



REVIEW ARTICLE

Bioactive compounds and therapeutic properties of Aloe vera – A review

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ARTICLE HISTORY

Received: 07 May 2022

Accepted: 03 August 2022

Available online

Version 1.0 : 19 March 2023



Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

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Indexing: Plant Science Today, published by Horizon e-Publishing Group, is covered by Scopus, Web of Science, BIOSIS Previews, Clarivate Analytics, NAAS, UGC Care, etc See https://horizonepublishing.com/journals/index.php/PST/indexing_abstracting

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CITE THIS ARTICLE

Mitra A, Singh M, Banga A, Pandey J, Tripathi S, Singh D. Bioactive compounds and therapeutic properties of Aloe vera – A review. Plant Science Today (Early Access). <https://doi.org/10.14719/pst.1715>

Abstract

Aloe vera is a popular herbal medicine and worldwide appreciated for its therapeutic potential. From ancient time, it has been used as a home remedy for different health issues. Many researchers have shown its therapeutic potential and there are many citations of characterization of bioactive compounds from it. A wide range of bioactive compounds have been characterized from Aloe vera. It has a wide range of antimicrobial, antioxidant, and antidiabetic properties. Aloe vera can also provide support for carbohydrate and lipid metabolism by maintaining the level of cholesterol and sugar in blood and it can also help to maintain body weight. Due to the presence of higher number of bioactive compounds and prolific therapeutic properties, it is widely used in medicine, cosmetics and food sector. In this review, the characterisation of bioactive compounds from Aloe vera along with the extraction of its gel and encapsulation is reviewed with a discussion on its medicinal properties.

Keywords

Aloe vera, bioactive compounds, phenolics, flavonoids, therapeutic properties

Introduction

Aloe vera (L.) Burm.f., which is also known as *Aloe barbadensis* Mill. is presently included in the Asphodelaceae family or to a broadly circumscribed family Liliaceae. It is an arborescent, perennial, xerophytic, succulent, thick and short-stemmed plant which is green in color and about 12–19 inches (30–50 cm) in length. Aloe vera reserves water in leaves and it is widely used for the treatment of skin injuries. Apart from this, it also has a large number of beneficial properties. Aloe vera is widely grown in the arid regions of Africa, Asia, Europe and the Americas. In India, it is widely grown in Maharashtra, Andhra Pradesh, Rajasthan, Gujarat and Tamil Nadu. The plant has triangular leaves with sharp edges, yellow tubular flowers and fruit. The leaf of Aloe vera can be distinguished into 3 layers:

- 1) The inside layer contains a gel like substance which consists of 99% water and rest is made of amino acids, glucomannans, vitamins, lipids and sterols.
- 2) The central layer holding latex, glycosides and anthraquinones.
- 3) The outer most thick layer having protective function that synthesizes carbohydrates and proteins.

Extraction of Aloe vera gel

Aloe vera plants have thick green leaves that contain gel and latex. The leaves are with curved edges and sharp points. The leaf is made up of three layers called rind, sap and mucilage. The leaves contain more than 75 nutrients and 200 active compounds, monosaccharides and polysaccharides (pectin, hemicellulose, cellulose, glucomannan, acemannan, and mannose derivatives). The unique healing and immunity stimulating property of Aloe vera is supposed to be provided by the long-acting acetylated mannose contained in it (1). The gel of Aloe vera is viscous in nature, colorless and clear and it forms an integral part of the healing properties of the Aloe vera leaf. Latex is a thick yellow liquid that is contained between the gel-portion and the inner layer of the leaf. It is important to distinguish the latex from gel, because the latex contains a bitter, yellow and red aloin which is also known as barbaloin, is a powerful laxative that can cause diarrhea and stomach cramps after consumption.

The process of preparing an extract of Aloe vera includes:-

- Trimming the peel and aloins from the gel
- Agitating under UV radiation in a digestion liquid containing amine, potassium ions and phosphorous ions apart from maintaining the pH of the liquid in the range of about 3 to 4.5.

