Proceedings of the Pakistan Academy of Sciences: B
Life and Environmental Sciences 60(3): 337-365 (2023)

ISSN (Print): 2518-4261; ISSN (Online): 2518-427X
http://doi.org/10.53560/PPASB(60-3)857

Pakistan Academy of Sciences

Review Article

A Wonder Plant *Aloe vera* L. (Liliaceae): An Overview of its Folk Traditional Uses, Phytoconstituents, Biological Activities, and Cosmaceutical Applications

Maira Batool[1], Malaika Khan[1], Maria Mubarak[2], Adil Hussain[3*], Muafia Shafiq[3], Shamma Firdous[3], and Asma Saeed[3]

[1]Department of Botany, Government Queen Mary Graduate College, Lahore, 54000 Pakistan
[2]Department of Botany, Government College University, Lahore, 54000 Pakistan
[3]Food and Biotechnology Research Centre, Pakistan Council of Scientific and Industrial Research (PCSIR) Laboratories Complex, Ferozepur Road, Lahore, 54600 Pakistan

Abstract: *Aloe vera* L. (Lililaceae) bears various medicinal applications that likely date back more than a thousand years ago. The current review provides an overview of the folk traditional uses, phytochemistry, biological activities, and cosmaceutical applications of the *A. vera* plant to date. The data have been retrieved from different scientific databases, including PubMed-Medline, Researchgate, Google Scholar, Science Direct, Scopus, SciELO, Taylor & Francis, Web of Science, books, conference papers, Masters and Ph.D. dissertations. As per the collected data of this review, almost 40 active phytoconstituents in *A. vera* have been reported so far with varying concentrations. Ethnobotanical data displayed that *A. vera* is still used as traditional medicine among communities against more than 20 different health-related problems. The DPPH, FRAP, TAC, and ABTS assays were commonly employed where *A. vera* extracts showed varying antioxidant activities against reactive oxygen species (ROS). Data on the biological activities showed *A. vera* plant extracts with remarkable anti-inflammatory activities through the inhibition of TNF-α and prostaglandin E2 factors and also exerts anti-diabetic activity against type 1 and type 2 diabetes. As per the collected data of this review, *A. vera* extracts have been reported with anti-microbial activities against more than 12 bacterial and 7 fungal strains and also obstruct the uncontrollable proliferation of specific types of cancer cells like HCT-116, HepG2, HeLa, A549, and MCF-7. Conclusively, *A. vera* possesses wide-ranging applications in the treatment of various diseases. However, more controlled investigations and clinical trials with the elucidation of the mechanism of action activities are prerequisites in the future to substantiate the outcomes and efficacies of *A. vera* under different circumstances. Any toxic effects of *A. vera* if associated with specific extracts or compounds should be addressed for safer consumption of *Aloe-based* food and cosmetic products.

Keywords: *Aloe vera*, Biological activities, Cosmeceutical uses, Folk traditional uses, Lililaceae, Phytoconstituents

1. INTRODUCTION

Plants have a wide background in the pharmaceutical and cosmetic industries along with food fields and are very significant in the development of human civilizations [1-4]. Some plants are used pliantly as folk medicine or herbal drugs since the time of the bible. Different classes of plants including bryophytes, tracheophytes, and their subclasses have been used to treat certain human diseases. It is well explained in the ethnobotanical field studies from different regions [5, 6]. The plants mostly used in traditional medicine belong to the tracheophyte's subclass angiosperm (94.6 %), followed by the pteridophytes (3.3 %), and gymnosperm (2 %) [7]. Mosses with ~29 species are the only group with the most uses, whereas liverworts only contributed 3 species and with no available data on traditional uses of hornworts [8].

The phytochemistry and biological activities of different plants and percentage of plant parts used

Received: February 2023; Revised: May 2023; Accepted: June 2023
*Corresponding Author: Adil Hussain <aadil.iiu07@gmail.com>

for therapeutic purposes globally were described by numerous authors [9-18].

Ali *et al*. [7] reported the percentages of parts of plants for ethnomedicinal use including leaves (44 %), stem (12 %), roos (10.66 %), fruit bark (5.33 %), rhizome (5.33 %), stem bark (2 %), blub (3 %), shoot (1.33 %), resin (1.33 %), and come pedicle, the capsule was 0.66 %. The contribution of trees was 16 %, shrubs 11 %, and herbs 73 % (Figure 1a-b).

Among all the higher plants, perennial succulent plants of the genus *Aloe* of the Liliaceae family are found in moderate and subtropical areas of the world. The word *Aloe*, which means a bitter, shining material, comes from the Arabic "Alloeh" or the Hebrew "Halal." Africa is where this plant genus first appeared [19]. There are almost 200 species in the genus some of them are grown for the sticky latex that their large, meaty leaves. *Aloe* plants have been used as purgatives and cure for skin conditions since the time of the Bible [20]. *A. vera* is also called elephant's gall, burn plant, "lily of the desert" and *Aloe*. This plant is sometimes known as *A. brobadensis* having green, stiletto-shaped, marginated, tapering, fleshy, spiky leaves that contain a clear viscid gel [21, 22].

A. vera leaves discharged two different forms of exudates on cutting, one is a sour reddish-yellow juice found in pericyclic cells under the leaves' heavily cutinized epidermis. This "juice" has often been used in dry form as a laxative [23]. Aloin, aloe-emodin, and other similar chemicals give it a bitter flavor. The thin-walled, cylindrical cells in the inner center region (parenchyma) of the foliage generate the other exudate, a translucent, slick mucilage or gel [20, 24].

The chemical makeup of *Aloe* varies by species, climate, and growth conditions and some important phytochemicals reported in *Aloe* include alkaloids, flavonoids, saponins, terpenoids, glycosides, tannins, phenolic compounds, carbohydrates, protein, sterols, protein, tri-terpenoids, glucose, and galactose, etc. and some derivatives [17, 25-27]. Vitamins, enzymes, micro and macro minerals, sugars, anthraquinones, campesterol, sitosterol and lupeol, salicylic acid, and amino acids were also reported [28].

The pharmaceutical and cosmaceutical industry most often uses the plant's latex and gel as it contains a range of organic components believed to contribute to the gel's alleged emollient, moisturizing, and are few skin conditions where *A. vera* is used to treat these complications. *A. vera* sap has healing potential [20] for cuts, burns, and eczema supposedly decreasing inflammation and relieving discomfort. However, there are still some disagreements on the benefits of *A. vera* sap on the healing process [1, 29-31]. Some important reported *A. vera-based* food, pharmaceutical, cosmaceutical, and other products developed are shown in Figure 2.

Considering the potentials of *A. vera*, the present review provides a brief account of ethnobotanical uses with the range of chemical

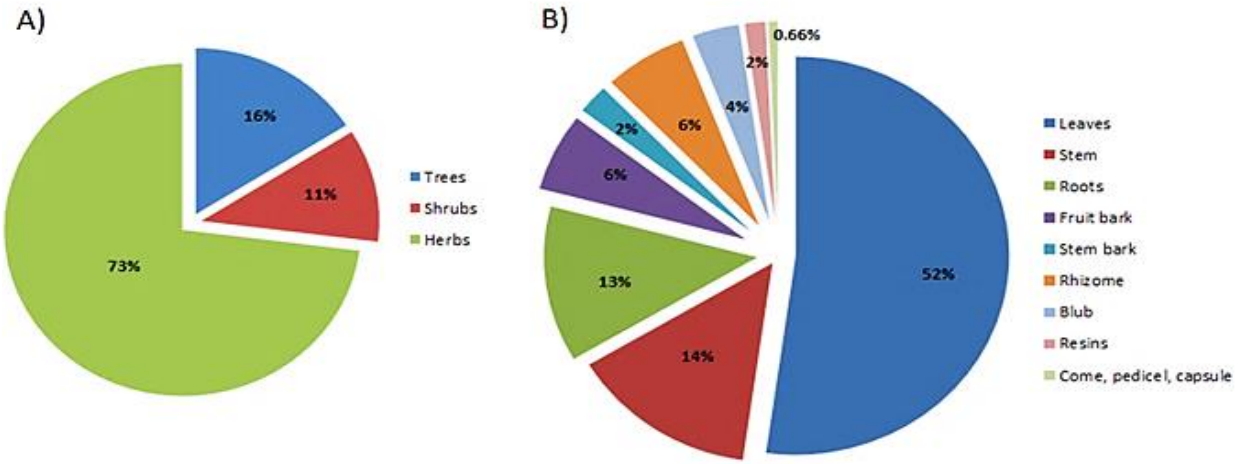


Fig. 1. A) Contribution of trees, herbs, and shrubs used as folk traditional medicine, B) Contribution of parts of plants used for ethnomedicinal purposes. Source: Ali *et al*. [7].

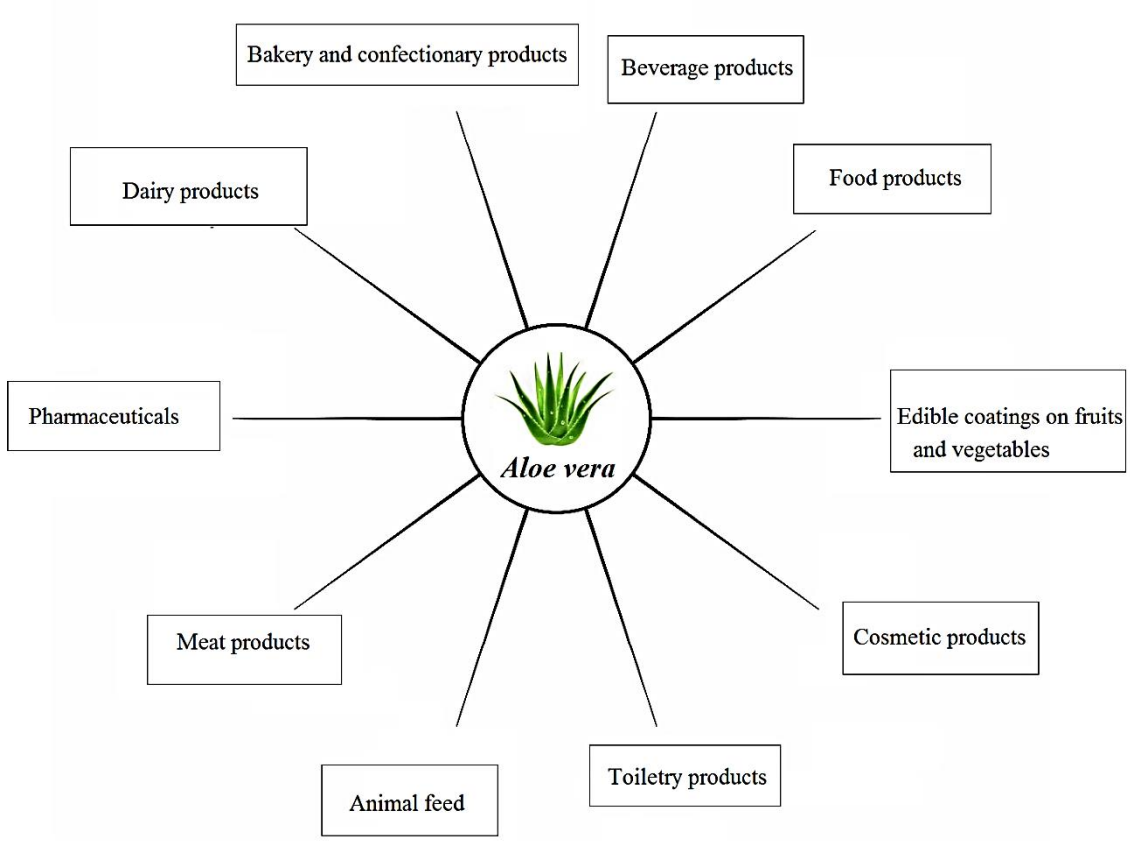


Fig. 2. Different *A. vera-based* food, pharmaceutical, cosmaceutical, and other products developed in the industries

compounds that make *Aloe* plants capable of providing antimicrobial, antioxidant, antidiabetic, anticancer, and anti-inflammatory activities. The review further emphasizes on *Aloe* based food and cosmetic products with improved nutritional and therapeutic effects.

2. METHODOLOGY

1.1. Data Search Approach

The data have been compiled after going through a detailed study on morphology, phytochemistry, folk traditional uses, biological activities, and cosmaceutical and food products of *A. vera* from different databases like Pubmed-Medline, Researchgate, Google Scholar, Science Direct, government reports, SciELO, Web of Science, Scopus, Springer Link, and Taylor & Francis, and from Masters and Ph.D. dissertations. While searching the data, specific keywords were used including ethnobotany of *Aloe vera*, *Aloe vera* morphology, *Aloe vera* phytochemistry, *Aloe vera* medicinal uses, *Aloe vera* biological activities, *Aloe vera* antioxidant activity, *Aloe vera* antimicrobial activity, *Aloe vera* antidiabetic, *Aloe vera* anti-inflammatory, *Aloe vera* cytotoxicity, and *Aloe vera* based cosmaceutical and food products, etc. The data for this review was collected from the articles published up to 2023 in the English language.

3. RESULTS

Overall, 132 articles were studied and the required data have been retrieved and compiled, and consequently presented. The detailed review of the selected articles showed that *A. vera* has been long used as traditional medicine in almost 12 countries against more than 20 different disease categories (Table 1). Almost 40 different types of active phytochemicals have been reported in the extracts of *A. vera* so for (Table 2) including phenols, flavonoids, alkaloids, tannins, saponins, etc. The total flavonoid content was estimated by the colorimetric method and the total phenol content was estimated by the folin-ciocalteu method.

Data showed that the total tannin content was mostly quantified by the vanillin-HCl method, and alkaloid content was determined with the bromocresol green method. For the antioxidant activities of *A. vera* extracts against reactive

oxygen species, DPPH, FRAP, ABTS, and TAEC were the most widely used techniques (Table 3). It was confirmed that the phytochemicals of *A. vera* extract have anti-inflammatory activities by targeting/inhibiting the TNF and MMP-9 factors (Table 4).

Aloe extracts also possess anticancer activity by preventing the uncontrollable division of specific types of cancer cells like HCT-116, HepG2, HeLa, A549, and MCF-7, hence reducing the chances of blood cancer/leukaemia, liver cancer, breast and lung cancer (Table 5). The restoration of insulin level was evident for the extracts of *A. vera* that authenticates its potential antidiabetic activity (Table 6). Antimicrobial activity data showed that the extracts of this plant were active against 12 bacterial and 7 fungal strains (Table 7). The current review also manifested that there are a lot of *Aloe-based* food and cosmetic products that have been commercialized with nutritional and cosmaceutical applications (Table 8).

3.1. Morphology of *A. vera*

The *Aloe* plant is comprised of leaves, short stems, roots, and flowers (Figure 3), and its morphology has been extensively studied by various authors [22-24, 32]. *A. vera* live for more than two years and has sukers at the base. The green, glabrous, glaucous, margin sparsely dentate leaves are sessile, erect, and linear-lanceolate with a length range from 15 – 35 cm and a width range from 4 – 8 cm [23, 24].

Malik *et al.* [22] explained some physical characteristics of the fresh and dried *Aloe* leaves such as length, weight, width, etc. In their study, the reported lengths of the fresh and dried leaves were 43.3 and 38.5 cm, weight was 5.4 g and 5.2 g, and width was 8.2 cm, and 6.1 cm respectively. The reduction in these physical parameters of fresh and dry weight, length, and width of the leaves is due to dehydration causing the reduction of gel weight [22].

