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The therapeutic properties and applications of *aloe vera*: a review

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Abstract

Aloe vera, a succulent perennial and drought resisting plant, is well known for its therapeutic potential. A number of beneficial effects of *aloe vera* have been reported, including immunomodulatory, wound and burn healing, hypoglycemic, anticancer, gastro-protective, antifungal, and anti-inflammatory properties. These beneficial therapeutic properties of *aloe vera*

have been employed for a number of commercial applications. The present review provides a survey of literature on its composition, rheology, processing and pharmaceutical uses as well as an outline of its application in foods and cosmetics. In addition, complications associated with the use of *aloe vera* and relevant precautions are summarised. Chemical characterization of *aloe vera* is in progress through scientific developments in the area of analytical chemistry. It is expected that further information will be available at a faster rate in the near future, resulting in enhanced applications.

Keywords: *Aloe vera*, composition, rheology, therapeutic, cosmetics, functional foods

1. Introduction

Complex carbohydrates are abundantly available from natural resources including plants (e.g. pectin, guar gum), animals (e.g. chitosan) and microorganisms (e.g. dextran). Carbohydrates derived from some of the plants (such as *aloe*) exhibit diverse biological activities. *Aloe* was previously considered in family Liliaceae, but now it has been placed in its own family Aloaceae (David, 1999). It finds its origin in South and East Africa as well as in Mediterranean regions. It has more than 400 species and is found throughout the world but mostly grows in subtropical areas. It is a perennial, succulent and shrubby plant with green leaves (color varies from bright green to gray) arranged in a rosette pattern at the stem. The leaves are triangular and fleshy with serrated edges consisting of a thick epidermis covered by cuticle surrounding the mesophyll. The leaves have a high capacity to retain water which enables the plant to survive in harsh circumstances, i.e., long periods of drought and warm dry climate (Akinyele and Odiyi, 2007; Ali et al., 2012; Hamman, 2008; Iwu, 2014; Jiang et al., 2013; Misir et al., 2014). The plant bears single or multiple bicolor flowers (depending upon variety) which are tubular inflorescences growing at the center of a rosette of leaves.

Among various species of *aloe*, *aloe vera* is considered to be the most potent, commercially important and the most popular plant in the research field. Various parts of the plant contain approximately 75 nutrients, as well as 200 active compounds including amino acids, sugars, enzymes, vitamins, minerals, saponins, anthraquinones, lignin and salicylic acid (Misir et al., 2014). Volatile components and ascorbic acid are present in the flowers while polysaccharides, lignin, pectin, hemicellulose and cellulose are present in the rind. Similarly, the leaves are the source of various organic acids, enzymes, phenolic compounds, minerals and vitamins (Ali et al., 2012; Boudreau, Mary D. and Beland, Frederick A., 2006).

Aloe vera is well known for its antioxidant, anti-inflammatory, antidiabetic, sunburn relief, immune boost, anti-ageing and anticancer properties (Langmead et al., 2004). Owing to its unique composition various industrial applications of *aloe vera* have been initiated. The present paper summarizes the therapeutic uses of *aloe vera* together with its applications in cosmetics and foods. In addition, complications associated with the use of *aloe vera* and related precautions are discussed.

For this review article, the authors searched the literature using two major search engines: Scopus and Google Scholar. Scopus is an abstract and citation database of peer-reviewed literature and is a part of SciVerse provided by Elsevier (https://doi.org/10.1016/j.mla.2011.05.006). Scopus was used as a first choice to ensure a systematic review process as it is capable of large scale data compilation and yields interesting statistics based on different bibliometric indicators (https://doi.org/10.1002/asi.21062). Alternatively, Google Scholar is a relatively straightforward search engine which retrieves scientific information through a number of source including articles, books, theses, abstracts, conference proceedings, professional societies, universities and research organizations,(https://doi.org/10.1016/j.mla.2011.05.006; https://doi.org/10.1016/j.joi.2016.04.017). Despite providing a wide range of scholarly literature, there are limited search features and less bibliometric tools in Google Scholar; therefore, it was only used to look for any missing information in regard to each section of this review article. An initial hit for the word '*aloe vera*' in Scopus and Google Scholar for 'all fields' returned 38,864 and 79,500 documents, respectively. Out the 38,864 documents returned from Scopus, 12,408 were directly available from the Scopus database, some of the statistics related to these published documents are represented in Appendix 1. The review process was continued by further refining of the search results by using the keywords (composition, rheology, therapeutic, cosmetics,

functional foods) one at a time through the 'Search within results' function of Scopus by specifically targeting 'article title, abstract and keywords'. Consequently, the abstracts of this keyword-based search were evaluated and the selected documents were imported and kept in separate groups in a bibliographic management software, EndNote. Afterwards, all the downloaded full text documents were carefully read and the writing process commenced. During the writing phase, specific searches were performed using Google Scholar for each of the sections/subsections to access any missing information. In both of the search phases, i.e., in the case of both Scopus and Google Scholar searches, the documents solely focusing on extraction of some specific components from different parts of *aloe vera* were excluded through abstract evaluation. The resulting data was organized according to manuscript outline and has been discussed in the following sections.

1.1 Composition of *Aloe vera*

Aloe vera is a succulent, tender plant containing a high water content (99-99.5%). Solid contents range from 0.5-1% and consist of a variety of active components i.e. fat and water soluble minerals, vitamins, simple/complex polysaccharides, organic acids, enzymes and phenolic compounds (Hamman, 2008). The leaf consists of three layers i.e. gel, latex and rind (figure 1):

1) *Gel:* Inner layer consisting of soft, clear, moist and slippery tissues having large parenchyma cells. This is a transparent mucilaginous jelly like material. It contains water (99%), glucomannans, amino acids, lipids, sterols and vitamins (Benítez et al., 2015; Hamman, 2008; Ramachandra and Rao, 2008).
2) *Latex:* The middle layer containing anthraquinones, bitter yellow sap and glycosides (Hamman, 2008).

3) *Rind:* The outer thick layer consisting of 15-20 cells which gives protection to gel matrix and helps in the synthesis of carbohydrates and proteins (Misir et al., 2014).

