

***ALOE VERA* PLANT - AN IMPORTANT SOURCE OF BIOACTIVE COMPOUNDS WITH FUNCTIONAL VALUE**

ELENA ENACHI^{1*}, MONICA BOEV², GABRIELA ELENA BAHRIM¹

¹*“Dunărea de Jos” University of Galati, Faculty of Food Science and Engineering, Domnească
Street 111, 800201, Galati, Romania*

²*“Dunărea de Jos” University of Galati, Faculty of Medicine and Pharmacy, 35 Al. I. Cuza
Street, Galati, Romania*

*Corresponding author: elena.ionita@ugal.ro (Elena Enachi)

Abstract: *Aloe vera* leaves and gel have been used since ancient times. The beneficial medicinal, cosmetic and nutritional effects have been described empirically by many users but there are not too many scientific experiments that validate all the information. Various sources in the literature describe the ability of the gel to quickly heal wounds and stimulate macrophages in the immune system. It is also known that anthraquinones in the parenchyma and cortex have laxative, antifungal and antimicrobial qualities. According to these studies, it can be stated that the medicinal, cosmetic and nutritional properties of the *Aloe vera* plant are due to the bioactive molecules synthesized by the plant.

Keywords: *Aloe vera*, bioactive compounds, therapeutic effects

Introduction

The *Aloe barbadensis* Miller plant, known as *Aloe vera*, has been known and used for centuries for the beneficial effects that it exerts on health, beauty and skin protection. The *Aloe vera* name has a complex etymology, coming from the Arabic word "Alloeh" = bright, bitter substance, while "vera" comes from Latin and means "true". *Aloe barbadensis* Miller is part of the *Asparagales* order, *Xanthorrhoeaceae* family, *Asphodelaceae* subfamily also known as *Aloe vulgaris* Lam., *Aloe indica* Royale or *Aloe perfoliata* var. *vera*. In order to compare different species, the DNA based techniques suggest that *Aloe vera* is related to *Aloe perryi*, an endemic

REVIEW ARTICLE

species from Yemen (Darokar *et al.*, 2003). Similar DNA techniques that target the comparison of sequences in chloroplasts, demonstrate the relationship between *Aloe vera* and *Aloe forbesii*, *Aloe inermis*, *Aloe scobinifolia*, *Aloe sinkatana*, and *Aloe striata*. Except for the last species that are specific to South Africa, the others are native to Socotra (Yemen), Somalia and Sudan (Treutlein *et al.*, 2003). Nevertheless, the lack of scientifically proven natural origins of these species led to several studies in which it was suggested the hypothesis that *Aloe vera* may have a hybrid origin (Jones and Sacamano, 2000).

Today, the whole *Aloe vera* plant is used for its therapeutic purposes especially in dermatology and cosmetology. *Aloe vera* is considered a perennial monocotyledonous plant, with green and fleshy leaves, that are gathered in a basal rosette. The green *Aloe vera* leaves consist of an epidermis (cortex) that is covered by a cuticle that covers the mesophyll, which includes chlorenchyma cells and the thin-walled cells that form the parenchyma. The mesophilic cells contain this polysaccharide-rich mucilaginous gel called by other scientists the *Aloe vera* gel (Femenia *et al.*, 1999). The *Aloe vera* plant comes from southern Africa and is part of the group of plants that are capable to assimilate CO₂ at night in order to achieve photosynthesis, these types of plants being called plants with *crassulacean acid metabolism* (CAM- *Crassulacean Acid Metabolism*). These species are especially adapted to arid and semi-arid areas that are free of precipitation, being able to keep the intra- and extracellular water at high temperatures. Recently, a significant increase has been observed regarding the applications of this plant extracts for various biomedical purposes (Alvarado-Morales *et al.*, 2019; Kudłacik-Kramarczyk *et al.*, 2021). *Aloe vera* possesses several phytotherapeutical properties such as germ-killing, anti-tumor and anti-swelling as many studies have proven (Hamman, 2018; Gao *et al.*, 2018; Farrugia *et al.*, 2019; Aghamohamadi *et al.*, 2019). Among these beneficial properties, the plant has been used for many purposes including wound healing (Hamman, 2018; Gao *et al.*, 2018; Farrugia *et al.*, 2019; Aghamohamadi *et al.*, 2019). The *Aloe vera* gel that is extracted from the leaf parenchyma has been used on several occasions to treat burns by being both a plasticizer and a strong humidity agent that improves the healing pathway of the damaged skin and helps to reduce the pain (Alvarado-Morales *et al.*, 2019; Kudłacik-Kramarczyk *et al.*, 2021). Furthermore, the use of the *Aloe vera* gel has been extended to the food industry, namely as a functional resource of bioactive compounds that are especially used for the development of healthy food ingredients, drinks and other beverages, including here the *Aloe vera* juice (Alvarado-Morales *et al.*, 2019;

REVIEW ARTICLE

Kudłacik-Kramarczyk *et al.* 2021). The objectives of the present study were to provide a review of the scientific literature on the *Aloe vera* main compounds (both nutrients and bioactive compounds) and its main biological activities.

Chemical composition in terms of bioactive compounds

The plant presents triangular, fleshy leaves with serrated edges, white or yellow tubular flowers and fruits with numerous seeds. Each leaf is composed of three layers:

- ❖ A transparent gel inside, which contains 99% water and 1% of glucomannan, amino acids, lipids, sterols and vitamins.
- ❖ The middle layer is latex, which is a yellowish and bitter sap, and contains anthraquinones and glycosides.
- ❖ The thin outer layer is composed of 15-20 cells that form the shell and has the function of protection and the carbohydrates and proteins' synthesis. Inside this layer, several vascular connections are presents and are responsible for the accumulation of starch (phloem) and water (xylem) (Tyler, 1993).

In cross section, the *Aloe vera* leaf is shown as in Figure 1.