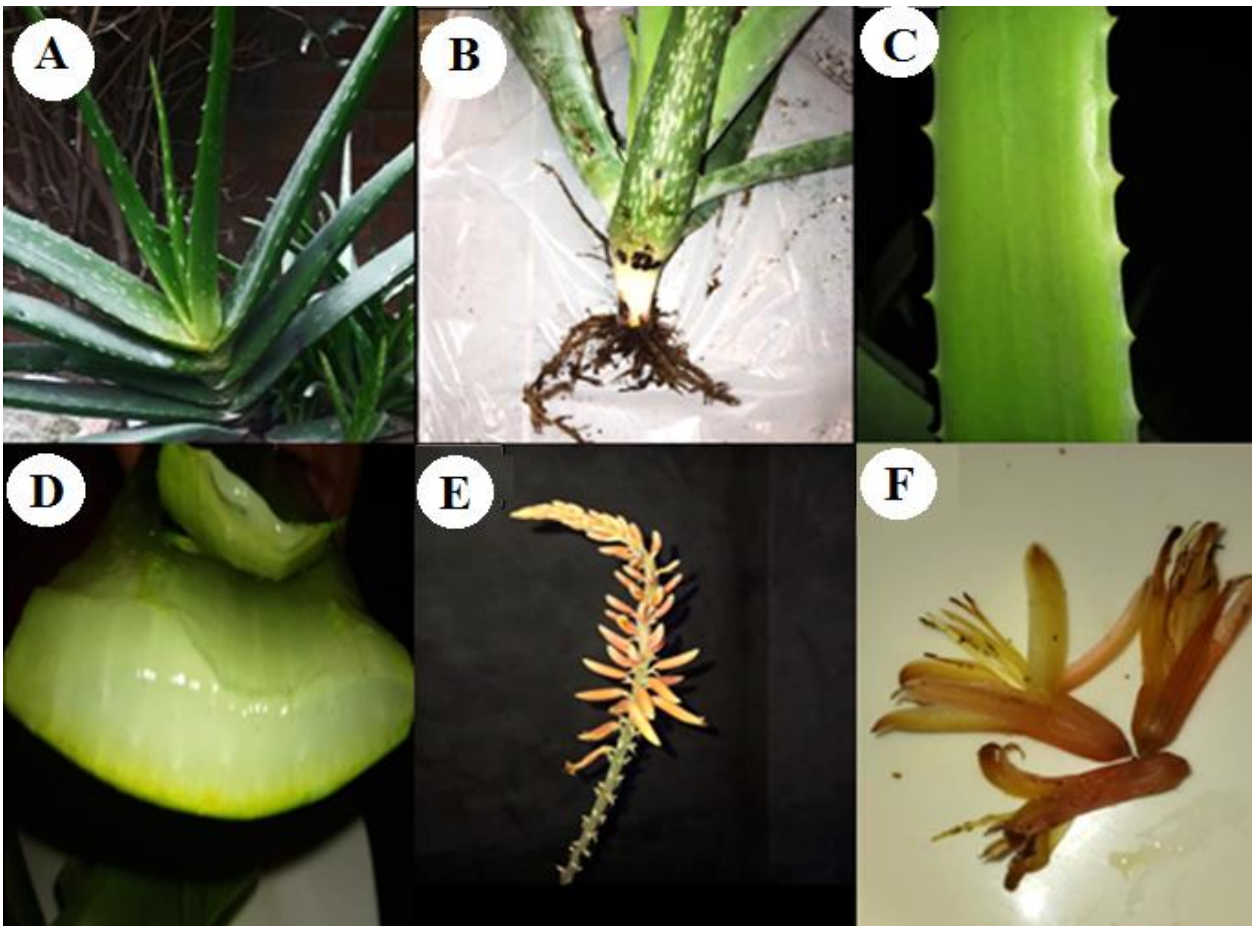


Fig. 3. Morphology of *A. vera* plant. **A)** Habitat**, B)** Roots, **C))** Abaxial surface of leaf and thrones, **D)** Leaf gel**, E)** Synflouresence, F) Flowers. Original photographs by Maira Batool.

The short stem had 1 – 2 branches on which erect pedunculate raceme inflorescence occurs which may be 60-100 cm in length. It has ovate-lanceolate and persistent bracts; 9-12 x 5-6 mm. The flower of *A. vera* formed on the short pedicel and the perianth is dull reddish, lobes 6, almost equalling the tube, and 2.5-3 cm long. The color of the flower ranges from reddish to pale yellow capsule of 1.5 cm [22, 33]. The roots are fibrous that absorb water and nutrients required for proper growth and development. Some physical parameters of *A. vera* roots studied [23] showed varying color, length, weight, and width. The color of the fresh roots is brown and became dark on drying. The fresh and dried root lengths reported were 35 cm, and 34 cm long, 5.4, and 5.2 cm wide with 0.5 g, and 0.4 g weight [22].

3.2. Folk Traditional Uses of *A. vera*

Plants have various beneficial traditional uses and different plant species are used as medicine by people of different regions according to the information they know about that particular plant [34-36]. The traditional uses depend on the cultural and religious knowledge of the plant. The ethnobotany of

Table 1. Folk traditional uses of *A. vera* reported from different regions of the world

Region	*Aloe* spp.	Part used	Folk medicinal use	Reference
Machakos	*A. vera*	Leaves	Hypoglycaemic effect	[46]
India	*Aloe barbadensis,* and *Aloe arborescens*	Gel and juice	Used against mild fever, diabetes, wound and burns, AIDS, liver infection, improve fertility and gastrointestinal disorder	[39]
Singapore		Leaves	Used to treat respiratory disorders, boost immunity, skin and hair care, mouth ulcer, control bleeding, itching and reduce muscle pain	[38]
Ghana		Leaves	Used against diabetes mellitus	[40]
Cameroon		Gel	Used for hair care, visage, sunblock, analgesic and anti-inflammatory agent	[41]
Tanzania	*A. vera*		Used against constipation, toothache, and skin complaints. Used to assist labor and induce abortion. Used to treat arthritis, pneumonia, gonorrhea, sleeping sickness, alleviate pain, inflammation, retarded growth of tongue, pneumonia, aid wound healing, syphilis, diseases in poultry and goats, testicular and scrotum cancer, chest pain, malaria, colds, reduce labor pain, cough, typhoid, ulcers, vomiting, swollen diaphragm, nosebleed, ringworm, skin diseases, diarrhea, anemia, backache, stomach ache, burns, gonorrhea	[42]
Yemen	*Aloe lavranosii*	Leaves	Used for wound healing, to treat malaria, abdominal pain, fever, gynaecological pain after childbirth intestinal infection, burns, intestinal colic, obesity, newborn infection, and intestinal infection,	[46]
	Aloe rubroviolacea			
	Aloe vacillans		Used against constipation, scabies, intestinal worm, low immunity by infant malaria, fever, low immunity, abdominal pain, body pain, and hair fall	
India			Used against dental problems	[44]
North Africa	*A. vera*		Used as a wound healer and taken against skin ulcers, mouth ulcers, herpes simplex, psoriasis, gastric ulcers, and age-related problems	[48]
Nigeria			Used against malaria	[43]
Kenya			Used to treat malaria, peptic ulcers, cough, wounds, and swelling of the diaphragm	[47]
Tanzania	*A. latcritia, A. secvndiflora,* and *A. duckcri*		Used to treat malaria, general stomach in humans, new castle disease in chicken, wounds, hernia, and typhoid	[45]

A. vera (Table 1) has been extensively studied among communities of different regions where it has been used as a traditional medicine against many diseases [37-45].

In one study, *A. vera* leaves gel was used to treat the hypoglycaemic effect (condition of blood when the glucose level is lower than the normal 70 mg/dL) because the gel controls diabetes [48]. The study by Siew *et al.* [38] in Singapore described local uses of *A. vera* against respiratory diseases and cancer by using its leaves as decoctions, eaten raw or in the form of juice. As per their data, it improves immunity and blood circulation and is a better remedy against acne, mouth ulcer, itching, and arthritic pain.

A study in India described two species of *A. vera* i.e, *Aloe barbadensis* miller and *Aloe arborescens,* whose gels and juices were used to treat mild fever, gastrointestinal disorders, AIDS, liver infection, muscle pain, and cancer [39]. Asase and Yohonu [40] proclaimed that in Ghana, *A. vera* leaves were used to treat diabetes mellitus when added 15 % of plants in food or taken in the form of decoctions. Fongnzossie *et al.* [41] reported that *A. vera* from the east of Cameroon was used to treat hair and skin problems. Moreover, *A. vera* was included in the top 10 cosmetic ingredients, and different phytochemical constituents present were used to treat inflammation, block UV rays for skin, and regenerate tissues.

From Tanzania, Amir *et al.* [42] found that malaria is frequently treated with *Aloe* leaves. Besides that, 11 species of *Aloe* were used as traditional medicine in Tanzania to treat diseases such as constipation, induction of abortion, toothache, skin complaints, assist labor, arthritis, pneumonia, gonorrhea, alleviation of pain, inflammation, retarded growth of tongue, pneumonia, wound healing, syphilis, diseases in poultry and goats, testicular and scrotum cancer, malaria, colds, ulcers, vomiting, swollen diaphragm, nosebleed, ringworm, skin diseases, reduce labor pain, anemia, backache, stomach ache, burns, gonorrhea, wounds, fever, pneumonia and skin diseases, edema, headache, chest pain, pneumonia, conjunctivitis were found to be treated with *Aloe* species.

Another study reported the ethnobotanical uses of *Aloe lavranosii, Aloe rubroviolacea, Aloe sabaea,* and *Aloe vacillans* against wounds, malaria, intestinal infection, fever, intestinal colic, obesity, gynaecological pain after childbirth, eye infection, eye pain, constipation, intestinal infection, eye allergy, face acne body pain, abdominal pain, newborn infection, intestinal worm, hair fall, and scabies [47]. Roy and Janbandhu [44] studied *A. vera* in Maharashtra and Saphale village of India and reported traditional uses of *A. vera* juice which was used to cure dental ailments and applied as a wound healing remedy. Oladeji *et al.* [43] in Nigeria documented that the decocted leaves of *A. vera* are used against malaria as it inhibits the growth of *the Plasmodium falciparum* strain.

Asif [48] reported that *A. vera* is a wound-healing remedy which has been utilized against skin ulcers, gastric ulcers, mouth ulcers, psoriasis, skin injury, herpes simplex virus, and age-related problems. Mutie *et al.* [49] reported different uses of *A. vera* plant gel from Kenya, where it was used against cough, swelling of the diaphragm, peptic ulcers, malaria, and wounds. A recent study in Tanzania showed that the *A. vera* leaves were used to treat malaria, general stomach problems, hernia, typhoid, wounds, ringworms in humans, and new castle disease in chickens [45]. *Aloe latcritia, Aloe secvndiflora,* and *Aloe duckcri* were the most frequently used species against diseases without any side effects whereas *A. secundiflora* was reported to cause death if taken in high doses.

As per the collected data of this review, the most commonly used parts of the *A. vera* plant as traditional medicine includes leaves (70 %), followed by the flowers (20 %), and roots (10 %) (Figure 4). It is found that despite of industrial use of *A. vera* it is also being used by people to treat almost more than ~20 different health problems.

3.3. Medicinal Uses of *A. vera*

The ancient *Aloe* plant has been proven to be medicinally significant by various research groups [1, 2, 4, 29- 31]. Manvitha and Bidya [39] reported various phytochemicals from the *Aloe* plant useful in medicine such as curing sunburn, tumor formation, and inflammation, maintaining cell growth and

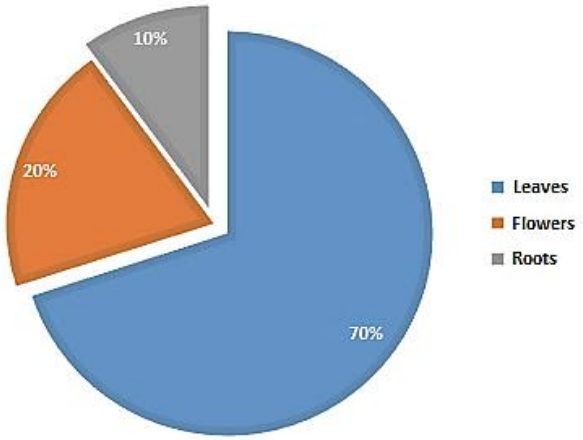


Fig. 4. Percentage of parts used in ethnobotantanical studies of *Aloe* species

development in the body, and maintaining sugar levels in diabetic patients. According to Grace *et al.* [29], natural products extracted from *A. vera* leaves such as carbohydrates, can be applied to treat skin diseases and a liquid matrix, can be used as an effective purgative or in veterinary medicines.

Gupta and Rarawt [30] reported the effectiveness of *A. vera* in reducing joint pain, muscle-related tendonitis, and other injuries. *Aloe* juice reduces stress (oxidation stress) and biological and physical alterations in the body. Tiwari and Upadhayay [31] reported that the latex in the leaves of *A. vera* contains anthraquinones which stimulate bowel contraction. Particularly, emodin found in latex act as an anticancer drug for lung, prostate, and skin cancers. Asif [48] studied the sugar-controlling ability of *A. vera* and showed improvement in carbohydrate metabolism, anti-hyperglycemic and anti-hyperchloremia effects in diabetic patients and hence maintaining the blood sugar, body fat, and body weight.

According to Danish *et al.* [1], *Aloe* contains high water content and can be used as a body moisturizer. Moreover, it cures thermal burn, stomach ailments, sunburn, and wounds caused by radiation and helps in cell growth, and provides relief against constipation. Sayar *et al.* [2] reported that *Aloe* possesses many anti-microbial and inflammatory properties and can cure gingivitis (a mild redness, irritation, and swelling in gums) and reduces bleeding and swelling of the gums.

Farid *et al.* [4] reported medicinal uses of the *A. vera* plant due to its exceptional features. It is considered a revolutionary weapon against various diseases in medical treatments and services. Traditionally *A. vera* has been used to cure dermal disorders but presently, more advanced advantageous therapeutic uses of this plant in bone marrow BM-MSC (mesenchymal stem cells) transplantation has been investigated which will help in curing liver complications.

3.4. Phytochemistry of *A. vera*

A lot of studies have reported diverse classes of phytochemicals (Table 2) in *Aloe* species using different methods [17, 25-27, 51-58]. Sathyaprabha *et al.* [51] found tannins, saponins, terpenoids, flavonoids, steroids, cardiac glycosides, phlobatannins, squalene oleic acid and dodecanoic acid in *A. vera*. In their study, some other phytochemicals including n-hexadecanoic acid, 1,2-benzenedicarboxylic acid, eugenol, phenol, 2,4-bis(1-phenylethyl) diisooctyl ester were also reported in *A. vera* using the GC-MS procedures.

Wintola and Afolayan [59] studied *Aloe ferox* leaf gel and quantified phenols (70.33 mg/g), flavanols (35.2 mg/g), proanthocyanidins (171.06 mg/g), alkaloid 60.9 mg/g) in the acetone extracts. In the ethanol extract, phenols (70.24 mg/g), flavanols (12.53 mg/g), proanthocyanidins (76.7 mg/g), and alkaloids (23.76 mg/g) were also quantified. Patel *et al.* [52] described the complexity of the *Aloe* gel extracted from the whole plant and analyzed using HPLC. The phytochemicals quantified were alkaloids, carbohydrates, tannins, steroids, triterpenoids, glycosides, flavonoids, and phenols.

Raphael *et al.* [33] and Kumar *et al.* [60] performed different tests for the analysis of the phytochemical constituents in the aqueously extracted gel from the leaf of *A. vera*. They reported tannins, phlorotannins, saponins, flavonoids, anthraquinones, terpenoids, steroids, and alkaloids in the extracts of *A. vera.*

Cardralli *et al.* [61] studied the *Aloe marlothii* and *Aloe melanacatha* to analyze the phytochemicals in the methanolic extracts of gel from leaves through Mass spectrophotometry. Aloeresins, *Aloe* resin A (843.4 g/100g), anthraquinones aloin (0.66- 4.96 g/100g), and hydroyaloins were found with a major part of gallic acid and polyphenols, flavonoids and flavonols as a phytochemical constituent in the studied *Aloe* species.

Dharajiya *et al.* [56] reported phytochemicals like saponins, alkaloids, tannins, cardiac glycoside, sterols, flavanoids, and phenol in the four different types of extracts (ethyl acetate, hexane, methanol, aqueous) from the fresh leave of *A. vera* by using thin layer chromatography.