Figure1

Rind and gel constitute the major portion of whole leaf weight (20-30% and 70-80%, respectively). On a dry matter basis the gel consists of 55% polysaccharides, 17% sugars, 7% proteins, 4% lipids, 16% minerals, 1% phenolic compounds and a variety of vitamins including vitamin A, C, E, B_1, B_2, B_{12}, niacin, choline and folic acid (Ahlawat and Khatkar, 2011; Femenia et al., 1999; Ni et al., 2004; Radha and Laxmipriya, 2015).

Figure2

Carbohydrates consist of mono and polysaccharides including glucomannans, xylose, rhamnose, galactose and arabinose (Ahlawat and Khatkar, 2011). Enzymes present in *aloe vera* gel include catalase, amylase, oxidase, cellulase, lipase and carboxypeptidase (Meadows, 1980). Potassium and chloride are present in excessive amounts whereas sodium, calcium, magnesium, copper, zinc, chromium and iron are present in small amounts. A series of glycosides (anthraquinones) are present in *aloe* gel with aloin A and aloin B being the most prominent. Anthraquinones and their derivatives are potent antimicrobials and analgesic agents. Around 20 amino acids are present in *aloe vera* gel among which seven are essential amino acids (Ahlawat and Khatkar, 2011). Table 1 summarizes various compounds present in *aloe vera* gel.

Table 1

1.2 Rheological behavior of *aloe vera* gel

Aloe vera gel generally exhibits elastic behavior which can be attributed to the network of polymeric fibrous chains. Elastic modulus increases with increasing temperature and exhibits damping behavior under oscillatory shear at low frequencies. Viscosity decreases with increasing shear rate (exhibiting shear thinning behavior); however, above certain critical value (100 S^{-1}) viscosity becomes constant. Such rheological behavior is attributed to the structural decomposition and rearrangement of weak network of polymeric fibers (Lad and Murthy, 2013).

Rheology of any formulation (e.g. creams, lotions, and foods) depends upon the combination of individual components as well as their mutual interactions. The addition of *Aloe vera* gel to different products can lead to complex rheological behaviors, developing from its interactions with product ingredients as well as process conditions. However, it has been suggested that the rheological properties of *aloe vera* can be tuned to meet product requirements. Moreover, it can also be used as a rheology modifier for various products.

2. Processing of *aloe vera*

Aloe vera has been employed as an ingredient in different formulations. This requires an adequate processing of *aloe vera* into different preparations that can easily be incorporated according to the nature of the product. The *aloe vera* as an ingredient is defined as the preparation which maximizes the desired constituents while keeping them in active and unaltered form, minimizes the ingredients with negative impact, preserves the benefits, and is present in the final product in amounts sufficient to produce desired results (Eshun and He, 2004). Different processing steps can be followed depending on the industry and requirement with variation in product quality. In a commonly used method, *aloe vera* is first drained with subsequent soaking of leaves in ethanol solution (15%) for 14 days in the dark. The resulting material is then finely chopped and is subjected to a mill press (Iwu, 2014). In another method, *aloe vera* juice is first prepared through

crushing, grinding or milling of entire leaves. After filtration and stabilization, the juice becomes ready for end use (Ramachandra and Rao, 2008). For various applications, *aloe vera* is generally prepared in the form of juice, concentrate and powder.

2.1. Aloe vera juice

Traditionally, for juice preparation, unwanted parts of the leaf (leaf base, leaf top, tapering point and spines at leaf margins) are removed and the fillet is washed. This material is added to the pulper where juice is extracted under refrigerated temperatures. The extracted juice is then stored at low temperature to prevent the loss of bioactivity of sensitive molecules (Ahlawat and Khatkar, 2011). In an alternative method of juice preparation, the base and tip of the leaf are removed and ground to form slurry that produces a soup like consistency. It is then treated with cellulose enzyme to release cell constituents. The material is then passed through a series of coarse filters to remove impurities (e.g. rind particles). The resulting liquid is subjected to the removal of large pieces of pulp and rind (through de-pulping extractor) formed during grinding process. The material is finally passed through a series of filters to remove aloin, emodin, traces of leaves, sand and other particles. Juice prepared by this method contains three times more bioactive components compared to the juice prepared with the traditional method (Ramachandra and Rao, 2008).

2.2. Aloe vera concentrate

Aloe vera juice is concentrated under vacuum (125 mm Hg) at temperature below 50 °C for 120 seconds. As bioactive components are sensitive to temperature and pressure, therefore, temperature and vacuum conditions should be tuned carefully to prevent the loss of bioactivity (Ramachandra and Rao, 2008). The juice is concentrated to the desired consistency suitable for various food applications including jams, jellies, squashes, tea and fruit juices.

2.3. ***Aloe vera powder***

Aloe vera fillets are washed, placed in a humidity chamber at desired temperature and relative humidity followed by drying with hot air passing over the fillets. Freeze drying and tray drying have also been reported (Ahlawat and Khatkar, 2011; Qian, 2002). The dried material is then ground to powder and packed.

Traditional drying techniques are detrimental to the temperature sensitive bioactive compounds present in *aloe vera*. The bioactivity can be preserved through freeze drying; however, the process is uneconomical and time consuming. Novel microwave-assisted drying techniques can be used as an effective alternate to conventional and freeze drying. This technique involves the removal of product moisture through microwave heating followed by complete drying using some conventional drying technique. The process is not only energy efficient and cost effective but also ensures speedy operation and improved product quality (Khan et al., 2016).

3. Applications of *aloe vera*

Aloe vera is applied to a variety of products in the form of *aloe vera* juice, concentrate and powder. Some of its applications in pharmaceuticals, foods and cosmetics are discussed in the following sections.

3.1 Pharmaceutical applications

Investigations have led to an increased importance of *aloe vera* due to its dependable medicinal properties, and it has been used in the preparation of pharmaceutical products including ointments, tablets and capsules (Eshun and He, 2004; He et al., 2005). Various components present in *aloe vera* have been found effective against many diseases, some of which are discussed below and which are summarized in table 2.

