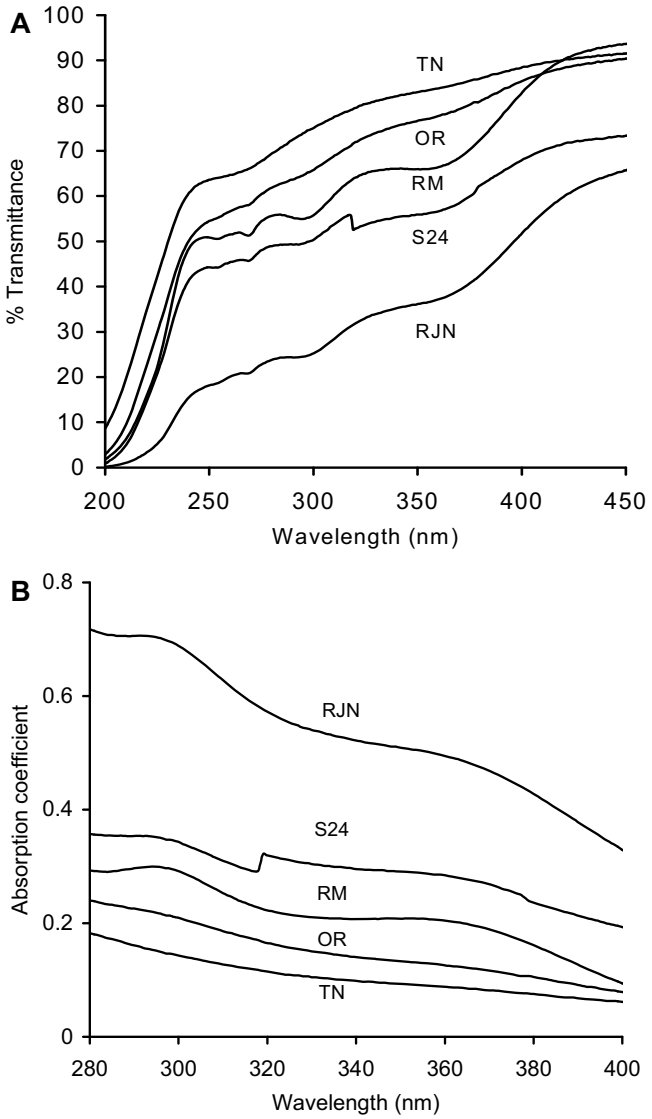

Fig. 4 Percent transmission (**A**) and absorption coefficient (**B**) of lyophilized gel of 5 *Aloe* germplasms at 4 mg/ml. Reproduced from **Kumar MS, Datta PK, Dutta Gupta S** (2009) *In vitro* evaluation of UV opacity potential of *Aloe vera* L. gel from different germplasms. *Journal of Natural Medicine* **63**, 195-199, ©2009 with kind permission of the Japanese Society of Pharmacognosy and Springer, Japan.

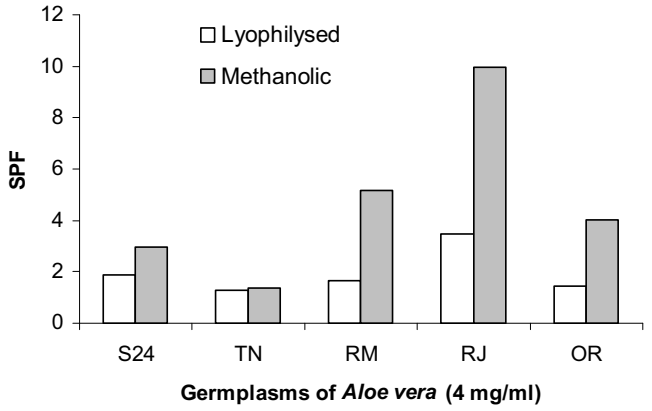

Fig. 5 SPF for lyophilized and methanolic extracts of aloe gel from 5 different germplasms at 4 mg/ml. Reproduced from **Kumar MS, Datta PK, Dutta Gupta S** (2009) *In vitro* evaluation of UV opacity potential of *Aloe vera* L. gel from different germplasms. *Journal of Natural Medicine* **63**, 195-199, ©2009 with kind permission of the Japanese Society of Pharmacognosy and Springer, Japan.

found but the effects of exposure were less deleterious following gel application up to 48 h after exposure. Photo-oxidative damage to both cellular RNA and DNA was observed by the pretreatment of cells with Aloe-derived anthraquinones and exposure to UVA (Wamer *et al.* 2003).

UV opacity potential was screened for five different aloe germplasms by Kumar *et al.* (2009). The UV opacity potential was expressed by UV absorption profiles, SPF and percentage blocking of UVA and UVB. Aloe extracts of all the germplasms showed UV absorption in the wavelength range of 250-400 nm (**Fig. 4**).

The spectral profile proved a strong UV absorption ability of AG extracts both at UVA-UVB range. Among the tested germplasms, the UV filtering potential was maximum with RJN. The SPF ranged from 1.29 to 3.49 (**Fig. 5**).

The UV protection level was tested by determining the percent blocking of UVA and UVB. The transmittance spectrum of a sunscreen in either region can be averaged in order to produce one value, which describes the amount of UVA or UVB blocking. The average transmittance in each region is given by (Springsteen *et al.* 1999):

$$T\left(UVA\right)_{AV} = \frac{\sum_{315\,nm}^{400\,nm} T_{\lambda} \times \Delta\lambda}{\sum_{315\,nm}^{400\,nm} \Delta\lambda}$$

$$T\left(UVB\right)_{AV} = \frac{\sum_{280\,nm}^{315\,nm} T_{\lambda} \times \Delta\lambda}{\sum_{280\,nm}^{315\,nm} \Delta\lambda}$$

where $\Delta\lambda$ is the measured wavelength interval. Consequently, the percent blocking for UVA or UVB, respectively, is 100% - $T(UVA)_{AV}$ or 100% - $T(UVB)_{AV}$ where T(UVA) or T(UVB) is expressed as a percentage. Maximum UVA blocking of 79% and UVB blocking of 91% was obtained. Polyphenols in AG may be responsible for the UV-opacity potential. It has been demonstrated that the flavonoids and sinaptate esters in methanolic extracts can absorb UV rays (Strid and Porra 1992; Landry *et al.* 1995).

CONCLUSION

The therapeutic potential of AG in myriad of varied responses has been proved over the years. With advanced scientific and technological developments the list of useful attributes is being expanded. More than 200 biologically active compounds present in the AG contributed synergistically to the varied nature of biological activities including the cosmetic attributes. Polysaccharides are identified as the major compounds for varied nature of biological response. However, the action of the other compounds such as anthraquinones, vitamins, enzymes and low-molecular weight substances cannot be ruled out. The modus operandi of synergistic activity between the polysaccharides and other gel components and interrelationships of biological functions warrants further investigation.

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