



Barbaloin: an amazing chemical from the 'wonder plant' with multidimensional pharmacological attributes

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Abstract

Aloe vera (L.) Burm.f. is nicknamed the 'Miracle plant' or sometimes as the 'Wonder plant'. It is a plant that has been used since ancient times for the innumerable health benefits associated with it. It is one of the important plants that has its use in conventional medicinal treatments. It is a perennial succulent, drought-tolerant member of the family Asphodelaceae. There are scores of properties associated with the plant that help in curing various forms of human ailments. Extracts and gels obtained from plants have been shown to be wonderful healers of different conditions, mainly various skin problems. Also, this plant is popular in the cosmetics industry. The underlying properties of the plant are now mainly associated with the natural phytochemicals present in the plant. Diverse groups of phytoingredients are found in the plant, including various phenolics, amino acids, sugars, vitamins, and different other organic compounds, too. One of the primary ingredients found in the plant is the aloin molecule. It is an anthraquinone derivative and exists as an isomer of Aloin A and Aloin B. Barbaloin belonging to the first group is a glucoside of the aloe-emodin anthrone molecule. Various types of pharmacological properties exhibited by the plant can be attributed to this chemical. Few significant ones are antioxidant, anti-inflammatory, anti-diabetic, anti-cancer, anti-microbial, and anti-viral, along with their different immunity-boosting actions. Recently, molecular coupling studies have also found the role of these molecules as a potential cure against the ongoing COVID-19 disease. This study comprehensively focuses on the numerous pharmacological actions of the primary compound barbaloin obtained from the *Aloe vera* plant along with the mechanism of action and the potent application of these natural molecules under various conditions.

Keywords *Aloe vera* · Barbaloin · Aloins · Anthraquinone · Pharmacological actions · Medicinal uses

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Introduction

Aloe vera, a drought-tolerant, perennial succulent member of the family Xanthorrhoeaceae/Asphodelaceae/Liliaceae family having various similarities with *Cactus* sp., is one plant of its type that can be considered a blessing for humankind for centuries to date (Añibarro-Ortega et al. 2019). A native plant species of the hot and dry regions of North Africa and different Mediterranean countries has yet to be widely cultivated in the Indian subcontinent as well and has become a naturalized plant species of the region. Around the world, almost more than 300 varieties of the plant have been identified. Since time immemorial it has been used in alternative treatment approaches for its multifarious medicinal benefits and at times also finds use as an ornamental plant (Khare et al. 2021; Anand et al. 2022a). It is often called the 'Miracle Plant' and also at times the 'wound healer' due to its amazing ability to counter various human ailments and in turn heal and comfort man, and hence the names (Habeb et al. 2007). Derived from the Arabic word 'Alloeh', the name *Aloe vera* means 'bitter substance with shine'. Two thousand years back, Greek scientists considered this plant to be the universal panacea. The Egyptians named it 'the plant of immortality'. The mucilage gel-like tissue obtained from the leaves of the *Aloe* plant has wide uses in the cosmetic industry as the *Aloe* gel and also has potent therapeutic and medicinal applications. Planned, detailed scientific investigations on various medical applications of *A. vera* as a medicinal plant have gained significant concentration, and research is carried out all over the globe on the different phytochemicals, their isolation, characterization, analysis, and estimation for their diverse use as the pharmaceutical as well as nutraceutical agent. This particular study aims at providing an overview of the multifaceted attributes of one of the chief chemical components of *Aloe vera*, Barbaloin that revolves primarily around the biological, medicinal, and phytochemical parameters. Focus is given on the effect of chemicals against various diseases and conditions, with some emphasis on the mode of action as well.

Taxonomic position of *Aloe vera*

Kingdom: Plantae

Clade: Tracheophytes

Clade: Angiosperms

Clade: Monocots

Order: Asparagales

Family: Xanthorrhoeaceae/Asphodelaceae/Liliaceae

Subfamily: Asphodeloideae

Genus: *Aloe*

Species: *vera* (L.) Burm.f.

