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# PHYTOCHEMISTRY, PHARMACOLOGY AND TOXICITY OF *Aloe vera* : A VERSATILE PLANT WITH EXTENSIVE THERAPEUTIC POTENTIAL

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**ABSTRACT**

*Aloe vera*, with its immense potential has a rich history of traditional medicine and cosmetic use, addressing various health issues from digestion to dermatological conditions. Its therapeutic versatility arises from a different pharmacological activities, encompassing anti-inflammatory, antibacterial, wound healing, antioxidant, laxative, immunomodulatory, anti-diabetic, skin protective, and potential anti-cancer effects. These effects are attributed to its bioactive compounds ranging from tannins, saponins, flavonoids, terpenoids, alkaloids to triterpenoids, glycosides, glucomannans, chromones, anthraquinones, and anthrone derivatives primarily located in the latex layer of the outer leaf. However, *A. vera's* toxicity varies with form, with some products exhibiting low toxicity, while others posing risks at high doses.
***Keywords:*** *Aloe vera,* pharmacology, phytochemistry, traditional, anthraquinones, toxicity.

## Introduction

As per World Health Organization (WHO) about 75–80 % of the global population depends on the plant based healthcare products including dietary supplements. The beliefs in the herbal remedies over allelopathic treatments have escalated over the years. The importance of herbal medicine lies in its historical significance, cultural acceptance, and effectiveness, particularly in regions with limited access to modern healthcare resources (Sam, 2019). The genus *Aloe* is native to Arabian Peninsula and has since undergone substantial diversification, resulting in the diversity of *Aloe* species we see today (Sung, 2006; Grace *et al.,* 2015). *Aloe vera*, sometimes known as the 'Plant of Immortality," has a long history that dates back thousands of years. It was utilized for therapeutic and healing purposes in ancient Egypt, Greece, and Sumeria (Mehta, 2017). In sanskrit, *A. vera* is referred to as "Ghrit Kumari". It is also known as *Aloe barbadensis* belonging to the family Asphodelaceae and has a long history of topical and oral therapeutic use, with its gel and latex derived from its leaves containing a variety of constituents with potential biological and toxicological effects (Boudreau and Beland, 2006). Thus, *A. vera* is traditionally employed for medicinal and cosmetic purposes, taken internally to address digestive issues, asthma, diabetes, and periodontal diseases, and applied externally to treat skin conditions, burns, and promote healthy skin (Shrestha *et al.,* 2015; Lanka, 2018). The traditional usage of *A. vera* for skin injuries and stomach disorders, based on its anti-inflammatory (Langmead *et al.,* 2004; Yagi *et al.,* 2002) antibacterial (Nejatzadeh-Barandozi, 2013; Danish *et al.,* 2020), and wound healing (Davis *et al.,* 1989; Maenthaisong *et al.,* 2007) characteristics, has evolved into modern medicine through substantial research (Sánchez *et al.,* 2020). A key compound in *A. vera*, well-documented is anthraquinones (Ravi *et al.,* 2011; Ali *et al.,* 2012; Logaranjan *et al.,* 2013), recognized for its bitter taste and laxative properties, primarily located in the outer leaf, specifically the latex layer just beneath the skin (Ramachandra and Rao 2008; Riaz *et al.,* 2021; Borges-Argáez *et al.,* 2019). Although *A. vera* features various other bioactive compounds, anthraquinones stands out historically for its laxative use. The current article concentrates on bioactive compounds anthraquinones in *A. vera* and its pharmacological activity emphasizing its potential therapeutic benefits and the need for more research.

### Botany

*Aloe vera* (L.) Burm.f. (syn. *Aloe barbadensis* Miller), is a perennial plant of the Asphodelaceae (Lily) family. The species is native to Oman and has a bushy look and a lush pea-green colour. A gel-like material is found in the inner section of its leaves (Fig. 1). *A. vera* looks like a spiky cactus and has thick leaves. It is a small, stemless plant that often grows in clusters, creating dense groups. Its succulent leaves grow upright, forming a compact rosette. These leaves are grayish-green, reaching lengths of about 50 cm, and they have pinkish margins adorned with numerous small spines. Sometimes, the leaf surfaces have white flecks or spots. The plant produces yellow, tubular flowers that can grow up to 3 cm in length, with anthers and stigma sticking out. These flowers are arranged in tall, branching clusters called racemes, which can reach heights of up to 90 cm.