The gel must be drawn out from the leaf for use and must be disinfected and stabilized before it can be commercially distributed in a long-lasting manner. Previous attempts to fix the extract usually involved crushing the leaves to remove the gel from the leaf. Aloe vera, however, contains a thin layer of coating between the crust and the gel, which is a bitter liquid. The crushing of the leaves causes the gel to be contaminated with aloins, making the extract unsatisfactory for internal use and changing the extracted color. The extract of Aloe vera juice is repaired first by killing all the leaves. The rind and aloin layer are then physically separated from the gel by leaf surgery to remove the crust and layer at a depth of about one and eight inches. The remaining gel is then processed under sterile conditions and ground under U.V. radiation at ambient temperature. Ascorbic acid is added during the digestion process to compensate for its loss through oxidation when exposed to air and as a source of potassium ions embedded in the digestive fluid. The pH is maintained at about 4.5 during the whole process so that quinone and lignin are stereochemically matched. The resulting extract is a clear liquid with a chemical composition almost identical to that of the fresh juice. The juice, however, can not be produced easily enough to be bottled and transported for use. Thanks to the stabilization and sterilization process, the extract has a high shelf life and retains its beneficial chemical composition from the beginning. As the juice is released under sterile conditions at local temperatures, decay is avoided. In addition, by extracting the aloins with their extracted crust, they retain a clear color and flavor of orange juice, which gives the product its ready-to-use internal function effectively next to that of a fresh gel. This and the other established benefits can be fully understood if taken with regard to the following detailed explanation.

In some cases, the Aloe vera leaves were carefully cut and washed, leaving the leaf standing to release exudate and immersed in clear water overnight. Later, the peeled leaf and the inner gel were cut into pieces, soaked in water for half an hour, then passed through a strainer, and then melted. Aloe vera was also cut into small pieces and washed with distilled water. The roots are carefully cut into small pieces and washed with distilled water and dried at room temperature (25-30°C). Glycolic extract needs to be adjusted step by step. After crushing, the goods were weighed and added to a wide-brimmed bottle. Separately, it is reported that 50% ethanol solution and 5% propylene glycol solution were prepared, and then added to a mucilage-containing flask, which was left to soak for 8 days with daily wrapping. After this time, the material was filtered, stored in amber glass, in a dry place and protected from light (2). The centrifugation method is used for the extraction of chemical compounds present in the gel (3).

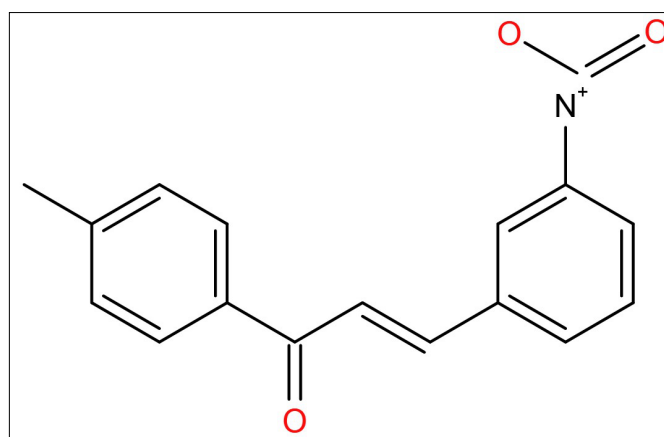


Fig. 1. Chemical Structure of Aloe vera

Encapsulation of Aloe vera gel

Hussain *et al.*, (4) demonstrated the incorporation effect of Aloe vera as an additive combining its solubility, antibacterial activity and roughness of the surface. Method: Compomer (Dytract XP). In this research, the sample1 (control), was added with 15% of prepared Aloe vera and encapsulated with chitosan nano-spheres; sample 2. In this research, discs of 15x1mm in size of every single sample were made and the characteristics evaluated. Total 21 number of discs of every single samples were evaluated in this experiment. Then, Antibacterial activity was examined against *Streptococcus mutans* (ATCC 25175) with the help of agar diffusion test by measuring the inhibition zone of each disc. After that, the surface roughness and solubility were also carried out after storing the sample with the help of artificial saliva at the temperature of 37°C for 5 minutes in lactic acid and maintaining at pH at 5.2 and the entire cycle is performed 3 times daily. Then after 6 months it was observed that the results of sample 2 had higher antibacterial property (2.21±0.21 mm) as compared with the sample 1 (0.05±0.22 mm). After the entire experiment, it was concluded that the incorporation of 15% change in solubility and surface roughness, freeze-dried Aloe vera infused by chitosan nano-spheres in the compound transmits antibacterial effect against *Streptococcus mutans*.