Mahendiran *et al.* [62] showed the presence of active chemical compounds in the aqueous extract of *A. vera* contained flavonoids, phenolic compounds, alkaloids, gums and mucilages, carbohydrates, tannins, saponins, and terpenoids by using FT IR

Table 2. Phytochemistry of *Aloe* plants reported from different regions of the world

***Aloe* spp.**	**Part used**	**Extract used**	**Phytochemicals/ derivatives**	**Detection method**	**Reference**
A. vera	Leaves	Aqueous	Phlobatannins, tannins, saponins, steroids, flavonoids, terpenoids, and cardiac glycosides, dodecanoic acid, squalene oleic acid. 1,2-benzenedicarboxylic acid ester, Eugenol, n-hexadecanoic acid, and phenol, 2,4-bis (1-phenylethyl)	GC-MS	[51]
A. ferox	Leaves	Aqueous and ethanol	Phenols, flavanols, pro-anthocyanidins, and alkaloids	Spectrophotometry	[59]
A. vera	Leaves	Chloroform and aqueous	Alkaloids, tannins, flavonoids, terpenoids, carbohydrates	ND	[33]
	Leaves	Ethanol	Alkaloids, carbohydrates, tannins, steroids, triterpenoids, glycosides, flavonoids, phenols	HPLC	[52]
	Leaves	Ethanol	Chromone, anthraquinone, or anthrone derivatives	HPLC	[69]
	Leaves	Methanol	Glycosides, alkaloids, tannins, reducing sugars, steroids and phenolic compounds, terpenoids, flavonoids, and saponin glycosides	Colorimetric method	[60]
	Dried leaves	Aqueous	Phenolic acids, catechins, flavonoids, proanthocyanidins, quinones, tannins, coumarins, alkaloids, amines, betalains vitamins, nitrogen compounds, terpenoids, and carotenoids	FTIR	[70]
	Leaves	Aqueous, ethanol, and methanol	Alkaloids, glycosides, flavonoids, steroids, reducing sugar, terpenoids, carbohydrates, phenolic compounds, amino acids, tannins, and saponins	Colorimetric method	[22]

***Aloe* spp.**	**Part used**	**Extract used**	**Phytochemicals/ derivatives**	**Detection method**	**Reference**
Aloe marlothii and *Aloe melanacatha*	Leaves	Methanol	Aloeresins, *Aloe* resin A, anthraquinones aloin and hydroyaloins	Mass spectrophotometry	[61]
A. vera	Leaves	Hexane, methanol, ethyl acetate, and aqueous	Saponins, cardiac glycoside, tannins, sterols, flavonoids, alkaloids, and phenols	TLC	[56]
	Leaves	Aqueous	Alkaloids, flavonoids, carbohydrates and saponins, gums, mucilages, phenolic compounds, terpenoids, and tannins	FT IR spectroscopy	[62]
	Leaves	Methanol	Flavonoid compounds such as merictin, quercitrin, apiginin, quercetin, rhamentin, naringin, kampferol, rutin, and phenolic compounds (ferulic, caffic, p-coumaric, vanillic, cinnami, chlorogenic, ellagic acids)	HPLC technique	[63]
	Leaves and flowers	Methanol	Flavonoids, phenols, saponins, terpenoids, carbohydrates, sterols, alkaloids, proteins, tannins, and triterpenes	RP-HPLC	[50]
	Leaves	Aqueous	Chromone, anthraquinone, flavonoids, phenylpropanoids, and coumarins phenylpyrone, phenol derivatives, and phytosterols	ND	[64]
	Leaves	Aqueous and methanol	Alkaloids, carbohydrates, tannin, steroids, tri-terpenoids, glucose, and galactose	HPLC and TLC	[26]
	Leaves	Aqueous	Alkaloids, saponin, tannins, and glycosides	ND	[65]
A. vera	Leaf	Ethanol	*Aloe*-emodindiglucoside, (S-2'-oxo-4'- hydroxypentyl2 (ß-glucopyranosyl-oxymethyl), aloenin 10-hydroxyaloin B, chromone, aloveroside B, aloenin B, aloin B, isoaloerisin D, 10-hydroxyaloin A, aloin A, and aloenin-2`-pcoumaroyl ester	LC-MS	[67]
A. vera	Leaf	Ethanol and aqueous	Alkaloids, saponins, flavonoids, terpenoids, glycosides, and tannins	ND	[71]
Aloe vacillans	Flower	Methanol	Flavonoids, carbohydrates, phenolic compounds, protein, and sterols	TLC	[72]
A. vera			Saponin, carbohydrate, flavonoid, steroids, protein, and phenolic compounds		

**LC-MS= Liquid chromatography-mass spectrophotometry, ND= Not Defined, TLC= Thin layer chromatography, FTIR= Fourier transform infrared spectrometer, HPLC= High-performance liquid chromatography, RP-HPLC= Reverse phase high-performance liquid chromatography*

spectra. Faid *et al.* [63] showed the occurrence of different active complexes including flavonoid compounds such as merictin, quercitrin, apiginin, rutin, quercetin, rhamentin, naringin, kampferol; phenolic compounds (ferulic, caffic, p-coumaric, vanillic, cinnami, chlorogenic, ellagic acids) in the methanol extract of *A. vera* leaves using HPLC technique.

Kahramanoğlu *et al.* [64] reported six different classes of chromone, anthraquinone, flavonoids, phenylpropanoids, and coumarins phenylpyrone and phenol derivatives; and phytosterols in *A. vera.* According to Babu *et al.* [50], flavonoids, phenols, saponins, terpenoids, carbohydrates, sterols, alkaloids, proteins, tannins, and triterpenes were present in the methanolic extracts of *A. vera* leaves and flower evaluated with RP-HPLC.

Usman *et al.* [65] also reported phytochemicals in *A. vera* leaves skin and gel extracted by the aqueous extraction method. They confirmed the presence of alkaloids (31.067 g/100g), saponin (10.67 g/100 g), tannins (25.66 g/100 g), glycosides (0.060 g/100 g), and minerals like phosphate and magnesium in the *Aloe* plant.

In a study, it has been validated that the extracts of *Aloe* species possess complex phytochemical components [66]. Tannins, phenolics, alkaloids, flavonoids, and tri-terpenes were present in the ethanolic extract from the gel made from the leaves of *A. barbadensis*. The n-hexane fraction showed only phenols, alkaloids, and flavonoids. The petroleum ether showed tannins, phenolic, and flavonoids. The chloroform fraction showed tannins, phenolics, saponins, alkaloids, and flavonoids. Tanning agents, saponins, alkaloids, and flavonoids were visible in the dichloromethane fraction. Tannins, flavonoids, phenolics, saponins, alkaloids, and tri-terpenes could be seen in the acetone fraction. Additionally, tannin, phenolics, alkaloids, and flavonoids were present in the methanol fraction [66]. Hamdeni *et al.* [17] evaluated the phytochemistry of *A. vera* and reported the presence of phenols, flavonoids, flavonols, and condensed tannins using various techniques.

Bendjedid *et al.* [67] reported phytochemicals in the leaves of *A. vera* by extracting the gel using ethanol as a solvent using the LC-MS method. They verified the presence of isoaloerisin D, aloenin B, aloenin 10-hydroxyaloin B, aloenin 10-hydroxyaloin A, aloveroside B, aloin B, aloe-emodindiglucoside, (S-2'-oxo-4'-hydroxypentyl2 (ß-glucopyranosyl-oxymethylene) chromone, aloin A, and aloenin-2 in the ethanol extract of *A. vera* leaves gel. Arsene *et al.* [68] reported phytochemicals like aloesin, 8-o-methyl-7-hydroxyaloin B, chlorogenic acid (3-o-caffeoylquinic acid), trans-5-p-coumaroylquinic acid, luteolin 6,8-di-c-glucoside, cis-5-p-coumaroylquinic acid, trans-5-O-caffeoylquinic acid, 8-o-methyl-7-hydroxyaloin A, aloe-emodin-glucoside, aloinoside B, aloinoside A, 2′-O-feruloyaloesin, aloin B, aloe-emodin-glucoside, aloin A, 2′-p-methoxycoumaroylaloeresin B, 6′-malonylnataloin, *aloe*-emodin-glucoside, aloe-emodin" in the methanolic extract of *A. vera* leaves using HPLC–MS/MS technique.

Overall, for the phytochemistry of *A. vera,* more than 40 diverse groups of chemicals have been reported with potential effects against numerous health-related disorders, however, still there is a possibility to quantify more novel groups of compounds in *Aloe* species using advanced analytical techniques to unveil the medicinal significance of individual compound. Some of the essential phytochemical groups reported from *Aloe* species are illustrated in Figure 5.

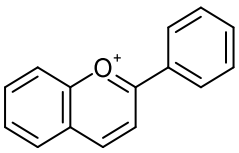
3.5. Biological Activities of A. vera

Some of the essential biological activities of *A. vera* extracts and chemical constituents are illustrated in Figure 6 and the details are discussed below.

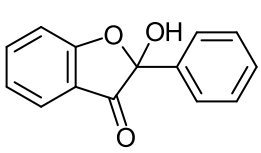
3.5.1. Antioxidant Activity

The activity of preventing oxidation (formation of free radicals), lowers the chances of tumors and various heart diseases. Antioxidants are a group of compounds that inhibits the free radicals and lipid oxidation reactions in the body [36, 77, 78]. A lot of studies have described the antioxidant activity of the *A. vera* plant [27, 57, 58, 70, 79-82] and the details of antioxidant activity conducted globally using various methods are given in Table 3.

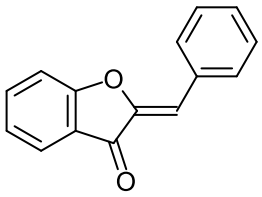
Vega-Gálvezv *et al.* [83] reported the effect of hydrostatic pressure on the antioxidant activity of *A. vera* gel ethanol extracts with DPPH (2,2′-diphenyl-



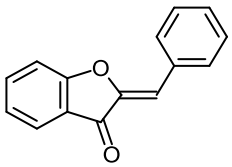
Anthocyanins



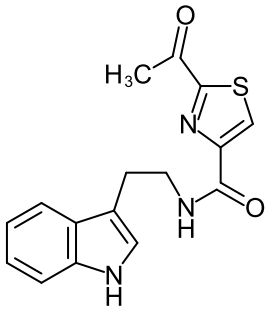
Auronols



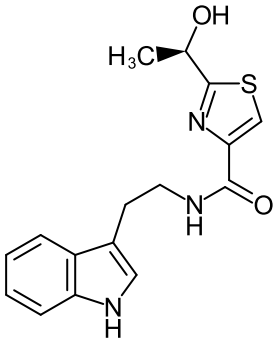
Aurones



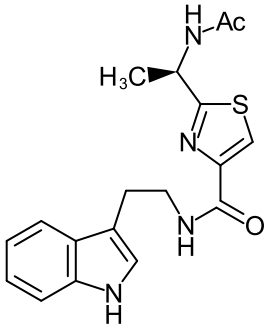
Cetophenones



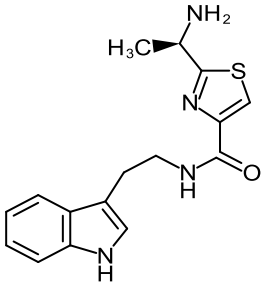
Bacillamide A



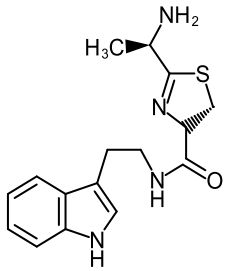
Bacillamide B



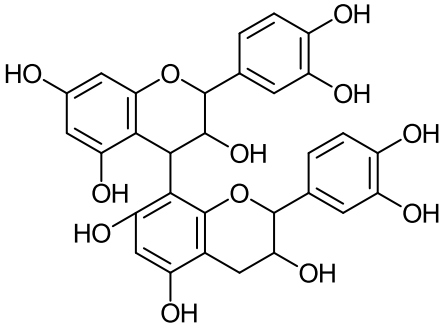
Bacillamide C



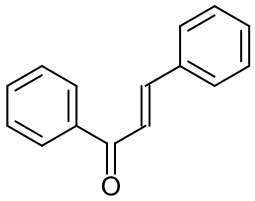
Bacillamide D



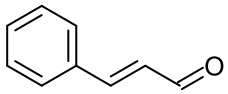
Bacillamide E aldehyde



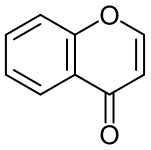
Biflavonoid procyanidin



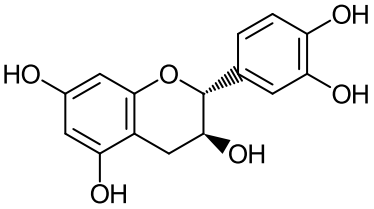
Chalcones



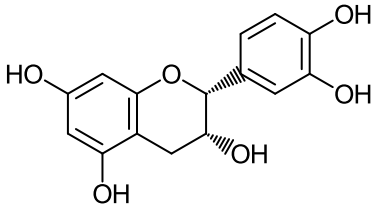
Cinnamic



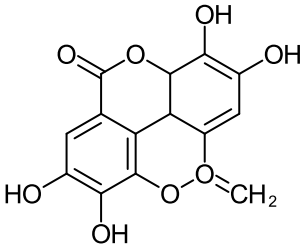
Chromones



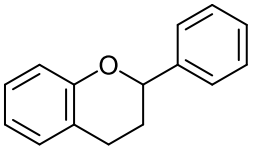
Catechin



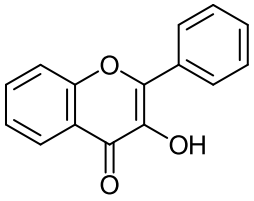
Epi-catechin



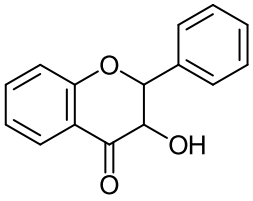
Ellagic acid



Flavonoids



Flavones



Flavon-3-ols

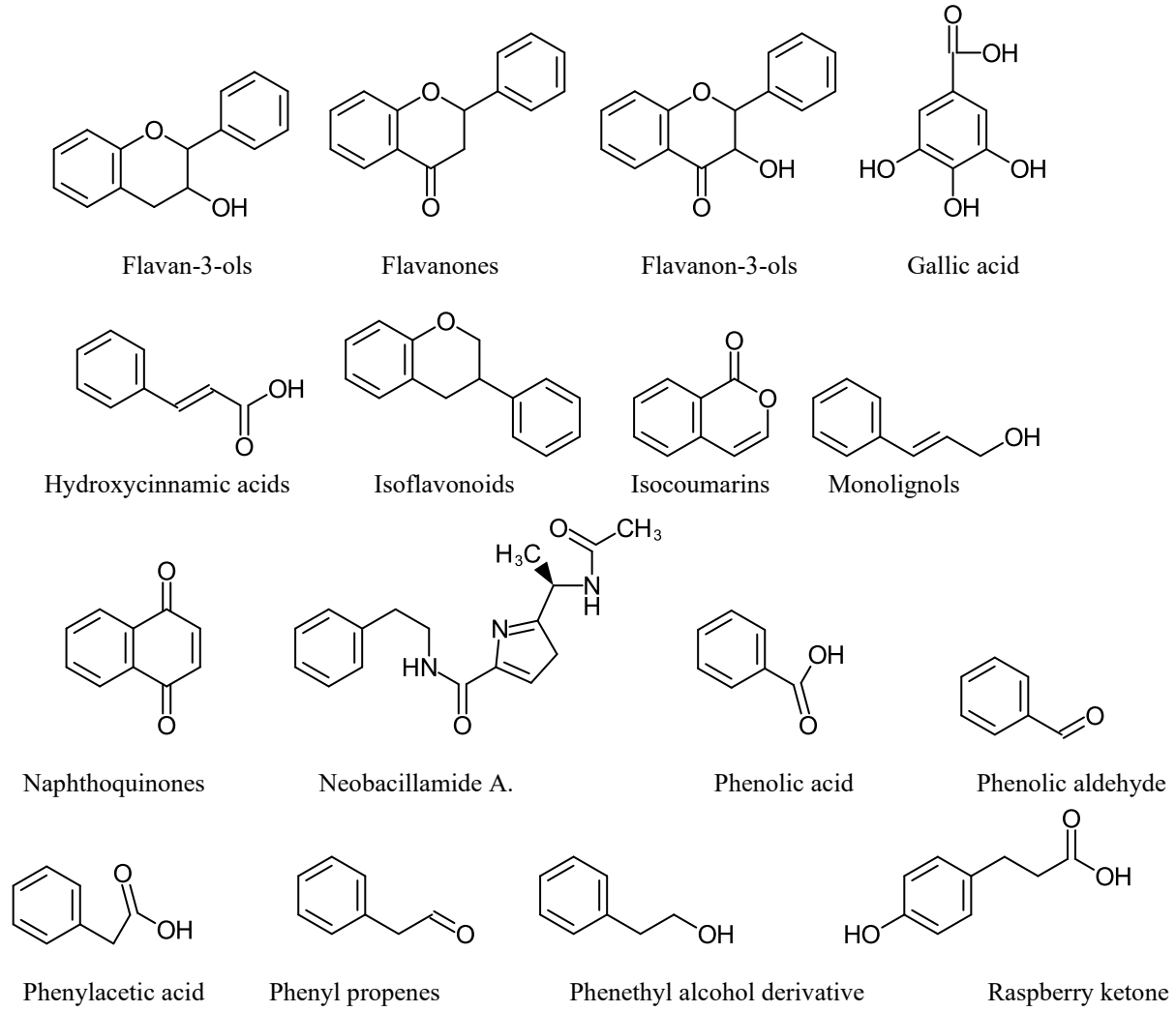


Fig. 5. Phytochemical groups and derivatives of flavonoid, phenols, tannins, and alkaloids from *Aloe* species. Adapted from: Multia *et al.* [73], Uivarosi *et al.* [74], Tsimogiannis *et al.* [75] and Vaca *et al.* [76]

1-picrylhydrazyl) activity and observed the activity range of 13.47 ± 0.72. Another study reported the potential antioxidant activity of methanol extract of *A. vera* gel was reported through hydrogen peroxide, DPPH, metal chelating, reducing power assay, and β carotene-linoleic assay [70]. Mahendiran *et al.* [62] documented the antioxidant activity with DPPH; hydrogen peroxide (H_2O_2), ABTS, superoxide radical, and hydroxyl radical scavenging assays in the aqueous extract of *A. vera* gel with a spectrophotometer. Lee *et al.* [84] verified the antioxidant activity of *A. vera* leaves in the methanol, acetonitrile, and aqueous extracts by ABTS and DPPH assays with positive results.

