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Ethnobotanical and pharmacological properties of *Aloe vera*: A review

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Aloe vera **belongs to the family of Alliaceae commonly known as Ghrit Kumari which is a popular medicinal plant. It has been used for centuries for its curative and therapeutic potential. More than 200 active ingredients of medical importance have been isolated from its inner gel. *A. vera* is rich in anthraquinones, vitamins, minerals, enzymes, amino acids, natural sugars and fatty acids. It has been used for an array of ailments such as mild fever, wounds and burns, gastrointestinal disorders, diabetes, sexual vitality and fertility, cancer, immunity modulation, AIDS and various skin diseases. *A. vera* gel is famous for facilitating digestion, aiding blood and lymphatic circulation, as well as improving kidney, liver and gall bladder functions. *A. vera* gained many reputations, such as "the champion among health care medicines", "the best health food in 21st century" and "new star in plant", due to its unique effective ingredients and special functions. The present review described the ethnobotanical and pharmacological properties plant of *Aloe vera*.**

Key words: *Aloe vera,* anthraquinones, ethnobotanical, therapeutic, pharmacological, *Aloe gel*.

INTRODUCTION

A. vera is the most significant plant family of Alliaceae and belongs to genus *Aloe* which contains about 420 species (Dagne et al., 2000). The name *A. vera* derives from the Arabic word "Alloeh" meaning "shining bitter substance," while "vera" in Latin means "true." Commonly it is also known as *Aloe barbadensis.* This plant has been used for a variety of medicinal purposes. Medicinal use of *A. vera* traces back to ancient literature of many countries. The Greek scientists considered *A. vera* as the universal panacea of 2000 years ago, (Surjushe et al., 2008). *A. vera* (Sanskrit-Ghrita kumari, Hindi-Guarpatha, Ghikanvar) is a perennial succulent xerophyte, which develops water-storage tissue in the leaves to survive in dry areas with low or erratic rainfall. It is found to grow in hot humid and high rainfall conditions. It is grown in all kinds of soil but well drained soil with high organic matter is most suitable. It grows well in bright sun light. Shady conditions results in disease infestation. It is highly sensitive to water stagnation (Manvitha and Bidya, 2014). The *A. vera* plant can be utilized in three basic forms: Aloe gel, Aloe latex and the whole leaf extract (Udo et al., 2014). This plant undergoes Crassulacean acid metabolism (CAM) metabolic pathway for conserving water within the parenchymatous tissues to withstand drought like conditions. *A. vera* grown under normal water conditions behaves as a typical CAM plant, but when exposed to stress condition of excess water supply, it shifts to CAM-idling (a dampened form of CAM). In

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which the stomata closes day and night but with a continued, low diurnal organic acid fluctuation (Joshi et al., 2014).

Higher K/Na ratio and lower Na/K ratio indicate its salt tolerance capacity. *Aloe* plants uptake to Na is mediated by increasing K mineral uptake. This avoidance of salt stress damage, increases the agronomic and physiological characteristics of *Aloe* plant under salt stress, making this species attractive for industrial production in arid or semiarid areas around the world associated with moderate saline soils (Amador et al., 2014). Over the years, this plant has been known by a number of names such as 'the wand of heaven', 'heaven's blessing' and 'the silent healer' (Gupta and Malhotra, 2012). Davis (1997) stated in his book namely *Aloe vera*: "No longer can anyone say that *A. vera* is a myth or the result of magic", because its efficacy is based on scientific dose-response curves. In Japan, it is known as "all-day service" and "doctor away" plant. Furthermore, *Aloe* is also "air pollution detector" because pollution of air retards its growth (Yang and Ma, 2000). The pharmacological attributes of *A. vera* have been revalidated in modern sciences through various *in vivo* and *in vitro* studies (Sajjad and Sajjad, 2014). Active ingredients of *Aloe* and its biological functions have attracted more and more researcher's attention (Shen et al., 2001; Zhang et al., 2009).

OCCURERRENCE AND BOTANICAL DESCRIPTION

A. vera probably originated in northern Africa and believed to be from Sudan. Subsequently it was introduced in the Mediterranean region and other warm areas of the world (Grindlay and Reynolds, 1986). The species was introduced to China and various parts of southern Europe in the 17th century (Farooqi and Sreeramu, 2001). It is widely naturalized in temperate and tropical regions of Australia, Barbados, Belize, Nigeria, Paraguay and the United States (Akinyele and Odiyi, 2007). The plant is also found in India, Mexico, Pacific Rim countries, South America, Central America, the Caribbean, Australia and Africa. It has been widely cultivated throughout the world. Certain species are now cultivated for commercial purposes, throughout India and some parts of Pakistan (Zakia et al., 2013). The species is popular with modern gardeners as a putative medicinal plant and as an ornamental plant. In India, it is found in Rajasthan, Haryana, Panjab, Andhra Pradesh, Gujarat, Maharashtra and Tamil Nadu (Bhuvana et al., 2014).