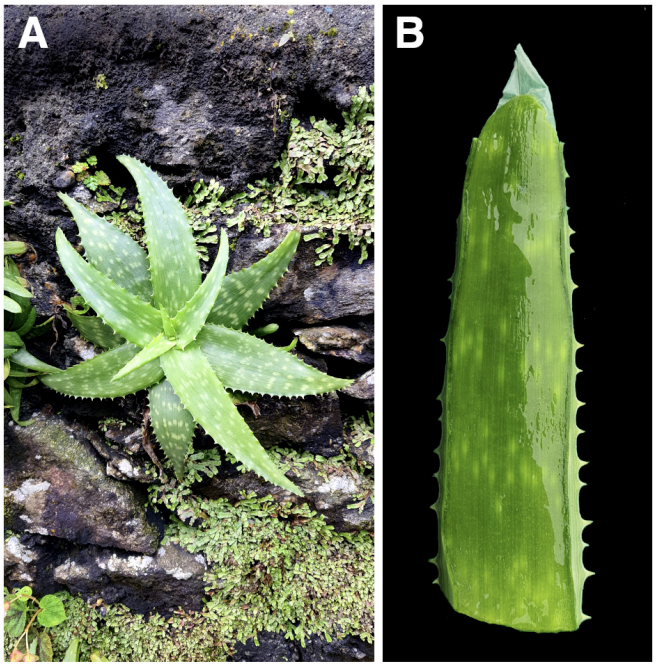


**Fig. 1: A.** Entire plant of *Aloe vera* **B.** Inner section of leaf showing gel

**Traditional use**

*Aloe vera* has traditionally been used for skin healing, as it soothes burns, irritations, and cuts, possesses bactericidal properties, and has anti-aging potential due to its nutrient-rich composition (Nirala *et al.,* 2020). In addition, it has also been used for detoxifying and immune-boosting qualities, digestive improvement, because of rich content of vitamins and amino acids (Rajeswari *et al.,* 2012). Futhermore, *A. vera* has traditionally been used for a wide range of medicinal purposes, including treating ailments like mild fever, wounds, burns, gastrointestinal disorders, diabetes, sexual vitality and fertility issues, cancer, immune modulation, AIDS, and various skin diseases (Manvitha and Bidya, 2014).

**Phytochemistry of *Aloe vera***

*Aloe vera* is rich in a diverse range of phytochemical compounds including tannins, saponins, flavonoids, terpenoids, alkaloids, carbohydrates, steroids, triterpenoids, glycosides, glucomannans, chromones, anthraquinones, and anthrone derivatives, benzene and furan derivatives, coumarins, phytosterols, pyrans and pyrones (Arunkumar and Muthuselvam, 2009; Patel *et al.,* 2012; Raphael, 2012; Mukherjee *et al.,* 2014; Cock, 2015). The leaves of *A. vera* have high moisture content, ash, crude fibre, crude protein, and crude lipid, as well as trace amounts of ascorbic acid, while enzymatic activities (superoxide dismutase, peroxidase, catalase, and amylase) and sugar content (total soluble and reducing sugars) vary within the plant with bacteriostatic properties (Lorenzetti, 1964; Ahmed and Hussain, 2013). The phenolic compounds traditionally recognized as laxatives can be found in the bitter reddish-yellow exudates situated beneath the plant's outer leaf. These compounds include anthraquinones and their derivatives (Fig. 2), such as barbaloin, aloeemodin-9-anthrone, lsobarbaloin, anthrone-c-glycosides, and chromones (Sharma *et al.,* 2014). However, the barbaloin, barbaloin (S)-isomer, barbaloin beta-D-isomer, barbaloin monoglucoside, and isobarbaloin are all the synonyms of Aloin (NCBI, 2023). Jawade and Chavan (2013) extracted Aloin from *A. vera* using ultrasound-assisted extraction (UAE) with methanol as the solvent, followed by quantification using HPLC. Aloin is a bitter-tasting chemical with laxative qualities found largely in the plant's outer leaf, notably the latex layer just beneath the epidermis (Ramachandra and Rao 2008; Riaz *et al.,* 2021). While *A. vera* contains a number of additional chemicals with medical and aesthetic qualities, Aloin is most well-known for its historic usage as a laxative. Aloin is represented by the chemical formula $C_{21}H_{22}O_9$ and its molecular weight is 418.4 g/mol (NCBI, 2023). In the study conducted by Ravi *et al.* (2011), *A. vera* leaf gel products were examined, showing that processed samples had low Aloin content (below 0.1 $mgL^{-1}$), while unprocessed ones contained over 10 $mgL^{-1}$, and Aloin A at low concentrations protected cells from hydrogen peroxide-induced toxicity. In addition, the anthraquinones present in *A. vera* include aloesaponarin-I and aloesaponarin-II, along with their derivatives obtained through methylation, acetylation, and O-glycosylation reactions, as well as a new Tetra-O-acetyl-β-d-glucopyranosyl derivative from aloesaponarin-II (Borges-Argáez *et al.,* 2019).

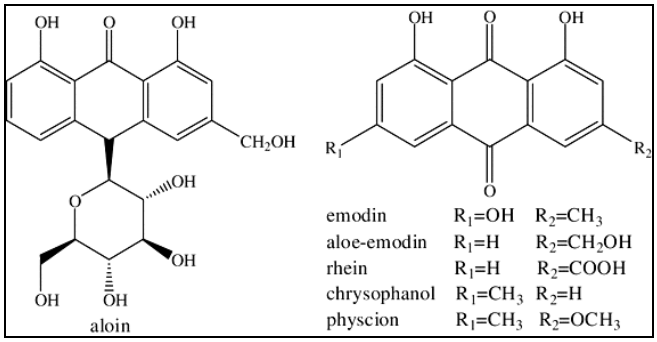


**Fig. 2 :** Key anthraquinone derivatives isolated from *A. vera* (Tan *et al.,* 2013)

**Pharmacological Properties**

*Aloe vera* exhibits various pharmacological properties (Table 1), such as anti-inflammatory (Langmead *et al.,* 2004; Yagi *et al.,* 2002) antibacterial (Nejatzadeh-Barandozi, 2013; Danish *et al.,* 2020), and wound healing (Davis *et al.,* 1989; Maenthaisong *et al.,* 2007), antioxidant (Hu *et al.,* 2003; Hęś *et al.,* 2019), laxative (Manvitha and Bidya, 2014; Surjushe *et al.,* 2008), immunomodulatory (Madan *et al.,* 2008; Kwon *et al.,* 2011), anti-diabetic (Tanaka *et al.,* 2006; Atanu *et al.,* 2018), skin protective (Foster, 1999; Gao *et al.,* 2019) and potential anti-cancer effects (Karpagam *et al.,* 2019; Ali *et al.,* 2020; Murugesan *et al.,* 2021) making it a versatile plant with medicinal potential. It has been employed in the pharmaceutical industry to manufacture topical drug products, ointments, gel preparations, tablets, and capsules (Manvitha and Bidya 2014).

