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REVIEW ARTICLE

REVIEW OF LITERATURE ON MEDICINAL USE OF ENDEMIC *ALOE* OF ETHIOPIA

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ABSTRACT

The plant world is a Pandora of active chemical compounds. Nearly half the medicines that we use today are of herbal origin, and a quarter contains plant extracts or active chemicals taken directly from plants. Aloe genus, which belongs to the family Xanthorrhoeaceae, produces a number of metabolites in good yields and some have been shown to possess useful biological activities. Many compounds belonging to different classes, including anthrones, chromones, pyrones, naphthalenes and flavonoids have so far been reported from the endemic aloe of Ethiopia. This review focuses on phytochemistry and medicinal use of endemic Aloe of Ethiopia to allow an evaluation of the potential for utilization of the largest biomass of endemic Aloe available.

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INTRODUCTION

Medicinal plants have a long history of use in most communities throughout the world. It has been confirmed by WHO that herbal medicines serve the health needs about 80% of the world's population, especially for millions of people in the vast rural areas of developing countries like Ethiopia (Akerele, 1984). In Africa, the use of traditional medicine has persisted over the years and the last few decades have witnessed an upsurge of interest in traditional medicine and other alternative forms of healthcare in the developing and developed countries (Duru, 2006). *Aloe* is a genus containing over 500 species of flowering succulent plants (Verma, 2008). The APG III system (2009) places the genus in the family Xanthorrhoeaceae, subfamily Asphodeloideae (Rai, 2000). In the past, it has also been assigned to families Aloaceae and Liliaceae or lily family. The genus is native to Africa; species are found in southern Africa, the mountains of tropical Africa, various islands off the coast of Africa including Sardinia, Madagascar, and the Arabian Peninsula (Samy, 2007). The term *aloe* is derived from the Arabic word alloeh, which means a shining bitter substance (Poaceae, 1997). Medicinally, the gel and dried leaf exudates of *aloe* species have been used since ancient civilizations of the Egyptians, Greeks and Mediterranean people (Poaceae, 1995).

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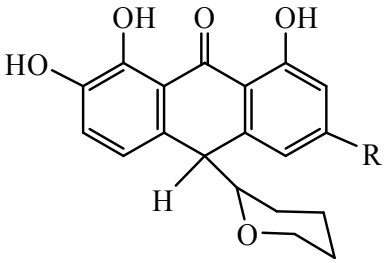
Aloe species have enjoyed a very wide folkloric usage and are also now used in modern medicine in many parts of the world. The bitter leaf exudates of some *aloe* species are commercially important sources of the laxative aloe drugs (Pittosporaceae to araliaceae, 1989), and are also used in the cosmetics industry as additives in shampoos, shaving and skin care creams (The Plant List, 2010), and in the treatment of skin disorders. The exudates have also been used as a bittering agent in alcoholic beverages (Stevens, 2001). The leaves and roots of *Aloe* species elaborate many interesting secondary metabolites belonging to different classes of compounds including, anthrones, chromones, pyrones, coumarins, alkaloids, glycoproteins, naphthalenes, anthraquinones and flavonoids ("Aloe", 2014).

Medicinal use and Biologically active compounds

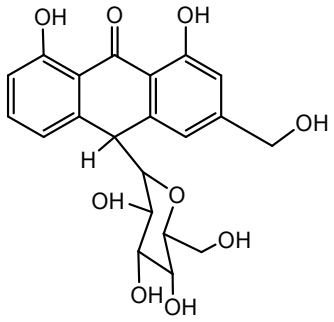
Aloe pulcherrima: Tekleab T.*et al* (2016), investigated the leaf latex of *A. pulcherrima* screened for its antimicrobial activity against 21 bacterial and 4 fungal strains using the disc diffusion method. The latex displayed a potent inhibitory effect against the majority of the tested bacterial pathogens. Owing to its promising activity, the latex was further subjected to PTLC, which led to the isolation of two major anthrones identified as 7-hydroxyaloin (1) and nataloin (2) Figure 1. The isolated compounds showed broad spectrum antibacterial activity against both Gram-positive and Gram-negative bacteria.