A. vera is a perennial, xerophytic, succulent plant with turgid green leaves. It is a stemless or very short-stemmed plant growing up to 60 to 100 cm tall, spreading by offsets. It has thick fleshy elongated and pointed leaves that are joined at the stem in a rosette pattern and grow to about 30 to 50 cm in length and 10 cm in breadth at the base in the adult plant. The margin of the leaf is serrated and has small white teeth. The leaf is composed of three layers. Outer protective layer known as rind is made up of 15 to 20 cells. The middle layer contains latex (a bitter yellow sap) and inner layer contains a clear mucilaginous gel. The flowers of *A. vera* comes out in summer on a spike up to 90 cm tall, each flower being pendulous, with a yellow tubular corolla and 2 to 3 cm long (Femenia et al., 1999; Boudreau and Beland, 2006). The succulent property enables the species to survive in areas of low natural rainfall, making it ideal for rockeries and other low-water use gardens. The species is hardy, although it is intolerant to very heavy frost or snow. The species is relatively resistant to most insect pests, though spider mites, mealy bugs, scale insects, and aphid species may cause a decline in plant health. During winter, *A. vera* may become dormant, during which little moisture is required. In areas that receive frost or snow, the species is best kept indoors or in heated glasshouses.

Techniques based on DNA comparison suggest that *A. vera* is relatively closely related to *Aloe perryi*, a species that is endemic to Yemen (Darokar et al., 2003). Similar techniques, using chloroplast DNA sequence comparison and ISSR profiling have also suggested that *A. vera* is closely related to *Aloe forbesii*, *Aloe inermis*, *Aloe scobinifolia*, *Aloe sinkatana* and *Aloe striata*. Large scale agricultural production of *A. vera* is undertaken in Australia, Bangladesh, Cuba, the Dominican Republic, China, Mexico, India, Jamaica, Kenya and South Africa, along with the USA to supply the *A. vera* gel to cosmetics industry (Varma, 2008).

ETHNO BOTANCAL DETAILS

A. vera is an important traditional medicinal plant in many countries throughout the world. The ethno botanical uses of this plant have been given in Table 1.

PHYTOCHEMISTRY

A. vera has complex chemical ingredients. The main chemical components found in *Aloes* can be classified into nine categories: anthraquinones, inorganic compounds, enzymes, vitamins, essential amino acids, non essential amino acids, carbohydrates, fatty acids, and other miscellaneous chemicals (Table 2). Among these constituents, anthraquinones are the most important active ingredient of high medical values. Blue light has been found to be beneficial for the accumulation of anthraquinones. *A. vera* also contains products of the isoprenoid pathway, which are carotenoids, steroids, terpenes and phytosterols (Samman, 1998). Isoprenoids can be regarded as sensory molecules because they contribute to the color and fragrance of the products in which they exist. In general, active ingredients content is

Table 1. Ethnobotanical uses of *A. vera* in different traditional medicine systems.