Changes in melting and solidification of the environment were in accepted limit as per ISO standards. The encapsulation process is demonstrated in Fig. 2.

potassium. Many of them are important for the functioning of the various enzymes in different metabolic pathways and few of them also have antioxidant properties.

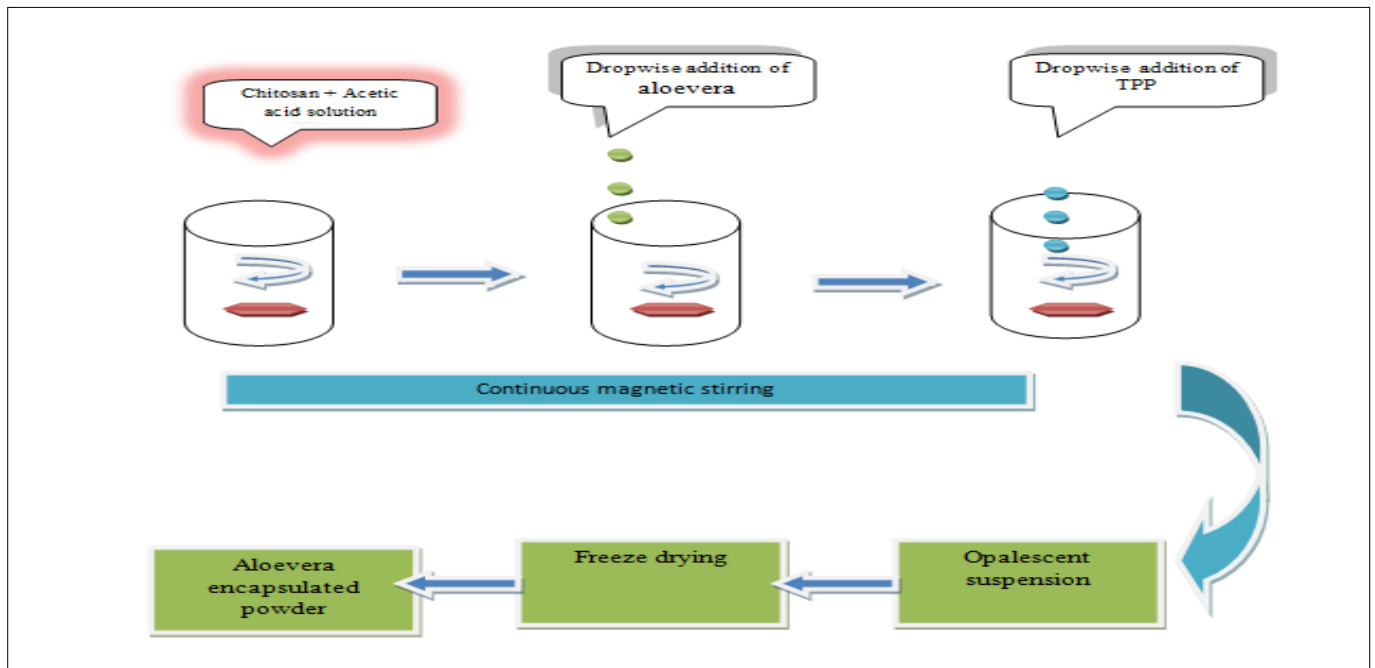


Fig. 2. Encapsulation process of Aloe vera.

Restorative properties of Aloe vera have been demonstrated by analysts through *in vitro* and *in vivo* conditions. All of these investigations were sufficient for the verification of the useful properties of Aloe vera due to the dynamic compounds like cinnamic acid, orientin and isovitexin. For the exploitation of the benefits, information on the traditional therapeutic usage of Aloe vera is vital. Aloe vera has the potential for a wide range of medical applications in pharmaceutical industry and treatment for dental disorders. However, more research is needed so that the activity of acemannan hydrogel can be experimentally proved and established.

Bioactive compounds present in Aloe vera

Aloe vera is known to contain around 75 potentially active constituents: vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids and amino acids (5).

Vitamins

Vitamin A, C and E are well known as antioxidants. Apart from this, Aloe vera also contains water soluble vitamins like B1, B2, B6, B12 and folic acid. Antioxidants help to protect the body from free radicals by neutralizing them.