3.1.1. Wound healing

Wound healing is the restoration of integrity of injured tissues. Amino acids that are essential in wound healing process are present in *aloe vera* (Robbers et al., 1996). It also contains many inorganic electrolytes like iron, potassium, magnesium, chromium, copper, sodium, calcium and zinc which are vital part of wound healing process. It stimulates the body to produce antibodies and starts wound healing by releasing growth factors (Bozzi et al., 2007). Many studies have shown fast healing of wounds with *aloe vera* treatment (Tarameshloo et al., 2012). *Aloe vera* prevents scar formation during skin injury by stimulating the cell production and promoting the regeneration process at the deepest layers of the skin (Eshun and He, 2004).

3.1.2. Anti-ulcer effects

Aloe vera gel has the potential to prevent and cure gastric ulcers through a number of mechanisms including anti-inflammatory properties, healing effects, mucus stimulation and regulation of gastric secretions (Suvitayavat et al., 2004). Mansour et al (2014) have reported that *aloe* and myrrh based gels were found effective in decreasing ulcer size, erythema and exudation. At concentrations of about 80%, *aloe vera* can be successfully used for treatment of skin ulcers including mouth ulcers, cold sores and leg ulcers (Sims and Zimmermann, 1971).

3.1.3. Anti-inflammatory

Aloe vera gel exhibits strong anti-inflammatory effects due to the presence of anthraquinones and chromone. An intake of oral aloe gel (2%) has been reported to be effective in decreasing the severity of pain and wound size in aphthous stomatitis patients (Radha and Laxmipriya, 2015). The anti-inflammatory effect of *aloe vera* is also helpful in relieving joint pain. The complex mechanisms of the body that cause painful inflammation involve the production of bradykinin (an

inflammatory mediator) in response to various types of injuries. Studies have shown that *aloe vera* possesses anti-bradykinin activity because it contains a bradykinase enzyme, which breaks down the bradykinin and reduces the inflammation (Peng et al., 1991). *Aloe vera* gel is more effective against inflammation caused by prostaglandin synthesis as well as infiltration of leukocytes and is less effective against inflammation caused by allergenic agents (Reynolds and Dweck, 1999).

3.1.4. Anticancer activity

Glycoproteins and polysaccharides present in *aloe vera* make it a potent chemo-preventive agent that is useful against various types of cancers (Reynolds and Dweck, 1999). These agents stimulate the immune system to fight against cancer (Steenkamp and Stewart, 2007). Barbaloin, aloe-emodin and aloesin extracted from a*loe vera* have shown cytotoxicity against acute myeloid leukemia (AML) and acute lymphocytes leukemia (ALL) cancerous cells. Administration of these active compounds have been reported to significantly extend the life span of tumor transplanted animals (El-Shemy et al., 2010).

3.1.5. Antidiabetic effects

Aloe vera gel is an effective antihyperglycemic agent against type 2 diabetes. It lowers the blood glucose level without disturbing the normal blood lipid level and liver/kidney function (Hamman, 2008; Huseini et al., 2012). It has been proposed that blood glucose level is lowered due to its increased metabolism (Boudreau, Mary D. and Beland, Frederick A., 2006). Devaraj et al (2008) have reported reduced body weight and reduced insulin resistance in diabetic patients treated with *aloe vera* gel complex. Jain et al (2010) have reported the antidiabetic activity of *aloe vera* gel through reduced oxidative stress and improved antioxidant status. Yongchaiyudha et al (1996) reported a 44 % reduction in blood glucose level in diabetic patients administered with *aloe vera*

gel. Similar results were also observed when *aloe vera* gel was administered in combination with glibenclamide (Syed et al., 1996).

3.1.6. Antioxidant effects

A number of antioxidants such as α-tocopherol, carotenoids, ascorbic acid, flavonoids, tannins vitamin C and E are present in *aloe vera* (Aburjai and Natsheh, 2003; Eshun and He, 2004; Radha and Laxmipriya, 2015). Antioxidant potential of the extracts of *aloe vera* (leaf and flower) have been reported by Lopez et al (2013). *Aloe vera* has a dose dependent antioxidant effect, which is helpful in treatment of various diseases (Hamman, 2008). Investigations of the antioxidant potential of a polysaccharide isolated from *aloe vera* gel showed that it had a protective effect against dihydrochloride induced oxidative stress and cell death in kidney epithelial cells (Kang et al., 2014).

3.1.7. Antihyperlipidemic activity

Aloe vera gel is claimed to have antihyperlipidemic activity. When administered to patients not responding to dietary interventions, it effectively reduced the blood cholesterol level (15.4%), triglycerides (25.2%) and LDL cholesterol (18.9 %) (Mulay, 2014). An investigation reported by Kumar and Rakesh (2013) also showed that *aloe vera* gel in combination with probiotic *lactobacillus rhamnosus* can improve the lipid profiles in hypercholesteremic rats together with enhanced cholesterol production and absorption resulting in reduced risk of cardiovascular diseases.

3.1.8. Teeth and gum protection

Aloe vera is widely used in the field of dentistry to treat a variety of dental complications, such as to relieve pain and accelerate healing after periodontal flap surgery (Eshun and He, 2004). Gum

diseases like gingivitis and periodontitis are treated by using *aloe vera* to reduce bleeding, control inflammation and stop the swelling of the gums (Sujatha et al., 2014).

3.1.9. Absorption and bioavailability of compounds

Aloe vera gel has potential to enhance the absorption of drugs with low bioavailability (Carien et al., 2013). Oral bioavailability of vitamin C and E was investigated with *aloe vera* gel and leaf extract. Absorption of vitamin C was found to decrease with both the gel and leaf extract. However, overall bioavailability of vitamin C and E was increased. The mechanism of action was proposed to be the protection against degradation as well as binding of polysaccharides resulting in slower absorption rates (Vinson et al., 2005). In addition to enhancing absorption and bioavailability through the gut, *aloe vera* oil has also been found beneficial in accelerating the penetration rate of drugs through the transdermal route. In a recent study by Vashisth et al (2014), the effect of *aloe vera* oil on skin penetration of losartan potassium (a drug used to treat hypertension) was investigated and compared with other essential oils such as tea tree oil, cumin oil and rose oil. Among these essential oils, only *aloe vera* oil could provide the target flux required to deliver the therapeutic transdermal dose of losartan potassium. The availability of such formulations provides an alternative and convenient route for drug administration as compared to the conventional oral route, which can result in poor patient compliance in case of long-term treatment.