S/No	System of medicine/ country	Ethno botanical uses	References
1	Indian system of medicine/ India.	In Ayurveda, *Aloe* is known as *Kumari*, or "young girl", because aloe is believed to bring back youthful energy and femininity. *Aloe* is used as a tonic for the female reproductive system. *Aloe* is said to have alliterative, tonic, rejuvenating, purgative and vulnerary actions in Ayurveda. *Aloe* is also believed to tone all three of the Ayurveda constitutions, Vatta, Pitta, and Kapha. It is used in traditional Indian medicine for constipation, colic, skin diseases, worm infestation and infections. *Aloe* is used internally as a laxative, antihelminthic, haemorrhoid treatment, and uterine stimulant (menstrual regulator). It is used topically, often in combination with liquorice root, to treat eczema or psoriasis. People in Tamil Nadu, a state of India, often prepare a curry using *A. vera* which is taken along with Indian bread (nan bread) or rice	Ghazanfar (1994) and Heber (2007)
2	Chinese medicine system/ China	The Chinese use of *Aloe*'s skin and the inner lining of its leaves as a cold and bitter remedy is used to clear constipation due to accumulation of heat (fire).The gel is considered cool and moist and recommended in the treatment of fungal diseases. Like their Ayurvedic peers, Chinese herbalists recognized aloe's potential as a purgative; they used aloe to expel worms, alleviate constipation and normalize bowel movements	Bensky et al. (1993), Heber (2007) and Babaeil et al. (2013)
3	Egyptian system of medicine/ Egypt	Ancient Egyptian Papyrus and Mesopotamian described *Aloe* as being useful in curing infections, treating skin problems and as a laxative. Cleopatra was said to include *Aloe* cream in her beauty regimen	Haller (1990) and Shelton (1991)
4	Arabian system of medicine/ Arab	In Arabian medicine, the fresh gel is rubbed on the forehead as a headache remedy or rubbed on the body to cool it in case of fever, as well as being used for healing wound, curing conjunctivitis, and as a disinfectant and laxative.	Ghazanfar (1994)
5	Western system of medicine	In Western society, *A. vera* is one of the few herbal medicines in common usage, and it is found useful in the cosmetic, pharmaceutical, and food industries. Therapeutically it is used for topical and oral applications.	Foster (2011)
6	Greek system of medicine	The *A. vera* plant is described in detail in the Greek Herbal of Dioscorides (ca 70 AD), and its use is promoted for the treatment of wounds, hair loss, genital ulcers and haemorrhoids	Davis (1997)
7	Spanish medicine system	*Aloe* was used by Hippocrates and Arab physicians, and was carried to the Western Hemisphere by Spanish explorers to treat the wounded soldiers	Atherton (1998)
8	United States	*A. vera* was officially listed as a purgative and skin protectant by the U.S. pharmacopoeia in 1820 and was clinically used in the 1930s for the treatment of radiotherapy, burns to the skin and mucous membranes. Little is known of aloe's role in Native American. They gained the information from the Spanish explorers who brought *Aloe* with them. Modern native healers of America use *Aloe* in the same way as their European counterparts	Collins and Collins, (1935), Manderville (1939) and Park and Jo, (2006)
9	Mexican	For the treatment of type 2 diabetes mellitus	Coronado et al. (2004)
10	Trinidad and Tobago	Used for the treatment of hypertension.	Lans (2006)
11	Roman	*A. vera* gel has been used for many purposes since the Roman era or even long before. Treating burns is one of the major application of *A. vera* gel used in many countries	Maenthaisong et al. (2007)
12	Japan	Commonly used as an ingredient in commercially available yogurt. There are also many companies that produce *A. vera* beverages	Calvin (2008)
13	Philippines	Used with milk for kidney infections	Calvin (2008)
14	Russia	Used for treating cuts, scraps, minor burns, cold sores, sun burns and other type of skin inflammations	Zevin (1996)

Table 1. Cont'd.

15	Africa	Cultivation in East Africa is primarily on a small scale for ornamental purposes. *A. vera* L. (Syn. *Aloe barbadensis* Miller) is most often encountered for its treatment of burns, however, a number of useful hair care references also exist. It was probably Dioscorides (in about AD 74), who made the observation that *A. vera* could stop hair loss, though it is not recorded whether this was the exudate, the gel or the whole leaf.	Dweck (1996) and Mukonyi et al. (2001)

Table 2. Chemical constituents of *Aloe vera.*

S/No	Name of the constituents	Types	Property and activity	References
1	Anthraquinones	Aloin, Barbaloin, Isobarbaloin, Anthranol, Aloetic acid, Ester of cinnamic acid, Aloe-emodin, Emodin, Chrysophanic acid, Resistannol.	Analgesic, antibacterial and antiviral activity.	Surjushe et al. (2008) and Balasubramanian et al. (2013)
2	Inorganic compounds	Calcium, Sodium, Chlorine, Manganese, Zinc, Chromium, Potassium sorbate, Copper, Magnesium, Iron, Selenium.	They are essential for the proper functioning of various enzyme systems in different metabolic pathways and few are antioxidants.	Shelton (1991) and Balasubramanian et al. (2013)
3	Enzymes	Bradykinase, Cyclooxygenase, Oxidase, Amylase, Catalase, Lipase, Alkaline phosphatase, Carboxypeptidase, Cellulase, Proteases, Creatine phosphokinase, Superoxide dismutase.	Helps with the breakdown of food sugars and fats, aiding digestion and enhancing nutrient absorbtion. Bradykinase which helps to reduce excessive inflammation.	Shelton (1991) and Vogler and Ernst, (1999)
4	Vitamins	A, B1, B2, B6, B12, Choline, Folic acid, C, α-tocopherol, β-carotene.	Antioxidant, neutralizes free radicals.	Obata et al. (1993) and Sies (1992)
5	Essential amino acids	Lysine, Threonine, Valine, Leucine, Isoleucine, Phenylalanine, Methionine.	Provides the basic building blocks of proteins in the production of muscle, tissue etc.	Shelton (1991) and Bhattacharya et al. (2011)
6	Nonessential amino acids	Histidine, Arginine, Hydroxyproline, Aspartic acid, Glutamic acid, Proline, Glycine, Alanine, Tyrosine.	Provides the basic building blocks of proteins in the production of muscle, tissue etc.	Shelton (1991) and Bhattacharya et al. (2011)
7	Sugars	Glucose, Galactose, Mannose, L-rhamnose, Aldopentose, Glucuronic acid, Cellulose, C-glucosyl chromone.	Anti-inflammatory action, anti viral, immune modulated activity.	Kahlon et al. (1991) and Lorenzetti et al., (1964)
8	Fatty acids	Cholesterol, β-sitosterol, Campestrol, Lupeol.	Anti-inflammatory action and lupeol possesses antiseptic and analgesic action.	Senan (2014) and Surjushe et al. (2008)
9	Miscellaneous	Lignins, Uric acid, Auxins,, Gibberellins, Lectin-like substance, Salicylic acid, Arachidonic acid, Saponins.	Lignin, an inert substance enhances penetrative effect of the other ingredients into the skin. Auxins and gibberellins help in wound healing and have anti-inflammatory action. Salicylic acid that possesses anti-inflammatory and antibacterial properties Saponins that are the soapy substances have cleansing and antiseptic properties.	Surjushe et al. (2008) and Misir et al. (2014)