***Anti-inflammatory***

The species has broad-spectrum anti-inflammatory effects, primarily due to anthraquinones (Davis *et al.,* 1989). Aloin and Aloe-Emodin, two of its components, also exhibit anti-inflammatory properties (Park *et al.,* 2009), making *A. vera* a potential therapeutic option for reducing inflammation. It works by inhibiting the production of reactive oxygen metabolites, prostaglandin E2, and interleukin-8, as shown in *in-vitro* assays, suggesting its potential use in inflammatory bowel disease (Langmead *et al.,* 2004). Moreover, *A. vera's* anti-inflammatory effects,

including the reduction of inflammation, may be linked to components such as mannose-6-phosphate, as observed in mouse studies (Davis *et al.,* 1994).

***Antimicrobial effects***

Aloins exhibit pharmacological potential by inhibiting microbial and human metalloproteinases, including *Clostridium histolyticum* collagenase (ChC) and granulocyte matrix metalloproteinases (MMPs), and their inhibitory effects are structurally similar to antimicrobial tetracyclines (Barrantes and Guinea 2003).

***Wound healing***

Aloin has been studied for its potential role in wound healing (Davis *et al.,* 1987; Maenthaisong *et al.,* 2007; Liang *et al.,* 2021). *A. vera* is known to improve wound healing, as demonstrated by studies involving mice where it enhanced the healing process compared to control groups. This wound-healing effect is likely due to its various beneficial components, including mannose-6-phosphate (Davis *et al.,* 1994). The wound healing properties of *Aloe vera* gel in the study are attributed to its optimized formulation with Carbopol 934, which improved spreadability and consistency, leading to faster wound healing and reduced inflammation (Khan *et al.,* 2013).

***Antioxidant***

Superoxide dismutase activity in *A. vera* plants, whether *in-vitro* generated or conventionally propagated, appears to be similar, possibly indicating a contribution from Aloin (Gantait *et al.,* 2011). Aloin was examined for its antioxidant properties, with ethanolic extracts from different *A. vera* accessions showing significant free radical scavenging capabilities, which can help protect tissues from oxidative damage caused by reactive oxygen species (ROS) (Anima *et al.,* 2012).

***Laxative effects***

*A. vera* appears to improve bowel movements and alleviate symptoms in patients with irritable bowel syndrome (IBS) based on a meta-analysis of randomized controlled trials. It showed a significant reduction in IBS symptom severity, a higher response rate, and no adverse effects, suggesting its potential as a safe and effective remedy for IBS (Hong *et al.,* 2018).

***Immune system support***

Aloin-containing *A. vera* products are used by some individuals to boost immune system function (Huang *et al.,* 2019). *A. vera* supplementation in the diet of rainbow trout improved their growth, immune responses, and resistance against a pathogenic oomycete, *Saprolegnia parasitica*, suggesting its supportive role in enhancing the fish's immune system and overall health (Mehrabi *et al.,* 2019). It appears to have an immunomodulatory effect by reducing cell-mediated immune responses (such as hypersensitivity reactions) while simultaneously enhancing humoral immunity, particularly the production of antibodies (Halder *et al.,* 2012).

***Antidiabetic activity***

Aloin A, a component found in *A. vera*, exhibits antidiabetic activity (Aldayel *et al.,* 2020). Oral administration of *A. vera* juice twice a day for at least 2 weeks in diabetic patients led to a reduction in blood sugar and triglyceride levels, indicating the potential of *Aloe vera* juice as an antidiabetic agent (Yongchaiyudha *et al.,* 1996). *A. vera* methanol extract (AVM) was found to significantly reduce the formation of advanced glycation end products (AGEs) and inhibit enzymes like α-amylase and α-glucosidase, suggesting its potential in preventing diabetes complications associated with AGEs (Muñiz-Ramirez *et al.,* 2020).

***Skin health***

Aloin was observed to induce melanin aggregation in tadpole melanophores, suggesting its potential as a safe melanolytic agent for treating hyperpigmentation by stimulating alpha adrenergic receptors and promoting skin lightening (Ali *et al.,* 2012).

***Anti-hyperlipidemic***

*Aloe vera* gel when administered alongside standard diabetes medications, has shown promise in reducing fasting blood glucose, HbA1c, total cholesterol, and LDL levels in hyperlipidemic type-2 diabetic patients, making it a potential safe option for managing both blood sugar and cholesterol levels (Huseini *et al.,* 2011). Aqueous extract of *Aloe vera* leaves displayed notable oral hypoglycemic effects in diabetic rats, especially at a dose of 500.00 $mgkg^{-1}$, and also exhibited antihyperlipidemic properties by lowering serum cholesterol levels, indicating its potential as a treatment for both diabetes and hyperlipidemia (Hasan *et al.,* 2020).

***Gastroprotective***

*A. vera's* gastroprotective properties are linked to its low molecular-weight gel fraction (lgfAv), which effectively reduces alcohol-induced gastric lesions in mice by inhibiting the activity of matrix metalloproteinase-9 (MMP-9), thus protecting the gastric mucosa (Park *et al.,* 2017). *A. vera* drink, known as Masfon, was investigated for its gastroprotective effects in rats. It increased basal gastric acid output but reduced acid output when histamine was administered, suggesting potential cytoprotective properties on the gastric mucus (Oka *et al.,* 2014).

***Antifungal***

In some studies, *A. vera* has exhibited antifungal activity against certain fungi, which could have implications for the treatment of fungal infections (Rosca-Casian *et al.,* 2007; Danish *et al.,* 2020; Bajwa, 2012).