Aloe harlana: Asamenew G.*et al*. (2011) investigated the latex of the medicinal plant *Aloe harlana Reynolds* from Ethiopia subjected to bioassay-guided fractionation, which led to the isolation of two known



1 R= CH_2OH
2 R= CH_3

Figure 1. Chemical structures of compounds isolated from leaf latex of *Aloe pulcherrima*



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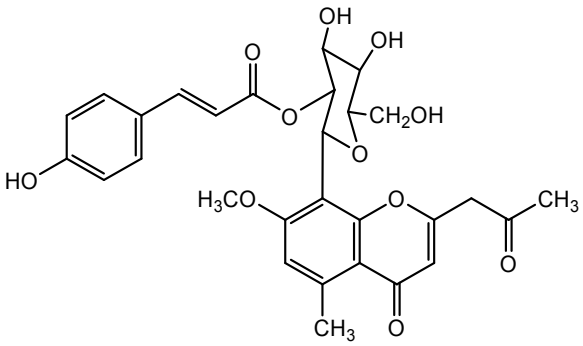

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Figure 2. Chemical structures of compounds isolated from latex of *Aloe harlana*

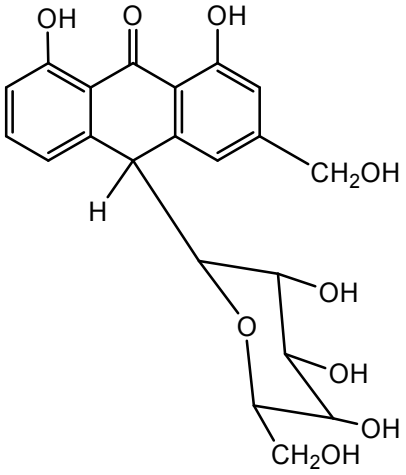

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Figure 3. Chemical structures of compounds isolated from leaf latex of *Aloe debrana*

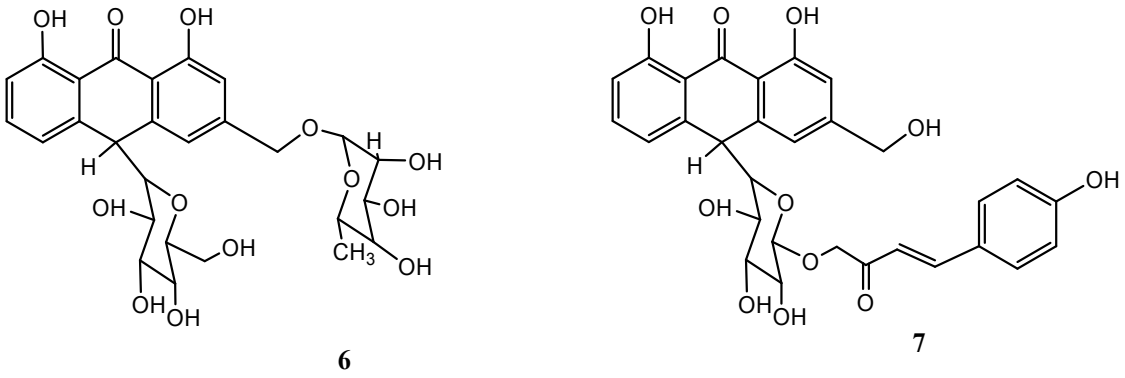
compounds, anthrone (aloin) (3) and chromone (7-O-methylaloeresin A) (4) Figure 2. The latex and its two constituents were assessed for their possible antimicrobial activities against 23 bacterial and four fungal strains using the disc diffusion method and their antioxidant activity by two complementary test systems, namely 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2-deoxyribose degradation assay methods. The isolated compounds showed promising results against various pathogenic bacterial and fungal strains in comparison with standard drugs. Moreover, "compound 4" exhibited good activity against multiple drug resistant Staphylococcus aureus (NCTC 11994) and Salmonella typhimurium (ATCC 1255) with MIC values of 0.72 and 0.18 mm, respectively.