determined by variety and ecological conditions (Wang et al., 2002). *A. vera* gel is rich in polysaccharides like acemannan (partially acetylated glucomannans) which has been reported as the primary active substance in the parenchymatous tissue. There are numbers of secondary metabolites found in plants which contribute significant biological activities (Xiong, 2002). The biological activities of *A. vera* are due to the synergistic action of a variety of compounds, rather than from a single defined component (Dagne et al., 2000; Hamman, 2008). The potential of constituents which exhibit antagonistic and competitive activities also influences the overall biological activity of a particular *A. vera* preparations (Hamman, 2008). A large number of biological activities related to health benefits have been determined including antimicrobial, anti-inflammatory, lipid and glucose lowering, antiproliferative, immunostimulatory, and antioxidant functions (Surjushe et al., 2008).

Anthraquinones

Anthraquinones are mostly found in high concentration in the sap trunk of the plant and smaller amount in sap derived from outer layer of the cuticle or skin of the *Aloe* leaves (Itrat and Zarnigar, 2013). *Aloe* consist of free anthraquinones and their derivatives. Aloin and emodin are major anthraquinones acts as analgesics and antiangiogenic properties (Balasubramanian et al., 2013). The leaf exudate contains anthraquinones, particularly barbaloin and iso barbaloin which appear to be responsible for its bitter taste and cathartic effect (Dagne et al., 2000; Boudreau and Beland, 2006). Both barbaloin and isobarbaloin undergo decomposition in the large intestine to form the active metabolites. Barbaloin and products of the phenylpropanoid pathway are commonly referred as polyphenolic compounds. These are derived from the precursor phenolic acids and they may act as antioxidants to inhibit free radical–mediated cytotoxicity and lipid peroxidation (Cook and Samman, 1996). In large amounts these compounds exert a powerful purgative effect, but in smaller amount they appear to aid absorption from the gut and act as potent antimicrobial agents (Mckeown, 1987). They also reduce the formation of melanin and any tendency to hyper-pigmentation (Strickland et al., 1993). *A. vera* has been used as a bittering agent in alcoholic beverages in dried forms. The chemical structure of major anthraquinones found in *A. vera* has been given in Figure 1.

Sugars

Sugars are derived from the mucilage layer of the plant under the rind which surrounds the inner parenchymatous gel. The most important are the long chain polysaccharides, comprising of glucose and mannose, known as the gluco-mannans. Glucomannan is a good moisturizer. Polysaccharides, particularly mannose-containing polysaccharides, cellulose, and pectic polysaccharides, comprises of the major part of *A.vera* gel. The polysaccharides act as immunomodulators which are absorbed directly in the blood stream (Kahlon et al.,1991; Lorenzetti et al., 1964). Acetylated glucomannan is primarily responsible for the gel's mucilaginous properties (Hamman, 2008).

Vitamins

Antioxidant vitamins A (beta-carotene), vitamin C, vitamins B (thiamine), niacin, vitamin B2 (riboflavin), vitamin B12, choline and folic acid reported by Obata et al., (1993). Vitamins A, C and E are the anti-oxidant which neutralizes free radicals. Vitamins B and Choline are involved in amino acid metabolism, Vitamin B12 is required for the production of red blood cells, and folic acid is required in the development of blood cells.

Enzymes

The main enzymes found in *A. vera* are amylase (breaks down sugars and starches), bradykinase (stimulates immune system, analgesic and anti-inflammatory), and carboxy-peptidase (inactivates bradykinins and produces an anti-inflammatory effect). During the inflammatory process, bradykinin produces pain associated with vasodilation and therefore, its hydrolysis reduces these two components and produces an analgesic effect (Shelton, 1991). Catalase (prevents accumulation of water in the body), cellulase (aids digestion-cellulose), lipase (aids digestion-fats), oxidase, alkaline phosphatase, proteases (hydrolyses proteins into their constituent elements) and creatine phosphokinase (aids metabolism) are the other enzymes found in *Aloe vera*.