***Anticancer properties***

Preliminary research has explored the potential anticancer effects of *A. vera* although more studies are needed to establish its efficacy in cancer therapy. *A. vera's* chief bioactive compounds have shown promise in pre-clinical studies for their potential anticancer effects, making *A. vera* a subject of interest in cancer prevention and treatment research due to its diverse mechanisms of action (Majumder *et al.,* 2019). The plants active compounds, such as anthraquinones (barbaloin, aloesin, aloe-emodin) and an octapeptide, exhibited significant anticancer effects by prolonging animal lifespan, inhibiting tumor growth, inducing cytotoxicity in leukemia and colon cancer cells, and promoting apoptosis (El-Shemy *et al.,* 2010). The ethanolic leaves extract displayed potent anticancer activity against liver, cervical, and lung cancer cell lines, suggesting its potential as a source of anticancer agents that require further characterization (Karpagam *et al.,* 2019).

***Antiviral properties***

An extract of *A. vera* gel exhibited antiviral activity against HSV-2 at different stages of virus replication, suggesting its potential as a natural source for developing antiviral drugs against HSV-2 with a favorable selectivity index (Zandi *et al.,* 2007). *A. vera* molecules were subjected to molecular docking studies with the main protease (3CLpro) responsible for coronavirus replication, revealing three potential enzyme inhibitors, with ligand 6 showing the highest binding energy and adhering to Lipinski's rule of five, indicating their potential as antiviral agents against SARS-CoV-2, the virus responsible for COVID-19 (Mpiana *et al.,* 2020). Anthraquinones present in *A. vera* were evaluated for their antiviral activity against influenza virus AH1N1 strains (Borges-Argáez *et al.,* 2019).

**Toxicity**

*Aloe vera* gel toxicity against *Aliivibrio fisheri* was assessed with values ranging from 0.03 to 0.09 mg $mL^{-1}$, indicating varying toxicity, with some samples having low toxicity (Kaparakou *et al.,* 2021). Wu *et al.,* (2021) found that *A. vera* soft capsules had no harmful effects at high doses in animal tests, and there was no evidence of genetic damage. This suggests that *A. vera* soft capsules is safe for use as a laxative and health food. Some study indicates that *A. vera* green rind and whole leaf extracts are safe at high doses for short periods. However, extended and high-dose use of whole leaf extract may lead to kidney issues, so caution is advised in such cases (Nalimu *et al.,* 2022). Moghbel *et al.,* (2007) tested *A. vera* cream for healing second-degree burn wounds in 30 patients. It showed superior wound healing (90.6%) compared to silver sulfadiazine (29.8%) by day 10. Importantly, *A. vera* didn't cause skin issues, suggesting it's a promising option for burn wound management. Some findings also suggest that *A. vera* can help counteract arsenic-induced oxidative stress without changing arsenic concentrations in organs (Gupta and Flora 2005).

**Table 1 :** Compounds found in *A. vera* with its pharmacological significance

| Compounds | Pharmacological activities | Source |
|---|---|---|
| Anthraquinones | Anti-inflammatory | Yagi *et al.* (2002); Langmead *et al.* (2004). |
| | Antibacterial | Nejatzadeh-Barandozi, (2013); Danish *et al.* (2020). |
| | Wound healing | Davis *et al.* (1989); Maenthaisong *et al.* (2007). |
| | Antioxidant | Hu *et al.* (2003); Hęś *et al.* (2019). |
| | Laxative | Surjushe *et al.* (2008); Manvitha and Bidya (2014). |
| | Immunomodulatory | Madan *et al.* (2008); Kwon *et al. (*2011). |
| | Anti-diabetic | Tanaka *et al.* (2006); Atanu *et al.* (2018). |
| | Skin protective | Foster (1999); Gao *et al.* (2019). |
| | Anti-Hyperlipidemic | Huseini *et al.* (2011); Hasan *et al.* (2020). |
| | Gastroprotective | Oka *et al.,* 2014; Park *et al.,* 2017. |
| | Antifungal | Rosca-Casian *et al.* (2007); Bajwa, (2012); Danish *et al.* (2020). |
| | Anticancer | Karpagam *et al.* (2019); Ali *et al.* (2020); Murugesan *et al.* (2021). |
| | Antiviral | Zandi *et al.* (2007); Borges-Argáez *et al.* (2019); Mpiana *et al.* (2020). |
| Polysaccharides | Immune-modulating | Yu *et al.* (2009). |
| | Anti-inflammatory | Tornero-Martínez *et al.* (2022). |
| Phytosterol | Chlolesterol-lowering | Pothuraju *et al.* (2016). |
| | Anti-inflammatory | Conte *et al.* (2017). |
| Saponins | Antimicrobial | Yebpella *et al.* (2011); Berniyanti and Mahmiyah (2015). |
| | Anti-inflammatory | Das *et al.* (2011); Paul *et al.* (2014) |
| Flavonoids | Antioxidant | Gorsi *et al.* (2019); Hęś *et al.* (2019). |
| | Anti-inflammatory | Kumar *et al.* (2020); Mir and Masodi (2020). |
| | Anticancer | Jose *et al.* (2014). |
| Enzymes | Anti-inflammatory | El-Shemy *et al.* (2010). |
| Vitamins | Nutritional support | Nagpal *et al.* (2012). |

## Conclusion

*Aloe vera*, known as the "Plant of Immortality," has been traditionally used for its medicinal and cosmetic properties, with applications ranging from digestive issues to skin conditions. It possesses various pharmacological activities, including anti-inflammatory, antibacterial, wound healing, antioxidant, laxative, immunomodulatory, anti-diabetic, skin protective, and potential anti-cancer effects, largely attributed to its bioactive compound anthraquinones primarily found in the outer leaf's latex layer. The species possess laxative phytochemical compounds, including anthraquinones like Aloin, predominantly found in the outer leaf and the latex layer. These compounds have notable laxative properties and can vary in concentration depending on processing methods. *A. vera* exhibits a range of toxicity levels depending on its form, with some products showing low toxicity, while others may pose risks at high doses, particularly in the case of unprocessed whole leaf extracts. Concurrently, *A. vera* demonstrates potential wound healing benefits and protective effects against arsenic-induced oxidative stress. Nevertheless, further research is needed to explore its therapeutic potential fully through modern scientific methods.