3.1.10. ***Laxative effects***

Aloe vera gel is one of the most potent laxative compounds and is used traditionally to treat constipation (Hamman, 2008). When taken in doses of 0.25mg, laxative effects start within 6 to 12 hours resulting in loose bowel movements. It is safe for nursing mothers, as no laxative effects are found in their infants (Mulay, 2014).

Table 2

3.1.11. Genital Herpes

Genital herpes (caused by Herpes Simplex Virus) is one of the most common sexually transmitted diseases. Treatment of this disease involves medication for faster healing of sores and lesions so that outbreaks can be reduced or prevented. *Aloe vera* extract (0.5%) in the form of a hydrophilic cream has shown effectively to treat genital herpes in men (Syed et al., 2009) through a more rapid healing process.

3.1.12. Asthma

Storage of *aloe vera* extract in the dark for a period of 3-10 days produces some active compounds (prostanoids) in the glycoprotein and polysaccharide fractions. These active compounds have shown effectiveness against chronic bronchial asthmatics. However, the activity against asthma becomes ineffective if the patient has been previously administered with steroid drugs (Capasso et al., 1998; Shida et al., 1985).

3.1.13. HIV Infection

Human immunodeficiency virus is increasingly becoming a serious threat to global health infecting around 10 million people worldwide every year. Various anti-HIV drugs have been approved for clinical use. However, such drugs have limitations including high cost, decreased sensitivity and adverse side effects (Wu et al., 2001). Hence, there is a need for less toxic and less expensive herbal therapies for HIV treatment. Polysaccharides and acemannans present in *aloe vera* have proved to be effective against HIV (Olatunya et al., 2012; Yu et al., 2009).

3.2 Food applications

The demand for functional foods with prolonged shelf life and without chemical preservatives has increased around the world. Recently, processing of *aloe vera* gel has converted to a big undertaking owing to its applications in the food industry (He et al., 2005). *Aloe vera* incorporation is made as a dietary supplement and functional ingredient in many food products including beverages, yoghurt, milk, ice creams, confectionary etc. (Kapoor et al., 2009; Ramachandra and Rao, 2008). Some important food applications are given below and are summarized in table 3.

3.2.1. Functional and nutraceutical foods

The use of *aloe vera* gel extract in the preparation of functional foods started in 1970s in Europe and United States (Park and Jo, 2006). Currently, its applications have been extended to the development of a variety of functional and nutraceutical foods. Mannose polymers with some sugars including glucose and acemannan are present in *aloe* gel. These together with glycoproteins, enzymes, amino acids and vitamins contribute to the functionality of foods without affecting their quality and acceptability (Rodr´iguez et al., 2010). Pushkala and Srividya (2011) formulated functional *dahi* (a fermented South Asian dairy product) by replacing skim milk with *aloe vera* gel. It not only added to its nutritional and therapeutic potency, but the quality parameters of *dahi* (whey syneresis, water holding capacity, total yield, whiteness index and viscosity) were also improved. *Aloe vera* gel enriched beverages (sweetened *aloe vera* juice, ready-to-serve juices and squashes) have also been reported which are claimed to have potential to maintain good health (Sharma et al., 2015). Other health foods developed from *aloe vera* include ice-cream (Manoharan and Ramasamy, 2013), *lassi* (a traditional fermented dairy beverage of South Asia) (Hussain et al., 2014), mango nectar (Elbandy et al., 2014) and carbonated beverages (Moore and McAnalley, 1995).

The foods described above are claimed to be both functional and nutraceutical based on their in vitro analysis which confirms the presence of bioactive compounds (e.g. flavonoids). However, their bio-functionality can be influenced by their interactions with food components. Biological studies are therefore recommended to confirm the nutraceutical potential of such products.

3.2.2. Antimicrobial agent

An antimicrobial agent is a substance having the ability to inhibit or delay the growth of microorganisms including bacteria, fungi, and viruses. *Aloe vera* gel can effectively inhibit the growth of food borne spoilage and pathogenic microorganisms including *Staphylococcus aureus, Salmonella, Stroptococcus, Escherichia coli, Aspergillus niger, Candida etc.* (Kedarnath et al., 2013; Lone et al., 2009; Nidiry et al., 2011; Shelton, 1991). Thus, incorporation of *aloe vera* gel not only contributes towards safety of foods but also prevents them from microbial spoilage. A variety of antimicrobial compounds are present in *aloe vera* gel and antimicrobial activity is exhibited due to their synergistic effect (Lawrence et al., 2009). Valverde et al (2005) have reported the improved safety of table grapes treated with *aloe vera* gel. The microbial load of mesophilic aerobic bacteria, yeasts and molds was effectively reduced during storage. Similar antimicrobial effects have also been reported for other foods like mango, green grape berries and sweet cherries (Castillo et al., 2010; Chauhan et al., 2014; Martínez-Romero et al., 2006; Sophia et al., 2014).

3.2.3. Edible coatings/films

An edible coating/film is a thin layer of eatable material that hinders the transfer of components between food and its environment; thereby increasing the shelf life of perishable commodities. *Aloe vera* gel is considered among one of the best edible and biologically safe coatings for various food applications due to its film-forming properties and biodegradability. The polysaccharides of

aloe vera act as a natural barrier to moisture and oxygen that are the main agents of deterioration of fruits and vegetables (Misir et al., 2014). They help to control respiratory rate, delay ripening, prevent moisture loss, delay oxidative browning, and provide firmness. Martinez-Romero et al (2006) investigated the post-harvest quality of sweet cherries coated with *Aloe vera* gel based coating. The respiration rate, weight loss, color changes, softening, ripening and stem browning were reduced as compared to uncoated fruits while maintaining the taste, aroma and flavor. Ahmad et al. (2009) and Castillo et al., (2010) have reported similar effects of *aloe vera* gel coating on post-harvest quality of grapes and nectarines. A novel trend of making edible coatings/films is to disperse lipids into polysaccharide solutions resulting into emulsions. Such coatings/films exhibit improved barrier and mechanical properties compared to lipids and polysaccharides alone. The emulsion based coatings/films of *aloe vera* gel are expected to exhibit better characteristics compared to the coatings reported above. However, preparation and application of such coatings/films (from *aloe vera* gel) are hardly reported in the literature.