Chemical components of *Aloe vera*

The primary chemical present in the *Aloe vera* plant is a bitter chemical that when dried produces a yellow color belonging to the class called Aloin, which, as per historical shreds of evidence, shows the potency to be used as the cathartic medicines. *Aloe vera* is made up of 99 to 99.5% water and has a pH of around 4.5. Aloins can again be classified into two groups according to the chemical compositions: (1) Nataloins that react with nitric acid produce oxalic acid and picric acid and do not produce any red colour; (2) Barbaloin that in reaction with nitric acid forms aloetic acid (C₇H₂N₃O₅), chrysammic acid (C₇H₂N₂O₆), picric and oxalic acids and forms reddish colouration with the acid (Rajeshwari et al. 2012). Bright yellowish scale-like substances are formed by Nataloins, whereas yellowish prismatic crystals are formed by Barbaloin (Rajeshwari et al. 2012).

Different other phytochemicals were also identified from other parts of *Aloe vera* plants, viz. Anthraquinones/anthrones (barbaloin, aloetic acid, aloe-emodin, anthranol, emodin, isobarbaloin, cinnamic acid esters); chromones [8-C-glucosyl-(2'-O-cinnamoyl)-7-omethylaloediol A, 8-C-glucosyl-noreugenin, 8-Cglucosyl-7-O-methylaloediol A, 8-C-glucosyl-(S)-aloesol, 8-C-glucosyl-7-O-methylaloediol, isorabaichromone, neoaloesin A, isoaloesin D]; lipids and other organic compounds (γ-linolenic acid, arachidonic acid); steroids (cholesterol, campesterol, β-sitosterol); triterpenoids; triglycerides; lignins; gibberellin; salicylic acid; potassium sorbate; and uric acid (Minwuyet et al. 2017). The plant houses vitamins A, B, B₂, choline, niacin, C, F, and folic acid with traces of vitamin B₁₂. Enzymes such as alkaline phosphatase, acid phosphatase, lactic dehydrogenase, amylase, and lipase were also present. Table 1 represents the main chemical ingredients of the *Aloe vera* plant, as well as the individual chemicals that are present.

Comprehensive applications of *Aloe vera*

There are numerous scientific studies that focus on the multiple uses of *Aloe vera* as a medicinal and cosmetic agent. There are different properties associated with the plant such as laxative, anti-microbial, analgesic, antioxidant, anti-inflammatory, anti-diabetic, anti-proliferative, anti-tumor, anti-mutagenic, wound healing, neuroprotective, hepatoprotective, immunoregulative, anti-aging, and radioprotective activities. Table 2 makes a comprehensive listing of a few

Table 1 The main chemical constituents found in the *Aloe vera* plant with the specific compounds present

Types of compounds	Name of compounds	Reference
Phenolic bitter compounds made of free anthraquinones/anthrones and their derivative compounds	Barbaloin, aloë-emodin, isobarbaloin, aloin A and B, anthrone C-glycosides, chromones	Rodríguez et al. 2010; Quispe et al. 2018; Shakib et al. 2019
Vitamins	A, B ₁ , B ₂ , B ₆ , B ₉ , B ₁₂ , C, E	Maan et al. 2018; Kahramanoğlu et al. 2019
Minerals	Potassium, sodium, calcium, magnesium, manganese, copper, zinc, iron, selenium	Rahmani et al. 2015; Sánchez et al. 2020
Sterols	Campesterol, sitosterol, lupeol	Ahlawat and Khatkar, 2011; Bawankar et al. 2013
Enzymes	Amylase, lipase, catalase, peroxidase, carboxypeptidase, cyclo-oxidase	Ray et al. 2013; Radha and Laxmipriya 2015; Heş et al. 2019
Sugars	Long-chain polysaccharides containing glucose and mannose combining together to form gluco-mannans	Hamman, 2008; Zhang et al. 2018
Essential and non-essential amino acids	Arginine, aspartic acid, alanine, glutamic acid, histidine, glycine, leucine, lysine, proline, methionine, tyrosine, threonine	Quispe et al. 2018; Martínez-Sánchez et al. 2020