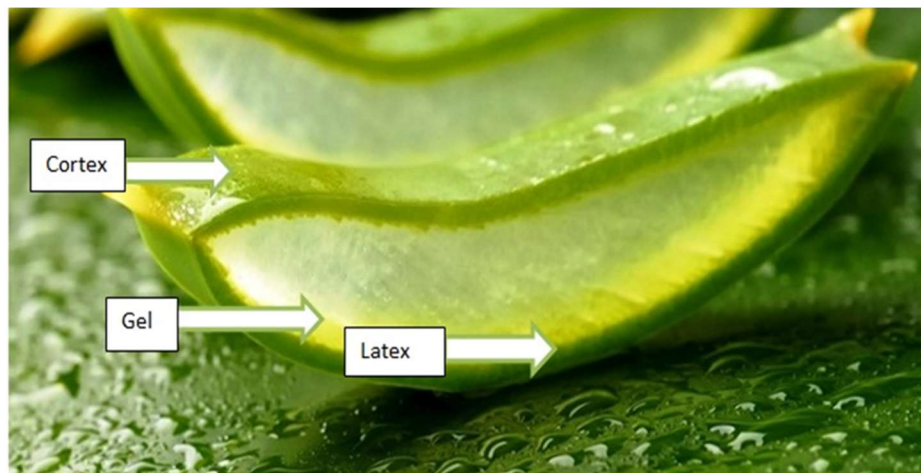


Fig. 1. *Aloe vera* leaf shown in section

The *Aloe vera* leaves contain 75 active ingredients that were shown to have a therapeutic potential: polysaccharides, amino acids, vitamins, enzymes, mineral salts, lignins, saponins and salicylic acid and some of these compounds are comprised in Table 1. The chemical composition of the plant is influenced by several factors such as the geographical area, soil quality,

REVIEW ARTICLE

precipitation, solar radiation and temperature. The amount of water is very important, as the main role of the gel is to retain the water. The amount of water in the gel represents up to 99.5% of the plant product, and more than 60% of this percentage is represented by polysaccharides (Femenia *et al.*, 1999; Silva *et al.*, 2010; Delatorre-Herrera *et al.*, 2010). To extract the compounds from this plant, the gel is separated from the cortex. The latex is found in the cortex and corresponds to the yellow, bitter juice from the green part of the leaf, produced in the epidermis and the extremely thorny portion. The bitter juice contains 15-40% hydroxyanthracene derivatives. The *Aloe vera* gel is the colorless, mucilaginous part of the central part of the leaf (Park, 2006), consisting almost entirely of water (> 98%) and polysaccharides (pectins, cellulose, hemicellulose and acetylated galactoglucomannan called acemannan). Acemannan is the main component that imprints the beneficial therapeutic effects discovered for this gel. It is composed of a long chain of acetylated mannose, intertwined with glucose, in which the mannose binds the galactose. Both classes of polysaccharides identified in the gel and leaves have been shown to be responsible for preventing the colon cancer and inducing wound healing. The polysaccharides' therapeutic action to stimulate the wound healing process has long been studied using *in vitro* cell lines in order to determine the rate of proliferation of fibroblasts and epi- and endodermal cells induced by these natural compounds (Mandrioli *et al.*, 2011; Dell-Agli *et al.*, 2007). A research study has reported the identification in the *Aloe vera* gel of a glycoprotein with antiallergic properties, called alprogen and a new bioactive anti-inflammatory component, C-glucosyl chromone (Ro *et al.*, 2000). The vitamins identified in the composition of the gel were: vitamin A (beta-carotene), vitamins C and E, with antioxidant action, vitamin B12, folic acid and choline (Surjushe *et al.*, 2008). *Aloe vera* synthesizes 8 enzymes: alkaline phosphatase, amylase, bradykinase, carbopeptidase, catalase, cellulase, lipase and peroxidase. The bradykinase has the role to reduce the excessive inflammation when applied topically to the skin, while the rest of the enzymes play a major role in the cellular metabolism. Furthermore, the *Aloe vera* plant is also a natural source of calcium, chromium, copper, selenium, magnesium, manganese, potassium, sodium and zinc. These minerals are essential for the proper functioning of various enzyme systems corresponding to different metabolic pathways, and some of them also manifest antioxidant action. In terms of phenolic compounds, the plant contains 12 anthraquinones, which are commonly used as laxatives. Aloin and emodin act as analgesics, antimicrobials and antivirals. The plant also presents four steroids among its constituents: cholesterol, campesterol,

REVIEW ARTICLE

β -sitosterol and lupeol. All these compounds have anti-inflammatory action, and lupeol also has analgesic and antiseptic properties. The plant also synthesizes 20 of the 22 amino acids needed by the human body, and 7 of the 8 essential amino acids. It also contains auxins, gibberellins and salicylic acid which have anti-inflammatory and antibacterial action with a proven effect in the wound healing. Lignin, an inert substance in the plant, however, has a beneficial effect when used in topical preparations, being an absorption promoter, i.e. it promotes the penetrating effect through the skin of active ingredients, increasing the therapeutic efficacy of pharmaceutical preparations used for external use. Saponins are found also in a proportion of about 3% in the gel and have cleansing and antiseptic properties.