Table 3

3.3 Cosmetic applications

Aloe vera gel is extensively used in the cosmetic industry, where it has become an important selling ingredient. It is used as a base material for various formulations including moisturizers and suntan lotions which are used as humectant in skin preparations (Iwu, 2014). *Aloe vera* gel and powder have many other applications in the cosmetic industry due to their valuable moisturizing and soothing effects in products like shampoos, soaps, cleansers and moisturizing creams. Soaps prepared with *aloe vera* have the advantage that they do not cause irritation and do not leave the skin dry. *Aloe* extracts are also added into some shaving creams and lotions in the USA and Asia

to enhance the healing of shaving wounds. The mucilaginous nature of *aloe vera* gel also helps it to serve as a protective barrier between skin and beard in shaving creams (Eshun and He, 2004; Lad and Murthy, 2013).

Many skin problems such as sunburns, flaky or dry skin, hair and scalp problems, psoriasis, stretch marks, and dandruff are being treated by lotions and sun-blocks. *Aloe vera* is famous for its powerful healing activity even at the epithelial level of the skin and thus provides a protective layer on the skin which allows the skin to heal at a faster rate due to its nutritional contents and antioxidant properties (Bouchey and Gjerstad, 1969; Meadows, 1980). The skin drying is prevented by the application of *aloe vera* before the use of mineral-based make-up. Its moisturizing effect (without giving a greasy feel) makes it perfect for oily skin. Giberellin (present in *aloe vera*) is a growth hormone which stimulates the growth of new cells and heals the skin with minimal scarring. *Aloe vera* is used in Ayurvedic medicines to heal chronic skin problems such as psoriasis, acne and eczema (Arunkumar and Muthuselvam, 2009). Antioxidants including β-carotene, vitamin C and E present in *aloe vera* leaves improve the natural firmness of the skin and keep the skin hydrated (Aburjai and Natsheh, 2003; Eshun and He, 2004).

Aloe vera gel can be added to any product where moisturization or mildness is required. However, successful development of such products depends upon the compatibility of the gel with the product system. Generally, *aloe vera* gel is compatible with cationic, anionic and non-ionic systems. However, with anionic systems only a limited amount of gel can be incorporated where quinones can react with the base to cause product discoloration. In addition, the natural pH of the gel (if added in conc. > 30%) can cause the neutralization of the product system (Meadows, 1980).

4.0. Recent technological advances to ensure effective utilization of *aloe vera*

As discussed in previous sections, the *aloe vera* plant possesses an enormous potential for various biomedical and cosmetic applications because of its bioactive components. It is notable that the latest research on *aloe vera* is focusing on getting maximum benefit from these natural compounds. This has been targeted through the development of improved formulations that can offer a better application and controlled release of the active components. The investigations conducted over the last few years are concentrating more on the wound-healing property of *aloe vera*, especially related to burn-healing. To effectively utilize the wound-healing property of *aloe vera*, several types of formulations such as functional films, hydrogels and sponges have been developed which can release the bioactive components along with providing a mechanical support to the tissue. These novel biomaterials have been formulated through combination of *aloe vera* gel with various biopolymers such as cellulose, gellan gum, alginate chitosan, or gelatin (Chen et al., 2010; Saibuatong and Phisalaphong, 2010; Silva et al., 2013a; Silva et al., 2014; Silva et al., 2013b). The development of such formulations offers many advantages over the conventional dosage forms (e.g., liquid or semisolid drug delivery products) such as providing uniform drug application, prolonged drug release, application over large surface area, mechanical support, absorption of skin secretions, and prevention of loss of body fluid.

Although the mammalian skin is capable of regenerating itself after minor injuries, in case of severe damages, a proper clinical treatment such as skin transplantation becomes indispensable (Shakespeare, 2001). However, there are some drawbacks associated with these conventional clinical procedures and therefore, much attention has been given to tissue engineering that employs different biomaterials and growth factors for the regeneration of neotissues from cells (Ikada,

2006). The excellent wound healing property of *aloe vera* has also made it an attractive material for skin tissue engineering applications. Recently, Suganya et al. (2014) studied naturally derived biofunctional nanofibrous scaffold composed of *aloe vera* and silk fibroin for skin tissue regeneration. They found that *aloe vera* and silk fibroin showed a synergistic effect with excellent physico-chemical properties.

Apart from polymer films, hydrogels and sponges that are discussed above, the biodegradable polymer micro- and nano-particles represent another form of drug delivery systems that offers a great stability to the encapsulated drug, and their application is gradually increasing in cosmetic and pharmaceutical products (Pereira et al., 2014). In the case of wound healing, the use of rough surfaced polymer microparticles offers some added benefits such as a better adhesion at the target site thus ensuring an effective drug release (Huang and Fu, 2010). In an investigation by Pereira et al. (2014), rough surfaced microparticles comprising Aloe vera, vitamin E and chitosan were developed specifically for skin burns. These rough surfaced microparticles exhibited good muco-adhesive properties together with prolonged drug release.

Solid-lipid particles represent another form of drug loaded particles for controlled drug release through various administration routes like oral, parenteral, ophthalmic and topical, and have been applied for delivering various drugs (Sawant and Dodiya, 2008). For the preparation of solid-lipid particles, stearic acid is commonly used as lipid matrix. However, the highly crystalline nature of stearic acid renders difficulties in the preparation of solid-lipid particles. Therefore, various polymeric forms of stearic acids are employed as lipid matrix in the preparation of solid-lipid particles. Recently, Joshy et al. (2016) reported preparation of solid-lipid nanoparticles of stearic acid modified with *aloe vera* for antiviral drug delivery applications, to ensure high loading

efficiency in addition to improved antiviral activity. Furthermore, these modified solid-lipid nanoparticles provided a better cellular interaction than the unmodified form.

Aloe vera has versatile skin care properties due to its different hydrophilic components. However, the absorption of these hydrophilic components through the skin is limited due to the presence of the stratum corneum, a water impermeable outer layer of the skin. In this regard, various strategies have been adopted; however, the liposomal drug delivery system has been found quite remarkable in enhancing the permeation of the hydrophilic substances of *aloe vera* gel through the skin (Takahashi et al., 2009).