The latex and isolated compounds also showed significant activities on both antioxidant assays with the highest activity being observed for "compound 4", which gave IC50 values of 0.026 mm and 0.021 mm for DPPH and 2-deoxyribose degradation assay, respectively.

Aloe debrana: Worku G.*et al*. (2014) investigated the leaf latex of *aloe debrana Christian* used for the treatment of several diseases including malaria. In search for effective, safe and cheap antimalarial agents from the plants, the leaf latex of *A.debrana* was tested for its in *vivo* antimalarial activity, in a 4-days suppressive assay against plasmodium berghei. Activity-guided fractionation of this latex which showed good antiplasmodial activity resulted in the isolation of two

compounds identified as 10-C-β-D glucopyranosyl-1,8-dihydroxy 3 (hydroxymethyl) -9 (10H) anthracenone, commonly known as aloin, (**3**) and (E)-2-(1-hydroxy-2-methylpropyl)-8-(6'-O-cinnamoyl)-β-D-glucopyranosyl-7-methoxy-5-methylchromone (HCGMM) (**5**) Figure 3. Aloin displayed a significant ($p< 0.05$) antimalarial activity at dose of 25, 50 and 100 mg/kg with chemosuppression values of 48.38, 69.66 and 78.31%, respectively, while the effect of HCGMM was slightly less than that of aloin inhibiting growth of the parasite by 35.49, 47.02 and 63.13%, at the same doses.

Aloe sinana: *Aloe sinana Reynolds* is endemic to Ethiopia, where its leaf latex is traditionally used in and around the town of Debre Sina and other central highlands as a wound-healing agent, insecticide and for the treatment of snake bite and malaria by the local people. The leaf latex of *A. sinana* has been investigated for its antibacterial and antifungal activities. Three anthrones, aloin (3), aloinoside (6) and microdontin (7) Figure 4. Which are responsible for the antimicrobial activity against both Gram-positive and Gram-negative bacteria, have been isolated and characterized (Japheth, 2015).



6 **7**

Figure 4. Chemical structures of compounds isolated from leaf latex of *Aloe sinana*

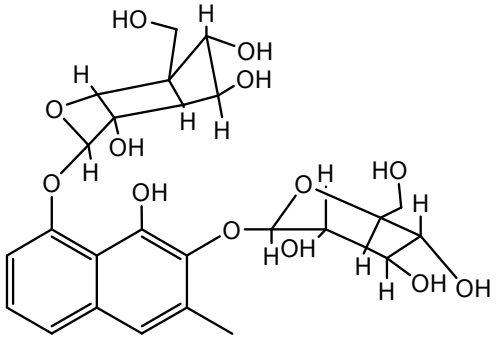


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Figure 5. Chemical structures of compound isolated from leaf exudates of *Aloe otallensis*

Aloe otallensis

Aloe otallensis Baker is endemic to Ethiopia where its leaf exudates is traditionally used in the southern part of the country for the treatment of malaria.The methanol soluble portion of the leaf exudates which was subjected to preparative thin layer chromatography (PTLC) over silica gel led to the isolation of naphthalene derivative identified as 2,8-O,O-di(*β*-D-gluco-pyranosyl)-1,2,8-trihydroxy-3-methylnaphtalene (plicataloside) (8) Figure 5. The exudate and plicataloside were evaluated for their in *vivo* antimalarial activity using a four days plasmodium berghei suppressive test method, and their in *vitro* antioxidant potential assessed by 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay. The exudate (300 mg/kg) and plicataloside (100 mg/kg) inhibited parasite growth by 60.7% and 40.7% respectively. They also exhibited comparable radical scavenging activity with an IC_{50} value of about 26 µg/ml. It was proposed that plicataloside may minimize oxidative stress thereby contributing to the antimalarial activity of the plant (Biniam, 2011).

