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Antimalarial *Aloe* Compounds

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ABSTRACT

Among the most prevalent diseases caused by protozoan parasites, malaria is caused by parasites of the genus Plasmodium and transmitted to humans by infected female anopheles' mosquito. Plants are considered to be the richest resource of active molecules in traditional systems of medicine and modern medicines. The use of plants and plant products both in medicines and as medicine could be traced as far back as the beginning of human civilization. In human history medicinal plants, a source of remedies, are widely used as alternative therapeutic tools for the prevention or treatment of many diseases. The genus *Aloe* is one of the top medicinal plants that have obtained its popularity from time to time. Aloe plants are used from immemorial time to nowadays. Combinations of active molecules extracted from Aloe species have been indicated to confer a variety of biological effects with different mechanisms of action. The chemical compositions that have been identified in *Aloe* plants include simple and complex polysaccharides, minerals, vitamins, enzymes, hydrocarbons, fatty acids, indoles, pyrimidines, aldehydes, and ketones, dicarboxylic acids, phenolic compounds, phytosterols, and alkaloids with potential biological and toxicological activities. Among these compounds several investigations revealed antimalarial activities. Generally, Anthraquinoes, anthrones, chromones and others are active compounds against malaria. Considering that natural molecules have acted as natural templates in the development of antimalarial agents, it is encouraged to investigate further analyses into *Aloe* constituents and their values against malaria. It should be followed with phytochemical and pharmacological analyses in order to give scientific ground to medicinal knowledge and future potential utilization. Therefore, further studies are needed to determine which compound act as a strong antimalarial agent or synergistic effects of the compounds are used for antimalarial activities. In addition, it is recommended to test other parts of *Aloe* plants like flowers, leaf gel, leaf skin, etc. against malaria.

Introduction

Among the most prevalent diseases caused by protozoan parasites, malaria is caused by parasites of the genus Plasmodium and transmitted to humans by infected female anopheles' mosquito [1]. Plasmodium falciparum, Plasmodium malaria, Plasmodium knowlesi Plasmodium ovale, and Plasmodium vivax are the five parasite species that cause malaria in humans. Among these species, P. falciparum causes the most severe form of malaria and

hence higher mortality rates [2]. The estimated number of malaria deaths stood at 627, 000 of the estimated 241 million cases of malaria in 2020 worldwide [3]. To control malaria, many popular practices exist to avoid the nuisance of mosquito bites such as fumigation, burning green leaves on the hut's threshold, mosquito coils, insecticide sprays, and repellents. Smoke is a common method of repelling biting mosquitoes that is used throughout the world from ancient times to current [4]. To treat infectious diseases such as malaria, herbal medicine plays a great role. Due to the vast metabolic diversity of plants, natural products may be an alternative treatment opportunity of cheap and easy to treat malaria infection. For instance, artemisinin and quinine are antimalarial drugs that were isolated from plants. As a result, it can be generalized that plants have potential as sources of active chemical components used for antimalarial drugs [5].

Plants are considered to be the richest resource of active molecules in traditional systems of medicine and modern medicines. The use of plants and plant products both in medicines and as medicine could be traced as far back as the beginning of human civilization [6]. In human history medicinal plants, a source of remedies, are widely used as alternative therapeutic tools for the prevention or treatment of many diseases [7]. The genus Aloe is one of the top medicinal plants that have obtained its popularity from time to time. *Aloe* plants are used from immemorial time to nowadays. Therefore, they become a popular household remedy exhibiting a range of beneficial health-promoting properties. *Aloe* in one form or another is a common domestic medicine and is the basis of most pharmaceutical preparations [8]. For instance, investigations have led to increased importance of the mostly known *Aloe* species, A. vera due to its dependable medicinal properties, and it has been used in the preparation of pharmaceutical products [9].