## References

Ahmed, M. and Hussain, F. (2013). Chemical composition and biochemical activity of *Aloe vera* (*Aloe barbadensis* Miller) leaves. *International Journal of Chemical and Biological Sciences,* 3: 29-33.

Aldayel, T.S., Grace, M.H., Lila, M.A., Yahya, M.A., Omar, U.M. and Alshammary, G. (2020). LC-MS characterization of bioactive metabolites from two Yemeni *Aloe* spp. with antioxidant and antidiabetic properties. *Arabian Journal of Chemistry,* 13: 5040-5049.

Ali, K., Saquib, Q., Siddiqui, M.A., Ahmad, J., Al-Khedhairy, A.A. and Musarrat, J. (2020). Anti-cancer efficacy of *Aloe vera* capped hematite nanoparticles in human breast cancer (MCF-7) cells. *Journal of Drug Delivery Science and Technology,* 60: 102052.

Ali, S.A., Galgut, J.M. and Choudhary, R.K. (2012). On the novel action of melanolysis by a leaf extract of *Aloe vera* and its active ingredient aloin, potent skin depigmenting agents. *Planta Medica,* 78: 767-771.

Anima, K., Srivastava, M.K. and Dutta, M. (2012). Free radical scavenging activity of ethanolic extracts and determination of aloin from *Aloe vera* L. leaf extract. *International Journal of Medicinal and Aromatic Plants,* 2: 612-618.

Arunkumar, S. and Muthuselvam, M. (2009). Analysis of phytochemical constituents and antimicrobial activities of *Aloe vera* L. against clinical pathogens. *World Journal of Agricultural Sciences,* 5: 572-576.

Atanu, F.O., Avwioroko, O.J. and Momoh, S. (2018). Anti-diabetic effect of combined treatment with *Aloe vera* gel and Metformin on alloxan-induced diabetic rats. *Journal of Ayurvedic and Herbal Medicine,* 4: 1-5.

Bajwa, R. (2012). Appraisal of antifungal activity of *Aloe vera*. *Mycopath,* 5: 5-9.

Barrantes, E. and Guinea, M. (2003). Inhibition of collagenase and metalloproteinases by aloins and aloe gel. *Life science,* 72: 843-850.

Berniyanti, T. and Mahmiyah, E. (2015). Microbiological studies on the production of antimicrobial agent by saponin *Aloe vera* linn against *Streptococcus sanguinis*. *Research Journal of Microbiology,* 10: 486-493.

Borges-Argáez, R., Chan-Balan, R., Cetina-Montejo, L., Ayora-Talavera, G., Sansores-Peraza, P., Gómez-Carballo, J. and Cáceres-Farfán, M. (2019). In vitro evaluation of anthraquinones from *Aloe vera* (*Aloe barbadensis* Miller) roots and several derivatives against strains of influenza virus. *Industrial Crops and Products,* 132: 468-475.

Boudreau, M.D. and Beland, F.A. (2006). An evaluation of the biological and toxicological properties of *Aloe barbadensis* (miller), *Aloe vera*. *Journal of Environmental Science and Health-Part C,* 24: 103-154.

Cock, I.E. (2015). The genus *Aloe*: Phytochemistry and therapeutic uses including treatments for gastrointestinal conditions and chronic inflammation. *Progress in Drug Research,* 70: 179-235.

Conte, R., Marturano, V., Peluso, G., Calarco, A. and Cerruti P. (2017). Recent advances in nanoparticle-mediated delivery of anti-inflammatory phytocompoundoles. *International Journal of Molecular Sciences,* 18: 709.

Danish, P., Ali, Q., Hafeez, M.M. and Malik, A. (2020). Antifungal and antibacterial activity of *Aloe vera* plant extract. *Biological and Clinical Sciences Research Journal,* 2020: e004.

Das, S., Mishra, B., Gill, K., Ashraf, M.S., Singh, A.K., Sinha, M., Sharma, S., Xess, I., Dalal, K., Singh, T.P. and Dey, S. (2011). Isolation and characterization of novel protein with anti-fungal and anti-inflammatory properties from *Aloe vera* leaf gel. *International Journal of Biological Macromolecules,* 48: 38-43.

Davis, R.H., Donato, J.J., Hartman, G.M. and Haas, R.C. (1994). Anti-inflammatory and wound healing activity of a growth substance in *Aloe vera*. *Journal of the American Podiatric Medical Association,* 84: 77-81.

Davis, R.H., Kabbani, J.M. and Maro, N.P. (1987). *Aloe vera* and wound healing. *Journal of the American Podiatric Medical Association,* 77: 165-169.

Davis, R.H., Leitner, M.G,, Russo, J.M. and Byrne, M.E. (1989). Wound healing. Oral and topical activity of *Aloe vera*. *Journal of the American Podiatric Medical Association,* 79: 559-562.

El-Shemy, H.A., Aboul-Soud, M.A.M., Nassr-Allah, A.A,, Aboul-Enein, K.M., Kabash, A. and Yagi, A. (2010). Antitumor properties and modulation of antioxidant enzymes' activity by *Aloe vera* leaf active principles isolated via supercritical carbon dioxide extraction. *Current Medicinal Chemistry,* 17: 129-138.

Foster, S. (1999). *Aloe vera*: The succulent with skin soothing cell protecting properties. *Herbs for Health Magazine,* 1999: 59-60.