Table 1. Compositional structure of the *Aloe vera*'s leaves

Class of compounds	Examples	References
Anthraquinones	➤ 7-hydroxyaloe emodin ➤ nataloe emodin and its ester ➤ aloechrysone ➤ chrysophanol ➤ aloesaponol ➤ aloe saponarin, ➤ 1,5-dihydroxy-3-hydroxy methylantraquinone, ➤ desoxyerythrolaccin ➤ isoxanthorin ➤ helminthosporin ➤ laccaic acid D methyl ester ➤ bianthracene, ➤ asphodelin	Tan <i>et al.</i>, 2011 Cock, 2015
Anthrones	➤ aloin ➤ aloe-emodin anthrone ➤ chrysophanol anthrone ➤ nataloin ➤ homonataloside ➤ aloinoside ➤ littoraloin ➤ barbendol ➤ deacetylittoraloin ➤ littoraloside ➤ microdentin ➤ microstigmin A	Zhifen <i>et al.</i>, 2012 Minale <i>et al.</i>, 2014; Kanama <i>et al.</i>, 2015;
Chromones	➤ aloesin A-F ➤ isoaloeresin A and D ➤ 7-O-methylaloesin ➤ 7-O-methylaloesinol ➤ 7-O-methylaloeresin A ➤ 2-acetonyl-7-hydroxy-8-(2-furanonyl)-7-hydroxy-5-methylchromone ➤ 7-hydroxy-2,5-dimethylchromone	Zhifen <i>et al.</i>, 2012 Kanama <i>et al.</i>, 2015 Lucini <i>et al.</i>, 2015

REVIEW ARTICLE

	➤ 20-p-O-methylcoumaroylaloenin	
Coumarins, pyrans and pyrones	➤ feralolide and dihydroisocoumarin glycoside ➤ bisbenzopyran ➤ aloenin ➤ aloenin aglycone ➤ aloenin acetal ➤ aloenin B	Cock, 2015 Lucini <i>et al.</i>, 2015 Sun <i>et al.</i>, 2016
Alkaloids	➤ N-methyltryamine ➤ O-N-dimethyltryamine, ➤ g-coniceine ➤ coniine	Kumar <i>et al.</i> , 2019
Benzene and naphthalene derivatives	➤ methyl-p-coumarate ➤ protocatechuic acid ➤ pluridone ➤ isoeleutherol ➤ isoeleutherol-5-O-glucoside ➤ plicataloside ➤ feroxidin ➤ furan derivatives ➤	Kumar <i>et al.</i> , 2019
Flavonoids	➤ naringenin ➤ apigenin, ➤ dihydroisorhamnetin ➤ isovitexin ➤ daidzenin ➤ genistein.	Lucini <i>et al.</i> , 2015
Carbohydrates and related compounds:	➤ mannan, ➤ acemannan ➤ acetylated glucomannan ➤ glucogalactomannan ➤ galactan ➤ arabinogalactan ➤ xylan ➤ cellulose ➤ fucose ➤ L-rhamnose ➤ aldopentose ➤ salicylic acid ➤ lignin	Kumar <i>et al.</i> , 2019
Amino acids and enzymes	➤ 20 amino acids ➤ carboxy-peptidase ➤ cyclooxygenase ➤ cyclooxygenase ➤ amylase ➤ lipase ➤ oxidase, ➤ alkaline phosphatase ➤ phosphoenol pyruvate carboxylase ➤ superoxide dismutase ➤ bradykinase	Cock, 2015 Kumar <i>et al.</i>, 2019
Lipoid components	➤ arachidonic acid	Kumar <i>et al.</i> , 2019

REVIEW ARTICLE

		➤ γ-linolenic acid ➤ triglycerides ➤ triterpenoid ➤ gibberillin, ➤ campesterol ➤ β-sitosterol ➤ lupeol	
Vitamins minerals	and	➤ vitamins A (β-carotene), C, E, B1,B2, B6, B12,folic acid ➤ choline ➤ sodium ➤ potassium ➤ calcium ➤ chromium, ➤ copper ➤ iron ➤ selenium ➤ magnesium ➤ manganese ➤ phosphorous ➤ zinc	Cock, 2015 Kumar <i>et al.</i>, 2019

Therapeutic effects and applications

Anti-inflammatory effect

The *Aloe vera* plant inhibits the cyclooxygenase (COX) pathway, which is responsible for causing inflammation and its associated manifestations, and it reduces the synthesis of prostaglandin E2 (PG-E2) in the arachidonic acid cycle. Also, the new compound called C-chromone has been isolated from the gel ([Vazquez *et al.*, 1996](#)), a compound that is well-known for its anti-inflammatory effect. The gel of *Aloe* reduces the inflammation that is induced by different agents through the prostaglandin synthesis and the increased infiltration of leucocytes. The whole process proved to be less effective against another type of inflammation caused by agents that produce allergic reactions ([Sanchez-Machado *et al.*, 2017](#); [Kumar *et al.*, 2019](#)). Furthermore, *Aloe vera* can determine the inhibition of the inflammatory process by reducing the leukocytes adhesion. The transcription levels of the albumin and the tumor necrosis factor genes are involved in the early phase of the acute inflammatory response. Some studies showed that in rats treated with aloe-emodin, there was an observed abolishment of the transcription of the albumin gene, the tumor necrosis factor being detectable in a very small concentration in the rats' protected livers after the *Aloe* emodin administration. The histological analysis displayed a lower inflammatory infiltration on the lymphocytes and Kuffer cells ([Sanchez-Machado *et al.*, 2017](#); [Kumar *et al.*, 2019](#)).

REVIEW ARTICLE

Antiviral and antitumor effect

These actions may occur as direct or indirect effects. The indirect effects are dependent on the stimulation of the immune system, and the direct effects are due to anthraquinones. Practically, aloin inactivates various types of encapsulated viruses, such as *Herpes simplex*, chickenpox and *Haemophylus influenzae*. Recent studies in mice have shown that a polysaccharide fraction of the *Aloe vera* extract can inhibit the binding of the benzopyrene to the primary hepatocytes, thus preventing the formation of pro-oncogene benzopyrene-DNA complexes. The *Aloe vera* gel contains also forbol-12-myristate-13-acetate, which has been shown to have potential benefits in preventing different sorts of cancer by inducing the glutathione S-transferase synthesis and inhibiting the cancer cell formation (El-Shemy *et al.*, 2010; Kumar *et al.*, 2019). Some other study performed on the HeLaS3 human uterine carcinoma cells, showed that the natural anthracycline aloin from *A. vera* exhibited an antiproliferative and cytotoxic potential. The aloin as a bioactive compound displayed the aforementioned antiproliferative effect at a physiological concentration, thus causing the cell cycle arrest in the S phase. This compound from *Aloe* increased the apoptosis of the HeLaS3 cells (Singh *et al.*, 2018). The Aloe-emodin can induce the cell death of the human colon carcinoma cell lines, DLD-1 and WiDr, depending on the concentration and time (Lin and Uen, 2010). Shalabi *et al.* (2015) stated that the process of upregulation of p53 and the downregulation of Bcl-2 in a concentration and time-dependent manner were responsible for cytotoxic activity of *A. vera* on the HepG2 cells.