Aloe calidophila

Fetene. A *et al*., (2014) investigated the antiprotozoal activity of the latex obtained from the Ethiopian plant *Aloe calidophila Reynolds* was evaluated by in vitro testing against *Leishmania aethiopica* and *Leishmania* major. It was found that the latex possesses moderate activity against both parasites with IC_{50} values of 64.05 and 82.29 µg/ml, respectively. Phytochemical investigation resulted in the isolation of three anthrones identified as aloinoside (6), aloin (3), and microdontin (7). The isolated compounds showed strong antileishmanial activity with IC_{50} ranging from 1.76 to 6.32 µg/ml against *L.aethiopica* and from 2.09 to 8.85µg/ml against L.major.

Aloe otallensis

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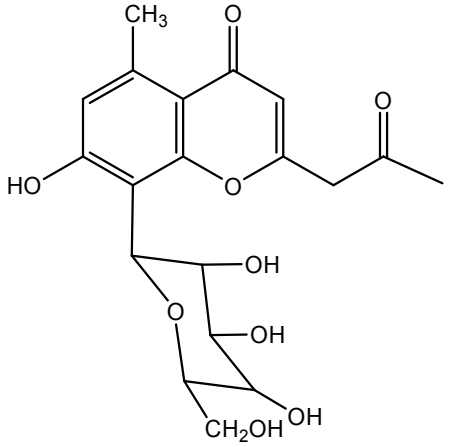
Aloe trigonantha

Mekdes.M et al. (2015), studied the leaves of *Aloe trigonantha* L.C. Leach, endemic Ethiopian plant, locally used for the Although these values were higher than those of amphotericin B (IC_{50} = 0.109 and 0.067 µg/ml), the selectivity indices (813.35 and 694.90, respectively, against *L.aethiopica* and L. major) of aloinoside were much better than those of the standard drug (423.49 and 688.96). the results indicate that the isolated compounds have the potential to be used as a scaffold for the development of safe and cost-effective antileishmanial agents.



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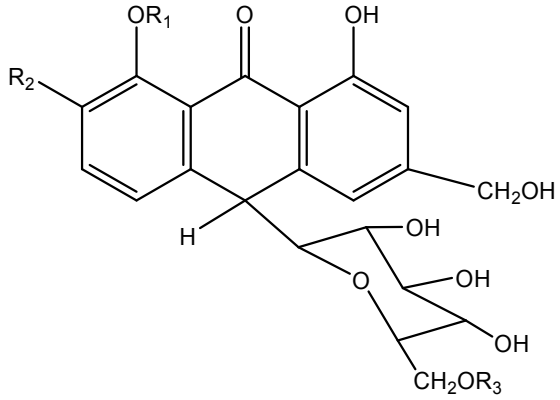
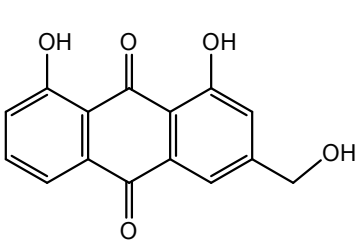


10 R_1= CH_3; R2=OH;R3=H
11 R_1= H; R2= H; R3= $COCH_3$

Figure 6. Chemical structures of compounds isolated from leaf latex *Aloe trigonantha*



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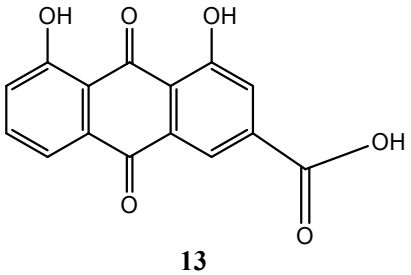

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Figure 7. Chemical structures of compounds isolated from exudate of *Aloe gilbertii*