Chemical Compositions of *Aloe*

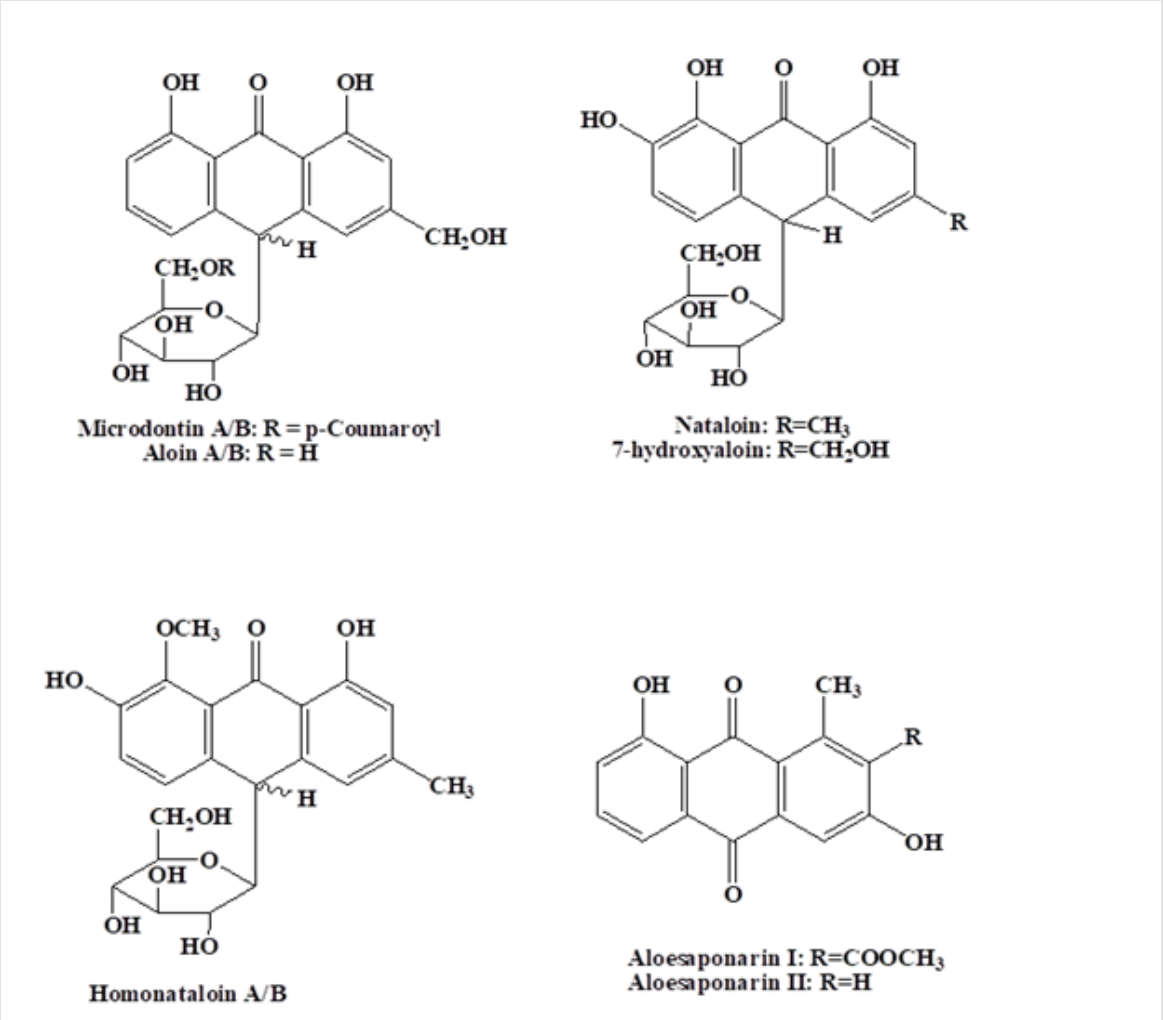

Figure 1: Structures of some antimalarial compounds.