Benzidia *et al.* [79] found that the tannins in *A. vera* are the major phytochemicals that can inhibit free radicals with DPPH assay using three different fractions (F1, F2, and F3) of the acetone-aqueous extracts of *A. vera* gel. The reported ranges of antioxidant activity were 1.9, 3.74, 5.55, and 2.8 mg/ml correspondingly.

Quispe *et al.* [85] evaluated the ethanolic extract of *A. vera* gel, peels, roots, and flowers for antioxidant activity with DPPH, ABTS, and FRAP methods. The highest antioxidant activities of peel recorded were 2.43 mM ET/g MF in the DPPH assay, 34.32 mM ET/g MF in the ABTS assay, and 3.82 mM ET/g MF in the FRAP assay.

Tariq *et al.* [57] validated that the extracts from *A. vera* gel using methanol, ethanol, n-hexane, and aqueous solvents scavenged the free radicals and

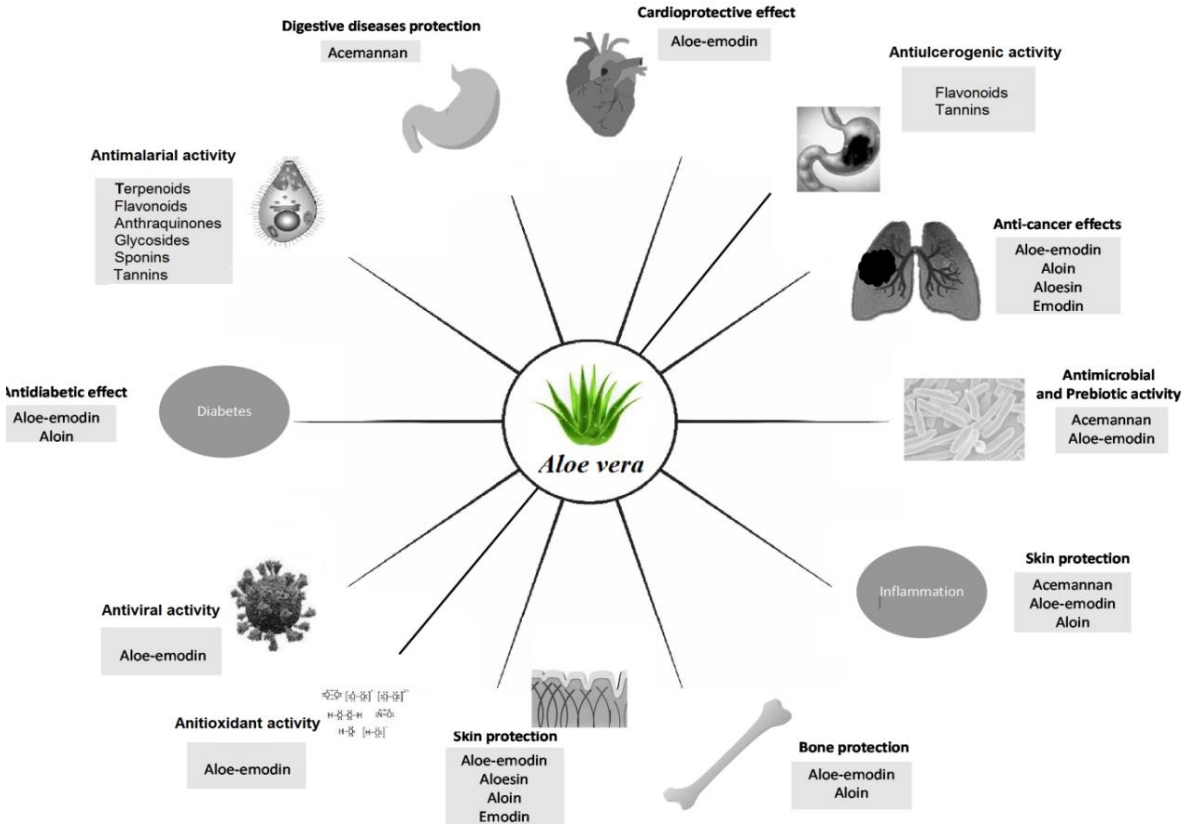


Fig. 6. Biological activities of some major chemical constituents of *A. vera*

Table 3. Anti-oxidant activity of *A. vera* extracts reported from different regions of the world

***Aloe* spp.**	**Part used**	**Extract used**	**Method of antioxidant activity**	**Reference**
	Leave gel	Ethanol	DPPH	[83]
	Leaves	Methanol	DPPH, metal chelating, and hydrogen peroxide	[70]
	Leaves gel	Acetone-aqueous	DPPH	[79]
	Leaves	Acetonitrile, aqueous, and methanol	ABTS and DPPH	[84]
	Peels, flowers, gel, and roots	Ethanol	ABTS, DPPH, and FRAP	[85]
A. vera	Leaves	Aqueous, ethanol, methanol, and n-hexane	DPPH and Ferric ion	[57]
	Leaves	ND	DPPH, FRAP, and TAC	[81]
	Flowers	ND	DPPH, ABTS, and FRAP	[80]
	Leave	Methanol	ABTS and DPPH	[86]
	Fresh latex of leaves	Lyophilized gel	Superoxide ions and hydrogen peroxide	[82]
	Leave gel	Acetone, aqueous, ethanol, and methanol,	DPPH	[58]
	Fresh leaves latex	Aqueous	DPPH	[27]

DPPH= 2,2- diphenyl-1-picrylhydrazyl, FRAP= Ferric ion reducing antioxidant power, ND= Not defined, TAC= Total antioxidant capacity, ABTS= 2,2'-azino-bis 3-ethylbenzothiazoline-6-sulfonic acid

the highest activities of ethanol extract with DPPH (11.82 to 75.54 %) andFRAP (228.9 ± 39.1 µg/mg) were recorded. The overall reported range of total antioxidant activity of different fractions of *A. vera* leaf was 28.77 ± 9.36 to 150.4 ± 25.8 µg EQ/mg. Yadav *et al.* (2020) evaluated *A. vera* leaves with peel (AL-P) and *A. vera* without –peel (AL-WP) where the free radical scavenging activity by FRAP was 156.83 ± 0.659 and 192.66 ± 1.416 mg Fe (II)E/g DWE, DPPH was 48.12 % and 68.88 % at 1mg/mL, NO scavenging potential was 38.43 % and 54.55 % at 0.1 mg/mL, and TAC was 89.66 ± 0.577 and 108.66 ± 1.000 AAE/g DWE.

Martínez-Sánchez *et al.* [80] documented the antioxidant activity of organic extract of *A. vera* flowers at different maturity stages with DPPH, ABTS, and FRAP radicals scavenging assays. The obtained values of antioxidation of free radicals were 179.91 ± 8.16 mg TEA/100g, which were highest in the first immature stage of the flower and decreased as the bud opens. Kaparakou *et al.* [86] reported the antioxidant potency of methanol extract of *A. vera* leaves gel with ABTS and DPPH assays and the range of recorded activities were 1.64 to 9.21 µmol Trolox mL^{-1} and 0.73 to 5.14 µmol Trolox $mL^{-1)}$ respectively. Ojha *et al.* [82] validated that *A. vera* possesses active phytochemicals with a considerable reduction in the oxidation of compounds and a decrease in the concentration of free radical superoxide ions (42.49 + 0.92 %) and hydrogen peroxide (35.95 + 0.97 %) in male albino rate when dosed with 6 mg/kg of extraction of *Aloe* plant.

Aida *et al.* [58] assessed the antioxidant activity of phytochemicals extracted from the *A. vera* gel using various solvents such as methanol (AVGM), ethanol (AVGE), aqueous (AVGW), and acetone (AVGA). Their obtained antioxidant activity results were highest for the *A. vera* gel extracted with methanol (1.015 ± 0.003) followed by AVGE (0.574 ± 0.007), AVGW (0.3525 ± 0.030) and AVGA (0.223 ± 0.008) expressed in Trolox equivalent per gram (mMTE/g). Another inquiry evaluated the *in vitro* antioxidant activity of aqueous extracts of fresh latex of *A. vera* leaves with the DPPH method where the recorded activity was 21.900 ± 0.0594 mg/ml [27].

The data compiled in this review for the antioxidant activity of *A. vera* showed that overall, 9 different organic extracts from various parts of the *A. vera* plant were proven to have potential antioxidant activities and DPPH and FRAP methods were the commonly used methods for the evaluation of antioxidant activity of *A. vera*. Nevertheless, it is proposed that some biological models to evaluate the activities of *A. vera* extracts on lipid peroxidation and activities on different enzymes with oxidizing potentials including adenine dinucleotide phosphate oxidase (NOX), nitric oxide synthase (NOS), monoxides and nicotinic and xanthine oxidoreductase (XO) etc should be explored.

3.5.2. Anti-inflammatory Activity

The activity of reducing redness, swelling, and pain in living organisms is termed anti-inflammatory activity. In many studies, the phytochemicals extracted from *A. vera* were reported (Table 4) to be active in reducing inflammatory effects [87-96]. In a study, Devaraj and Karpagam [88] tested the aqueous extract of *A. vera* leaf for its ability to reduce inflammation. They employed albino Wistar rats as substrates and varied extract concentrations and observed the effects of carrageenan and formaldehyde on rat paw edema to unveil the anti-inflammatory efficacy of *A. vera*. It was confirmed that the leaf extracts at a dosage of 600 mg/kg reduce the development of edoema brought on by carrageenan and formaldehyde with no mortality and gives anti-inflammatory effects.

Vijayalakshmi *et al.* [90] performed MMP inhibition tests on peripheral blood mononuclear cells (PBMC) isolated from heparinized venous blood using the ficoll diatrizoate gradient centrifugation method. *A. vera* aqueous extract was proven to inhibit the MMP-9 in a dose-dependent manner with gelatin zymography and RT-PCR procedures. Williams *et al.* [87] and Huseini *et al.* [89] corroborated that *A. vera* chromones inhibit the cyclooxygenase pathway and reduce the production from arachidonic acid of prostaglandin E2 in rats with carrageenin-induced paw edema. Whereas, mice with Croton oil-induced edema show a significant decrease in inflammation due to

Table 4. Reported anti-inflammatory activity of *A. vera* in different models

Inflammatory condition	Model/cells used	Extract/part used	Result	Reference
Carrageenan and formaldehyde-induced rat paw edema	Albino Wistar rats	Leaves aqueous extract	Decrease in the formation of edema	[88]
MMP inhibition studies on PBMC	Peripheral blood mononuclear cells (PBMC)	Leaves	Inhibition in MMP-9	[90]
HMA ointment on epidermal cell	Albino Wister rats	Leaves	Reduce edema	[91]
Immune-modulation of inflammatory arthritis condition	RBC membrane	Gel homogenate	Prevent the tissue damage & immune-modulation of inflammatory arthritis condition	[93]
Colitis	Albino Wistar rats	Leaves gel	Reduction in inflammatory agents in colonic tissue	[92]
Cytokine during an immune response	Human gingival fibroblasts	Leaves	Inhibition of TNF-α	[96]

TNF-α= Tumor necrosis factor, PBMC= Peripheral blood mononuclear cells, MMP-9= Matrix metallopeptida

β-sitosterol, campesterol, lupeol, and cholesterol in the *A. vera* gel.

Farzadinia *et al.* [91] documented the antiinflammatory effect of *A. vera* using it as honey milk *A. vera* ointment on the burning part of male albino rats. The burn was induced artificially and treated with HMA ointment containing dried *Aloe* gel powder, honey, and dry milk powder displayed observable anti-inflammatory effects, hence reducing edema by drying out, granulation, and closing of the wound edges, and increase in catalase activity. It also lowered the amount of collagen fiber and the hardness of the skin and increased the formation of connective tissue.

Paul *et al.* [93] reported the anti-inflammatory activity of *A. vera* gel homogenate for immune modulation of inflammatory arthritis conditions. It was validated that hypotonicity-induced (74.89 ± 1.26 %) and heat-induced (20.86 ± 0.77 %) RBC membrane lyses can be inhibited by the use of *A. vera* gel homogenate at a concentration of 1000 µg/ml. The same concentration can be used for the *in vitro* inhibition of protein denaturation (39.35 ± 4.25 %). The effect of *A. vera* was also assessed *in vivo*, and the results showed a reduction in tissue damage thus maintaining the normal functioning of TNF-α and Cox-2 gene expressions for the immune-modulation of inflammatory arthritis condition.

Naini *et al.* [92] investigated the anti-inflammatory activity of *A. vera* on experimental colitis (Inflammatory disease) in Wistar rats. Trinitrobenzenesulfonic acid (TNBS) was used for the induction of experimental colitis in rats and the extracts of *A. vera* were administered to the rats orally or rectally. Tumor necrosis factor, interleukin-6, and nitric oxide levels were higher in colonic tissue from rats with experimental colitis, and malondialdehyde and myeloperoxidase concentrations were also higher. *A. vera* treatment had a healing impact with an anti-inflammatory effect in rats.

Villarreal *et al.* [96] confirmed the anti-inflammatory effect of *A. vera* with ELISA assays (enzyme-linked immunosorbent assay) and reported an increase in the expression of cytokine and IL-1β (released during immune-response) levels in human gingival fibroblasts. The *A. vera* gel extract was able to decrease cyclooxygenase-2, 5-lipoxygenase biosynthesis, inducible nitric oxide synthase (iNOS), and TNF-α concentration hence proving a major role in lowering inflammation.

Overall, 9 organic extracts from *A. vera* were used *in vitro* and *in vivo*, showing anti-inflammatory action by inhibiting enzymes and factors such as TNF-α in humans. It is further proposed that extracts from *A. vera* should be evaluated against

more factors other than TNF-α and inflammation-causing pathways at the cellular level should be targeted to better explore the anti-inflammatory potentials of this plant.