Enzymes

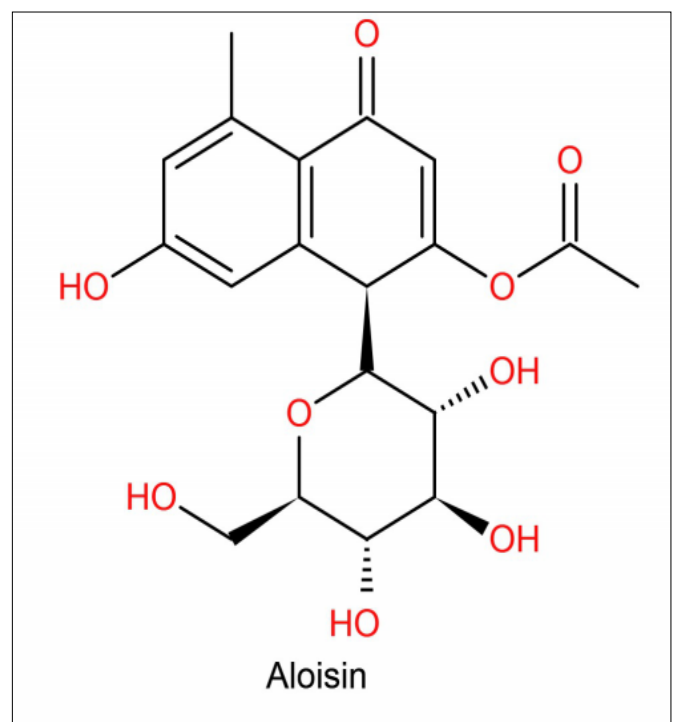
Major enzymes present in Aloe vera are amylase, alkaline phosphatase, oxidase, catalase, brady kinase, carboxypeptidase, cellulase, lipase, peroxidase and cylooxygenase. These enzymes help for the breakdown of fats, proteins and sugar. Brady kinase enzyme minimizes the excessive inflammation of skin.

Minerals

Minerals are considered as minor nutrients. Aloe vera is a rich source of minerals like calcium, magnesium, manganese, chromium, sodium, copper, selenium, zinc and

Sugars

Aloe vera is a good source of monosaccharides like glucose and fructose. It also contains polysaccharides like glucomannans or polymannose. Mannose-6-phosphate is the most prominent monosaccharide and glucomannans [β -(1,4)-acetylated mannan] is the most common polysaccharide. Apart from that acemannan is also found in Aloe vera which is the most prominent glucomannan. Alprogen, a glycoprotein which has anti-allergic properties and c-glucosyl chromone having anti-inflammatory properties also have been isolated from Aloe vera gel.