Antiseptic effect

Aloe vera contains six compounds with antiseptic action: lupeol, salicylic acid, urea, cinnamic acid, phenols and sulfur. For all these compounds, the inhibitory action on bacteria, viruses and fungi has been demonstrated (Gharibi *et al.*, 2016; Kumar *et al.*, 2019). The clinical use of the *Aloe vera* derivatives is largely supported by empirical data. Although many of the uses are interesting, controlled trials are required to determine their scientific efficacy in treating various conditions. Scientifically based studies have also been carried out, based on animal and / or human trials to determine its therapeutic effects. Their safety and efficacy have not always been demonstrated. The main conditions on which the trials were performed were:

- seborrheic dermatitis (Vardy *et al.*, 1999);
- psoriasis vulgaris (Syed *et al.*, 1996; Paulsen *et al.*, 2005);

REVIEW ARTICLE

- genital herpes (Syed *et al.*, 1996; Syed *et al.*, 1997);
- skin burns (Visuthikosol *et al.*, 1995);
- type II diabetes wounds (Takeda *et al.*, 2006);
- ulcerative colitis (Langmead *et al.*, 2004);
- wound healing studies are mixed, some with positive results (Fulton, 1990); without any benefit (Thomas *et al.*, 1998) or with worsening potential (Schmidt and Greenspoon, 1991);
- decubitus ulcers (Hegggers *et al.*, 1996);
- dermatitis (Bosley *et al.*, 2003);
- acne vulgaris (Takeda *et al.*, 2006);
- lichen planus (Hayes, 1999), frostbite (McCauley *et al.*, 1991);
- foot-and-mouth disease (Paulsen *et al.*, 2005);

There are also conditions such as alopecia, bacterial or fungal infections of the skin, chronic wounds (varicose ulcers), parasitic infections, (systemic lupus erythematosus) SLE, painful arthritis, in which the use was based on some traditional or unscientific unfounded theories. For these conditions, complete human trials have not been performed, and their efficacy and safety have not always been proven (Kumar *et al.*, 2019).

Prebiotic effect

Most of the beneficial effects on the human health are due to the bioactive compounds that this miracle plant possesses. Furthermore, given that the extracts obtained from this plant may be a supplement as a nutrient substrate in which several probiotic lactic acid bacteria can grow, it is important to demonstrate the potentially beneficial effect it can bring in the adaptation and growth of the lactic acid bacterial cells (Kumar *et al.*, 2019). The ability of lactic acid bacteria to transform the phenolic compounds into new and smaller molecules, which can be more easily absorbed in the gut, may support the hypothesis of using these natural bioactive compounds as prebiotics, thus making *Aloe vera* a good ingredient for the cultivation of different species of *Lactobacilli*. Moreover, certain probiotic strains, for example *L. johnsonii*, can generate a higher concentration of free phenolic acids from the plant substrate during fermentation than it would normally be obtained in the presence of other species (Hole *et al.*, 2012). *L. johnsonii* NCC 533 synthesizes esterases and hydroxycinnamate decarboxylases, responsible for the

REVIEW ARTICLE

biotransformation of chlorogenic and caffeic acids. The complete *in vitro* hydrolysis of 5-caffeochinic acid was performed in the first 16 hours of incubation whereas after 48 hours, the caffeic acid was completely converted to 4-vinylcatechol. In this case, the presence of lactic acid bacteria increased the amount of caffeic acid released and produced the release of aromatic compounds from phytophenols (Bel-Rhlid *et al.*, 2013; Kumar *et al.*, 2019).

Healing properties

Glucomannan, a polymanosic saccharide, and gibberellin, a growth hormone, interact with the fibroblast growth factor receptors, stimulating their proliferative activity and hence enhancing the collagen synthesis after the topical or systemic use of *Aloe vera* gel (Chitra *et al.*, 1998). The *Aloe* gel not only increases the amount of regenerating collagen in the wound, but also changes the composition of the collagen (more type III collagen - elastin) and enhances the network of tissue restructuring collagen fibers. Due to this, it will accelerate the reduction of the wound and reduce the risk of scarring of the injured tissue (Heggers *et al.*, 1996). The literature has reported an increase in the synthesis of hyaluronic acid and dermatan sulfate in the granulation tissue of the healed wound, following the oral or topical treatment (Chitra *et al.*, 1998).

Hepatoprotective effect

The compounds that are mainly responsible for the hepatoprotective effect of the *Aloe vera* are the anthraquinones, compounds that can act as bioactive antioxidants and that are directly involved in free radical-mediated reactions during the inflammatory response. Mainly, the reactive oxygen species and free radical reactions are considered to be involved in the inflammatory response and liver necrosis. A type of aqueous extract of the aerial parts of *A. vera* significantly reduced the hepatic damage induced by carbon tetrachloride (CCl₄) in mice and rats and reversed the associated damaged biochemical parameters. The histopathological studies confirmed the curative efficacy of the aqueous extract of *A. vera* against the damaged induced by CCl₄ on the liver and showed that whole process happens by reversing the centrilobular necrosis, macro-vascular fatty changes, and scattered lymphomononuclear cell infiltrate in the hepatic parenchyma. Other researchers carried out *in vivo* studies on rats with CCl₄ intoxication in which they administered aloe-emodin to observe the hepatoprotective activity of the anthraquinones (Sanchez-Machado *et al.*, 2017; Kumar *et al.*, 2019). It has been shown that the *A. vera* extract alone or combined with two other extracts (*Azadirachta indica* and *Moringa*