Gantait, S., Mandal, N. and Das, P.K. (2011). In vitro accelerated mass propagation and ex vitro evaluation of *Aloe vera* L. with aloin content and superoxide dismutase activity. *Natural Product Research,* 25: 1370-1378.

Gao, Y., Kuok, K.I., Jin, Y. and Wang, R. (2019). Biomedical applications of *Aloe vera*. *Critical Reviews in Food Science and Nutrition,* 59: S244-S256.

Gorsi, F.I., Kausar, T. and Murtaza, M.A. (2019). Evaluation of antibacterial and antioxidant activity of *Aloe vera* (*Aloe barbadensis* Miller) gel powder using different solvents. *Pure and Applied Biology,* 8: 1265-1270.

Grace, O.M., Buerki, S., Symonds, M.R., Forest, F., van Wyk, A.E., Smith, G.F., Klopper, R.R., Bjorå, C.S., Neale, S., Demissew, S. and Simmonds, M.S. (2015). Evolutionary history and leaf succulence as explanations for medicinal use in aloes and the global popularity of *Aloe vera*. *BMC Evolutionary Biology,* 15: 1-12.

Gupta, R. and Flora, S.J. (2005). Protective value of *Aloe vera* against some toxic effects of arsenic in rats. *Phytotherapy Research,* 19: 23-28.

Halder, S., Mehta, A.K. and Mediratta, P.K. (2012). Augmented humoral immune response and decreased cell-mediated immunity by *Aloe vera* in rats. *Inflammopharmacology*, 20: 343-346.

Hasan, A.K., Jat, R.K. and Khan, A.M. (2020). Pharmacological screening of anti-diabetic and antihyperlipidemic activity of aqueous extracts of leaves of *Aloe barbadensis*. *International Journal of Research in Pharmaceutical Sciences,* 11: 1197-1203.

Hęś, M., Dziedzic, K., Górecka, D, Jędrusek-Golińska, A. and Gujska, E. (2019). *Aloe vera* (L.) Webb.: natural sources of antioxidants–a review. *Plant Foods for Human Nutrition,* 74: 255-265.

Hong, S.W., Chun, J., Park, S., Lee, H.J., Im, J.P. and Kim, J.S. (2018). *Aloe vera* is effective and safe in short-term treatment of irritable bowel syndrome: a systematic review and meta-analysis. *Journal of Neurogastroenterology and Motility,* 24: 528-535.

Hu, Y., Xu, J. and Hu, Q. (2003). Evaluation of antioxidant potential of *Aloe vera* (*Aloe barbadensis* Miller) extracts. *Journal of Agricultural and Food Chemistry,* 51: 7788-7791.

Huang, C.T., Hung, C.Y., Hseih, Y.C., Chang, C.S., Velu, A.B., He, Y.C., Huang, Y.L., Chen, T.A., Chen, T.C., Lin, C.Y., Lin, Y.C., Shih, S.R. and Dutta, A. (2019). Effect of aloin on viral neuraminidase and hemagglutinin-specific T cell immunity in acute influenza. *Phytomedicine,* 64: 152904.

Huseini, H.F., Kianbakht, S., Hajiaghaee, R. and Dabaghian, F.H. (2011). Anti-hyperglycemic and anti-hypercholesterolemic effects of *Aloe vera* leaf gel in hyperlipidemic type 2 diabetic patients: a randomized double-blind placebo-controlled clinical trial. *Planta medica,* 78: 311-316.

Jawade, N.R. and Chavan, A.R. (2013). Ultrasonic-assisted extraction of aloin from *Aloe vera* gel. *Procedia Engineering,* 51: 487-493

Jose, J.O., Sudhakaran, S.U., Kumar, S., Jayaraman, S.O. and Variyar, E.J. (2014) 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: 319-22.

Kaparakou, E.H., Kanakis, C.D., Gerogianni, M., Maniati, M., Vekrellis, K., Skotti, E. and Tarantilis, P.A. (2021). 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: 414-423.

Karpagam, T., Firdous, J., Priya, S., Varalakshmi, B., Gomathi, S., Geetha, S. and Muhamad N. (2019). Anti-cancer activity of *Aloe vera* ethanolic leaves extract against in vitro cancer cells. *Research Journal of Pharmacy and Technology,* 12: 2167-2170.

Khan, A.W., Kotta, S., Ansari, S.H., Sharma, R.K., Kumar, A. and Ali, J. (2013). Formulation development, optimization and evaluation of *Aloe vera* gel for wound healing. *Pharmacognosy Magazine,* 9: S6-S10.

Kumar, A., Mahajan, A. and Begum, Z. (2020). Phytochemical screening and in vitro study of free radical scavenging activity of flavonoids of aloe vera. *Research Journal of Pharmacy and Technology,* 13: 593-598.

Kwon, K.H., Hong, M.K., Hwang, S.Y., Moon, B.Y., Shin, S., Baek, J.H. and Park, Y.H. (2011). Antimicrobial and immunomodulatory effects of *Aloe vera* peel extract. *Journal of Medicinal Plants Research,* 5: 5384-5392.

Langmead, L., Makins, R.J. and Rampton, D.S. (2004). Anti□inflammatory effects of *Aloe vera* gel in human colorectal mucosa in vitro. *Alimentary Pharmacology & Therapeutics,* 19: 521-527.

Lanka, S. (2018). A review on *Aloe vera*-The wonder medicinal plant. *Journal of Drug Delivery and Therapeutics,* 8: 94-99.

Liang, J., Cui, L., Li, J, Guan, S., Zhang, K. and Li, J. (2021). *Aloe vera*: a medicinal plant used in skin wound healing. *Tissue Engineering Part B: Reviews,* 27: 455-474.