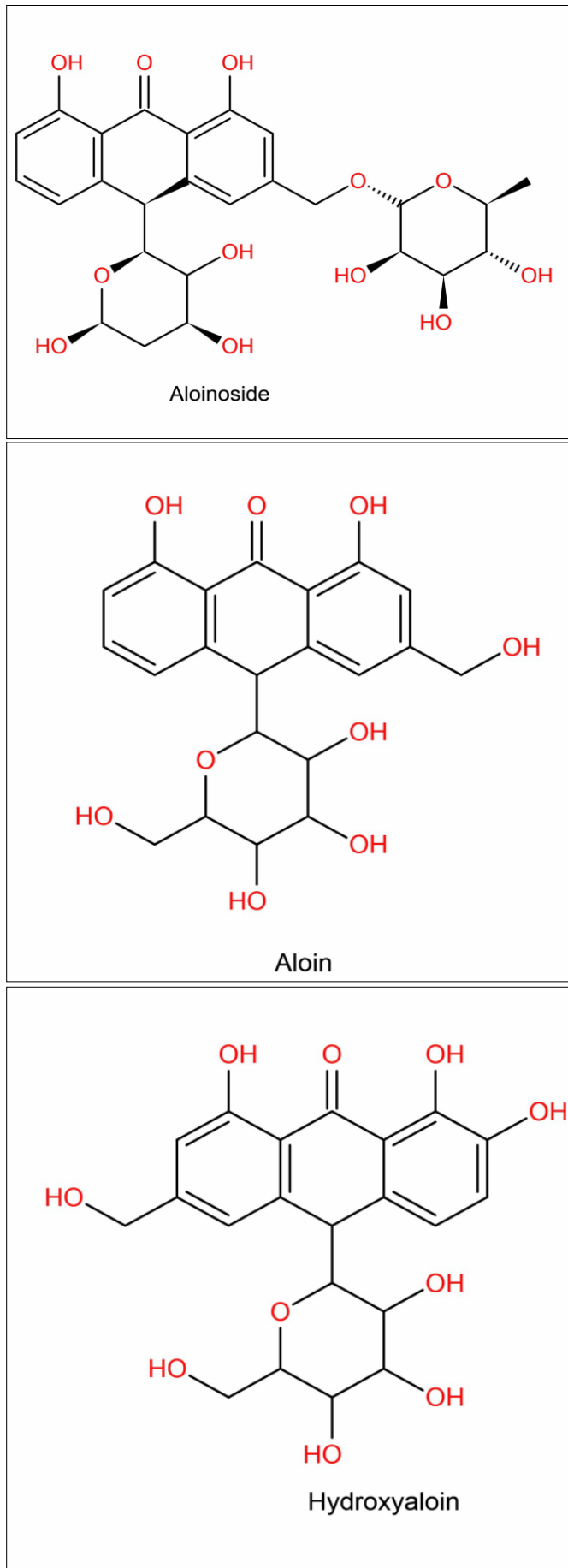


Fig. 3. Phenolic compounds found in Aloe vera

Anthraquinone

Bioactives like aloin, anthranol, barbaloin, isobarbaloin, aloetic acid, aloe-emodin and ester of resistanol,

cinnamic acid, chrysophanic acid and emodin also are present in Aloe vera which have great laxative effects. Most importantly, emodin and aloin also have antiviral and antibacterial properties.

Organic Acids

Aloe vera is a good source of different organic acids like sorbate, uric acid, salicylic acid. Salicylic acid has antibacterial and anti-inflammatory properties.

Essential and non-essential amino acids

Different essential amino acids like methionine, phenylalanine, leucine, isoleucine, valine, lysine and threonine. Apart from that different non-essential amino acids like histidine, arginine, aspartic acid, glutamic acid, proline, alanine, glycine, tyrosine and hydroxyl proline also found in Aloe vera.

Steroids and fatty acids

Aloe vera is a good source of cholesterol, campesterol, β -sitosterol and lupeol. Fatty acids like γ -linolenic acid and arachidonic acid, have great anti-inflammatory properties and lupeol also has analgesic and antiseptic properties.

Hormones

Aloe vera is a good source of hormones like auxins and gibberellins which has anti-inflammatory and wound-healing properties.

Other Bioactives

Other important bioactives like lignin is an inert substance which helps to enhance the penetrative effect of the other ingredients into the skin. Saponin is a soapy substance that form about 3% of the gel which has antiseptic as well as cleansing properties.

Table 1. Some major bioactive Components of Aloe vera

Phytochemicals	Aloe vera gel	Sources
Total Phenols (mg/g)	37.29±0.19	[7]
Total Flavonoids(RE/mg)	60.95±0.97	[8]
DPPH Radical Scavenging (%)	11.93	[9]
Total Proanthocyanidin (mg/g)	12.04±0.89	[7]
Total Tanins (μ g catechin equivalent)	21.11±1.92	[8]
Saponins (mg/g)	8.34±0.01	[7]
Sugars –Mannose (%)	84.9	
Glucose (%)	7.2	[6]
Galactose (%)	3.9	
Amino Acids (%)	15.33	[22]
Minerals (%)	16	[9]

Major Health Benefits

Aloe vera has a variety of beneficial effects on health. The beneficial properties are discussed below (6-8).

Effects on the immune system

Alprogen restrain calcium deluge into pole cells and in this manner hinders the antigen-antibody-mediated discharge of histamine and leukotriene from pole cells (9). In a ponder on mice that had already been embedded with murine sarcoma cells, acemannan fortifies the blend and discharge of interleukin-1 (IL-1) and tumor corruption figure