REVIEW ARTICLE

oleifera) exhibited a higher hepatoprotective action against the CCl₄- induced acute liver damage in mice (Salama *et al.*, 2016). The anthraquinones were likely to protect against the hepatocyte death and the inflammatory response that comes along subsequent to the lipid peroxidation. Moreover, the phytosterols that are also found in *Aloe*, specifically two compounds, iophenol and cycloartanol, possess the ability to induce the downregulation of the fatty acid synthesis and the upregulation of the fatty acid oxidation in the liver (Sanchez-Machado *et al.*, 2017; Kumar *et al.*, 2019). The study undertaken by Misawa *et al* (2012) displayed an improvement of the metabolic syndrome-related disorders and liver steatosis in fatty rats treated with Aloesterol. The hepatoprotective effect was attributed also to the liver's metabolizing enzymes through the high antioxidant activity (Sharma *et al.*, 2019).

Effects on the epidermis exposed to UV radiation or γ radiation

The *Aloe vera* gel has been shown to have beneficial protective effects on the skin against the UV radiation (Singh *et al.*, 2010). The mechanism by which the *Aloe vera* gel protects the skin from the harmful actions of radiation is not fully elucidated, but it is assumed that by administering *Aloe vera* gel on the skin, the production of metallo-thionine, an antioxidant protein is stimulated. This protein has the property to bind hydroxyl radicals and prevents the inactivation of superoxide dismutase and glutathione peroxidase in the skin. Moreover, the production and release of keratinocyte-derived immunosuppressive cytokines, such as IL-10 (interleukin 10) is reduced, thus preventing the UV-induced suppression of delayed-type hypersensitivity (Choi *et al.*, 2001).

Effects on the immune system

Several studies have indicated that the compounds found in the *Aloe vera* displayed the effect to boost the immune system (Kumar *et al.*, 2019). Hence, alprogen inhibits the influx of calcium into mast cells, blocking the formation of the antigen-antibody complex that involves the release of histamine and leukotrienes from the mast cells. A study on guinea pigs in which sarcomatous cells were implanted showed that the acemanan from the *Aloe vera* gel stimulated the synthesis and release of IL-1 and tumor necrosis factors in macrophages, which generated an immune response that led to the necrosis and the regression of the cancerous cells. It has also been shown that some low molecular weight compounds are also able to inhibit the release of the oxygen free radicals from the activated human neutrophils (El-Shemy *et al.*, 2010; Kumar *et al.*, 2019).

REVIEW ARTICLE

Laxative effect

The anthraquinones present in the latex have a strong laxative effect. After oral administration, they increase the water content of the intestine, stimulate the mucus secretion and increase the intestinal peristalsis (Baby *et al.*, 2010). The active anthraquinones found in the plant such as aloin, aloe emodin and emodin are directly linked to the purgative action of *Aloe*. The aloin was proven to be metabolized by the colonic flora and transformed into a reactive aloe-emodin, this final compound being responsible for the purgative activity of plant. Other compounds that presented a similar reaction were the probiotic bacteria originating from the *Aloe* leaf, specifically *Lactobacillus brevis*, a type of bacteria that has been isolated from the naturally fermented *Aloe vera* gel. This bacterial strain has been demonstrated to inhibit the growth of harmful pathogens without restraining the growth of normal commensals in the gut (Kang *et al.*, 2014). Another study investigated the effect of gel and whole leaf extracts from three species of *Aloe* on the modulation of drug efflux all across the rats' intestinal tissues (Beneke *et al.*, 2013). The obtained results demonstrated an increase of the drug permeability in the presence of the gel separated from *Aloe vera* and whole leaf materials (Beneke *et al.*, 2013; Kumar *et al.*, 2019).

Moisturizing and anti-aging effect

Mucopolysaccharides (MPZs) have the role of promoting and maintaining the skin hydration. *Aloe vera* stimulates the fibroblasts with a role in the production of collagen and elastin fibers, which gives the skin a more elastic appearance and reduces the wrinkles. It also has a co-adhesive effect on the cells of the epidermis, keeping them together, giving the appearance of silky, velvety skin. The amino acids also determine the hydration of skin cells whereas the zinc acts as an astringent to close the pores. The moisturizing effect was studied in the treatment of dry skin, this effect being determined by aggravating occupational factors, where the gloves impregnated with *Aloe vera* gel significantly improved the condition and integrity of the skin while decreasing the appearance of fine wrinkles and erythema (Eshun and He, 2004). Another effect on the skin was the anti-acne effect.

Conclusions

The *Aloe vera* plant through its rich phytochemical content represents an important source of functional bioactive compounds that are very important and beneficial constituents thus inducing various therapeutic effects, with the potential to be used not only in the pharmaceutical or

REVIEW ARTICLE

cosmeceutical industry but also in the food industry. As such, due to these functional bioactive compounds, the *Aloe vera* products or extracts have been used to treat different sort of conditions such as seborrheic dermatitis, psoriasis vulgaris, genital herpes, skin burns, type II diabetes, HIV, cancer prevention, ulcerative colitis, wound healing, decubitus ulcers dermatitis; acne vulgaris; lichen planus, frostbite, foot-and-mouth disease and constipation. Nonetheless, although the plant has been used to treat all sorts of conditions, its use as a cosmeceutical has no equal. Numerous studies sustain the various therapeutic effects that *Aloe vera* extract could manifest against different skin disorders, thus it became a frequently used active ingredient in hundreds of dermato-cosmetical products.