Combinations of active molecules extracted from *Aloe* species have been indicated to confer a variety of biological effects with different mechanisms of action [10]. The chemical compositions that have been identified in Aloe plants include simple and complex polysaccharides, minerals, vitamins, enzymes, hydrocarbons, fatty acids, indoles, pyrimidines, aldehydes, and ketones, dicarboxylic acids, phenolic compounds, phytosterols, and alkaloids with potential biological and toxicological activities [11]. Various components present in *Aloe* species have been found effective against many diseases, including malaria. In every application of Aloe species, preparing extracts of *Aloe* parts is mandatory. The leaves of *Aloe* plants are the most commonly used are heterogeneous and can be divided into three major parts. These are,

1. The majorly consists of structural components of the leaf part, the outer green epidermis.
2. The part that vascular bundles are placed where the bitter latex or sap is obtained, the outer pulp region below the epidermis; and
3. The inner leaf pulp, which consists of Aloe gel and containing parenchyma cells [12,13]. Although leaves are the most used part of the plant, recently some studies have reported the bioactive roots [14] and flowers [15] of the plant. *Aloe* species have become of great interest to researchers who have tried to identify the compounds responsible for these beneficial effects. Several constituents from various classes such as alkaloids, anthrones, chromones, flavonoids, glycoproteins, naphthalene's, and pyrones have been isolated from the genus *Aloe* [16]. Aloin, aloesin, aloenin, aloeresin, aloe-emodin, apigenin, acemannan, and chrysophanol are some examples of such bioactive compounds Table 1 and Figure 1 [17-25].

Table 1: The bioactive compounds in the genus Aloe.

Class of phytoconstituents	Components	Ref.
Carbohydrates	Pure mannan, acetylated mannan, acetylated glucomannan, glucogalactomannan, galactan, galactogalacturan, arabinogalactan, xylan, pectic, cellulose, acemannan, glucose, galactose, manose, fucose, and aldopentose	[17-20]
Anthraquinones	*Aloe*-emodin, aloesaponarin, desoxyerythrolaccin, chrysophanol, 1,5-dihydroxy-3-hydroxy methylanthraquinone, helminthosporin, 7-hydroxyaloe emodin, nataloe emodin and its ester nataloe emodin-8-methyl ester, aloechrysone, aloesaponol, bianthracene O-glycosides: aloe emodin-11-O-rhamnoside, aloesaponol-6-O-glucoside, aloesaponol-8-O-glucoside, aloesaponol-O-methyl-4-O-glucoside, and elgonicardine	[17-18]
Anthrones	Aloin A and B (collectively called aloin and also often referred to as barbaloin), 5-hydroxyaloin A, 7-hydroxyaloin, 10-hydroxyaloin B, 5-hydroxyaloin A 6'-O-acetate, 7-hydroxyaloin-6'-O-monoacetate, homonataloin, nataloin, aloinoside, barbendol, aloe-emodinanthrone, chrysophanolanthrone, aloe emodin-10-C-rhamnoside, 8-O-methyl-7-hydroxyaloin, 6'-O-cinnamoyl-8-O-methyl-7-hydroxyaloin, 6'-O-p-coumaroyl-7-hydroxyaloin, 7-hydroxyaloin-4',6'-O- diacetate, 6'-O-cinnamoyl-5-hydroxyaloin A, microstigmin A, littoraloin, littoraloside, microdontin, homonataloside, and deacetyllittoraloin,	[17-21]
Chromones	Aloesin, iso-aloeresin, 7-O-methylaloesin, 8-[C-β-D-[2-O-(E)- cinnamoyl] glucopyranosyl]-2-[(R)- 2-hydroxypropyl]-7-methoxy-5-methylchromone, 8 -C-glycosyl-7-O-methylaloediol, and 8-C-glucosyl-7-methoxy-(S)-aloesol	[19, 21]
Coumarins	Feralolide and dihydroisocoumarin glycoside	[20-21]
Flavonoids	Naringenin, dihydroisorhamnetin, apigenin, isovitexin, isorhamnetin, genistein, saponarin, kaempferol, and quercetin	[17-22]
Alkaloids	N-methyltryamine, O, N-dimethyltryamine, γ-coniceine, coniine	[19-22]