Table 2 Multiple properties and uses of *Aloe vera*

Properties	Functions	Reference
Laxative effect	Effective as a cure for constipation, irritable bowel syndrome, indigestion, and other intestinal disorders	Foster et al. 2011; Heş et al. 2019
Anti-microbial property	Effective against various classes of microorganisms such as virus and bacteria	Goudarzi et al. 2015; Forno-Bell et al. 2019; Arbab et al. 2021
Anti-inflammatory action	Effective as a cure for arthritis and other inflammations such as different types of wounds	Klaikeaw et al. 2020; Farid et al. 2021
Immuno-boosting action	Enhances immunity through various modes of actions that involve different immune cells and other associated chemicals	Gao et al. 2019; Mehrabi et al. 2019; Darzi et al. 2021
Antioxidant	Prevents cell damage by destroying unwanted free radicals and inhibits different harmful oxidation reactions within the cell	de Oliveira et al. 2018; López-Cervantes et al. 2018; Bendjedid et al. 2021; Kaparakou et al. 2021; Reza Nazifi et al. 2019
Anti-tumor	Inhibits tumor formation and potential malignant tumors	Majumder et al. 2019; Medina-Cruz et al. 2021; Xie et al. 2021
Anti-diabetic	Hypoglycemic effect by lowering insulin levels in the blood	Aldayel et al. 2020; Muñiz-Ramirez et al. 2020
Cosmetic uses	Moisturizing and anti-aging properties help in the use for skin care and various beauty related products	Pressman et al. 2019; Martínez-Burgos et al. 2022

of the well-known properties. Figure 1 presents the diverse pharmacological attributes of barbaloin.

Barbaloin

One of the principal ingenious phytoconstituents of the *Aloe vera* plant is barbaloin (10-beta-D-glucopyranosyl-1, 8-dihydroxy-3-hydroxymethyl-9(10H)-anthracenone) (Groom and Reynolds, 1987). A yellowish-brown colour latex-based chemical with a persistent taste and having C₂₁H₂₂O₉ as the molecular formula. It is the C-glucoside of the aloë-emodin anthrone, located mainly in the outer part of the plant. According to historical evidence, this compound found its

use as a laxative before World War II. A salient feature of this compound is the production of yellow fluorescence. The content of barbaloin is generally higher in the younger parts of the *Aloe* plant mainly in the leaves than in the older leaves. The diverse range of medicinal properties is associated with this particular compound having universal distribution and isolated from the *Aloe vera* plant.

This particular ingredient is responsible for the typical bitterness of bitter aloes and helps protect the plant against an attack by herbivores and acts as the defense molecule for the plants. According to a report, 30% of the dried leaf extract of the *Aloe vera* plant contains barbaloin and aloins. Barbaloin is found to occur mainly in two forms: the pure form and the impure form, which is available on the market

Fig. 1 The diverse pharmacological attributes of barbaloin



as various types of formulations. Conventionally having its use as cathartics but also possessing several other properties such as antioxidant, anti-cancer, anti-inflammatory, anti-microbial, and anti-fungal (Zhang et al. 2017a; Brilhante et al. 2021).