Acknowledgments

This research was supported by the project “Excellence, performance and competitiveness in the R&D&I activities at “Dunarea de Jos” University of Galati”, acronym "EXPERT", financed by the Romanian Ministry of Research and Innovation, Programme 1 – Development of the national research and development system, Sub-programme 1.2 – Institutional Performance – Projects for financing excellence in R&D&I, Contract no. 14PFE/17.10.2018. The work of the Elena Enachi was supported by the project ANTREPRENORDOC, in the framework of Human Resources Development Operational Programme 2014–2020, financed from the European Social Fund under the contract number 36355/23.05.2019 HRD OP/380/6/13—SMIS Code: 123847.

References

- Aghamohamadi, N., Sanjami, N.S., Majidi, R.F., Nasrollahi, S.A (2019) Preparation and characterization of *Aloe vera* acetate and electrospinning fibers as promising antibacterial properties materials. *Materials Science and Engineering C*, 94, 445–452.
- Alvarado-Morales, G., Minjares-Fuentes, R., Contreras-Esquivel, J.C., Montañez, J., Meza-Velázquez, J., Femenia, A. (2019) Application of thermosonication for *Aloe vera* (*Aloe barbadensis* Miller) juice processing: Impact on the functional properties and the main bioactive polysaccharides. *Ultrasonics - Sonochemistry*, 56, 125–133.
- Baby, J., Raj, J.S. (2010) Pharmacognostic and phytochemical properties of *Aloe vera* linn -An overview, *International Journal of Pharmaceutical Sciences Review & Research*, 4, 106-110.

REVIEW ARTICLE

Bel-Rhliid, R., Thapa, D., Kraehenbuehl, K., Hansen, C.E., Fischer, L. (2013) Biotransformation of caffeoyl quinic acids from green coffee extracts by *Lactobacillus johnsonii* NCC 533, *AMB Express*, 3, 28.

Beneke, C., Viljoen, A., Hamman, J. (2013) Modulation of drug efflux by *Aloe* materials: An in Vitro investigation across rat intestinal tissue, *Pharmacognosy Magazine*, 9, 44-48.

Bosley, C., Smith, J., Baratti, P., Prichard, D.L., Xiong, X., Li, C., Merchant, T.E. (2003) A phase III trial comparing an anionic phospholipid-based (APP) cream and *Aloe vera* based gel in the prevention and treatment of radiation dermatitis, *International Journal of Radiation, Oncology, Biology and Physics*, 57(2), 01404-4.

Chitra, P., Sajithal, G.B., Chandrakasan, G. (1998) Influence of *Aloe vera* on the glycosaminoglycans in the matrix of healing dermal wounds in rats, *Journal of Ethnopharmacology*, 59, 179-186.

Choi, S, Son B.W., Son Y.S. (2001) The wound-healing effect of a glycoprotein fraction isolated from *Aloe vera*, *British Journal of Dermatology*, 145, 535-545.

Cock, I.E, (2015) The genus *Aloe*: phytochemistry and therapeutic uses including treatments for gastrointestinal conditions and chronic inflammation, In: novel natural Products: therapeutic effects in pain, arthritis and gastro-intestinal diseases. In: Rainsford, K.D., Powanda, M.C., Whitehouse, M.W. (Eds.), *Progress in Drug Research* 70. Springer, Basel, pp. 179–235.

Darokar, M.P., Rai, R., Gupta, A.K., Shasany, A.K., Rajkumar, S., Sunderasan, V., Khanuja, S.P.S. (2003) Molecular assessment of germplasm diversity in *Aloe* spp. using RAPD and AFLP analysis, *Journal of Medical and Aromatic Plant Sciences*, 25(2), 354–361.

Delatorre-Herrera, J., Delfino, I., Salinas, C., Silva, H., Cardemil, L. (2010) Irrigation restriction effects on water use efficiency and osmotic adjustment in *Aloe vera* plants (*Aloe barbadensis* Miller), *Agricultural Water Management*, 97(10), 1564-1570.

Dell'Agli, M., Giavarini, F., Ferraboschi, P., Galli, G., Bosisio, E. (2007) Determination of aloesin and aloeresin a for the detection of *Aloe* in beverages, *Journal of Agriculture and Food Chemistry*, 55, 3363-3367.

REVIEW ARTICLE

El-Shemy, H.A., Aboul-Soud, M.A., Nassr-Allah, A.A., Aboul- Enein, K.M., Kabash, A, Yagi, A. (2010) Antitumor properties and modulation of antioxidant enzymes' activity by *Aloe vera* leaf active principles isolated via supercritical carbon dioxide extraction, *Current Medicinal Chemistry*, 17, 129-38.

Eshun, K., He, Q. (2004) *Aloe vera*: A valuable ingredient for the food, pharmaceutical and cosmetic industries - A review, *Critical Reviews in Food Science and Nutrition*, 44, 91-96.

Farrugia, C.-J.E., Burke, E.S., Haley, M.E., Bedi, K.T., Gandhi, M.A. (2019) The use of *Aloe vera* in cancer radiation: an updated comprehensive review. *Complementary Therapies in Clinical Practice*, 35, 126–130.

Femenia, A., Sánchez, E.S., Simal, S., Rosselló, C. (1999) Compositional features of polysaccharides from *Aloe vera* (*Aloe barbadensis* Miller) plant tissues, *Carbohydrate Polymers*, 39(2), 109-117.

Fenig, E., Nordenberg, J., Beery, E., Sulkes, J., Wasserman L. (2004) Combined effect of aloemodin and chemotherapeutic agents on the proliferation of an adherent variant cell line of Merkel cell carcinoma, *Oncology Reports*, 11(1), 213–217.

Fulton, J., 1990, The stimulation of postdermabrasion wound healing with stabilized *Aloe vera* gel-polyethylene oxide dressing, *Journal of Dermatology Surgery and Oncology*, 16(5), 460–467.

Furukawa, F., Nishikawa, A., Chihara, T., Shimpo, K., Beppu, H., Kuzuya, H., Lee, I.S., Hirose, M., 2002, Chemopreventive effects of *Aloe arborescens* on N-nitrosobis (2-oxopropyl) amine-induced pancreatic carcinogenesis in hamsters, *Cancer Letters*, 168(2): 117–122.