Amino acids

These are the building blocks of proteins. *A. vera* contains seven of the eight essential amino acids (Lysine, threonine, valine, leucine, isoleucine, phenylalanine and methionine) required by human body that cannot be synthesized. The nine non essential amino acids (Histidine, Arginine, Hydroxyproline, Aspartic acid, Glutamic acid, Proline, Glycine, Alanine and Tyrosine) are also found in *A. vera* juice (Shelton, 1991; Bhattacharya et al., 2011).

Minerals

Minerals are essential for the proper functioning of

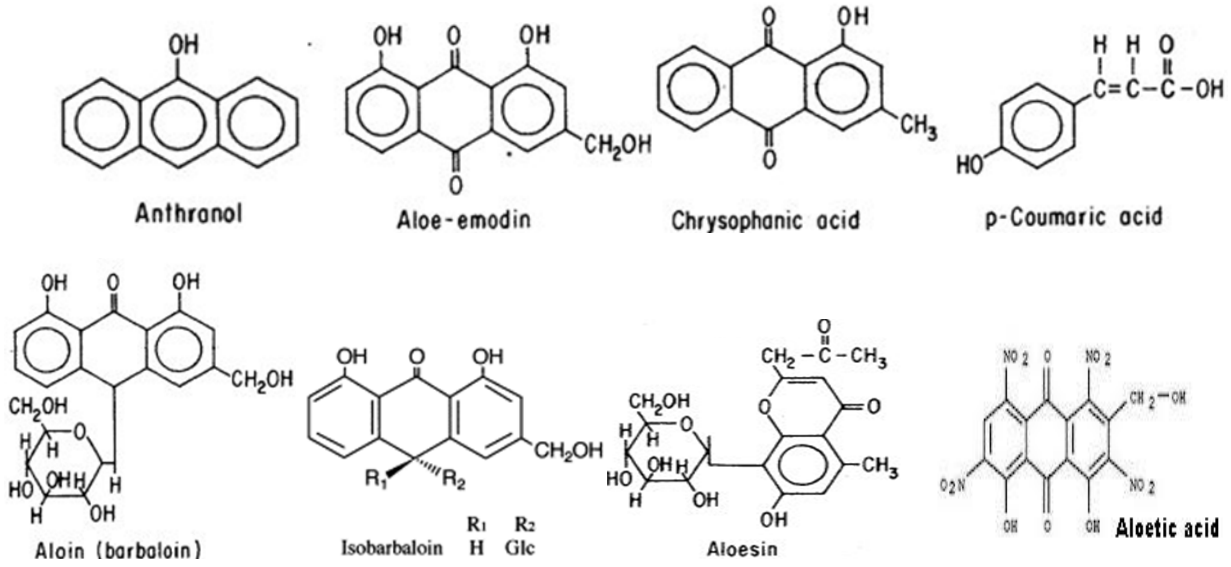

Figure 1. Chemical structure of anthraquinones.

various enzyme systems in different metabolic pathways. 13 out of 17 minerals necessary for human nutrition have been found in *A. vera* including calcium, sodium, chlorine, manganese, chromium, potassium sorbate, copper, magnesium, iron, selenium and zinc (Shelton, 1991; Balasubramanian et al., 2013). Magnesium lactate inhibits histidine decarboxylase and prevents the formation of histamine from the amino acid (Shelton, 1991). Histamine is released in many allergic reactions and causes intense itching and pain. The prevention of its formation may explain the antipyretic effect of *A. vera* (Bhattacharya et al., 2011).

PHARMACOLOGICAL PROPERTIES

Laxative

A. vera latex is commonly used in the treatment of constipation (De Witte, 1993). The laxative effect of the anthraquinone glycosides found in *A. vera* latex is well established (Ulbricht et al., 2008). The bitter yellow juice found between the gel and the outer skin of the leaf is dried and used as laxative. It increases intestinal water content, stimulates mucus secretion and increases intestinal peristalsis (Ishii et al., 1994). *Aloe*-emodin-9-anthrone and *Aloe*-emodin, which induce laxation via multiple mechanisms. In vitro and in vivo studies in rats demonstrated that *Aloe*-emodin-9-anthrones reduce the absorption of water from the intestinal lumen by inhibiting the activity of Na^+, K^+-adenosine triphosphatase (ATPase) and stimulate water secretion by increasing the paracellular permeability across the colonic mucosa (Ishii et al., 1990). Secretion of water into the lumen by a prostaglandin-dependent mechanism has also been reported. The net result is a reduction in water absorption and the formation of softer stools (Boudreau and Beland, 2006).

Antioxidative property

Phenolic compound from *A. vera* plant has potent antioxidative activity. Aloe barbendol, Aloe emodin, barbaloin A and Aloe chrysone are the compounds having the antioxidative effects (Lee et al., 2000).