Logaranjan, K., Devasena, T. and Pandian, K. (2013). Quantitative detection of aloin and related compounds present in herbal products and *Aloe vera* plant extract using HPLC method. *American Journal of Analytical Chemistry,* 4: 600-605.

Lorenzetti, L.J., Salisbury, R., Beal, J.L. and Baldwin, J.N. (1964). Bacteriostatic property of *Aloe vera. Journal of Pharmaceutical Sciences,* 53: 1287.

Madan, J., Sharma, A.K., Inamdar, N., Rao, H.S. and Singh, R. (2008). Immunomodulatory properties of *Aloe vera* gel in mice. *International Journal of Green Pharmacy,* 29: 31-37

Maenthaisong, R., Chaiyakunapruk, N., Niruntraporn, S. and Kongkaew, C. (2007). The efficacy of *Aloe vera* used for burn wound healing: a systematic review. *Burns,* 33: 713-718.

Majumder, R., Das, C.K. and Mandal, M. (2019). Lead bioactive compounds of *Aloe vera* as potential anticancer agent. *Pharmacological Research,* 148: 104416.

Manvitha, K. and Bidya, B. (2014). *Aloe vera*: a wonder plant its history, cultivation and medicinal uses. *Journal of Pharmacognosy and Phytochemistry,* 2: 85-88.

Mehrabi, Z., Firouzbakhsh, F., Rahimi-Mianji, G. and Paknejad, H. (2019). Immunostimulatory effect of *Aloe vera (Aloe barbadensis)* on non-specific immune response, immune gene expression, and experimental challenge with *Saprolegnia parasitica* in rainbow trout (*Oncorhynchus mykiss*). *Aquaculture,* 503: 330-338.

Mehta, I. (2017). 'History of *Aloe vera'*- (A Magical Plant). *IOSR Journal of Humanities and Social Science,* 22: 21-24.

Mir, R.H. and Masoodi, M.H. (2020). Anti-inflammatory plant polyphenolics and cellular action mechanisms. *Current Bioactive Compounds,* 16: 809-817.

Moghbel, A., Ghalambor, A. and Allipanah, S. (2007). Wound healing and toxicity evaluation of *Aloe vera* cream on outpatients with second degree burns. *Iranian Journal of Pharmaceutical Sciences,* 3: 157-160.

Mpiana, P.T,, Tshibangu, D.S., Kilembe, J.T., Gbolo, B.Z., Mwanangombo, D.T., Inkoto, C.L., Lengbiye, E.M., Mbadiko, C.M., Matondo, A., Bongo, G.N. and Tshilanda, D.D. (2020). Identification of potential inhibitors of SARS-CoV-2 main protease from *Aloe* vera compounds: a molecular docking study. *Chemical Physics Letters,* 754: 137751.

Mukherjee, P.K., Nema, N.K., Maity, N., Mukherjee, K. and Harwansh, R.K. (2014). Phytochemical and therapeutic profile of *Aloe vera*. *Journal of Natural Remedies,* 14: 1-26.

Muñiz-Ramirez, A., Perez, R.M., Garcia, E. and Garcia, F.E. (2020). Antidiabetic activity of *Aloe vera* leaves. *Evidence-Based Complementary and Alternative Medicine,* 2020: 1-9.

Murugesan, M.P., Ratnam, M.V., Mengitsu, Y. and Kandasamy, K. (2021). Evaluation of anti-cancer activity of phytosomes formulated from *Aloe vera* extract. *Materials Today: Proceedings,* 42: 631-636.

Nagpal, R., Kaur, V., Kumar, M. and Marotta, F. (2012). Effectof *Aloe vera* juice on growth and activities of Lactobacilli in-vitro. *Acta Biomedica,* 83: 183-188.

Nalimu, F., Oloro, J., Peter, E.L. and Ogwang, P.E. (2022). Acute and sub-acute oral toxicity of aqueous whole leaf and green rind extracts of *Aloe vera* in Wistar rats. *BMC Complementary Medicine and Therapies,* 22: 1-14.

National Center for Biotechnology Information. (2023). PubChem Compound Summary for CID 12305761, Aloin A. from https://pubchem.ncbi.nlm.nih.gov/compound/Aloin-A. Retrieved September 8, 2023.

Nejatzadeh-Barandozi, F. (2013). Antibacterial activities and antioxidant capacity of *Aloe vera*. *Organic and Medicinal Chemistry Letters,* 3: 1-8.

Nirala, R.K., Raj, P,, Anjana, K. and Mandal, K.G. (2020). A review on *Aloe vera* and its traditional uses in India. *Journal of Pharmacognosy and Phytochemistry*, 9: 2571-2573.

Oka, V.O., Ikpi, D.E., Udo, N.V., Bassey, A.A. and Osim, E.E. (2014). Gastroprotective effects of masfon-*Aloe vera* drink: its effects on gastric acid and mucus. *European Journal of Medicinal Plants,* 4: 394-403.

Park, C.H., Son, H.U., Yoo, C.Y. and Lee, S.H. (2017). Low molecular-weight gel fraction of *Aloe vera* exhibits gastroprotection by inducing matrix metalloproteinase-9 inhibitory activity in alcohol-induced acute gastric lesion tissues. *Pharmaceutical Biology,* 55: 2110-2115.

Park, M.Y., Kwon, H.J. and Sung, M.K. (2009). Evaluation of aloin and aloe-emodin as anti-inflammatory agents in aloe by using murine macrophages. *Bioscience, Biotechnology, and Biochemistry,* 73: 828-832.

Patel, D.K., Patel, K. and Dhanabal, S.P. (2012). Phytochemical standardization of *Aloe vera* extract by HPTLC techniques. *Journal of Acute Disease,* 1: 47-50.