Gao, Y., Kuok, K.I., Jin, Y., Wang, R. (2018) Biomedical applications of *Aloe vera*. *Critical Reviews in Food Science and Nutrition*, 59, 3, 1–48.

Gharibi, D., Khosravi, M., Hosseini, Z., Boroun, F., Barzegar, S. K., Far, A. F. (2016) Antibacterial Effects of *Aloe Vera* Extracts on some Human and Animal Bacterial Pathogens, *Journal of Medical Microbiology and Infectious Diseases*, 3, 6-10.

REVIEW ARTICLE

Hamman, J.H. (2018) Composition and applications of *Aloe vera* leaf gel. *Molecules*, 13, 8, 1599–1616.

Hayes, S.M. (1999) Lichen planus--report of successful treatment with *Aloe Vera*, *General Dentistry*, 47(3), 268-72.

Heggers, J.P., Kucukcelebi, A., Listengarten, D., Stabenau, J., Ko, F., Lyle D. Broemeling, L.D., Robson, M.C., Winters, W.D., (1996) Beneficial effect of *Aloe* on woundhealing in an excisional wound model, *Journal of Alternative and Complementary Medicine*, 2(2):271-277.

Hole, C.R., Wormley, F.L. Jr. (2012) Vaccine and immunotherapeutic approaches for the prevention of cryptococcosis: lessons learned from animal models, *Frontiers in Microbiology*, 28, 3-29.

Ishii, Y, Tanizawa, H, Takino, Y. (1994) Studies of *Aloe vera*: Mechanism of cathartic effect, *Biological and Pharmaceutical Buletin*, 17, 651–653.

Jones, W.D., Sacamano, C., (2000) *Landscape Plants for Dry Regions: More Than 600 Species from Around the World*, California Bill's Automotive Publishers. USA.

Kanama, S.K., Viljoen, A.M., Kamatou, G.P.P., Weiyang, C., Maxleene, S., Hamid, R.A., Ben-Erik, V.W. (2015) Simultaneous quantification of anthrones and chromones in *Aloe ferox* (*Cape aloes*) using UHPLC-MS, *Phytochemistry Letters*, 13, 85–90.

Kang, M. C., Kim, S. Y., Kim, Y. T., Kim, E. A., Lee, S. H., Ko, S. C. (2014), In vitro and in vivo antioxidant activities of polysaccharide purified from *Aloe vera* (*Aloe barbadensis*) gel, *Carbohydrate Polymers*, 99, 365-371.

Kudłacik-Kramarczyk, S., Drabczyk, A., Głąb, M., Alves-Lima, D., Lin, H., Douglas, T.E.L., Kuciel, S. Zagorska, A., Tylińczak, B. (2021) Investigations on the impact of the introduction of the *Aloe vera* into the hydrogel matrix on cytotoxic and hydrophilic properties of these systems considered as potential wound dressings. *Materials Science & Engineering C*, 123, 111977.

Kumar, R., Singh, A.K., Gupta, A., Bishayee, A., Pandey, A.K., (2019) Therapeutic potential of *Aloe vera*—A miracle gift of nature, *Phytomedicine*, 60, 152996.

REVIEW ARTICLE

Langmead, L., Feakins, R.M., Goldthorpe, S., Holt, H., Tsironi, E., De Silva, A., Jewell, D.P., Rampton, D.S. (2004) Randomized, double-blind, placebo-controlled trial of oral *Aloe vera* gel for active ulcerative colitis, *Alimentary Pharmacology and Therapeutics*, 19(7), 739–747.

Lin, K.Y., Uen, Y.H. (2010) Aloe-emodin, an anthraquinone, in vitro inhibits proliferation and induces apoptosis in human colon carcinoma cells, *Oncology Letters*, 1, 541–547.

Lucini, L., Pellizzoni, M., Pellegrino, R., Molinari, G.P., Colla, G. (2015) Phytochemical constituents and in vitro radical scavenging activity of different *Aloe species*. *Food Chemistry*, 170, 501–507.

Mandrioli, R., Mercolini, L., Ferranti, A., Fanali, S., Raggi, M.A. (2011) Determination of aloe emodin in *Aloe vera* extracts and commercial formulations by HPLC with tandem UV absorption and fluorescence detection, *Food Chemistry*, 126(1): 387–93.

McCauley, R., Hegger, J.P., Martin, C.R. (1991) Frosbite: methods to minimize tissue loss, *Postgraduate Medicine*, 88(8), 67-68, 73-77.

Misawa, E., Tanaka, M., Nomaguchi, K., Nabesima, K., Yamada, M., Toida, T., Iwatsuki, K, (2012) Oral ingestion of *Aloe vera* phytosterols alters hepatic gene expression profiles and ameliorates obesity-associated metabolic disorders in Zucker diabetic fatty rats, *Journal of Agricultural and Food Chemistry*, 60, 2799–2806.

Montaner, J.S., Gill, J, Singer, J. (1996) Double-blind placebo-controlled pilot trial of acemannan in advanced human immunodeficiency virus disease, *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*, 12(2), 153–157.

Park, Y.I., Jo, T.H. (2006) Perspective of industrial application of *Aloe vera*. In: Park, Y.I., Lee, S.K. (Eds.), *New Perspectives on Aloe*. Springer, pp 191-200.

Paulsen, E, Korsholm, L, Brandrup, F. (2005) A double-blind, placebo-controlled study of a commercial *Aloe vera* gel in the treatment of slight to moderate psoriasis vulgaris, *Journal of European Academy of Dermatology/Venereology*, 19(3), 326–331.

Ro, J.Y., Lee, B., Kim, J.Y., Chung, Y., Chung, M.H., Lee, S.K. (2000) Inhibitory mechanism of *Aloe* single component (Alprogen) on mediator release in guinea pig lung mast cells activated

REVIEW ARTICLE

with specific antigen-antibody reactions, *Journal of Pharmacology and Experimental Therapeutics*, 292, 114–21.