Healing properties

Glucomannan, a mannose-rich polysaccharide, and gibberellin, a growth hormone, interact with growth factor receptors on the fibroblast, thereby stimulating its activity and proliferation, which in turn significantly increases collagen synthesis after topical and oral administration (Chithra et al., 1998). According to Heggers et al. (1996) "*Aloe* gel not only increased collagen content of the wound but also changed collagen composition (more type III). Gel accelerates wound contraction and increases the breaking strength of resulting scar tissue". An increased synthesis of hyaluronic acid and dermatan sulfate in the granulation tissue of a healing wound following oral or topical treatment has also been reported (Chithra et al., 1998). *A. vera* juice enables the body to heal itself from cancer and also from the damage caused by radio and chemotherapy that destroys healthy immune cells crucial for the recovery (Sahu et al., 2013). It also improves blood circulation due to its detoxification property. It is

also a natural healer, and hence any internal ulcers or lesions to be soothed and healing is enhanced (Manoharan et al., 2013).

Protection of skin exposure to ultraviolet (UV) and gamma radiation

A. vera gel has been reported to have a protective effect against radiation damage to the skin (Sato et al., 1990; Roberts and Travis, 1995). The exact role is not known, but following the administration of *A. vera* gel, an antioxidant protein, metallothionein, are generated in the skin, which scavenges hydroxyl radicals and prevents suppression of superoxide dismutase and glutathione peroxidase in the skin. It reduces the production and release of skin keratinocyte-derived immunosuppressive cytokines such as interleukin-10 (IL-10) and hence prevents UV-induced suppression of delayed type hypersensitivity (Byeon et al., 1988).

Anti-inflammatory action

Extracts of *A. vera.* gel have shown anti-inflammatory activity and suggested its inhibitory action on the arachidonic acid pathway via cyclooxygenase (Vazquez et al., 1996). It inhibits the cyclooxygenase pathway and reduces the prostaglandin E2 production from arachidonic acid. Veracylglucan B and veracylglucan C, two maloyl glucans isolated from *Aloe vera* gel have been demonstrated *in vitro* for its potent anti-inflammatory effects, although their effects on cell proliferation appear antagonistic (Esua and Rauwald, 2006). A novel anti-inflammatory compound called C-glucosyl chromone was also isolated from gel extracts (Hutter et al., 1996).

Immunomodulatory

The gels of *Aloe* species contain immunomodulatory components such as aloctin A and acemannan. *In vitro* and *In vivo* studies prove that *Aloe* gel modulates the immune system (through macrophage activation and cytokine production) which accelerates wound healing (Ulbricht et al., 2008). Most studies on these gels were performed *in vitro* cell culture systems (Sun et al., 2010). Alprogen inhibit calcium influx into mast cells, thereby inhibiting the antigen-antibody-mediated release of histamine and leukotriene from mast cells (Ro et al., 2000). The study revealed that acemannan stimulates the synthesis and release of interleukin-1 (IL-1) in mice injected with murine sarcoma cells which in turn initiated an immune attack that resulted in necrosis and regression of the cancerous cells (Peng et al., 1991). Several low-molecular-weight compounds are also capable of inhibiting the release of reactive oxygen free radicals from activated human neutrophils (Hart et al., 1990). *A. vera* juice enables the body to heal itself from cancer and also from the damage caused by radio and chemotherapy that destroys healthy immune cells (Sahu et al., 2013). Recently Choche et al. (2014) proved that *A. vera* juice stimulates the body's immune system.

Antimicrobial activity

Agarry et al. (2005) have shown the potent antimicrobial activities of the gel and leaf of *A. vera* against a wide range of bacteria and fungi. Antifungal activity of *A. vera* was analyzed against strains of *Aspergillus niger*, *Aspergillus fumigatus* and *Neurospora crassa*. The maximum antifungal activity was observed from petroleum ether and ethanol extracts (22mm in each). The antimicrobial activity of *A. vera* plant extract has also been studied by Kedarnath et al. (2012). Anthraquinone aloin inactivates various enveloped viruses such as *Herpes Simplex, Varicella zoster* and *Influenza* (Sydiskis et al., 1991). *A. vera* contains 6 antiseptic agents: Lupeol, salicylic acid, urea nitrogen, cinnamonic acid, phenols and sulfur. They all have inhibitory action on fungi, bacteria and viruses (Surjushe et al., 2008). Therefore, it has strong antiseptic, antibacterial, fungicidal and virucidal properties. It also promotes cell growth and is neurologically calming and acts as a detoxifying agent (Subhash et al., 2014).

Antitumor activity

The two fractions from *Aloes* that are claimed to have anti-cancer effects include glycoproteins (lectins) and polysaccharides (Reynolds and Dweck, 1999). The anti-tumour activity of polysaccharides isolated from *A. vera*, specifically acemannan has been investigated *in vitro* models using different animal species. In recent studies, a polysaccharide fraction has been shown to inhibit the binding of benzopyrene to primary rat hepatocyte, thereby preventing the formation of potentially cancer-initiating benzopyrene-DNA adducts. An induction of glutathione S-transferase and an inhibition of the tumor-promoting effects of phorbol myristic acetate has also been reported which suggested a possible benefit of using *Aloe* gel in cancer chemoprevention (Kim and Lee, 1997; Kim et al., 1999).