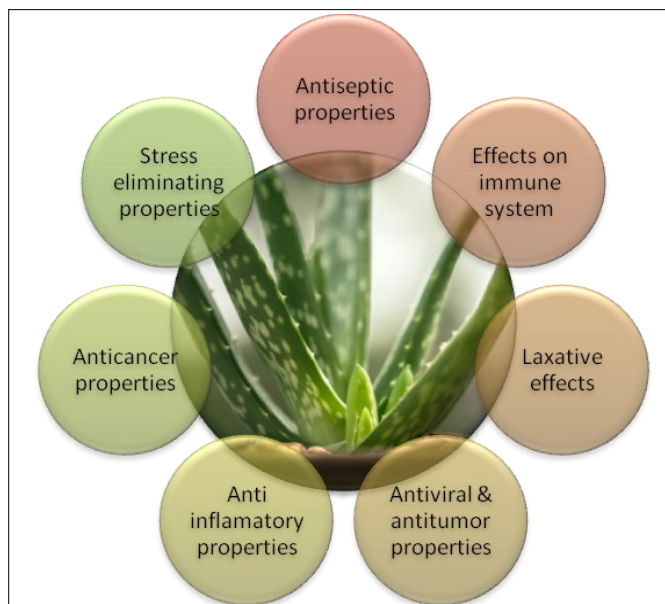


Fig. 4. Beneficial properties of Aloe vera.

from macrophages in mice which in turn started a safe assault that brought about in corruption and relapse of the cancerous cells (10). A few low-molecular-weight compounds are too competent for restraining the discharge of receptive oxygen free radicals from actuated human neutrophils.

Laxative Effects

Anthraquinones are powerful purgatives. It increments intestinal water substance, intestinal peristalsis and invigorates bodily fluid discharge.

Antiviral and Anti-tumor properties

These activities may be due to round about or coordinated impacts. Back-handed impact is due to incitement of the resistant framework and coordinated impact is due to anthraquinones. The anthraquinone aloin inactivates different wrapped infections such as herpes simplex, varicella zoster and influenza (11). In later considers, a polysaccharide division has appeared to hinder the official of benzopyrene to essential rodent hepatocytes, in this manner avoiding the arrangement of possibly cancer-initiating benzopyrene-DNA adducts (29). An acceptance of glutathione S-transferase and a restraint of the tumor-promoting impacts of phorbol myristic acetic acid derivation was also detailed which proposed a conceivable advantage of utilizing Aloe vera gel in cancer preventing chemotherapy.

Antiseptic properties

Aloe vera contains 6 sterile specialists: lupeol, salicylic acid, urea nitrogen, cinnamonic acid, phenols and sulfur. They all have inhibitory activity on microscopic organisms and infections.

Anti-inflammatory Properties

Aloe vera restrains the cyclooxygenase pathway and decreases prostaglandin E2 generation from arachidonic acid. As of late, the novel anti-inflammatory compound called C-glucosyl chromone was disconnected from gel extracts (12).

Anticancer Properties

Diverse bioactives like aloe-emodin (1,8- dihydroxy-3-(hydrxymethyl)anthraquinone) which is found in Aloe vera leaf, aloin found within the Aloe vera gel extricate, separated from that crysophanol, aloe-saponarin I & II, acemannan, aloesin, umbeliferone, esculetin are found in Aloe vera plant which makes a difference to battle against cancer (13).

Stress eliminating properties

Within the advanced situation, numerous individuals endure from pressure. Today's quick unpleasant life causes a few bio-chemical and physiological changes within the body, making it prone to illnesses and leading to breakdown of organ systems. Aloe juice is supportive in smooth working of the body mechanism (14). It diminishes the cell-damaging processes amid stress conditions and minimizes bio-chemical and physiological changes within the body. Oxidative stress alludes to chemical responses in which compounds have their oxidative state changed. A few cancer prevention agents form part of the body's normal directing apparatus whereas other dietary cancer prevention agents are inferred from slim-down sources. Aloe vera is an amazing illustration of how a natural agent can play a noteworthy part in protecting the body from the destructive effects of oxidative stress (15, 16).

Use of Aloe vera for the prevention of Covid-19

Herbal medications, derived from natural resources has a great importance in the development of anti-viral drugs. Recognition of the action mechanisms apart from the interaction site and the viral life cycle including entry, replications and release by targeting of host-specific interactions. In a paper, Majumder R., *et al.*, have shown that the antiviral potential of Aloe vera is quite high among many natural products and herbal products against a lot of viral infections including infections caused by coronavirus. Aloe vera has high-potential against Covid-19 infections and its management (17). In perspective of the toxicity, the non-toxic effect of the extracts of this plant has been proven experimentally by Majumder R., *et al.*, both *in vitro* and *in vivo* (17).. Virucidal secondary metabolites such as anthraquinones is also present in Aloe vera which is similar of Lopinavir ritonavir, an antiviral drug that is capable of acting alone or in combination with pharmaceutical targets like SARS Cov-2 protease 3CLPro (22). Most importantly, many research studies have shown that the Aloe vera plant extracts are capable of fighting against RNA and DNA viruses.