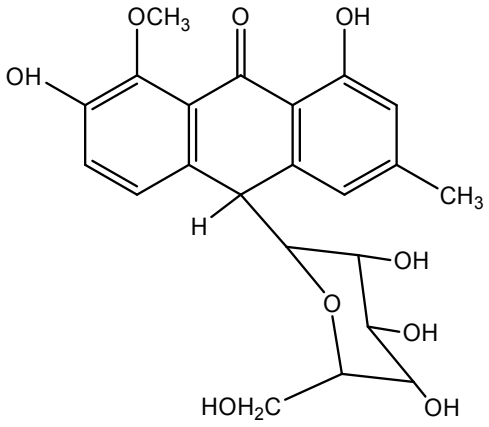

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Figure 8. Chemical structures of compounds isolated from leaf latex of *Aloe citrina*

treatment of infectious and inflammatory diseases. The potential of the latex of the plant and compounds isolated thereof have been studied for their in vitro antibacterial and antifungal properties. A C-glycosylated chromone identified as aloesin (9), and three C-glycosylated anthrones characterized as 8-Omethy-7-hydroxyaloin A/B (10), aloin A/B (3) and aloin-6'-O-acetate A/B (11) Figure 6 were isolated. The latex and isolated compounds exhibited in *vitro* antibacterial activity against the tested pathogens. In some cases the activity of the isolated compounds (MIC = 10 µg/mL) was comparable with that of the standard drug ciprofloxacin, particularly against some of the Gram-negative bacterial strains tested. However, their activity towards the fungal pathogens tested was relatively weaker showing maximum activity against Candida albicans with MIC value of 400 µg/mL.

Aloe gilbertii: Yitagesu.T *et al*. (2014) reported that the exudate of *Aloe gilbertii*, an endemic *Aloe* species of Ethiopia, aloin (3), aloe-emodin (12) and rhein (13) Figure 7 were tested for their in *vitro* and in *vivo* antitrypanosomal activities against Trypanosoma congolense field isolate. Aloin was prepared from the leaf exudate of *A. gilbertii* by acid catalyzed hydrolysis. Aloe-emodin was obtained by oxidative hydrolysis of aloin, while rhein was subsequently derived from aloe-emodin by oxidation. In *vitro* trypanocidal activity tests were conducted on parasites obtained from infected mice, while mice infected with Trypanosoma congolense were used to evaluate in *vivo* antitrypanosomal activity of the test substances. Among the tested substances, rhein showed superior activity with minimum inhibitory concentration (MIC) of 0.4 mg/ml. No adverse reactions were observed when the test substances were administered at a dose of 2000 mg/kg.

Rhein at doses of 200 and 400 mg/kg, and the exudate, aloin and aloe-emodin at a dose of 400 mg/kg reduced the level of parasitaemia significantly ($P < 0.05$) and improved anaemia.

Aloe citrina

Biruktawit.G et al (2015), examined the leaf latex of *A. citrina* was dissolved in methanol and subjected to preparative thin layer chromatography. The latex and its isolated compound were tested for their in *vivo* antimalarial activity using a 4-day suppressive test against chloroquine sensitive ANKA strain of Plasmodium berghei in mice. Homonataloin A/B (14) Figure 8 was isolated as a major component of the latex. Both the latex and isolated compound exhibited significant ($P < 0.001$) antimalarial activity at a dose of 400 mg/kg with parasite suppression of 60.59% and 67.52%, respectively. No significant adverse signs of toxicity were observed in mice treated with the leaf latex up to the highest dose (5000 mg/kg).

CONCLUSION

In order to enhance Ethiopian herbal drugs and traditional use of medicinal plants, there is a need to evaluate the therapeutic potential of the drugs as per the WHO guidelines. Bioactive extracts should be validated and standardized on the basis of phytochemical constituents. Phytochemical studies on the endemic Aloe of Ethiopia have shown are rich sources of different classes of compounds such as anthrones, chromones, pyrones, coumarins, naphthalenes and flavonoids. These classes of compounds have been shown to possess antifungal, antimalarial, antidiabetic, antileishmaniasis and antibacterial activities. As a result, plants from Aloe genus should be explored further as an alternative source of medicine.

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