Chemical structure of barbaloin

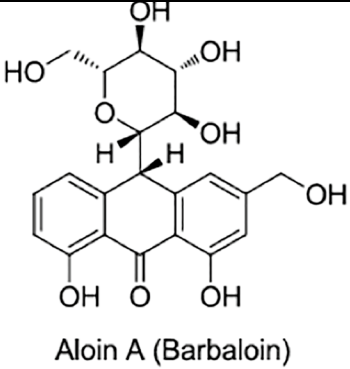
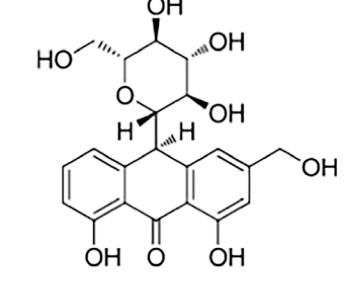
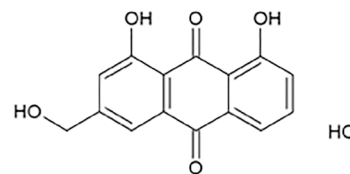
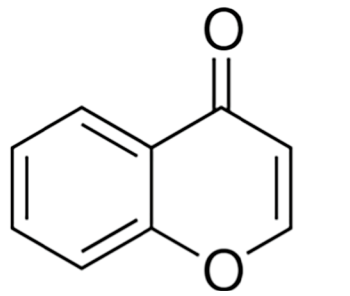
Aloin isolated from different natural sources is found to exist as a combination of two diastereomers, namely Aloin A (or barbaloin) and Aloin B (or isobarbaloin), with similar chemical attributes. Aloin, being an anthraquinone glycosyl is an anthraquinone containing a skeletal structure with the addition of one sugar moiety. Anthraquinones are naturally occurring phenolic compounds containing a 9,10-anthraquinone skeleton and are the common and largest family of indigenously occurring quinones that contain some of the significant chemicals such as emodin, chrysophanol, aloe-emodin, physcion, and rhein, that are found in various types of natural orange, yellow, and red pigments, and many possess the purgative action similar to that of aloins. Aloin was found to share

similarities with aloe-emodin that has similar biological characteristics as aloins but does not contain the sugar group. The chemical structures of some of the main bioactive compounds found in *Aloe vera* leaf extracts are listed below in Table 3.

Methodology

The data presented in this manuscript were obtained from different available international databases and electronic resources such as Google Scholar, PubMed, Science Direct, Scopus, Wiley, etc. as well as from certain textbooks. The main keywords such as *Aloe vera*, Barbaloin, medicinal values of Barbaloin, pharmacological activity, chemical components, treatment, prevention, pharmacological activities, nutraceutical uses, health, clinical trials, and other related words were used singly or in combination. A thorough and careful reading of all sources of the available literature was carried out to obtain the best possible information.

Table 3 Chemical structures of the chief aloins present in the Aloe leaf extract

Name of the bioactive compound	Class of the compound	Structure of the compound
Barbaloin	Anthraquinone	 <p>Aloin A (Barbaloin)</p>
Isobarbaloin	Anthraquinone	 <p>Aloin B (Isobarbaloin)</p>
Aloe emodin	Dihydroxanthraquinone	 <p>Aloe-emodin</p>
Chromones	Phenylpropanoids	

Barbaloin isolation and extraction methods

Fresh leaves from the *Aloe* plant are collected mainly from some local nurseries, and then the outer portion of the leaves is peeled off and the leaves are cleaned by placing

them under clean water and thoroughly washing them. The inner gel obtained after the process can be scrapped and then smaller pieces cut from it. Various standardized protocols are available for barbaloin extraction, such as the Soxhlet extraction procedure, ultrasound-assisted

extraction methods, batch extraction experiments (Singh et al. 2020). An elaborate drying process is followed using the solar drying method for 3 weeks at 30–45 °C. Standard barbaloin was retrieved with the Fluka method and ultra-assisted sonication for the calibration process. Analysis by HPLC involves a diverse range of solvents of different grades manufactured by S.D. Fine Chemicals, India. Taiwan-made ultrasonic probes were used in the sonication technique and the probes were 20 kHz and had dimensions of 1.5 cm diameter or 30 cm length. Maintaining a constant temperature for the process is important. Subsequently, the samples were collected at certain time gaps to estimate the barbaloin quantity from the *Aloe vera* sample.

Medicinal importance and pharmacological activities of barbaloin

As already mentioned above, Barbaloin is one of the primary and functional phytochemicals of the *Aloe vera* plant for its innumerable benefits. Due to the multifarious and beneficial properties of this compound, it is in high demand as a remedy for treatment of various diseases. Various research studies point to the efficacy of barbaloin due to its varied pharmacological and medicinal aspects. The usefulness of the compound against different ailments because of its various properties like antioxidant, anti-inflammatory, anti-cancer, anti-diabetic, and anti-microbial is discussed through this study.