The review made by Mpiana *et al.* has demonstrated antiviral activity of Aloe vera against different viruses including Varicella-Zoster virus, haemorrhagic Viral Rhodavirus Septicaemia, herpes simplex virus type 1 and 2, human immunodeficiency virus, poliovirus, influenza virus, cytomegalovirus, human papilloma virus and most importantly coronavirus SARS-CoV-1. The alloe vera is mostly consumed orally in different forms and it has already demonstrated effects on viruses by few mechanisms including breakdown of the viral envelope interaction with enzymes etc. Aloe vera is also a good source of

minerals like Zinc which has great effect on SARS-CoV-1 (23).

As we already discussed Aloe vera is mostly consumed orally as tablets, tea, juices, capsules, yogurt, jam and so on. The main reason behind its wide usage is the safety associated with it, both *in vitro* (24) and *in vivo* (25). It has been observed that in many cases oral administration of methanol extract with dosage like 4, 8 and 16 g/kg of body weights up to 14 days does not have any toxic effects (26). Apart from this, another study has also proved that it does not have any toxicity after oral application on F344 rats up to 13 weeks in the form of locally available decolorized beverage (27). But, apart from all of these, study an unpropitious effect (hepatotoxicity) was shown by (28). This has an indication that Aloe vera should be used with precaution and most importantly excessive doses should be avoided.

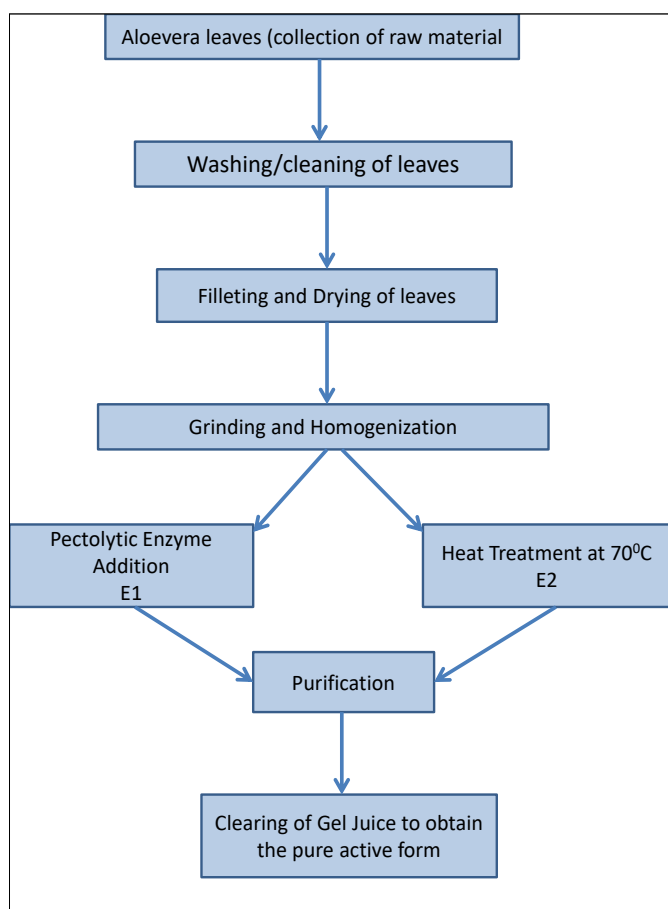


Fig.5. Extraction Process of Aloe vera Gel.

Conclusion

Aloe vera has huge beneficial properties to our health as it loaded with bioactive compounds. Due to various beneficial properties of Aloe vera and its compounds, it can be used to maintain healthy skin with moisture and integrity. Apart from that it also helps to prevent various health issues. The application of Aloe vera, as a traditional medicine with improved technologies will minimize many diseases and would be contributing towards the existence of a healthy society.

Acknowledgements

We gratefully acknowledge Invertis University for providing immense support and encouragement for this work.

Authors contributions

AM participated in the sequence alignment and drafted the manuscript. SST participated in the sequence alignment. MS participated in the design and planning. AB conceived the study and participated in its coordination. JP and DS did the final revision. All authors have read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest: There is no conflict of interest in between the authors.

Ethical issues: None.

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