5.0. Complications and precautions

Aloe vera is generally considered as safe; however, a few side effects and complications have been reported. When used for the treatment of constipation, some side effects including abdominal cramps, flatulence and griping may occur (Mulay, 2014). Use of *aloe vera* can promote bleeding during surgical procedures; therefore, its use should be discontinued at least two weeks before any surgery. The oral use of *aloe vera* with furosemide or digoxin treatment for irregular heart rhythms and congestive heart failure can lower the level of potassium in the body; therefore, it should not be consumed with these drugs. Use of *aloe* juice or *aloe* latex for longer times or in high doses can cause an imbalance of electrolytes - loss of sodium can result in secondary hyperaldosteronism, and loss of potassium can result in hypokalemia leading to fatigue, muscular weakness, weight loss, mental problems and dis-functioning of kidneys (Mulay, 2014). Skin applications of *aloe vera* along with steroid creams (such as hydrocortisone containing creams) can increase their absorption. Allergic reactions such as skin rashes may occur if *aloe vera* gel is applied on open or deep wounds, but it can be used on the skin surface safely if there is no injury (Surjushe et al., 2008). Recently, anthraquinone and aloin present in *aloe vera* gel have been related to the risk of

tumours and colon cancer (Aldhous, 2011; Mulay, 2014). It is also recommended that in cosmetic products containing *aloe vera*, anthraquinone content (especially aloe emodin) should not exceed 50 ppm to avoid phototoxicity caused by photo-oxidative damage to both RNA and DNA (Boudreau, M. D. and Beland, F. A., 2006; Christaki and Florou-Paneri, 2010).

6.0. Conclusion

Aloe vera, owing to its beneficial therapeutic effects, has found applications in a variety of products including foods, pharmaceuticals and cosmetics. Its consumption in various fields can be maximized by developing appropriate processing techniques. Establishment of standards for its incorporation in various foods are under discussion in the international *aloe* science council as well as in countries including European Union, China and Korea. It is expected that its application in functional foods and cosmetics will increase with time. However, there are some complications linked to the use of *aloe vera* which need to be addressed. Precautions need to be considered while using *aloe vera* in some specific conditions and with some specific compounds. It is recommended that its continuous use for extended period of time should be avoided in order to avoid any possible complications.

Conflict of interest statement

We hereby confirm that we do not have any financial and personal relationships with other people or organizations that could inappropriately influence (bias) our work.

Conflict of interest: None

7.0. References

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Figures

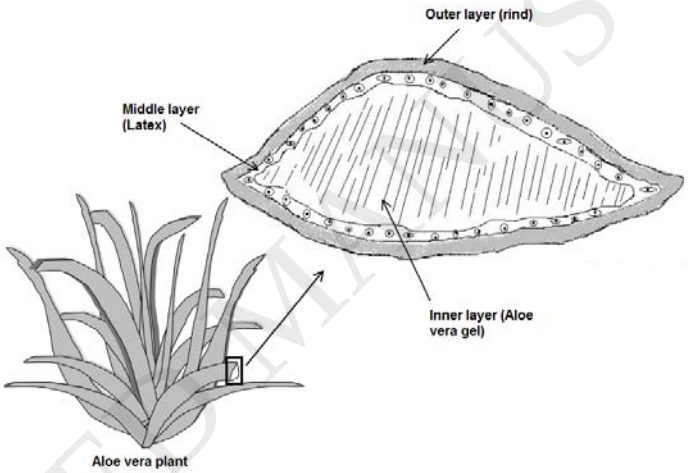

Figure1: A cross sectional view of *aloe vera* leaf showing inner, middle and outer layers (Adapted from Beland and Boudreau (2006)).

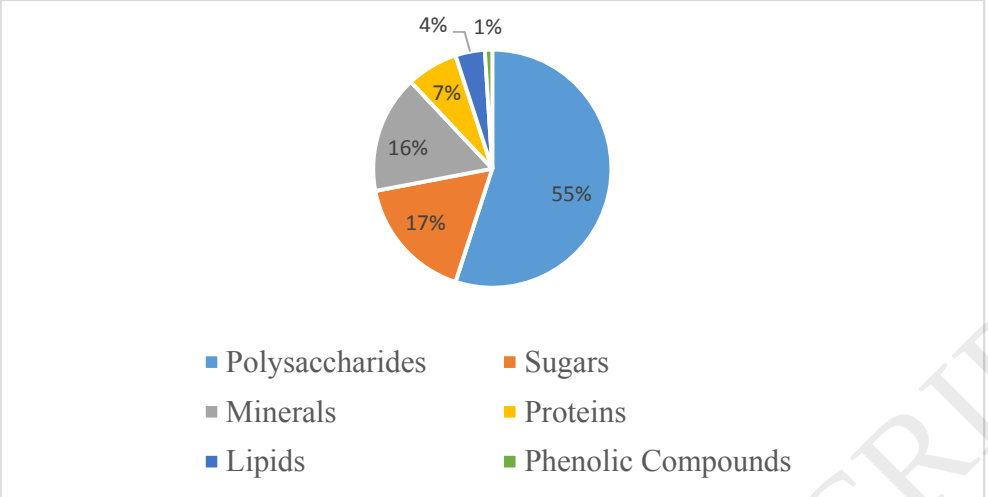

Figure2: Chemical composition of *aloe vera* gel on dry matter basis.