Antioxidant property

Barbaloin has been found to possess an antioxidant property by helping in the process of destroying free radicals produced in the process of oxidative stresses taking place within the cell. It exhibited its antioxidant properties in the regions of free radical induced with the deoxyribonucleic acid (DNA) component (Singh et al. 2020). Barbaloin also offered protection against the OH-induced components of DNA and broke it compared to another control group. At lower concentrations, it improved DNA damage or indicated its antioxidant attributes. The highest effect of barbaloin is reduced in a minimum ratio. On the other hand, there was a gradual decrease in the power of the free radical effects of barbaloin, and this may have led to results to protect the component of deoxyribonucleic acid (Singh et al. 2020). The presence of enzymes glutathione peroxidase, superoxide dismutase enzymes, and phenolic antioxidants were responsible for the antioxidant property of *Aloe vera* and its phytochemicals (Sharma et al. 2014).

Anti-cancer property

Various scientific reports are available that pointed to some of the anti-cancer activities of the aloins, especially the barbaloin. A study by Zhang et al. (2017a, b) showed that different types of conventional treatment approaches for non-small cell lung carcinoma (NSCLC), one of the most common types of lung cancer, had their own set of side effects (Mitra et al. 2022c; Anand et al. 2022b). However, in contrast, cells treated with barbaloin because of its anti-cancer potential were found to inhibit metastasis and cell growth both in vitro and in vivo and without any side effects as traditional treatment methods (Anand et al. 2020; Halder et al. 2021). An increase in the levels of different proteins related to apoptosis such as caspase-3, -8, and -9 and alteration in the concentrations of various cyclin A, p53, p27, and other such checkpoint proteins associated with the cell cycle process gave convincing evidence in A549 cells regarding the anti-viability effect of barbaloin. In addition, barbaloin was found to significantly cause a reduction in invasion and migration of A549 cells and showed controlled expression of proteins involved in the tumor metastasis process. Further studies were also conducted investigating the initiation of various pro-survival or pro-metastasis signaling pathways such as AKT, nuclear factor kappa B (NF- κ B), mitogen-activated protein kinase (MAPK) and β -catenin. The results showed that barbaloin hindered the p38MAPK/Cdc25B/Hsp27 pathway by blocking nuclear translocation of p38, but no other notable effects were found in other pathways. Lastly, this compound was also found to inhibit in vivo liver metastases and growth of A549 cells in vivo. The results of these studies, if combined, showed the inhibiting action of barbaloin in vitro and in vivo of NSCLC cells that point to safer and more efficient treatment approaches of NSCLC (Zhang et al. 2017a).

A research study by El-Shemy et al. (2010) tried to analyze the possible anti-cancer and immune modulatory effects of different phytochemicals isolated from the *Aloe vera* plant. The primary anthraquinone molecules were selected and verectin, a N-terminal octapeptide derived from a biologically active 14 kDa glycoprotein present in *A. vera*, was also examined. In vivo active chemicals demonstrated a notable expansion of longevity of the tumor-transplanted animals in the order: barbaloin > octapeptide > aloesin > aloe-emodin. The active principles of *A. vera* also showed substantial inhibition of the number of Ehrlich ascites carcinoma cells (EACC) in the order: barbaloin > aloe-emodin > octapeptide > aloesin. Furthermore, in the trypan blue cell viability assay, the active constituents exhibited remarkable concentration-dependent cytotoxicity against acute myeloid leukemia (AML) and acute lymphocyte leukemia (ALL) cell lines (El-Shemy et al. 2010). The data was strong enough to indicate the chemopreventive

activity of *A. vera* phytochemicals and that they can be potential, efficient, safe, specific, and economical treatment strategies. Therefore, because of the anti-neoplastic properties of barbaloin, aloe-emodin, these chemicals have been found to be used against the growth of malignant cells, and hence they have been used as a treatment for different types of cancers (Mitra et al. 2022a).