Pyrans and pyrenes	Bisbenzopyran, aloenin, aloenin aglycone, aloenin acetal, aloenin B, and aloe-2''-p-O-coumaroyl ester,	[19-21]
Benzene, naphthalene and furan derivatives	Protocatechuic acid, methyl-p-coumarate, pluridone, isoeleutherol, isoeleutherol-5-O-glucoside, feroxidin, feroxidin A, feroxidin B, plicataloside, 5-OH-3-methylnaphto[2,3-c] furan-4(1H)-one, 3-methylnaphto[2,3-c] furan-4(9H)-one, and 3- methylnaphto[2,3-c] furan-4,9-dione	[17-20]
Sterols	Cholesterol, campesterol, β-sitosterol, and lupeol	[20-22]
Proteins	Lectins, lectin-like substance	[20-21]
Enzymes	Alkaline phosphatase, amylase, cyclooxidase, cyclooxygenase, lipase, oxidase, phosphoenolpyruvate carboxylase, and superoxide dismutase	[18-22]
Vitamins	B1, B2, B6, B12, C, E, β-carotene, choline, folic acid, α-tocopherol	[21-23]
Inorganic compounds	Calcium, chlorine, chromium, copper, iron, magnesium, manganese potassium, phosphorous, sodium, and zinc.	[19-23]
Miscellaneous including lipids	Arachidonic acid, γ-linolenic acid, triglicerides, triterpenoid, gibberillin, lignins, potassium sorbate, salicylic acid, and uric acid	[21-25]

The Antimalarial *Aloe* Compounds

Anthraquinones

Above all the genus *Aloe* is rich in anthraquinones which play a crucial role in medicinal applications. Many investigators showed the antimalarial activities of anthraquinones of *Aloe* species. In the literature, the leaves and roots of different *Aloe* species were tested and showed variable antimalarial activities. One of the most known anthraquinones, *aloe*-emodin emodin which was isolated from leaf latex of *Aloe*, A. macrocarpa Todaro showed potential antimalarial activity against malaria when compared with chloroquine [26]. In addition to this the chrysophanol, aloesaponarin I, and aloesaponarin II are anthraquinones that were isolated from the root of A. pulcherrima showed ant plasmodial activity against both chloroquine-resistant and -sensitive malaria parasites, P. falciparum [27].

Anthrones

The most studied *Aloe* constituents against malaria were anthrones. Anthrones are large classes of the genus *Aloe* and they are biologically active. Table 2 shows the specific anthrones of *Aloe* species against malaria along with parts of the plant [28-30].

Table 2: Antimalarial anthrones of Aloe species.

Aloe spp.	Part of plant	Name of the isolated compounds	Ref.
A. percrassa Todaro	Leaf latex	Aloin A/B and microdontin A/B	[28]
A. citrina	Leaf latex	Homonataloin A/B	[29]
A. pulcherrima Gil. and Seb.	Leaf latex	nataloin and 7-hydroxyaloin	[30]
A. debrana Chrstian	Leaf latex	Aloin	[31]
A. macrocarpa Todaro	Leaf latex	Aloin and aloinoside	[26]

Chromones

Chromones also showed potential antimalarial compounds isolated from the *Aloe* species. In the literature, the compound, (E)-2-(1-hydroxy-2-methylpropyl)-8-(6'-O-cinnamoyl)-β-D-glucopyranosyl-7-methoxy-5-methylchromone (HCGMM) has been reported as is a potential antimalarial compound from A. debrana Chrstian. When compared to the mice in the negative control group HCGMM showed significant suppression ($p<0.05$) against P. berghei at dose levels of 25, 50, and 100 mg/kg/day [31].

Other Compounds

The potential of *Aloe* species means the molecules in them have wide applications in combating malaria. From A.otallensis, naphthalene derivative identified as 2,8-O,O-di(β-D-gluco-pyranosyl)-1,2,8-trihydroxy-3-methylnaphtalene (plicataloside) evaluated for its in vivo antimalarial activity using a 4- day Plasmodium berghei suppressive test method. The plicataloside (100 mg/kg) inhibited parasite growth by 40.7%. It was proposed that plicataloside may minimize oxidative stress thereby contributing to the antimalarial activity of the plant [32]. The literature shows that some flavonoid derivatives, xanthones,

stilbenes, coumarins, lignans, tannins, quinones, terpenoids, steroids, and alkaloids possess antimalarial activity [33]. Among these, natural, semi-synthetic, and synthetic quinones are effective antimalarials [34]. Several investigations showed that many naturally occurring compounds possess antimalarial activity when tested in different malarial diseases [31].