Tables

Table 1: Summary of various compounds present in *aloe vera* gel

Class	Compounds	References
Amino Acid	Alanine, arginine, aspartic acid, cysteine, glutamic acid, glycine, histidine, hydroxyproline, isoleucine, leucine, lysine, methionine, phenylalanine, proline, threonine, serine, tyrosine and valine	(Nwaoguikpe et al., 2010; Saeed et al., 2004; Samuelsson and Bohlin, 2004)
Anthraquinone	Aloe-emodin, aloetic acid, anthranol, aloin A& B, anthracine, anthranon, barbaloin, chrysophanic acid, emodin, ethereal oil, ester of cinnemonic acid, isobarbaloin, and resistannol	(Kilic, 2005; Saeed et al., 2004)
Carbohydrates	Lignins and sugars such as arabinose, cellulose, fructose, fucose, galactose, glucose lactose, maltose, mannose, pectic substance, rhamnose,	(Bozzi et al., 2007; Femenia et al., 1999; Ni et al., 2004; Saeed et al., 2004; Samuelsson and Bohlin, 2004)

	sucrose, uronic acids and xylose	
Chromones	8-C-glucosyl-(2'-O-cinnamoyl)-7-O-methylaloediol A, 8-C-glucosyl-(S)-aloesol, 8-C-glucosyl-7-O-methyl-(S)-aloesol, 8-C-glucosyl-7-O-methylaloediol, 8-C-glucosyl-noreugenin, isoaloeresin D, isorabaichromone and neoaloesin A	(Hamman, 2008)
Dietary Fibers		(Femenia et al., 1999)
Enzymes	Alkaline phosphotase, amylase, carboxypeptidase, catalase, cellulase, cyclooxidase, cyclooxygenase, lipase, oxidase, peroxidase, phosphoenolpyruvate carboxylase and superoxide dismutase	(Saeed et al., 2004; Samuelsson and Bohlin, 2004)
Hormones	Auxins and gibberllins	(Saeed et al., 2004; Samuelsson and Bohlin, 2004)
Inorganic Compounds	Minerals such as calcium, chlorine, chromium, copper, iron, magnesium, manganese, phosphorous, potassium, sodium and zinc	(Femenia et al., 1999; Mohamed, 2011; Nwaoguikpe et al., 2010; Saeed et al., 2004; Samuelsson and Bohlin, 2004)
Miscellaneous including organic compounds and lipids	Arachidonic acid, γ-linolenic acid, triglicerides, triterpenoid, potassium sorbate, salicylic acid and uric acid	(Femenia et al., 1999)
Organic Acids	Acetic acid, citric acid, formic acid, fumaric acid, lactic acid, malic acid, pyruvate, succinic acid and tartaric acid	(Bozzi et al., 2007)
Proteins	Lectins, lectin-like substance	(Femenia et al., 1999)
Sterols	Cholesterol, campesterol, lupeol and beta sitosterol	(Kilic, 2005; Saeed et al., 2004; Samuelsson and Bohlin, 2004)

Vitamins	Vitamin A, C, E, B_1, B_2, B_6, B_9 and choline	(Mohamed, 2011; Nwaoguikpe et al., 2010; Saeed et al., 2004; Samuelsson and Bohlin, 2004; Serrano et al., 2006)

Table 2: Summary of pharmacological applications of *aloe vera*.		
Effect	**Plant parts used**	**Reference**
Wound dressing	Leaf	(Iwu, 2014)
Vertigo treatment	Leaf	(Iwu, 2014)
Guinea worm infestation treatment, colds and asthma	Leaf exudate+ egg white	(Iwu, 2014)
Stomach ulcer	Leaf exudate+ sea water	(Bozzi et al., 2007; Iwu, 2014)
Constipation	Dried exudate, *aloe* latex	(Bozzi et al., 2007; Hamman, 2008; Iwu, 2014)
Wound healing	*Aloe* gel, inorganic electrolytes, amino acids	(Bozzi et al., 2007; Maenthaisong et al., 2007; Robbers et al., 1996)
Varicella zoster, herpes simplex type I and II, influenza and pseudo rabies	Anthraquinone glycosides	(Yongchaiyudha et al., 1996)
AIDS	*Aloe* extract	(Yongchaiyudha et al., 1996)
Antidiabetic effects	*Aloe* gel	(Bozzi et al., 2007; Maenthaisong et al., 2007; Syed et al., 1996)
Hypolipidemic effects	*Aloe* gel	(Kumar et al., 2013)
Cardiovascular and hypercholesteremic effects	*Aloe* gel	(Maenthaisong et al., 2007; Zandi et al., 2007)
Weight loss	*Aloe* gel	(Zandi et al., 2007)
Breast cancer, gastrointestinal cancer and brain glioblastoma	*Aloe vera*+ honey	(Kumar et al., 2013)
Burning mouth symptoms treatment	*Aloe* gel+ glycerine	(Borra et al., 2011)
Inflammation and anti-bradykinin activity	*Aloe* bradykinase enzyme	(Peng et al., 1991)
Genital herpes and psoriasis	*Aloe* gel	(Maenthaisong et al., 2007)
Burns	*Aloe* gel lectin	(Eshun and He, 2004)
Anti-virucidal effect, burns, skin irritations and wounds	*Aloe* gel	(Bozzi et al., 2007; Eshun and He, 2004)
Headaches, immune-system deficiencies, coughs and arthritis	*Aloe* gel	(Bozzi et al., 2007)
Antibacterial and antiviral effects and effects on immune system	*Aloe* polysaccharides (glucomannan, acemannan)	(Bozzi et al., 2007)
Antitumor and antiulcer effects	*Aloe* gel glycoproteins	(Bozzi et al., 2007)
Anti-inflammatory effects	Anthraquinones and chromone	(Radha and Laxmipriya, 2015)

Aphthous stomatitis treatment, antidiabetic activity, cardio-protective activity, antioxidant status and carbohydrate metabolism	*Aloe* gel	(Radha and Laxmipriya, 2015)
Protection from gastrointestinal irritation and damaged mucous membrane of the stomach	*Aloe* juice or drinks	(Agarry and Olaleye, 2005)
Antimicrobial activity against gram positive and gram negative bacteria	*Aloe vera* extracts	(Arowora et al., 2013; Misir et al., 2014)

Table 3: Summary of food applications of *aloe vera*

Function	**Foods**	**References**
Antimicrobial	Table grapes, mangoes, sweet cherry	(Castillo et al., 2010; Chauhan et al., 2014; Martínez-Romero et al., 2006; Sophia et al., 2014; Valverde et al., 2005)
Functional and neutraceutical agent	Dahi, sweetened *aloe vera* juice, ready to serve juices and squashes, ice-cream, lassi, carbonated beverages	(Hussain et al., 2014; Manoharan and Ramasamy, 2013; Moore and McAnalley, 1995; Pushkala and Srividya, 2011; Sharma et al., 2015)
Edible coating	Nectarines, grapes, sweet cherries, kiwifruit, pomegranate, blueberries, stonefruits	(Ahmed et al., 2009; Benítez et al., 2015; Castillo et al., 2010; Martínez-Romero et al., 2006; Martínez-Romero et al., 2013; Paladines et al., 2014; Vieira et al., 2016)