3.5.3. Anticancer Activity

The activity of controlling the proliferation of cells or reduction of cancer-developing cells by *A. vera* extracts was reported by various authors [80-100] as shown in Table 5. Jose *et al.* [94] performed an MTT test to assess how well flavonoids derived from *A. vera, Mimosa pudica,* and *Phyllanthus niruri* inhibits the growth of the human breast carcinoma cell line (MCF-7) to evaluate their potent effects. The extracts of *A. vera* (IC_{50} = 54.970.36 g/ml), *P. niruri* (IC_{50} = 35.520.50g/ml), and *M. pudica* (IC_{50}= 35.520.50 g/ml) showed the highest inhibition against the tested cells. It was proposed that the extracts could be utilized effectively to treat cancer. In another study, the *in vitro* anticancer activities of *Calligonum comosum* and *A. vera* extracts against HepG2 cells by MTT test, the cells' viability was evaluated [96]. The cytotoxicity against HepG2 cells was individually boosted by the extracts in a time and dose-dependent manner. It was found that the extracts could, at least in part, via modulating apoptosis have anti-hepatocarcinogeniceffects.

Mahendiran *et al.* [62] reported the anti-cancer activity of aqueous extracts of *A. vera* gel against three cancerous cell lines such as cervical (HeLa), human breast adenocarcinoma (MCF-7) and epithelioma (Hep-2), and one normal human dermal fibroblast (NHDF) cell lines with MTT assay and found positive results.

Karpagam *et al.* [97] investigated human cancer cell lines HeLa, HepG2 (liver cancer cell line), and A549 were used to test the anticancer properties of the ethanolic leaf extract of *A. vera* using the 3-(4, 5-dimethylthiazole-2yl)-2, 5-diphenyl tetrazolium bromide assay (human lung adenocarcinoma epithelial cell line). Their outcomes confirmed the presence of several active compounds with anticancer potential in the ethanolic leaf extract of *A. vera*. In another study, *A. vera* gel was used as a capping and reducing agent for the creation of Ag@TiO2 nanoparticles. It was also found that the nanoparticles containing *A. vera* gel have activity against lung cancer cell lines (A549). After being administered systemically *in vitro*, the Ag@TiO2 NPs produced a significant amount of reactive oxygen species (ROS), which completely suppressed the development of cancer cells [98].

Mohamed and Masry [99] reported that *A. vera* gel extract and sunlight were used to synthesize silver nanoparticles with anti-cancer activity. After 72 hours of incubation with AgNPs-AV *in vitro*, a rapid fall in breast cancer cells was observed. This greenly synthesized nano-formulation offers a lot of promise to be studied from a variety of angles.

Ahmad *et al.* [101] evaluated the methanolic extracts of the healing herbs *Aloe castellorum* and *Aloe pseudorubroviolacea* to reduce the human colon cancer, cell line (HCT-116). The methanolic extract of *A. castellorum* has more cytotoxic activity than *A. pseudorubroviolacea* against HCT-116, which was confirmed with the GC-MS technique. Murugesan *et al.* [100] developed a potent and efficient anti-carcinogenic gel material that represents a cutting-edge medicine delivery technique. The cytotoxic tests revealed that a loaded phospholipid *A. vera* was biocompatible and was

Table 5. Anticancer activity of *A. vera* against various cancer cell lines

Cancer type	Study model/ assay	Cell line	Reference
Breast cancer	MTT assay	MCF-7	[94]
Liver cancer	*In vitro*	HepG2	[95]
Breast adenocarcinoma, cervical and epithelioma cancer	MTT assay	MCF-7, HeLa and Hep-2	[62]
Liver cancer	*In vitro*	HepG2, HeL, and A549	[97]
Blood cancer	Gas chromatography	HCT-116	[101]
Lung cancer	*In vitro*	A549	[98]
		MCF-7	[100]

MTT= 3-(4, 5-dimethyl thiazolyl-2)-2, 5-diphenyltetrazolium bromide

effective against the MCF-7 cancer cell line. The outcomes demonstrated that phytosome carriers have the potential to enhance *A. vera* oral delivery by opening the door for its use in the treatment of cancer. Overall, for the anticancer activity of *A. vera*, the data reviewed here substantiated that *A. vera* possesses a broad-spectrum anticancer activity by preventing the uncontrollable division of specific types of cancer cells like HCT-116, HepG2, HeLa, A549, MCF-7 and hence reduces the chances of blood cancer/leukaemia, liver cancer, breast and lung cancer. However, it is believed that the bioactive compounds present in different extracts of *A. vera* should be isolated and screened extensively against further cancer types, and interpreting the anticancer mechanism of action of *A. vera* extracts at the molecular level could be a possible research line to be explored for *Aloe* based cancer therapies.

3.5.4. Antidiabetic Activity

The high sugar level in the blood of the organisms causes diabetes and different health effects and high cholesterol in the body can be controlled by the extract of the *A. vera* plant. A lot of studies have reported the activity of *A. vera* extracts against diabetes [50-107] and the details are given in Table 6.

Mohamed [102] conducted an experiment on diabetic and control rats to delineate the consequence of *A. vera* gel extract in the control of diabetes. Experimentation was conducted on 4 groups of forty rats, and the result showed that oral administration of *A. vera* gel extract can reduce serum glucose, total cholesterol, and triacylglycerols. The hypoglycemic effect of *A. vera* gel extract may be due to the occurrence of hypoglycemic trace elements such as Cr, Zn, and Mn which potentiate insulin action. *A. vera* gel extract possesses an antidiabetic effect due to an increase in serum cholesterol and tri-acylglycerols.

In another inquiry, Babu *et al.* [50] studied the flower and epidermis extract of *A. vera* that possesses amylase and alpha-glucosidase with anti-diabetic properties. The flower and gel have phytoconstituents like proteins, phytosterols, carbohydrates, and mineral components making it suitable for use as an anti-diabetic drug. Their outcomes also validated that the gel and flower of *A. vera* are more anti-diabetic than the epidermis of leaves. Muñiz-Ramirez *et al.* [103] applied different assays for the evaluation and determination of methanol extract of *A. vera* for the prevention of diabetes caused by AGEs (Advanced glycation end products) formation. AVM was found to be effective

Table 6. Activity of *A. vera* plant extracts on different types of diabetes

Type of diabetes	Part used	Extract used	Concentration of extract	Results	Reference
All types of diabetes	Whole plant	Gel extract	ND	Decreased serum glucose, total cholesterol, and triacylglycerols	[102]
	Flower			Regulated blood glucose levels	[50]
AGEs induced diabetes	Whole plant	Methanol extract (AVM)	5 mg/ml	Inhibition of diabetes caused by AGEs	[103]
Streptozotocin induced diabetes	Leaves	Gel extract	ND	Restoration of the FPG and insulin levels	[104]
Type 2 diabetes				Normalized hyperglycemic conditions	[105]
Streptozotocin-induced diabetes mellitus	Whole plant			Anti-hyperglycemic in STZ-induced diabetic models	[107]
Diabetes	Leaves			Controlled blood glucose homeostasis	[108]
All types of diabetes	Whole plant	*A. vera* juice		Controlled blood sugar level	[106]

FPG= Fasting plasma glucose, ND= Not defined

against the formation of AGEs as well as carbonyl protein, CML, and fructosamine.

The best results were obtained at the concentration of 5 mg/ml of AVM. AVM also worked for the inhibition of enzymes like α-amylase and α-glucosidase. Whereas thiol group content was found to be increased with the period within 4 weeks. It was found that AVM is effective against AGEs and inhibits the formation of postprandial glucose, so reducing the chances of diabetes associated with AGE.

Babu *et al.* [104] observed the mechanisms involved in the mitigation of streptozotocin-induced diabetes in rats by using *A. vera* gel extract through the proteomics approach. They validated that *A. vera* extract (AVE) alleviates diabetes by regulating the pathways involved in the development of diabetes. In AVE, both the components carbohydrate fraction and polypeptide fraction (CF & PPF) synergistically work to regulate the insulin fraction. Hasan and Abdulla [105] studied the gel extracted from *A. vera* with polysaccharide which regulates the blood sugar level. The gel was prepared by dissolving 7.5 g *Aloe* gel in 100 ml distilled water.

Their outcomes confirmed that the hyperglycaemic state could be normalized by the treatment of *A. vera* extracts as they possess phytochemicals, minerals, and many primary metabolites that regulate blood glucose levels.

Haghani *et al.* [107] assessed the chemical properties of *A. vera* and its effects on Streptozotocin-induced diabetes mellitus. *A. vera* can control blood glucose, recover plasma insulin, decrease oxidative stress, and stimulate the production of collagen and elastin fibers and hence leading to the healing effect of STZ-induced diabetic ulcers. *A. vera* inhibits oxidative stress due to its properties of inducing antioxidant enzymes and glutathione levels. *Aloe vera* is also capable of reducing the manufacture of inflammatory mediators, thus causing the suppression of inflammatory responses in STZ-induced diabetic models.

Deora and Venkatraman [108] evaluated the active components of *A. vera,* which possess hypoglycaemic and hypolipidemic activities beneficial to cure diabetes. It not only reduces the hypoglycaemic and hypolipidemic activities beneficial to cure diabetes. It not only reduces the chances of diabetes but also maintains a healthy life by reducing the adverse impact of diabetes on the liver. It was found that the oral administration of *A. vera* gel extracts improves blood glucose homeostasis and imparts variations in glucose-lowering effects.

Ankita *et al.* [106] confirmed that by taking *Aloe* juice, a person can maintain sugar levels in the blood due to the presence of polysaccharides that can control blood sugar and cholesterol levels. The possession of polysaccharides makes it suitable for the treatment of all diabetic situations as it exhibits hyperglycemia properties and increases the glycerin level.

Overall, in this review, the collected data on the antidiabetic activity of *A. vera* validated that the extracts from different parts of the *Aloe* plant help in controlling blood glucose and restoring insulin levels. It is believed that the isolation of novel compounds with the exploration of their antidiabetic mechanisms of action at the cellular level from *A. vera* extracts is a promising research mark for *Aloe-based* diabetes treatment.

3.5.5. Antimicrobial Activity

The inhibition of the growth of microbes like bacteria, fungi, viruses, etc., or prevention of the formation of microbial colonies and their destruction can be controlled by the phytochemicals obtained from the extracts of various plant species [109, 110]. There is a huge literature available with reported antimicrobial activities of *A. vera* on various pathogenic microbial strains [22, 111-118] (Table 7).

Stanley *et al.* [111] reported the antimicrobial activities of ethanolic, methanolic, and aqueous extracts of *A. vera* against *Escherichia coli, Staphylococcus aureus,* and *Candida albican* through the agar diffusion technique. Gentamycin was considered a positive and dimethyl sulfur oxide (DMSO) was considered a negative control. Of all, methanol extract was best with maximum inhibitory effects followed by ethanolic and aqueous extracts of *A. vera*.

Table 7. Antimicrobial activity of *A. vera* against different pathogenic microbial strains

Aloe spp.	Part used	Extraction method	Microorganism tested	Result	Reference
A. vera	Gel from leaves	Ethanolic, methanoic, aqueous extraction	*E. coli, S. Aureus* and *Candida*	+	[111]
		Aqueous, ethanol and methanol	*A. niger* and *Rhizopus*	+	[22]
A. vera, A. volkensi, A. secundriflora		Methanolic extraction	*S. aureus, Bacillus subtilis, E. coli* and *Erwinia carotovora*	+	[112]
A. barbadensis		Methanolic, ethanolc and acetone extraction	*Bacillus* and *Staphylococcus*	+	[113]
		ND	*S. Aureus, E. coli, Pseudomonas* and *Enterobacter*	+	[114]
		Methanol	*E. coli, S. aureus, P. aeruginosa* and *Yeast*	*E. coli* showed positive results while *S. Aureus, P. Aeruginosa, yeast* showed negative results	[116]
		Ethanol with other fractions	*Salmonella tylhi, E. coli* and *Aeromonas*	*Aeromonas* showed positive results while *S. tylhi* and *E. coli* showed negative results	[115]
A. vera		Methanol	*H. pylori*	+	[118]
		Ethanol	*S. aureus, Streptococcus, E. coli* and *Salmonella*	Inhibits only gram-positive bacteria	[117]

+ = Represents positive result, – = Represents negative result, E. coli= Escherichia. coli, S. aureus= Staphylococcus aureus, P. aeruginosa= Pseudomonas aeruginosa, H. pylori= Helicobacter pylori

Dharajiya *et al.* [56] reported the anti-microbial activity of *Aloe* gel against strains of various types of bacteria and fungi such as *Bacillus cereus, Serratia marcescens, Pseudomonas aeruginosa, Aspergillus flavus, E. coli, Aspergillus oryzae, Trichoderma viride, Penicillium chrysogenum* with thin layer biography method. Their outcomes showed that the *A. vera* gel has inhibitory effects on *S. marcescens* and three species of *Aspergillus*.

Malik *et al.* [22] documented methanol and ethanol extracts of *A. vera* with significant inhibitory actions as compared to the aqueous extracts which showed lower inhibition against *A. niger* and *Rhizopus.* Their outcomes recommended *A. vera* leaves extracts using ethanol and methanol solvents as better antifungal agents.

Waithaka *et al.* [112] revealed antimicrobial properties of the methanolic extract of leaves of *A. vera*, *A. volkensii,* and *A. secundriflora*. Mueller Hinton agar and potato dextrose agar for bacteria and fungi was used respectively containing *S. aureus, Erwinia carotovora, Klebsiella pneumonia, E. coli, Bacillus subtilis, Candida albicans, Fusarium oxysporum*.

These extracts showed positive results with various zone of inhibition on the tested strains. Gorsi *et al.* [113] showed that gel from *Aloe barbendis* leaves extracted with ethanol, methanol, and acetone inhibits the growth of bacterial strains

like *Salmonella typhi, E. coli, B. subtilis,* and *S. aureus*. Among the tested extracts, ethanol extract was found to be more effective with 20.33 and 18.63 zone of inhibition for *Bacillus* and *Staphylococcus*, whereas, acetone extraction was found to be better than aqueous extract with 13.60 mm inhibition zone for *S. typhi.*

Anju *et al.* [114] proclaimed that silver nanoparticles made from *A. vera* can be used to inhibit microbial growth. After extraction of *A. vera* gel naturally containing acemannan, the formation of silver nanoparticles (AgNPs) was analyzed through a spectrophotometer with 400 nm absorption. Their results showed that AgNP has anti-microbial properties against both gram-positive (*S. aureus*) and gram-negative (*E. coli, P. aeruginosa,* and *Enterobacter*) bacteria. These activities were analyzed through the disk diffusion technique.

Ahmed *et al.* [116] evaluated the inhibitory effects of *A. vera* gel on different biological agents like bacteria, yeast, and fungi strains. For this purpose, the gel was extracted from leaves of *Aloe barbadensis miller* and after blending it properly powder was formed by the cold maceration method. Using the solid medium method anti-microbial activities were analyzed through nystatin and gentamycin tests for fungi and bacteria respectively. *E. coli* showed inhibition zones whereas *S. aureus* and *P. aeruginosa* showed resistance against *A. vera* gel extract. On the other hand, lower activity was observed against yeast i.e., *Candida albicans.* Bajalanlou and Pakbin [115] obtained the transparent gel from *A. barbadensis* using methanol, aqueous, dichloromethane (DSM), acetone, chloroform, n-hexane, and PET solvents and analyzed the antimicrobial activity through the disk diffusion method. The ethanol extracts displayed the overall highest inhibitory activity against *Aeromonas* with a 9.6 mm inhibition zone. The *n*-hexane extract showed the least anti-bacterial activity with 0.12 mm inhibition zones. Other extracts such as PET, chloroform, DCM, and acetone showed 0.25 to 2 mm inhibition zones whereas methanol and aqueous extracts showed 0.93 to 3.75 mm inhibition zones. *Aeromonas* showed resistance in PET fraction and *Pseudomonas* and *Chryseobacterium meningospticum* were resistant to the aqueous fraction of *A. barbadensis.* Yahya *et al.* [118] studied the methanol extracts of *A. vera* and found effective results against *Helicobacter pylori* which causes gastric infection in humans.