Drug/vitamin bioavailability

A. vera gel has been shown to enhance vitamin C and E's bioavailability in a double-blind, randomized, controlled trial (Vinson et al., 2005). *A. vera* gel protects the degradation of vitamins in the intestinal tract. The gel polysaccharides may bind to vitamins and slow down

their absorption rate. *A. vera* gel has been shown to significantly increase the transport of insulin in a cell model, and limited information suggests that if co administered, it may also enhance the intestinal absorption of other poorly absorbed drugs (Hamman, 2008).

Moisturizing and anti-aging effect

It has a wonderful moisturizing activity (Choche et al., 2014). The presence of mucopolysaccharides helps in binding moisture into the skin. *Aloe* stimulates fibroblast which in turn produces the collagen and elastin fibers making the skin more elastic and less wrinkled. It also has been shown that the cohesive effects on the superficial flaking epidermal cells by sticking them together, softens the skin. The amino acids also soften hardened skin cells and zinc acts as an astringent to tighten the pores. Its moisturizing effects have also been studied in the treatment of dry skin associated with occupational exposure where *A. vera* gel gloves were found to improve the skin integrity, decrease in appearance of fine wrinkle and decrease erythema (West and Zhu, 2003).

Antidiabetic and Hypolipidemic Activity

A. vera is a traditional remedy for diabetes mellitus (DM) in many parts of the world, including Latin America (Coronado et al., 2004) and the Arabian Peninsula (Yeh et al., 2003). Some evidences in humans and animals suggests that *A. vera* is able to alleviate the chronic hyperglycemia and perturbed lipid profile that are characteristics of DM, which are major risk factors for cardiovascular complications in the disease. Phytosterols are not extensively absorbed from the intestine but can bind cholesterol and prevent it from being absorbed (Ralph and Provan, 2000). Phytosterols have been shown to lower plasma cholesterol concentrations, including the atherogenic low-density lipoprotein (LDL) fraction (Moghadasian and Frohlich, 1999). The mechanism by which *A. vera* modulates blood glucose level is unknown, but it has been suggested that it may interact with insulin. It has been hypothesized that *Aloe* stimulates insulin synthesis or its release from pancreatic β cells (Ajabnoor, 1990). Processed *A. vera* gel was found to suppress the expression of the adipogenic genes *SREBP-1a*, fatty acid synthase (FAS) and glycerol-3-phosphate acyltransferase (GPAT), suggesting that the gel improves insulin resistance by reducing the toxic effects of lipids in the liver (Kim et al., 1999). The administrations of PAG (Processed *Aloe vera* Gel) lowers the triacylglyceride levels in liver and plasma. Histological examinations of periepididymal fat pad showed that PAG reduced the average size of adipocytes (Kim et al., 2009). This showed the hypolipidemic effects of processed *A. vera* gel.

Cosmetic and therapeutic effectiveness

Scientific evidence for the cosmetic and therapeutic effectiveness of *A. vera* are limited and mostly are contradictory (Ernst, 2000; Marshall, 2000). Despite this, the cosmetic and alternative medicine industries regularly make claims regarding the soothing, moisturizing, and healing properties of *Aloe vera*, especially via Internet advertising (Boudreau and Beland, 2006; Kunkel, 1984). Today *A. vera* gel is an active ingredient in hundreds of skin lotions, sun blocks and cosmetics (Grindlay and Renolds, 1986). *A. vera* gel is also used as an ingredient in commercially available yogurt, beverages, and some desserts (Reynolds, 2004). Although at certain doses, it has toxic properties when used either for ingestion or topical applications. Furthermore, the dried powder obtained from *A. vera* gel was successfully used to manufacture directly compressible matrix type tablets. These tablets slowly release a model compound over an extended period of time, thereby showing potential to be used as an excipient in modified release dosage forms (Jani et al., 2007). *A. vera* is now widely used on facial tissues, where it is promoted as a moisturizer and/or anti-irritant to reduce chafing of the nose of users suffering from hay-fever or cold. It is a common practice for cosmetic companies to add sap or other derivatives from *A. vera* to products such as makeup, tissues, moisturizers, soaps, sunscreens, incense, shaving cream and shampoos (Reynolds, 2004). Other uses for extracts of *A. vera* include the dilution of semen for the artificial fertilization of sheep (Rodriguez et al, 1988), fresh food preservation (Serrano et al., 2006) and water conservation in small farms. It has also been suggested that biofuels may be obtained from *A. vera* seeds (Shukla, 2008). *Aloe* is also used as a food substance. Some molecular gastronomists have begun to take advantage of its gelling properties.