Anti-inflammatory property

Different studies aimed to show the anti-inflammatory action of barbaloin. These compounds had been shown to gradually retard the synthesis of nitric oxide by showing a negative effect on the expression of nitric oxide mRNA (Singh et al. 2020). Also, the effect was shown with respect to the manufacture of Prostaglandin E2. Studies showed that the inflammatory action of barbaloin was exhibited by reducing and restricting the mRNA expression of the nitric oxide synthase effect and the effect of cytoxygenase-2 mRNA in the body (Singh et al. 2020). The anti-inflammatory action of barbaloin was also found to contribute to its use in the case of inflammatory bowel disorder (Langmead et al. 2004). Due to its anti-inflammatory properties, *Aloe vera* has already been used in different types of inflammatory disorders such as gout, arthritis, etc. It is also used to strengthen joint muscles and reduces pain, inflammation, and redness. Often *Aloe*-based phytochemicals have been used to reduce different types of arthritis (Nandal and Bhardwaj, 2012).

Anti-diabetic and hypoglycemic effect

As already discussed, *Aloe vera* extract is known to contain a high quantity of polyphenols with the highest ratio of barbaloin. Barbaloin administered by oral route in rats for a long time up to 4 weeks was effective in controlling blood glucose levels and reduced the weight of mice compared to the control group (Singh et al. 2020).

Anti-microbial property

Barbaloin was found to possess anti-microbial activities against different classes of microorganisms ranging from bacteria, protozoa, viruses, etc. The phytoconstituent barbaloin from the *Aloe* extract showed high anti-microbial efficacy against the bacterium *Neisseria gonorrhoeae*. Pure barbaloin had been found to inhibit the growth of the bacteria *Neisseria gonorrhoeae* responsible for causing sexually transmitted disease gonorrhoeae (Kambiz and Afolayan 2008; Khare et al. 2021). Barbaloin, when administered with phyto-extracts from *Withania somnifera*, was found to show anti-viral properties against the herpes simplex type 1 virus (Singh et al. 2020). Also, a study by Van et al. (2002) pointed at the anti-plasmodial property

of Barbaloin (Van et al. 2002). *Aloe* extract containing Aloins was found to exert an anti-mycobacterial effect on tuberculosis-causing bacteria *Mycobacterium tuberculosis* and a strong anti-bacterial effect against bacteria, namely *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, and *Salmonella typhi* (Banik and Sharangi, 2019). When taken in large quantities, the compounds were found to show a purgative effect, but when taken in little concentration they helped in the absorption process in the gut and act as anti-microbial agents (Banik and Sharangi, 2019).

Anti-viral actions

There is clear evidence in favor of the anti-viral actions of *Aloe vera* and its different components. There are several documentations regarding the anti-viral properties of *Aloe vera* and its associated phytochemicals. The gel fractions comprising lectins had shown a direct inhibitory effect on cytomegalovirus (CMC) in cell cultures (Saoo et al. 1996). Alves et al. (2004) reported that a chemical called chrysophanic acid obtained from *A. vera* at concentrations of 0.21 and 0.02 µg/mL demonstrated 50% inhibition of viral replication in type 2 and 3 polioviruses. Aloin had been found to exert an anti-viral rather virostatic effect on an RNA-negative enveloped virus HSV (hemorrhagic rhabdovirus septicemia virus) (Alves et al. 2004). *Aloe vera* was found to exert an inhibitory effect on a negative RNA enveloped viral hemorrhagic septicemia rhabdovirus (VHSV) (Alves et al. 2004). Vlietinck et al. (1998), showed the anti-viral effect of *Aloe* compounds like lectins on different viral groups including the human immunodeficiency virus (HIV).