APPENDIX 1

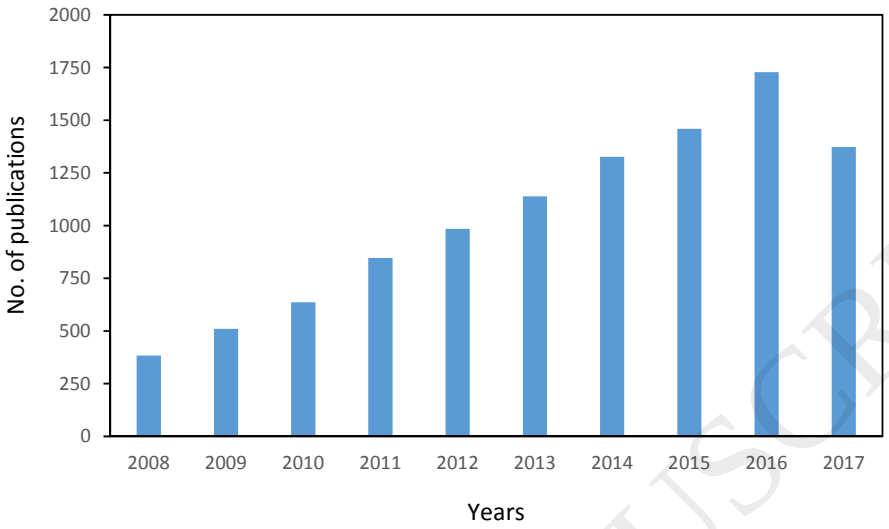

Figure 1a: Year-wise distribution of publications on *Aloe Vera* for the last ten years.

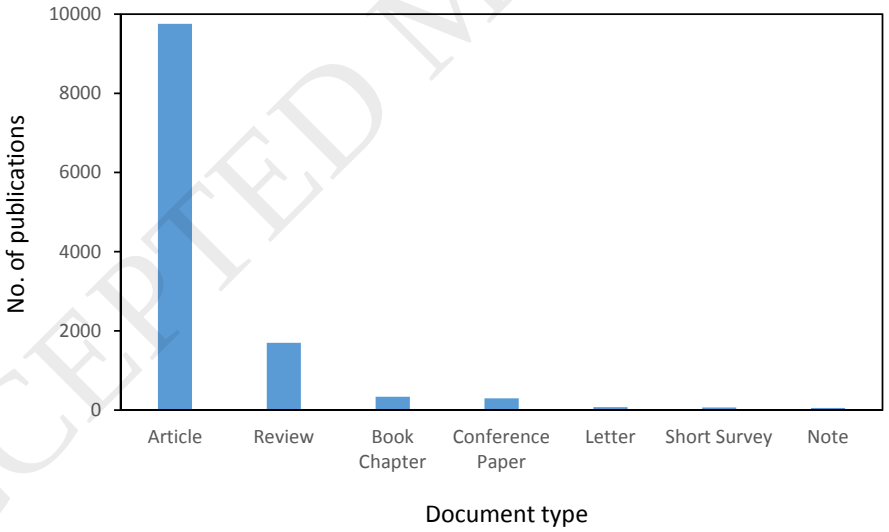

Figure 1b: The distribution of publications on *Aloe Vera* with respect to document type.

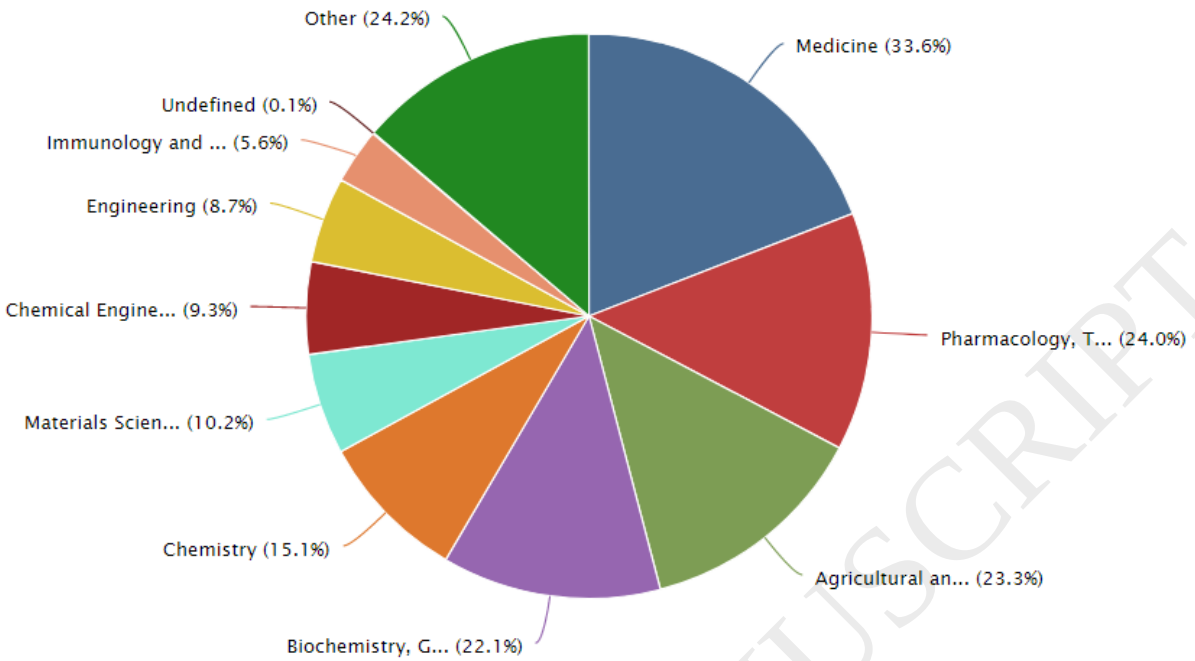

Fig. 1c: The subject-wise distribution of publications on *Aloe Vera*