Toxicological studies

No serious adverse reactions were reported from *A. vera* administration in clinical trials (Foster, 2011). Hypersensitivity and allergic responses were reported as the most common adverse effects of *A. vera* (Wang et al., 2003). Chronic ingestion of 100 mg/kg *A. vera* (extracted in ethanol) given orally in experimental rats produced reproductive toxicity, significant sperm damage, inflammation, and mortality compared to control animals (Shah et al., 1989). In a safety assessment of *Aloe*, the cosmetic ingredient review expert panel (2007) concluded that *Aloe* latex, derived from the inner

gel is cytotoxic. The topical application of *A. vera* gel resulted in contact dermatitis, and oral use may cause diarrhea or vomiting (Morrow et al., 1980; Ernst, 2000; Wang et al., 2003; Chinnusamy et al., 2009). Many of these reactions appear to be associated with anthraquinone contaminants of the gel product (Boudreau and Beland, 2006; Bottenberg et al., 2007).

Carcinogenicity

Tumor-promoting and antimutagenic activities have been ascribed to the latex of *A. vera* (Boudreau and Beland, 2006). Multiple *in vitro* studies have demonstrated the potential genotoxicity of anthraquinones; however, anthraquinones in *A. vera* do not appear to be well absorbed (Brusick and Mengs, 1997). In *vivo* studies revealed that there was no genotoxicity from *Aloe*-emodin and emodin (Brusick and Mengs, 1997). Anthranoid-containing laxatives such as *Aloe*-emodin have been suggested to cause colorectal cancer (Siegers et al., 1993); A 2-year long carcinogenicity study in rats reported that whole-leaf *Aloe* powder was not carcinogenic at nontoxic dose levels in the colon (Yokohira et al., 2009).

CONTRAINDICATIONS

Allergy

The use of *A. vera* preparations should be avoided in individuals with a known allergy to plants of the Liliaceae family, garlic, onions, and tulips etc. (Ulbricht et al., 2008).

Pregnancy

The use of *A. vera* as a laxative during pregnancy may pose potential teratogenic and toxicological effects on the embryo and fetus (Ulbricht et al., 2008).

Renal or cardiac disease

Prolonged use of *A. vera* latex has been associated with watery diarrhea resulting in electrolyte imbalance (Cooke, 1981; Boudreau and Beland, 2006), and anecdotal reports suggest that the increasing loss of potassium may lead to hypokalemia. Therefore, the *A. vera* latex is contraindicated in patients with a history of renal or cardiac disorders.

Drug interactions

The potential interactions of *A. vera* with drugs have been suggested by many researchers. Possible hypokalemia-related arrhythmia suggests a potential herb–drug interaction with cardiac glycosides (Boudreau and Beland, 2006). Caution is warranted in patients taking hypoglycemic agents as interactions with *A. vera* gel have been reported (Boudreau and Beland, 2006). Application of *Aloe* to skin may also increase the absorption of steroid creams such as hydrocortisone (Surjushe et al., 2008). It reduces the effectiveness and may increase the adverse effects of digoxin and digitoxin, due to its potassium lowering effect (Meena et al., 2013). Combined use of *A. vera* and furosemide may increase the risk of potassium depletion. It decreases the blood sugar levels and thus may interact with oral hypoglycemic drugs and insulin (Rajeswari et al., 2012).

Safety and efficacy

Safety and efficacy of *A. vera* is difficult to determine due to the lack of standardization of commercially available *A. vera* products. The lack of a detailed understanding of the plant's active components makes it difficult to evaluate the optimal dose of a particular *A. vera* preparations for the treatment of specific disorders. Despite this, topical application of *A. vera* gel or extract is safe for the treatment of mild to moderate skin conditions, burns, wounds, and inflammation (Ulbricht et al., 2008). Reports of its use in psoriasis, dermatitis, and surgical wound healing are contradictory. The Natural Standard Research Collaboration concluded that the oral use of *A. vera* gel for its potential hypoglycemic effects and the short-term use of oral *Aloe* latex as a laxative are possibly safe; however, prolonged use of the latex is likely to be unsafe due to a theoretical risk of dehydration and electrolyte imbalance (Ulbricht et al., 2008). In short, *A. vera* has wide spectrum of the properties and uses, some of them could be myths and some of which could be the real magic. In future, controlled studies are required to prove the effectiveness of *A. vera* under various conditions.

CONCLUSION

There has been an increase in demand for the phytopharmaceuticals all over the world. *A. vera* is well known for its therapeutic effects and as an effective medication for treating chronic diseases. The present study shows the traditional, pharmacological and phytochemical properties of various bioactive compounds present in *A. vera.* In spite of these positive benefits, contraindications about the plant also suggest that *A. vera* industry urgently needs reliable testing protocols to assess the quality and quantity of bioactive chemicals present in the final products. The information shared in this review update on *A. vera* might be fruitful for better understanding in the direction for search of plant origin drugs.

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Conflict of interest

All authors declare that they have no conflict of interest.

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