Conclusion and Future Aspects

Based on the indigenous antimalarial effects of *Aloe* plants, the scientific studies, in vitro and in vivo reports confirmed that the leaves and roots of *Aloe* plants possessed genuine antimalarial activities which could be attributed to the presence of the active chemical constituents. More, the activity of the active constituents along with their relative margin of safety merit the use of these compounds as leads to the development of safer, cost-effective, and more potent alternative drugs for the treatment of malaria. Considering that natural molecules have acted as natural templates in the development of antimalarial agents, it is encouraged to investigate further analyses into *Aloe* constituents and their values against malaria. It should be followed with phytochemical and pharmacological analyses in order to give scientific ground to medicinal knowledge and future potential utilization. Therefore, further studies are needed to determine which compound act as a strong antimalarial agent or synergistic effects of the compounds are used for antimalarial activities. In addition, it is recommended to test other parts of *Aloe* plants like flowers, leaf gel, leaf skin, etc. against malaria. Further analysis is important to identify the result; if malaria drugs like chloroquine are incorporated into *Aloe* extracts/ isolated compounds. Although most studies are directed towards the curative effect of the test substances, in-depth pharmacokinetic and pharmacodynamic studies are needed to elucidate their mechanism of action.

References

1. Paulos B, Bisrat D, Gedif T, Asres K (2011) Antimalarial and antioxidant activities of the leaf exudate and a naphthalene derivative from Aloe otallensis Baker. Ethiop Pharm 29: 100-107.
2. Koning-Ward TF De, Dixon MWA, L Tilley, Gilson PR (2016) *Plasmodium* species: Master renovators of their host cells". Nature Reviews Microbiology 14(8): 494-507.
3. (2022) World Health Organization (WHO).
4. Moore SJ, Lenglet AD (2004) An overview of plants used as insect repellents.
5. Kumar S, Yadav M, Yadav A, Rohilla P, Yadav JP (2017) Antiplasmodial potential and quantification of aloin and aloe-emodin in A. vera collected from different climatic regions of India. BMC complementary and alternative medicine 17(1): 1-10.
6. Dluya T, Daniel D, Yusuf U (2017) *In vitro* antioxidant activity and phytochemical evaluation of five medicinal plants extract. The Pharmaceutical and Chemical Journal 4(5): 73-82.
7. Kaur S, Mondal P (2014) Study of total phenolic and flavonoid content, antioxidant activity and antimicrobial properties of medicinal plants. J Microbiol Exp 1(1): 23-28.
8. Tom R (2004) Aloes: the genus Aloe. CRC Press LLC, p. 24-27.
9. Eshun K, He Q (2004) A. vera: A valuable ingredient for the food, pharmaceutical and cosmetic industries: A review. Crit Rev Food Sci Nutr 44(2): 91-96.
10. Sánchez M, González-Burgos E, Iglesias I, Gómez-Serranillos MP (2020) Pharmacological update properties of *A. vera* and its major active constituents. Molecules 25(6): 1324.
11. Yadeta AT (2022) Food applications of *Aloe* species: A review. J Plant Sci Phytopathol 6: 024-032.
12. Joseph B, Justin RS (2010) Pharmacognostic and phytochemical properties of A. vera Linn an overview. International Journal of Pharmaceutical Sciences Review and Research 4(2): 1-5.
13. Ahmed M, Hussain F (2013) Chemical composition and biochemical activity of *A. vera* (*A. barbadensis Miller*) leaves. International Journal of Chemical and Biochemical Sciences 3: 29-33.
14. Abdissa N, Gohlke S, Frese M, Sewald N (2017) Cytotoxic compounds from *Aloe* megalacantha. Molecules 22(7): 1136.
15. Martínez-Sánchez A, López-Cañavate ME, Guirao-Martínez J, Roca MJ, Aguayo E (2020) *Aloe* vera flowers, a byproduct with great potential and wide application, depending on maturity stage. Foods 9(11): 1542.
16. Amoo SO, Aremu AO, Van Staden J (2014) Unraveling the medicinal potential of South African *Aloe* species. J Ethnopharmacol 153 (1): 19-41.
17. Salehi B, Albayrak S, Antolak H, Kręgiel D, Pawlikowska E, et al. (2018) *Aloe* Genus Plants: From Farm to Food Applications and Phytopharmacotherapy. Int J Mol Sci 19(9): 2843.
18. Ni Y, Turner D, Yates KM, Tizard I (2004) Isolation and characterization of structural components of *A. vera* L. leaf pulp, Int. Immunopharmacol 4(14): 1745-1755.
19. Akaberi M, Sobhani Z, Javadi B, Sahebkar A, Emami SA (2016) Therapeutic eff ects of *Aloe* spp. in traditional and modern medicine: A review. Biomed Pharmacother 84: 759-772.
20. Cock IE (2015) The genus Aloe: Phytochemistry and therapeutic uses including treatments for gastrointestinal conditions and chronic inflammation, Progress in Drug Research, Birkhauser Verlag AG, pp. 179-235.
21. E Dagne, D Bisrat, A Viljoen, BE Van Wyk (2000) Chemistry of Aloe species. Curr Org Chem 4(10): 1055-1078.
22. Kahramanoğlu İ, Chen C, Chen J, Wan C (2019) Chemical constituents, antimicrobial activity, and food preservative characteristics of *A. vera* gel. Agronomy 9(12): 831.
23. Sharrif Moghaddasi M, M Res (2011) A. vera their chemicals composition and applications: A review. Int J Biol Med Res 2(1): 466-471.
24. Mahor G, Ali SA (2016) Recent update on the medicinal properties and use of *Aloe* vera in the treatment of various ailments. Biosci Biotechnol