Vadiati Saberi *et al.* [117] evaluated the effect of *A. vera* gel on the growth of gram-positive and gram-negative bacteria. The acetoacetate compound extracted from the ethanol extract of the gel repressed growth of gram-positive bacteria as compared to gram-negative bacteria.

Overall, the collected data here for the antimicrobial activity of *Aloe* species authenticated that the *Aloe* extracts are effective against almost 12 bacterial and 7 fungal species. It is still believed that the elucidation of proper mechanisms of action of *Aloe* extracts against pathogenic microbes is a possible research line for advanced *Aloe-based* natural antimicrobial therapies.

3.6. *Aloe*-Based Food and Cosmeceutical Products

There is extensive data available on the uses of *A. vera* in cosmetic items such as night creams, soaps, cleansers, shampoos, suntan creams, and lotions (Table 8). In a study, Pounikar *et al.* [119] prepared a cosmetic herbal hydrogel using the inner part of *A. vera* leaf by mixing other substances through heating. Mainly, the mixing of acacia, hydroxyl propyl methyl cellulose (HPMC), and carbopol 934 in a ratio of 1:1:2 done to make a product to increase moisture content in the skin, making skin clear by increasing transparency, and smoothness and reducing skin microbial growth. According to Estrada-Caslillon *et al.* [120], *A. vera* leaves are used in cosmetics to make shampoo, hair dye, and hair health products and are reported to be used in rituals. Rajkumar *et al.* [121] proclaimed the use of *A. vera* gel in goat meat nuggets to enhance the quality of food items in India. Different quantities of 0 %, 2.5 %, and 5 % gel were applied to nuggets before storing them in the refrigerator for 9 days. As a result, 2.5 % of *A. vera* gel in nuggets was said to be preferred because it does not affect the yield and does not decrease the protein content like 5 % of *A. vera*. It enhanced the quality of the item by improving its texture and nutritive value.

Mahmoudi *et al.* [122] developed yogurt by adding *A. vera* extract and *Lactobacillus casei* in cow milk and then stored it for different days like

Table 8. Details of *Aloe*-based food and cosmeceutical products reported globally

Region	*Aloe* spp.	Part used	Food/ cosmetic product	Nutritional or cosmaceutical uses	Reference
India	*A. vera*	Leaves gel	Herbal hydrogel	Moisturise skin, make skin smooth and transparent and inhibit microbial growth	[131]
			Applied in meat nuggets	Increase nutritional parameters	[121]
Iran			Yoghurt	Provide better physiochemical and microbiological properties	[122]
India	*A. barbadensis*		Herbal ice cream	Increase storage capacity with improved taste	[125]
Indonesia	*A. chinensis baker*		Lotion	Reduce irritation, prevent dryness and clear skin	[123]
	A. vera		Face mask	Makes the skin clear, soft and clean and increases vitamin C content	[124]
India			Edible coating on fruits	Increase the shelf life of fruit, delay oxidative browning, increase storage capacity with high total soluble solids	[126]
			Khoa burfi	Increase moisture content with desirable taste for eating	[127]
	A. barbadensis		Peel off mask	Clear skin, UV protection and healing potentials	[3]
			Kulfi	A film of *A. vera* increase thickness and density and reduce water vapor transmission and increases taste	[129]
Pakistan	*A. vera*	Juice	Cookies	High quantity of crude fiber, proteins, *β*-carotene, and low fat with healthy food	[128]
		Leaves gel	Coating on strawberry fruit	Strawberry fruit coated with *A. vera* gel prolongs post-harvest life and maintains nutritional quality	[130]
India	*A. barbadensis miller*	Leaves gel	Mouthwash	Antiplaque and antimicrobial activity	[125]
		Leaves extract	Coating on pink guava	Retention of *β*-carotene increases the antioxidant capacity of guava	[132]

1, 3, 5, 7, and 10 at 4 ^{0}C. The results showed that the concentration of lactobacillus was less in yogurt with *A. vera* extract and did not affect the quality of yogurt when added with 2.5 % concentration rather it improved the physiochemical, microbiological, and sensory properties of yogurt.

Hendrawati *et al.* [123] developed an *A. vera* gel extract mask for improving skin quality. The composition of this *A. vera* mask was polyvinyl Pirolidon K30, poly vinyl chloride, methylparaben, propylparaben, BHT, and water in 7.55, 1.51, 0.10, 0.12 and 90.61 % respectively. The preferred amount of *A. vera* gel extract was 0.15 % for better results and was used to make the skin soft, enhance color and increase vitamin C content.

The same authors Hendrawati *et al.* [124] developed *A. vera* gel extract-based lotion by using gel from leaves. The ingredients in the lotion were heated and then melted by adding different concentrations of gel extract like 33.33 % in 50 ml, 50 % in 775 ml 66.67 % in 100 ml and 100 % in 150 ml. The best concentration with positive effects was said to be 66.67 % in 100 ml. It provided a lot of therapeutic effects on the skin like reducing

irritation, retaining moisture, preventing dryness, and making it clear.

Verma *et al.* [125] prepared herbal ice cream using *A. vera* and mint. *A. Barbandis* species was used to extract *A. vera* juice. The best concentration of ingredients was 10 % fat, 15 % sugar, 0.5 % stabilizer, and emulsifier, 20 % *A. vera* juice, and 0.5 % mint extract. After blending all ingredients, pasteurizing, homogenizing, and cooling, 10 % of *A. vera* juice and mint was added and then stored. The product was analyzed and total solids, acidity, protein, carbohydrates, and ash were determined showing the best chemical characteristics. The product showed good storage capacity and taste and due to *A. vera* juice, it increases blood circulation, and detoxification by improving the digestive system.

Another edible coating of *A. vera* gel was done by Kumar and Bhatnagar [126] on oranges, grapes, sweet cherries, and papaya. The gel coating increased antifungal activity and shelf life along and reduced moisture content and the appearance of brown color due to oxidation. It maintained the time of maturation of fruits by increasing storage capacity. In oranges, it caused no weight loss and increased acidity and total soluble solids.

Chaudhary *et al.* [127] developed Khoa Burfi by adding *A. vera* juice at different concentrations (5, 10, 15 and 20 %). The optimum concentration was found to be 15 % after analyzing moisture, pH, color, and texture. The pH and moisture content were increased due to *A. vera* juice and adhesiveness and hardness were decreased. The addition of *A. vera* showed improved shelf life of burfi.

Masood *et al.* [128] developed *A. vera-based* cookies where the ingredients of the cookies were wheat, butter, sugar, salt, baking soda, and water with 10, 20, and 30 % of *A. vera*. They found improved moisture content, crude fiber, protein content, beta carotene, and reduced fat. Other properties of the product like flavor, texture, and color were also analyzed and the product was found to be very effective for health.

Asthana *et al.* [3] developed a peel-off mask for skin care as a product using gel from *A. Barbadensis* leaves. This mask was prepared by mixing the gel with montmorillonite (MMT) clay which is helpful in external detoxification and polyvinyl chloride (PVC) which is environment-friendly and provides homogeneity to the skin. This product was useful in protecting skin from UV radiation with healing properties. Moreover, it has antiseptic properties and an antiaging effect for batter and shiny skin.

In India, Mahajan *et al.* [129] prepared *A. vera*-based edible film for frozen dairy products using kulfi as a modal product. A standardized file was prepared by mixing carrageenan, glycerol, and gel from *A. barbadensis*. The film reduced lipid oxidation, water vapor transmission, microbial growth, and antioxidant capacity with an increase in storage capacity, thickness, and density.

Haider *et al.* [130] studied the effects of *A. vera* gel coating on the shelf life and nutritional quality of strawberry fruit. They claimed that the use of 15 % *A. vera* gel as a coating material in strawberries prolongs post-harvest life and maintains nutritional quality for a considerable duration.

Pattnaik *et al.* [131] developed a mouthwash using *A. vera* gel which showed antiplaque and antibacterial activities. *A. vera* gel can also be used to prevent the deposition on teeth where bacteria can proliferate which shows its antiplaque activity for healthy teeth.

According to Otalora *et al.* [132], a mucilage extract from *A. vera* leaf is used as coating material with small capsules on pink guava using a spray-drying method. The coating with beta carotene in fruit increased the antioxidant activity and total carotenoid contents by 14 % and 36 %. The coating keeps the fruit healthy, acted as a natural colorant, and increased the content of dietary fiber.

Overall, the data reviewed here validated the applications of different *Aloe*-based food and cosmetics products such as cosmetic herbal hydrogel, lotion, *A. vera* gel extract mask, peel-off mask, mouthwash, and food products including meat nuggets, yogurt, herbal ice cream, edible coating of *A. vera* on fruits, khoa burfi, Kulfi, cookies, coating on pink guava.

It is believed that the consumption of *Aloe-based* food products and the utilization of *Aloe-based* cosmetics can be improved and increased by

adopting suitable procedures. Conversely, the study of complications associated with some specific conditions and with some specific compounds in *Aloe* is the possible research line for the valuation of safe utilization of *Aloe-based* food and cosmetic products.

4. CONCLUSION

In the history of plant-based medications, *A. vera* has a major contribution because of its frequent use for the treatment of various diseases. It is one of the most globally utilized plants as its extracts provide therapeutic effects due to the presence of a wide variety of phytoconstituents. The phytochemicals from *A. vera* extracts are employed against reactive oxygen species, diabetes, cancer, inflammation, and bacterial and fungal microbes. The data presented here on *A. vera* could be very vital to advance the research of clinical uses and the development of *Aloe-based* food and medicinal products with improved nutrition and therapeutic effects. It is recommended that more controlled investigations and clinical trials are prerequisites in the future to substantiate the outcomes and efficacies of *A. vera* under different circumstances. Also, some complications associated with specific compounds in *Aloe* should be addressed for the safer consumption of *Aloe-based* food products and the utilization of cosmetic products.

5. CONFLİCT OF INTEREST

The authors declared that there is no competing interests.

6. REFERENCES

1. P. Danish, Q. Ali, M.M. Hafeez, and A. Malik. Antifungal and antibacterial activity of *Aloe vera* plant extract. *Biological and Clinical Sciences Research Journal* (1): 2708-2261(2020).
2. F. Sayar, A.H. Farahmand, and M. Rezazadeh. Clinical efficacy of *Aloe vera* toothpaste on periodontal parameters of patients with gingivitis—A randomized, controlled, singlemasked clinical trial. *The Journal of Contemporary Dental Practice* 22(3): 242-247 (2021).
3. N. Asthana, K. Pal, A.A. Aljabali, M.M. Tambuwala, F.G. de Souza, and K. Pandey. Polyvinyl alcohol (PVA) mixed green–clay and aloe vera based polymeric membrane optimization: Peel-off mask formulation for skin care cosmeceuticals in green nanotechnology. *Journal of Molecular Structure* 1229: 129592 (2021).
4. A. Farid, H. Haridyy, S. Ashraf, S. Ahmed, and G. Safwat. *Aloe vera* gel as a stimulant for mesenchymal stem cells differentiation and a natural therapy for radiation induced liver damage. *Journal of Radiation Research and Applied Sciences* 15(3): 270-278 (2022).
5. R.P. Shirsat. Ethnomedicinal uses of some common bryophytes and pteridophytes used by tribals of Melghat region (Ms), India. *Ethnobotanical Leaflets* 2008(1): 92 (2008).
6. W. Hussain, L. Badshah, M. Ullah, M. Ali, A. Ali, and F. Hussain. Quantitative study of medicinal plants used by the communities residing in Koh-e-Safaid Range, northern Pakistani-Afghan borders. *Journal of Ethnobiology and Ethnomedicine* 14(1): 1-18 (2018).
7. D. Ali, A.H. Shah, K.R. Khan, M. Farooq, M. Hussain, G.M. Shah, and A. Mehmood. Ethnomedicinal exploration of tracheophytes of Hangrai, district Mansehra, Khyber Pakhtunkhwa, Pakistan. *Journal of Biodiversity and Environmental Sciences* 14(1): 105-120 (2019).
8. E. Hernández-Rodríguez, and C. Delgadillo-Moya. The ethnobotany of bryophytes in Mexico. *Botanical Sciences* 99(1): 13-27 (2021).
9. W. Tang, G. Eisenbrand. Chinese drugs of plant origin: chemistry, pharmacology, and use in traditional and modern medicine. *Springer Science & Business Media* 27:3145-543210 (2013).
10. A.K. Shakya. Medicinal plants: Future source of new drugs. *International Journal of Herbal Medicine* 4(4): 59-64 (2016).
11. S. Madani, B. Amel, H. Noui, S. Djamel, and H. Hadjer. An ethnobotanical survey of galactogenic plants of the Berhoum District (M'sila, Algeria). *Journal of Intercultural Ethnopharmacology* 6(3): 311 (2017).
12. N. Jadid, E. Kurniawan, C.E.S. Himayani, I. Prasetyowati, K.I. Purwani, W. Muslihatin, D. Hidayati, and I.T.D. Tjahjaningrum. An ethnobotanical study of medicinal plants used by the Tengger tribe in Ngadisari village, Indonesia. *Plos One* 15(7): e0235886 (2020).
13. F. Zatout, B. Benarba, A. Bouazza, B. Babali, N.N. Bey, and A. Morsli. Ethnobotanical investigation on medicinal plants used by local populations in Tlemcen National Park (extreme North West Algeria). *Mediterranean Botany* 15(30): 12 (2021).
14. G. Dastagir, S. Bibi, N. U. Uza, R.W. Bussmann, and I. Ahmad. Microscopic evaluation, ethnobotanical and phytochemical profiling of a traditional drug *Viola odorata L.* from Pakistan. *Ethnobotany Research and Applications* 25: 1-24 (2023).
15. M. Saxena, J. Saxena, R. Nema, D. Singh, and A. Gupta. Phytochemistry of medicinal plants. *Journal of pharmacognosy and phytochemistry* 1(6) (2013).