In the treatment of various skin diseases

Skin is the largest, most widely, and most varied organ of the human body. It is present as the external barrier of the body that acts as a defense organ against various deleterious external factors found in the environment. Often, various harmful overlying symptoms are found to affect the skin mainly caused by some microbial activities and other modes of action too. Products obtained from the *Aloe* plant have diverse beneficial effects on the skin as well as the discussed compound barbaloin. Table 4 focuses on all such skin disorders as well as the preventive mode of action shown by the compound barbaloin, which may play a significant role in developing treatment strategies against such skin ailments.

Immunity-boosting property

One property that has gained high attention in modern pandemic times is the property of immunity boost. Humans are trying to consume different types of foods that can function as immunity and energy boosters (Paul et al. 2021; Mandal

Table 4 The use of barbaloin against a variety of skin disorders

Skin ailments	Signs and symptoms	Responsible property	References
Acne	The formation of closed and open plugged pores in the skin along with the development of pus-filled papules on skin	Anti-bacterial property	Akhoondinasab et al. 2014
Wounds and burns	Redness of the skin, blister formation, peeling of the skin, mild pain	Anti-inflammatory property	Moriyama et al. 2016
Cold sores	Itching, tingling, and burning sensation around the lips, formation of blisters	Anti-inflammatory property	Rajeshwari et al. 2012
Dandruff	Small white flakes on the scalp mainly around the hairlines, itching, irritation, inflammation	Anti-inflammatory, antioxidant, moisturizing properties	Mazzarello et al. 2018
Eczema	Itching, dryness, red to brownish-gray patches around eyelids, hands, and feet	Anti-microbial and anti-inflammatory properties	Klein and Penneys, 1988
Psoriasis	Red patches and silvery scale-like structures that cause inflammation, itching, and pain	Anti-bacterial and anti-inflammatory property	Laxmi et al. 2013
Rashes	Red in colour, inflammation, itching on the skin, dryness, formation of minute blisters filled with fluid	Anti-inflammatory and anti-microbial property	Singh et al. 2020
Sunburns	Pinkish to redness of the skin with irritation, pain, headaches, and at times fever also	Anti-inflammatory and moisturizing property	Qadir, 2009

et al. 2022). The *Aloe vera* plant has long been found to possess this quality and this feature can be associated with the principal phenolic compound barbaloin. The bitter aloes found in the *Aloe vera* plant are found to contain various types of free anthraquinones and their derivatives such as barbaloin, isobarbaloin, anthrone-C-glycosides, aloe-emodin-9-anthrone, and chromones as discussed previously. Studies suggest that barbaloin has immunity-boosting properties. It is found to enhance the immune system. Shreds of evidence suggest the use of these phytoingredients as immunomodulators and can hence be found effective against cold and cough conditions, fatigue, and other such related diseases associated with low immunity such as cold, fatigue, and other diseases caused by a low immune system. In larger quantities, these chemicals are found to possess purgative actions, but in minute amounts they act as a powerful antimicrobial agent and help in the process of absorption in the gut and many other related functions. Madan et al. (2008) in their study showed that mice when administered with *Aloe vera* extract (150 mg/kg and 300 mg/kg) respectively for 5 days showed a substantial increase in the total count of WBC and the number of macrophages count, indicating the immunomodulatory action of these compounds.

Barbaloin and COVID-19 disease

As already discussed above, barbaloin is found to contain anti-viral properties, and in modern times this word virus is the most discussed one. Although vaccination and different forms of medications are already available against the pandemic disease (Anand et al. 2021a, b; Anand et al.

2021b; Iyer et al. 2021), the role of different nutraceuticals and various phyto-based foods is not less, too. Often, such phytochemicals are used in complementary alternative treatment approaches as prophylactic measures against this disease (Banerjee et al. 2021; Dutta et al. 2021). Various study reports indicate the efficacy of barbaloin against COVID-19 disease. A study conducted by Ho et al. (2007) pointed to the use of aloe-emodin against the novel coronavirus (SARS-CoV) and its ability to inhibit the SARS-CoV spike protein and the ACE-2 receptor protein. Abd-Alla et al. (2012) showed the use of phytoconstituents such as barbaloin and aloe-emodin against various hemagglutinating viruses. Molecular coupling studies identified various *Aloe*-based compounds as potential inhibitors of the main protease enzyme of SARS-CoV-2 in the SARS-CoV-2 virus (Mpiana et al. 2020a, b). Several other studies also pointed to the usage of aloin compounds as a potential candidate against COVID-19 disease, which can also be of great use in this time of pandemic in the near future. But a more detailed study about the mode of action and other areas is needed in this field.