Salama, R.A., Mohamed, M.M., Abd Elwahab, M.B., Shakweer, M.M. (2016) Assessment effect of *Aloe vera*, *Azadirachta indica* and *Moringa oleifera* aqueous extracts on carbon tetrachloride-induced hepatotoxicity in rats. *International Journal of Pharmacy and Pharmaceutical Sciences*, 8, 83–89.

Sanchez-Machado, D.I., Lopez-Cervantes, J., Sendon, R., Sanches-Silva, A. (2017) *Aloe vera*: Ancient knowledge with new frontiers, *Trends in Food Science & Technology*, 61, 94-102.

Schmidt, J.M., Greenspoon, J.S. (1991) *Aloe vera* dermal wound gel is associated with a delay in wound healing, *Obstetrics and Gynecology*, 78(1), 115–117.

Shalabi, M., Khilo, K., Zakaria, M.M., Elsebaei, M.G., Abdo, W., Awadin, W. (2015) Anticancer activity of *Aloe vera* and *Calligonum comosum* extracts separately on hepatocellular carcinoma cells, *Asian Pacific Journal of Tropical Biomedicine*, 5, 375–381.

Sharma, U.K., Kumar, R., Gupta, A., Ganguly, R., Singh, A.K., Ojha, A.K., Pandey, A.K. (2019) Ameliorating efficacy of eugenol against metanil yellow induced toxicity in albino Wistar rats. *Food and Chemical Toxicology*, 126, 34–40.

Silva, H., Sagardia, S., Seguel, O., Torres, C., Tapia, C., Franck, N., Cardemil, L. (2010) Effect of water availability on growth and water use efficiency for biomass and gel production in *Aloe vera* (*Aloe barbadensis* M.), *Industrial Crops and Products*, 31, 20-27.

Singh, A.K., Bishayee, A., Pandey, A.K. (2018) Targeting histone deacetylases with natural and synthetic agents: an emerging anticancer strategy, *Nutrients*, 10, 731.

Singh, S., Sharma, P.K., Kumar, N., Dudhe, R., (2010) Biological activities of *Aloe vera*, *International Journal of Pharmacy and Technology*, 2(3), 259-280.

Sun, Y.N., Li, W., Yang, S.Y., Kang, J.S., Ma, J.Y., Kim, Y.H. (2016) Isolation and identification of chromone and pyrone constituents from *Aloe* and their anti-inflammatory activities. *Journal of Functional Foods*, 21, 232–239.

REVIEW ARTICLE

Surjushe, A., Vasani, R., Saple, D.G. (2008) *Aloe vera*: A short review, Indian Journal of Dermatology, 53(4),163-166.

Syed, T.A., Afzal, M., Ashfaq, A.S. (1997) Management of genital herpes in men with 0.5% *Aloe vera* extract in a hydrophilic cream A placebo-controlled double-blind study, Journal of Dermatological Treatment, 8, 99–102.

Syed, T.A., Ahmad, S.A., Holt, A.H., Ahmad, S.H., Afza, M. (1996) Management of psoriasis with *Aloe vera* extract in a hydrophilic cream: A placebo-controlled, double-blind study, Tropical Medicine and International Health, 1(4), 505–509.

Syed, T.A., Cheema, K.M., Ahmad, S.A., Ashfaq, A. (1996) *Aloe vera* extract 0.5% in hydrophilic cream versus *Aloe vera* gel for the measurement of genital herpes in males: A placebo-controlled, double-blind, comparative study, Journal of European Academy of Dermatology/Venereology, 7, 294–295.

Takeda, K., Suzuki, T., Shimada, S.I., Shida, K., Nanno, M., Okumura, K. (2006) Interleukin-12 is involved in the enhancement of human natural killer cell activity by *Lactobacillus casei* Shirota, Clinical & Experimental Immunology, 146, 109-115.

Tan, Z., Li, F., Xing, J. (2011) Separation and purification of *Aloe* anthraquinones using EG/salt aqueous two-phase system, Separation Science and Technology, 46, 1503–1510.

Thomas, D.R., Goode, P.S., LaMaster, K., Tennyson, T. (1998) Acemannan hydrogel dressing for pressure ulcers: A randomized, controlled trial, Advances in Wound Care, 11(6), 273–276.

Treutlein, J., Smith, G. F. S., van Wyk, B. E., Wink, W. (2003) Phylogenetic relationships in *Asphodelaceae* (*Alooideae*) inferred from chloroplast DNA sequences (rbcL, matK) and from genomic finger-printing (ISSR), Taxonomy, 52, 193.

Tyler, V. (1993) The Honest Herbal: A sensible Guide to Use of Herbs and Related Remedies, 3rd Edition, Binghamton; N.Y: Pharmaceutical Products.

Vardy, A.D., Cohen, A.D., Tcheto, T. (1999) A double-blind, placebo-controlled trial of *Aloe vera* (*A. barbadensis*) emulsion in the treatment of seborrheic dermatitis, Journal of Dermatological Treatment, 10, 7–11.

REVIEW ARTICLE

Vazquez, B., Avila, G., Segura, D., Escalante, B. (1996), Antiinflammatory activity of extracts from *Aloe vera* gel, Journal of Ethnopharmacology, 55, 69-75.

Visuthikosol, V., Chowchuen, B., Sukwanarat, Y., Sriurairatana, S., Boonpucknavig, V. (1995) Effect of *Aloe vera* gel to healing of burn wound a clinical and historic study, Journal of the Medical Association of Thailand, 78, 403-409.

Zhifen, C., Lu, Z., Junyang, Y., Zhuanbo, Y., Zhijie, Z., Zhen, L. (2012) Promotion of adiponectin multimerization by emodin: a novel AMPK activator with PPAR γ -agonist activity. Journal of Cellular Biochemistry, 113, 3547–3558.