Paul, S.U., Dutta, S.O., Chaudhuri, T.K. and Bhattacharjee, S. (2014). Anti-inflammatory and protective properties of *Aloe vera* leaf crude gel in carrageenan induced acute inflammatory rat models. *International Journal of Pharmacy and Pharmaceutical Sciences,* 6:368-371.

Pothuraju, R., Sharma, R.K., Onteru, S.K., Singh, S. and Hussain, S.A. (2016). Hypoglycemic and hypolipidemic effects of *Aloe vera* extract preparations: A review. *Phytotherapy Research,* 30: 200-207.

Rajeswari, R., Umadevi, M., Rahale, C.S., Pushpa, R., Selvavenkadesh, S., Kumar, K.S. and Bhowmik, D. (2012). *Aloe vera*: the miracle plant its medicinal and traditional uses in India. *Journal of Pharmacognosy and Phytochemistry,* 1: 118-124.

Ramachandra, C.T. and Rao, P.S. (2008). Processing of *Aloe vera* leaf gel: a review. *American Journal of Agricultural and Biological Science,* 3: 502-510.

Raphael, E. (2012). Phytochemical constituents of some leaves extract of *Aloe vera* and *Azadirachta indica* plant species. *Global Advanced Research Journal of Environmental Science and Toxicology,* 1: 014-017.

Ravi, S., Kabilar, P., Velmurugan, S., Kumar, R.A. and Gayathiri, M. (2011). Spectroscopy studies on the status of aloin in *Aloe vera* and commercial samples. *Journal of Experimental Sciences,* 2: 10-13.

Riaz, S., Hussain, S., Syed, S.K. and Anwar, R. (2021). Chemical Characteristics and Therapeutic Potentials of *Aloe vera*. *RADS Journal of Biological Research & Applied Sciences,* 12: 160-166.

Rosca-Casian, O., Parvu, M., Vlase, L. and Tamas, M. (2007). Antifungal activity of *Aloe vera* leaves. *Fitoterapia,* 78: 219-222.

Sam, S. (2019). Importance and effectiveness of herbal medicines. *Journal of Pharmacognosy and Phytochemistry,* 8: 354-357.

Sánchez, M., González-Burgos, E., Iglesias, I. and Gómez-Serranillos, M.P. (2020). Pharmacological update properties of *Aloe vera* and its major active constituents. *Molecules,* 25: 1324.

Sharma, P., Kharkwal, A.C., Kharkwal, H., Abdin, M.Z. and Varma, A. (2014). A review on pharmacological properties of *Aloe vera*. *International journal of Pharmacy research and Review,* 29: 31-37.

Shrestha, A., Acharya, A. and Nagalakshmi, N.C. (2015). *Aloe vera* as traditional medicinal plant: a review on its active constituents, biological and therapeutic effects. *World Journal of Pharmaceutical research,* 4: 2146-61.

Sung, C.K. (2006). The history of *Aloe*. In: New perspectives on *Aloe*, M.A. Boston (ed): Springer US, 7-17.

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

Tan, Z.J., Li, F.F. and Xu, X.L. (2013). Extraction and purification of anthraquinones derivatives from *Aloe vera* L. using alcohol/salt aqueous two-phase system. *Bioprocess and Biosystems Engineering,* 36: 1105-1113.

Tanaka, M., Misawa, E., Ito, Y., Habara, N., Nomaguchi, K., Yamada, M., Toida, T., Hayasawa, H., Takase, M., Inagaki, M. and Higuchi, R. (2006). Identification of five phytosterols from *Aloe vera* gel as anti-diabetic compounds. *Biological and Pharmaceutical Bulletin,* 29: 1418-1422.

Tornero-Martínez, A., del Carmen Silva-Lucero, M., Sampedro, E.C., Ramón-Gallegos, E., Pérez-Cruz, C., Pérez-Grijalva, B. and Mora-Escobedo, R. (2022). *Aloe vera* and fermented extracts exhibit an anti-inflammatory effect on human glioblastoma/ astrocytoma U373 MG cells. *Plant Foods for Human Nutrition,* 77: 37-43.

Wu, J., Zhang, Y., Lv, Z., Yu, P. and Shi, W. (2021). Safety evaluation of *Aloe vera* soft capsule in acute, subacute toxicity and genotoxicity study. *PloS One,* 16: e0249356.

Yagi, A., Kabash, A., Okamura, N., Haraguchi, H., Moustafa, S.M. and Khalifa, T.I. (2002). Antioxidant, free radical scavenging and anti-inflammatory effects of aloesin derivatives in *Aloe vera*. *Planta medica,* 68: 957-960.

Yebpella, G.G., Adeyemi, H.M.M., Hammuel, C., Magomya, A.M., Agbaji, A.S. and Okonkwo, E.M. (2011). Phtyochemical screening and comparative study of antimicrobial activity of *Aloe vera* various extracts. *African Journal of Microbiology Research,* 5: 1182-1187.

Yongchaiyudha, S., Rungpitarangsi, V., Bunyapraphatsara, N. and Chokechaijaroenporn, O. (1996). Antidiabetic activity of *Aloe vera* L. juice. I. Clinical trial in new cases of diabetes mellitus. *Phytomededicine,* 3: 241-243.

Yu, Z., Jin, C., Xin, M. and JianMin, H. (2009). Effect of *Aloe vera* polysaccharides on immunity and antioxidant activities in oral ulcer animal models. *Carbohydrate Polymers*, 75: 307-311.

Zandi, K., Zadeh, M.A., Sartavi, K. and Rastian, Z. (2007). Antiviral activity of *Aloe vera* against herpes simplex virus type 2: An in vitro study. *African Journal of Biotechnology,* 6: 1770-1773.