Discussion

Through this review, we can find the multidimensional usage of the *Aloe* plant with special reference to one of its chief phyto-components Barbaloin. This single phenolic compound, like several other phytoingredients, is found to possess diverse properties, ranging from antioxidant, anti-inflammatory, antiseptic, anti-tumor, hypoglycemic, to moistening anti-aging properties as well. As a result, it is

very clear that if this single chemical can be given more focus and importance in terms of both research and commercialization, it can serve so many ailments and disorders (Anand et al. 2019). Although there is a significant amount of studies on this chemical, much more needs to be done in the field of isolation, purification, availability, and tissue culture techniques to grow the plant, as well as to harvest the particular compound and commercialization of this product. In the current perspective, this chemical is found to have anti-viral properties as well as immunity-boosting properties, too. Hence, it can be used in alternative treatment approaches too against viral diseases, COVID-19 disease being the most focused of the present time. Furthermore, the inclusion of *Aloe*-based products containing these aloins can also improve our immune system and help boost our immunity protecting us from various foreign attacks. Therefore, more research work is required on this wonder chemical from the miracle plant.

The entire process of research based on natural products-based research surrounds the applicability of different naturally obtained molecules (Mitra et al. 2022b). But in reality, it calls for a lot of patience and endurance. The entire process of natural products-based research is in itself time-consuming, and the desired results call for perseverance compared to those confined mainly to the synthetic molecules (Biswas et al. 2021). Although the quality associated with these products and their environmentally friendly impacts are much higher compared to synthetic ones. Hence, the speed of generating the molecules is a major constraint. But there is definitely a surplus of global pharmaceutical companies that are also focused on this avenue of research. Furthermore, the phytochemical purification of the obtained phytochemical is another important step that requires a lot of standardizations, and any error in the steps can disrupt the entire process of isolation and the obtaining of the natural compound. There are many more protocols based on tissue culture to cultivate plants and isolate the compounds. Therefore, more cutting-edge research needs to be done in this field to utilize this astounding chemical to its full potential.

Conclusions

Numerous applications of the miracle herb have been made possible in different cosmetic products, as well as a potential drug for the cure of different diseases along with traditional drugs (Bandopadhyay et al. 2022). Although there is evidence in respect of its uses, more and more controlled trials have to be carried out to find out the true potency along with the interaction between the herb and the drug. Several preclinical studies indicate the great potential of *Aloe*-based compounds as curative remedies against various diseases. However, more randomized clinical trials

are needed for the firm establishment of these efficacies and the realization of the utmost potential of the drug and its derived phytochemicals. To conclude, it can be said that *Aloe vera* is a very potent plant that produces various types of an extremely useful plant-based drug against various diseases including COVID-19 disease, also. Through discussion of various study results, the broad-range antiviral activity of the drug has been highlighted. It has been found to show efficacy against both DNA and RNA viruses. Anthraquinone-based phytochemicals such as barbaloin, isobarbaloin, and aloe-emodin are found to have anti-viral actions comparable with conventional anti-viral drugs such as Lopinavir and Ritonavir. The mechanism of action mainly centers on inhibition or binding to a variety of different viral proteins such as ACE-2 receptors, spike proteins, and 3CLPro. However, more research is needed in this field, and an elaborate mode of action must be deciphered to strongly establish these *Aloe*-based phytochemicals against various kinds of viruses. Therefore, the diverse range of activities of the principal phytoingredients of the *Aloe vera* plant truly justifies its name as ‘wonder plant’ or ‘miracle plant’.

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