Res Commun 9(2): 277-292.

25. Josias H Hamman (2008) Composition and applications of A. vera leaf gel (review). Molecules13: 1599-1616.
26. Tewabe Y, Assefa S (2018) Antimalarial potential of the leaf exudate of Aloe macrocarpa Todaro and its major constituents against Plasmodium berghei. Clin Exp Pharmacol 8(1): 1-6.
27. Abdissa D, Geleta G, Bacha K, Abdissa N (2017) Phytochemical investigation of *Aloe* pulcherrima roots and evaluation for its antibacterial and antiplasmodial activities. PLoS ONE 12(3): e0173882.
28. Geremedhin G, Bisrat D, Asres K (2014) Isolation, characterization and *in vivo* antimalarial evaluation of anthrones from the leaf latex of *Aloe* percrassa Todaro. Journal of Natural Remedies 14(2): 119-125.
29. Girma B, Bisrat D, Asres K (2015) Antimalarial evaluation of the leaf latex of *Aloe* citrina and its major constituent. Ancient Science of Life 34(3): 143-147.
30. Teka T, Bisrat D, Yeshak MY, Asres K (2016) Antimalarial activity of the chemical constituents of the leaf latex of *Aloe* pulcherrima Gilbert and Sebsebe. Molecules 21(1415): 1-10.
31. Gemechu W, Bisrat D, Asres K (2014) Antimalarial anthrone and chromone from the leaf latex of Aloe debrana Chrstian, Ethiop Pharm J 30: 1-9.
32. Paulos B, Bisrat D, Gedif T, Asres K (2011) Antimalarial and antioxidant activities of the leaf exudate and a naphthalene derivative from Aloe otallensis Baker. Ethiop Pharm J 29: 100-107.
33. Bero J, Frédérich M, Quetin-Leclercq J (2009) Antimalarial compounds isolated from plants used in traditional medicine. J Pharm Pharmcacol 61: 1401-1433.
34. Imperatore C, Persico M, Aiello A, Luciano P, Guiso M, et al. (2015) Marine inspired antiplasmodial thiazinoquinones: Synthesis, computational studies and electrochemical assays. RSC Adv 5: 70689-70702.

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