16. A. Hussain, M. Q. Hayat, S. Sahreen, Q.U. Ain, and S.A.I. Bokhari. Pharmacological promises of genus *Artemisia* (*Asteraceae*): a review. *Proceedings of the Pakistan Academy of Sciences: B. Life and Environmental Sciences* 54(4): 265-287 (2017).
17. I. Hamdeni, I. Yangui, A. Sanaa, S. Slim, M. Louhaichi, C. Messaoud, A. Boulila, and T. Bettaieb. *Aloe vera* L. (Asphodelaceae): Supplementation of in-vitro culture medium with *Aloe vera* gel for production of genetically stable plants. *South African Journal of Botany* 147:1206-1213 (2022).
18. A. Hussain, M.Q. Hayat, and S.A.I. Bokhari. Some important species of the genus *Artemisia* L (Asteraceae) from northeastern (Gilgit-Baltistan) Pakistan and their folk medicinal uses. *Proceedings of the Pakistan Academy of Science: B Life and Environmental Sciences* 57(2): 35-48 (2020).
19. S. Sharma, and S. Sharma. *Aloe vera*: An ancient herb its components and applications. *Journal of Pharmacognosy and Phytochemistry* 7(6): 514-516 (2018).
20. E.V. Christaki, and P.C. Florou-Paneri. *Aloe vera*: a plant for many uses. *Journal of Food Agriculture and Environment* 8(2): 245-249 (2010).
21. D.I. Sánchez-Machado, J. López-Cervantes, R. Sendón, and A. Sanches-Silva. *Aloe vera*: Ancient knowledge with new frontiers. *Trends in Food Science & Technology* 61: 94- 102 (2017).
22. N.Z. Malik, M. Riaz, Q.Q. Noshad, N. Rashid, Q.U. Ain, and A. Hussain. Morphological, phytochemical and antifungal analysis of *Aloe vera* L. leaf extracts. *Asian Journal of Agriculture and Biology* 5(4): 177-187 (2017).
23. A.F. Nia, A.F. Sardrodi, M.M. Habibi, and S. Bahman. Morphological and physiological changes of *Aloe* (*Aloe barbadensis Miller*.) in response to culture media. *International Journal of Agronomy and Agricultural Research* 6(6): 100-105 (2015).
24. R.M. Beiu, V.F. Duma, C.A. Mnerie, A.C. Beiu, M.A. Dochia, L. Copolovici, G. Dobre, A. Bradu, and A. Podoleanu. Optical coherence tomography versus microscopy for the study of *Aloe vera* leaves. *In: Optics, Photonics and Digital Technologies for Imaging Applications VII* 12138: 60-68 (2022).
25. S. Bendjedid, R. Djelloul, A. Tadjine, C. Bensouici, and A. Boukhari. In vitro Assessment of Total Bioactive Contents, Antioxidant, Anti-Alzheimer and Antidiabetic Activities of Leaves Extracts and Fractions of Aloe vera. *Journal of Natural Sciences* 19, pp.469-485 (2020).
26. A. Kumar, A. Mahajan, and Z. Begum. Phytochemical screening and in vitro study of free radical scavenging activity of flavonoids of *Aloe vera. Research Journal of Pharmacy and Technology* 13(2): 593-598 (2020).
27. C.K. Nakiguli, V.J. Kosgei, J.K. Cherutoi, and J. Odda. Quantification of aloin in *Aloe barbadensis Miller* leaf gel and latex from selected regions of Kenya. *Open Access Library Journal* 9(4): 1-12 (2022).
28. A. Joseph, and S.J. Raj. Pharmacognostic and phytochemical properties of *Aloe vera* linn an overview. *International Journal of Pharmaceutical Sciences Review and Research* 4(2): 106-110 (2010).
29. O.M. Grace, S. Buerki, M. R. Symonds, F. Forest, A.E. van Wyk, G.F. Smith, R.R. Klopper, C.S. Bjorå, S. Neale, S. Demissew, and M.S. Simmonds. Evolutionary history and leaf succulence as explanations for medicinal use in *Aloe* and the global popularity of *Aloe vera*. *BMC evolutionary biology* 15(1): 1-12 (2015).
30. A. Gupta, and S. Rawat. Clinical importance of *Aloe vera*. *Research Journal of Topical and Cosmetic Sciences* 8(1): 30 (2017).
31. M. Tiwari, and M. Upadhayay. The medicinal plant components and applications (*Aloe vera*). *Journal of Medicinal Plants Studies* 6(3): 89-95 (2018).
32. R. Rahimi-Dehgolan, Z. Tahmasebi Sarvestani, S.A. Rezazadeh, and A. Dolatabadian. Morphological and physiological characters of *Aloe vera* subjected to saline water irrigation. *Journal of herbs, spices & medicinal plants* 18(3): 222-230 (2012).
33. E. Raphael. Phytochemical constituents of some leaves extract of *Aloe vera* and Azadirachta indica plant species. *Global Advanced Research Journal of Environmental Science and Toxicology* 1(2): 014-017 (2012).
34. B.B. Petrovska. Historical review of medicinal plants usage. *Pharmacognosy Reviews* 6:1-5 (2012).
35. A. Hussain. The genus *Artemisia* (*Asteraceae*): a review on its ethnomedicinal prominence and taxonomy with emphasis on foliar anatomy, morphology, and molecular phylogeny. *Proceedings of the Pakistan Academy of Science: B Life and Environmental Sciences* 57: 1-28 (2020a).
36. A. Hussain. A preliminary up-to-date review on Pakistani medicinal plants with potential antioxidant activity. *RADS Journal of Biological Research and Applied Sciences* 11(1):61-88 (2020b).
37. E. Estrada-Castillón, M. Garza-López, J.A. Villarreal-Quintanilla, M.M. Salinas-Rodríguez, B.E. Soto-Mata, H. González-Rodríguez, D.U. González-Uribe, I. Cantú-Silva, A. Carrillo-Parra, and C. Cantú-Ayala. Ethnobotany in Rayones, Nuevo León, México. *Journal of Ethnobiology and Ethnomedicine* 10(1): 1-13 (2014).
38. Y.Y. Siew, S. Zareisedehizadeh, W.G. Seetoh, S.Y. Neo, C.H. Tan, and H.L. Koh. Ethnobotanical survey of usage of fresh medicinal plants in Singapore. *Journal of Ethnopharmacology* 155(3): 1450-1466 (2014).

39. K. Manvitha, and B. Bidya. *Aloe vera*: a wonder plant its history, cultivation and medicinal uses. *Journal of Pharmacognosy and Phytochemistry* 2(5): 85-88 (2014).
40. A. Asase, and D. T. Yohonu. Ethnobotanical study of herbal medicines for management of diabetes mellitus in Dangme west district of southern Ghana. *Journal of Herbal Medicine* 6(4): 204-209 (2016).
41. E. F. Fongnzossie, Z. Tize, P.F. Nde, C.N. Biyegue, I.B. Ntsama, S.D. Dibong, and B.A. Nkongmeneck. Ethnobotany and pharmacognostic perspective of plant species used as traditional cosmetics and cosmeceuticals among the Gbaya ethnic group in Eastern Cameroon. *South African Journal of Botany* 112: 29-39 (2017).
42. H.M. Amir, O.M. Grace, E. Wabuyele, and M.L.K. Manoko. Ethnobotany of *Aloe* L.(Asphodelaceae) in Tanzania. *South African Journal of Botany* 122: 330-335 (2019).
43. O.S. Oladeji, A.P. Oluyori, D.T. Bankole, and T.Y. Afolabi. Natural products as sources of antimalarial drugs: ethnobotanical and ethnopharmacological studies. *Scientifica* Article ID 7076139, 22 pages (2020).
44. A. Roy, and S. Janbandhu. An ethnobotanical analysis on flora-medicine continuum among the tribal inhabitants of Ratnagiri and Palghar district, Maharashtra, India. *Ethnobotany Research and Applications* 20:1-23 (2020).
45. S. Abihudi. Ethnobotanical use, threat status and optimal environmental germination conditions for conservation of *Aloe* species in Tanzania. (2022). https://dspace.nmaist.ac.tz/handle/20.500.12479/1548
46. L.K. Keter, and P.C. Mutiso. Ethnobotanical studies of medicinal plants used by Traditional Health Practitioners in the management of diabetes in lower eastern Province, Kenya. *Journal of Ethnopharmacology* 139(1): 74-80 (2012).
47. M. Al-Fatimi. Ethnobotanical survey of medicinal plants in central Abyan governorate, Yemen. *Journal of Ethnopharmacology* 241: 111973 (2019).
48. R.I. Asif. Phytochemical and ethnobotanical effect of *Aloe vera*. NUST *Journal of Natural Sciences* (2021).
https://pdfs.semanticscholar.org/2013/8c3304d3cdfe50dda8855519f3f8651c1a57.pdf
49. F.M. Mutie, L.L. Gao, V. Kathambi, P.C. Rono, P.M. Musili, G. Ngugi, G.W. Hu, and Q.F. Wang. An ethnobotanical survey of a dryland botanical garden and its environs in Kenya: the Mutomo hill plant sanctuary. *Evidence-Based Complementary and Alternative Medicine* 22 pages (2020). Article ID 1543831.
50. S.N. Babu, S. Govindarajan, M.A. Vijayalakshmi, and A. Noor. Evaluation of in vitro anti-diabetic and anti-oxidant activities and preliminary phytochemical screening of gel, epidermis and flower extract of *Aloe vera*. *Research journal of pharmacy and technology* 12(4): 1761-1768 (2019).
51. G. Sathyaprabha, S. Kumaravel, D. Ruffina, and P. Praveenkumar. A comparative study on antioxidant, proximate analysis, antimicrobial activity and phytochemical analysis of *Aloe vera* and *Cissus quadrangularis* by GC-MS. *Journal of Pharmacy Research* 3(12): 2970-2973 (2010).
52. D.K. Patel, K. Patel, and S.P. Dhanabal. Phytochemical standardization of *Aloe vera* extract by HPTLC techniques. *Journal of Acute Disease* 1(1): 47-50 (2012).
53. A. Ray, S.D. Gupta, and S. Ghosh. Evaluation of anti-oxidative activity and UV absorption potential of the extracts of *Aloe vera* L. gel from different growth periods of plants. *Industrial Crops and Products* 49: 712-719 (2013).
54. C.Ibe, C.C. Jacobs, C. Imo, K.U. Osuocha, and M.U. Okoronkwo. Evaluation of the antioxidant activities of *Psidium guajava* and *Aloe vera*. *British Journal of Pharmaceutical Research* 4(3): 397 (2014).
55. U. Taukoorah, and M.F. Mahomoodally. Crude *Aloe vera* gel shows antioxidant propensities and inhibits pancreatic lipase and glucose movement in vitro. *Advances in Pharmacological and Pharmaceutical Sciences* 2016 (2016).
56. D. Dharajiya, N. Pagi, H. Jasani, and P. Patel. Antimicrobial activity and phytochemical screening of *Aloe vera* (*Aloe barbadensis Miller*). *International Journal of Current Microbiology and Applied Sciences* 6(3): 2152-2162 (2017).
57. H. Tariq, M. Zia, S.A. Muhammad, S.A. Khan, N. Fatima, A. Mannan, A.M. Abbasi, and M. Zhang. Antioxidant, antimicrobial, cytotoxic, and protein kinase inhibition potential in *Aloe vera* L. *BioMed Research International* 14 pages (2019). Article ID 6478187.
58. P.U.I.A. Aida, V.S. Chedea, A.M. Levai, I.C. Bocsan, and A.D. Buzoianu. Pot *Aloe vera* gel–a natural source of antioxidants. *Notulae Botanicae Horti Agrobotanici ClujNapoca* 50(2): 12732-12732 (2022).
59. O.A. Wintola, and A.J. Afolayan. Phytochemical constituents and antioxidant activities of the whole leaf extract of *Aloe ferox* Mill. *Pharmacognosy Magazine* 7(28):325-33 (2011).
60. S. Kumar, A. Yadav, M. Yadav, and J.P. Yadav. Effect of climate change on phytochemical diversity, total phenolic content and in vitro antioxidant activity of *Aloe vera* (L.) Burm. f. *BMC Research Notes* 10(1): 1-12 (2017).
61. M. Cardarelli, Y. Rouphael, M. Pellizzoni, G. Colla, and L. Lucini. Profile of bioactive secondary metabolites and antioxidant capacity of leaf exudates

from eighteen *Aloe* species. *Industrial Crops and Products* 108: 44-51(2017).
62. D. Mahendiran, G. Subash, D. Arumai Selvan, D. Rehana, R. Senthil Kumar, and A. Kalilur Rahiman. Biosynthesis of zinc oxide nanoparticles using plant extracts of *Aloe vera* and *Hibiscus sabdariffa*: Phytochemical, antibacterial, antioxidant and anti-proliferative studies. *Bio Nano Science* 7(3): 530-545 (2017).
63. S.F. Faid. Phytochemical Constituents from *Aloe vera* leaves and garden grass seeds and their utilization as anticancer activity. *International Journal of Engineering Research & Technology* 8(11) (2019).
64. I.Kahramanoğlu, C. Chen, J. Chen, and C. Wan. Chemical constituents, antimicrobial activity, and food preservative characteristics of Aloe vera gel. *Agronomy*, 9(12), p.831 (2019).
65. R.B. Usman, M. Adamu, I.M. Isyaku, and H.A. Bala. Quantitative and qualitative phytochemicals and proximate analysis of *Aloe vera* (*Aloe barbadensis miller*). *International Journal of Advanced Academic Research* 6(1): 95-104 (2020).
66. F. Iqbal, and A. Ahmed. Antibacterial activity of *Aloe barbadensis* Mill. *Polish Journal of Environmental Studies* 30(4): 3637-3643 (2021).
67. S. Bendjedid, I. Bazine, A. Tadjine, R. Djelloul, A. Boukhari, and C. Bensouici. Analysis of phytochemical constituents by using LC-MS, antifungal and allelopathic activities of leaves extracts of *Aloe vera*. *Jordan Journal of Biological Sciences* 15(1): 21-28 (2022).
68. M.M. Arsene, P.I. Viktorovna, G.V. Sergei, F. Hajjar, Y.N. Vyacheslavovna, Z.A. Vladimirovna, V.E. Aleksandrovna, S.A. Nikolayevich, and N. Sachivkina. Phytochemical analysis, antibacterial and antibiofilm activities of *Aloe vera* aqueous extract against selected resistant gram-negative bacteria involved in urinary tract infections. *Fermentation* 8(11): 626 (2022).
69. P.K. Mukherjee, N.K. Nema, N. Maity, K. Mukherjee, and R.K. Harwansh. Phytochemical and therapeutic profile of *Aloe vera*. *Journal of Natural Remedies* 1-26 (2014).
70. S. Kumar, M. Yadav, A. Yadav, P. Rohilla, and J.P. Yadav. Antiplasmodial potential and quantification of aloin and aloe-emodin in *Aloe vera* collected from different climatic regions of India. *BMC Complementary and Alternative Medicine* 17(1): 1-10 (2017).
71. P. Goyal, R. Chhabra, and S. Kaur. *Aloe vera*: Phytochemical composition and its pharmacological properties. *Indian Journal of Agricultural Biochemistry* 35(1): 15-19 (2022).
72. A.M. Al-Wajih, A.M. El-Shaibany, S.M. Raweh, and M.M. El–Aasser. Preliminary phytochemical screening for various secondary metabolites, quantitative and qualitative analysis of Yemeni *Aloe vera* and *Aloe vacillans* flower extracts. *GSC Biological and Pharmaceutical Sciences* 21(2): 202-210 (2022).
73. E. Multia. Potential and utilization of water extracts from spruce bark. *School of Chemical Engineering* (2018). DOI:10.13140/RG.2.2.18886.16963/1
74. V. Uivarosi, A.C. Munteanu, and G.M. Nițulescu. An overview of synthetic and semisynthetic flavonoid derivatives and analogues: perspectives in drug discovery. *Studies in Natural Products Chemistry* 60(2019): 29-84 (2019).
75. D. Tsimogiannis, and V. Oreopoulou. Classification of phenolic compounds in plants. In: *Polyphenols in plants* 263-284 (2019). Academic Press.
76. J. Vaca, F. Salazar, A. Ortiz, and E. Sansinenea. Indole alkaloid derivatives as building blocks of natural products from *Bacillus thuringiensis* and *Bacillus velezensis* and their antibacterial and antifungal activity study. *The Journal of Antibiotics* 73(11): 798-802 (2020).
77. L.S. Lai, S.T. Chou, and W.W. Chao. Studies on the antioxidative activities of Hsian-tsao (*Mesona procumbens* Hemsl) leaf gum. *Journal of Agricultural Food Chemistry* 49:963-8 (2001).
78. K. Tkacz, A. Wojdyło, I.P. Turkiewicz, L. Bobak, and P. Nowicka. Anti-oxidant and anti-enzymatic activities of Sea buckthorn (*Hippophae rhamnoides* L.) fruits modulated by chemical components. *Antioxidants (Basel)* 8(12): 618 (2019).
79. B. Benzidia, M. Barbouchi, H. Hammouch, N. Belahbib, M. Zouarhi, H. Erramli, N.A. Daoud, N. Badrane, and N. Hajjaji. Chemical composition and antioxidant activity of tannins extract from green rind of *Aloe vera* (L.) Burm. F. *Journal of King Saud UniversityScience* 31(4): 1175-1181 (2019).
80. A. Martínez-Sánchez, M.E. López-Cañavate, J. Guirao-Martínez, M.J. Roca, and E. Aguayo. *Aloe vera* flowers, a byproduct with great potential and wide application, depending on maturity stage. *Foods* 9(11): 1542 (2020).
81. R.B. Yadav, B. Kumar, A. Vats, S.N. Singh, D.P. Pathak, and R. Arora. Development, standardization and validation of analytical method for quality assurance and quality control of *Aloe*-based pharmaceuticals and nutraceuticals. *Trakia Journal of Sciences* 4: 294-309 (2020).
82. S. Ojha, K. Sonker, M. Pandey, and S. Saraf. *Aloe vera* gel: A potent nutraceutical. *Journal of Natural Pharmaceuticals* 2(1): 36-36 (2011).
83. A.Vega-Gálvez, E. Uribe, M. Perez, G. Tabilo-Munizaga, J. Vergara, P. Garcia-Segovia, E. Lara, and K. Di Scala. Effect of high hydrostatic pressure pretreatment on drying kinetics, antioxidant activity,

firmness and microstructure of *Aloe vera* (*Aloe barbadensis Miller*) gel. *LWT-Food Science and Technology* 44(2): 384-391 (2011).

84. S. Lee, S.G. Do, S.Y. Kim, J. Kim, Y. Jin, and C.H. Lee. 2012. Mass spectrometry-based metabolite profiling and antioxidant activity of *Aloe vera* (*Aloe barbadensis Miller*) in different growth stages. *Journal of Agricultural and Food Chemistry* 60(45): 11222-11228.
85. C. Quispe, M. Villalobos, J. Bórquez, and M. Simirgiotis. Chemical composition and antioxidant activity of *Aloe vera* from the Pica Oasis (Tarapacá, Chile) by UHPLCQ/Orbitrap/MS/MS. *Journal of chemistry* 12 pages (2018). Article ID 6123850.
86. E.H. Kaparakou, C.D. Kanakis, M. Gerogianni, M. Maniati, K. Vekrellis, E. Skotti, and P.A. Tarantilis. Quantitative determination of aloin, antioxidant activity, and toxicity of *Aloe vera* leaf gel products from Greece. *Journal of the Science of Food and Agriculture* 101(2): 414-423 (2021).
87. L.D. Williams, G.A. Burdock, and E. Shin. Safety studies conducted on a proprietary high-purity *Aloe vera* inner leaf fillet preparation, Qmatrix. *Regul Toxicology and Pharmacology* 57:90-98 (2010).
88. A. Devaraj, and T. Karpagam. Evaluation of anti-inflammatory activity and analgesic effect of *Aloe vera* leaf extract in rats. *International Research Journal Pharmacy* 2(3): 103-10 (2011).
89. H.F. Huseini, S. Kianbakht, R. Hajiaghaee, F.H. Dabaghian. Anti-hyperglycemic and antihypercholesterolemic effects of *Aloe vera* leaf gel in hyperlipidemic type 2 diabetic patients: A randomized double-blind placebocontrolled clinical trial. *Planta Medica* 78: 311-316 (2012).
90. D. Vijayalakshmi, R. Dhandapani, S. Jayaveni, P.S. Jithendra, C. Rose, A.B. Mandal. In vitro anti inflammatory activity of *Aloe vera* by down regulation of MMP-9 in peripheral blood mononuclear cells. *Journal of Ethnopharmacology* 141(1): 542-546 (2012).
91. P. Farzadinia, N. Jofreh, S. Khatamsaz, A. Movahed, S. Akbarzadeh, M. Mohammadi, A. Bargahi. Anti-inflammatory and wound healing activities of *Aloe vera*, honey and milk ointment on second-degree burns in rats. *The International Journal of Lower Extremity Wounds* 15(3): 241-247 (2016).
92. M.A. Naini, A. Zargari-Samadnejad, S. Mehrvarz, R. Tanideh, M. Ghorbani, A. Dehghanian, M. Hasanzarrini, F. Banaee, O. Koohi-Hosseinabadi, N. Tanideh, A. Iraji. AntiInflammatory, antioxidant, and healing-promoting effects of *Aloe vera* extract in the experimental colitis in rats. *Evidence-Based Complementary and Alternative Medicine* 12 pages (2021). Article ID 9945244.
93. S. Paul, D. Modak, S. Chattaraj, D. Nandi, A. Sarkar, J. Roy, T.K. Chaudhuri, and S. Bhattacharjee. *Aloe vera* gel homogenate shows anti-inflammatory activity through lysosomal membrane stabilization and downregulation of TNF-α and Cox-2 gene expressions in inflammatory arthritic animals. *Future Journal of Pharmaceutical Sciences* 7(1): 1-8 (2021).
94. J. Jose, S. Sudhakaran, S. Kumar, S. Jayaraman, and E.J. Variyar. A comparative evaluation of anticancer activities of flavonoids isolated from *Mimosa pudica*, *Aloe vera* and *Phyllanthus niruri* against human breast carcinoma cell line (MCF-7) using MTT assay. *International Journal of Pharmacy and Pharmaceutical Sciences* 6(2): 319-322 (2014).
95. M. Shalabi, K. Khilo, M.M. Zakaria, M.G. Elsebaei, W. Abdo, and W. Awadin. Anticancer activity of *Aloe vera* and *Calligonum comosum* extracts separetely on hepatocellular carcinoma cells. *Asian Pacific Journal of Tropical Biomedicine* 5(5): 375-381 (2015).
96. S.M. López Villarreal, J.H. Elizondo Luévano, R.A. Pérez Hernández, E. Sánchez García, M.J. Verde Star, R. Castro Ríos, M. Garza Tapia, O.E. Rodríguez Luis, and A. Chávez Montes. Preliminary study of the antimicrobial, anticoagulant, antioxidant, cytotoxic, and anti-inflammatory activity of five selected plants with therapeutic application in dentistry. *International Journal of Environmental Research and Public Health* 19(13): 7927 (2022).
97. T. Karpagam, J. Firdous, S. Priya, B. Varalakshmi, S. Gomathi, S. Geetha, and N. Muhamad. Anti-cancer activity of aloe vera ethanolic leaves extract against in vitro cancer cells. *Research Journal of Pharmacy and Technology* 12(5) pp.2167-2170 (2019).
98. D. Hariharan, P. Thangamuniyandi, A.J. Christy, R. Vasantharaja, P. Selvakumar, S. Sagadevan, A. Pugazhendhi, and L.C. Nehru. Enhanced photocatalysis and anticancer activity of green hydrothermal synthesized Ag@ TiO2 nanoparticles. *Journal of Photochemistry and Photobiology B: Biology* 202: 111636 (2020).
99. N. Mohamed, and H.M. El-Masry. *Aloe vera* gel extract and sunlight mediated synthesis of silver nanoparticles with highly effective antibacterial and anticancer activity. *Journal of Nanoanalysis* 7(1): 73-82 (2020).
100. M.P. Murugesan, M.V. Ratnam, Y. Mengitsu, and K. Kandasamy. Evaluation of anti-cancer activity of phytosomes formulated from *Aloe vera* extract. *Materials Today: Proceedings* 42: 631-636 (2021).
101. A. Ahamed, A Panneerselvam, A. Alaklabi, I.A. Arif, V. Ambikapathy, and N. Thajuddin. Molecular perspective and anticancer activity of medicinal plants. *Saudi Journal of Biological Sciences* 27(2): 666-675 (2020).
102. A.K. Mohamed. Antidiabetic, antihypercholestermic

and antioxidative effect of *Aloe vera* gel extract in alloxan induced diabetic rats. *Australian Journal of Basic and Applied Sciences* 5(11): 1321-1327 (2011).
103. A. Muñiz-Ramirez, R.M. Perez, E. Garcia, and F.E. Garcia. Antidiabetic activity of *Aloe vera* leaves. *Evidence-Based Complementary and Alternative Medicine* (2020).
104. S.N. Babu, S. Govindarajan, and A. Noor. *Aloe vera* and its two bioactive constituents in alleviation of diabetes–proteomic & mechanistic insights. *Journal of Ethnopharmacology* 280: p.114445 (2021).
105. Z.Y.M. Hasan, and J.M. Abdullah. Effects of gel extract from *Aloe vera* cultivated in Iraq on blood glucose level and lipid profile in induced diabetic mice. *Iraqi Journal of Science* 2022:124-130 (2022).
106. S.N. Ankita, and R. Ray. Effectiveness of *Aloe vera* in patients with diabetes mellitus. *The Pharma Innovation Journal* 11(2): 1821-1826 (2022).
107. F. Haghani, M.R. Arabnezhad, S. Mohammadi, and A. Ghaffarian-Bahraman. *Aloe vera* and Streptozotocin-Induced Diabetes Mellitus. *Revista Brasileira de Farmacognosia* 2022: 1-14 (2022).
108. N. Deora, and K. Venkatraman. *Aloe vera* in diabetic dyslipidemia: Improving blood glucose and lipoprotein levels in pre-clinical and clinical studies. *Journal of Ayurveda and Integrative Medicine* 13(4): 100675 (2022).
109. I. Amir, D.L. Martino, A. Marandino, H. Lamia, H. Mohsen, and E. Sacndolera. 2013. Chemical composition and biological activities of the essential oil from *Artemisia herba-alba* growing wild in Tunisia. *Natural Product Communication* 8: 407-410 (2013). PMID:23678823.
110. A. Hussain, M. Sajid, H. Rasheed, M. Hassan, M.A. Khan, and S.A.I. Bokhari. Phytochemistry and antibacterial efficacy of Northeastern Pakistani *Artemisia rutifolia* Stephan ex Spreng. extracts against some clinical and phyto-pathogenic bacterial strains. *Acta Pharmaceutica Sciencia* 60: 247-271(2022)
111. M.C. Stanley, O.E. Ifeanyi, and O.G. Eziokwu. Antimicrobial effects of *Aloe vera* on some human pathogens. *International Journal of Current Microbiology and Applied Sciences* 3(3): 1022-1028 (2014).
112. P.N. Waithaka, E.M. Gathuru, B.M. Githaiga, and R.Z. Kazungu. Antimicrobial properties of *Aloe vera, Aloe volkensii* and *Aloe secundiflora* from Egerton university. *Acta Scientific Microbiology* 1(5): 06-10 (2018).
113. F.I. Gorsi, T. Kausar, and M.A. Murtaza. Evaluation of antibacterial and antioxidant activity of *Aloe vera* (*Aloe barbadensis Miller*) gel powder using different solvents. *Pure and Applied Biology* 8(2): 1265-1270 (2019).
114. T.R. Anju, S. Parvathy, M.V. Veettil, J. Rosemary, T.H. Ansalna, M.M. Shahzabanu, and S. Devika. Green synthesis of silver nanoparticles from *Aloe vera* leaf extract and its antimicrobial activity. *Materials Today: Proceedings* 43: 3956-3960 (2021).
115. F. Bajalanlou, and B. Pakbin. Chemical properties and sensory evaluation of probiotic yoghurt manufactured with aqueous extract of *Aloe vera*. *Journal of Biology and Today's World 5*(11): 197-202 (2016).
116. T. Ahmed, B. Khedidja, D. Mounir, and C. Salah. Physicochemical and Biological Characteristics of *Aloe Barbadensis Miller* Gel Extract from Ghardaia, Algeria. *In 2nd International Conference on Industry 4.0 and Artificial Intelligence* 175: 99-105 (2022).
117. B. Vadiati Saberi, M. Haddadian, and N. Rasooli. The antibacterial activity of *Aloe vera*: An invitro study. *Journal of Dentomaxillofacial Radiology, Pathology and Surgery* 11(2):1 (2022).
118. R. Yahya, A.M. Al-Rajhi, S.Z. Alzaid, M.A. Al Abboud, M.S. Almuhayawi, S.K. Al Jaouni, S. Selim, K.S. Ismail, and T.M. Abdelghany. Molecular docking and efficacy of *Aloe vera* gel based on chitosan nanoparticles against Helicobacter pylori and its antioxidant and anti-inflammatory activities. *Polymers* 14(15): 2994 (2022).
119. Y. Pounikar, P. Jain, N. Khurana, L.K. Omray, S. Patil, and A. Gajbhiye. Formulation and characterization of *Aloe vera* cosmetic herbal hydrogel. *International Journal of Pharmacy and Pharmaceutical Sciences* 4(4): 85-86 (2012).
120. E. Estrada-Castillón, M. Garza-López, J.A. Villarreal-Quintanilla, M.M. Salinas-Rodríguez, B.E. Soto-Mata, H. González-Rodríguez, D.U. González-Uribe, I. Cantú-Silva, A. Carrillo-Parra, and C. Cantú-Ayala. Ethnobotany in Rayones, Nuevo León, México. *Journal of Ethnobiology and Ethnomedicine* 10(1), pp.1-13 (2014).
121. V. Rajkumar, A.K. Verma, G. Patra, S. Pradhan, S. Biswas, P. Chauhan, and A.K. Das. Quality and acceptability of meat nuggets with fresh *Aloe vera* gel. *Asian Australasian Journal of Animal Sciences* 29(5): 702-7 (2015).
122. R. Mahmoudi, F. Bajalanlou, P. Ghajarbeygi, and B. Pakbin. *Journal of Biology and Today's World* 5(11): 197-202 (2016).
123. T.Y. Hendrawati, H. Ambarwati, R.A. Nugrahani, S. Susanty, and U.H. Hasyim. The effects of *Aloe vera* gel addition on the effectiveness of sunscreen lotion. *Jurnal Rekayasa Proses* 14(1): 116 (2020).
124. T.Y. Hendrawati, L. Aristio, U.M. Hasyim, R.A. Nugrahani, and A.I. Ramadhan. The effects of adding *Aloe* chinensis baker gel extract on the formulation of lotion as a cosmetic product. *ARPN Journal of*

Engineering and Applied Sciences 13(23): 9291-9297 (2018).
125. A.Verma, R. Ansari, and A.A. Broadway. Preparation of herbal ice cream by using *Aloe vera* with mint flavour. *Journal of Pharmacognosy and Phytochemistry* 7(3): 391-394 (2018).
126. S. Kumar, and T. Bhatnagar. Studies to enhance the shelf life of fruits using *Aloe vera* based herbal coatings: A review. *International Journal of Agriculture and Food Science Technology* 5(3): 211-218 (2014).
127. V. Chaudhary, S. Bishnoi, and A. Argade. Development and characterization of *Aloe vera* juice incorporated burfi. *The Pharma Innovation Journal* 8(5): 407-411(2019).
128. S. Masood, A. un Nisa, F. Arif, M. Ashraf, S. Ashraf, H. ur Rehman, S. Hina, I. Ahmad. *Aloe vera* based cookies as a functional food. *Bangladesh Journal of Scientific and Industrial Research* 56(4): 293-298 (2021).
129. K. Mahajan, S. Kumar, Z.F. Bhat, Z. Naqvi, T.E. Mungure, and A.E.D.A. Bekhit. Functionalization of carrageenan based edible film using *Aloe vera* for improved lipid oxidative and microbial stability of frozen dairy products. *Food Bioscience* 43: 101336 (2021).
130. T. Haider, S. Ahmad, M. Abbas, N. Sharif, N. Mahreen, K. Aslam, and A. Noreen. Effect of *Aloe vera* gel coating on postharvest quality of strawberry fruit (*Frageria ananassa*). *Journal of Agricultural Research.* 60(4): 295-303 (2022).
131. N. Pattnaik, R. Mohanty, A. Satpathy, R. Nayak, R. Shamim, and A.K. Praharaj. *Aloe vera* mouthwashes can be a natural alternative to chemically formulated ones–A randomized-controlled trial. *Journal of Taibah University Medical Sciences* 17(3): 424-432 (2022).
132. M.C. Otálora, A. Wilches-Torres, and J.A. Gómez Castaño. Spray-drying microencapsulation of pink guava (*Psidium guajava*) carotenoids using mucilage from opuntia *ficus-indica cladodes* and *Aloe vera* leaves as encapsulating materials. *Polymers* 14(2): 310 (2022).

LIST OF ABBREVIATIONS

ABTS=2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid, AOAC= Association of Official Analytical Chemists, *A. vera= Aloe vera*, DPPH= 2,2- diphenyl-1-picrylhydrazyl, DW= Dry weight, FPG= Fasting plasma glucose, FRAP= Ferric ion reducing antioxidant power, FTIR= Fourier transform infrared spectrometer, HPLC= High-performance liquid chromatography, LC-MS= Liquid chromatography-mass spectrophotometry, mg/g= Milli gram per gram, Mg CE/g= Milligram catechin per gram, MgQE/g= Milli gram quercetin/ gram, MMP-9= Matrix metallopeptidase 9, MTT= 3-(4,5-dimethyl thiazolyl-2)-2,5-diphenyltetrazolium bromide, MWCO= membrane molecular weight cut-off, PBMC= Peripheral blood mononuclear cells, TAC= Total alkaloid content, TAC= Total antioxidant capacity, TFC= Total flavonoid content, TLC= Thin layer chromatography, TNF-α= Tumor necrosis factor, TPC= total phenolic content, TTN = Total tannin content, μg CE mg-1= Micro gram catechin per milli gram, μg GAEmg-1= Micro gram gallic acid per gram, μg RE mg-1= Microgram rutin per gram.