Traditional Medicines for Treatment African Diseases by Artemisia Annua

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ABSTRACT

The isolation of bioactive compounds from medicinal plants, based on traditional use or ethno medical data, is a highly promising potential approach for identifying new and effective antimalarial drug candidates. Today, a vast store of knowledge concerning therapeutic properties of medicinal plants has accumulated through either experiences or knowledge evolved and transferred to the generation of tribal people, traditional healers or practitioners. The herbs can provide starting material for isolation or synthesis of conventional drugs. The purpose of this review is giving the information regarding the medicine plant in Ethiopia. The history, availability in Ethiopia and application has been also discussed.

Keywords: Abiotic; Biological; Composition; Herbal; Traditional

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1 INTRODUCTION

The history of herbal medicine is as old as human civilization. The widespread use of herbal remedies and healthcare preparations, as those described in ancient texts such as the Vedas and the Bible, and obtained from the commonly used traditional herbs and medicinal plants, has been traced to the occurrence of natural products with medicinal properties. World Health Organization (W.H.O.) currently encourages, recommends and promotes traditional/herbal remedies in National Health Care Programmers because such drugs are easily available at low cost, are comparatively safe and the people have faith in such remedies [1]. Plants synthesize a tremendous number of secondary metabolites, in addition to compounds that are necessary for the growth and reproduction such as carbohydrates, proteins and lipids. As our understanding of chemistry and other natural sciences has increased, the active chemical compounds of the plants have been successfully isolated and identified. Extraction of crude drugs can be done by various processes depending on the physical nature of the drug and chemical properties of the constituents present in it [2]. Various traditional methods used for the extraction of drugs include Infusion, Decoction, Digestion, Maceration and Percolation. Out of these Maceration and Percolation are of particular importance and most Pharmacopoeias refer to these processes for the extraction of crude drugs. The conventional extraction processes are time consuming, if use maceration, it will takes 2–7 days and involves bulk amount of solvents and ultimately there might be thermal decomposition of the target molecule [3].

Artemisia annua is an aromatic annual herb traditionally grown in China as a medicinal plant for treating different types of ailments including malaria, stomach complaints, and hemorrhoids. It has been successfully introduced in many African countries including Ethiopia, it is considered one of the most effective treatments against malaria in the world. It has become the source of income and a life-saver for the community [4]. Actually, this herb used for the crafting of aromatic wreaths, as a source of essential oils used in the beverages industry and also as a source of Artemisinin, a potent antimalarial drug. Currently the plant grows in many regions as Australia, North- and South America, Southern Europe and Africa. Now farmers in Ethiopia are discovering its virtues. Frequently used extraction methods are liquid solvent extraction, Pressurized Solvent Extraction (PSE), Ultrasonic Assisted Extraction (UAE), Accelerated Solvent Extraction (ASE), Microwave-assisted Extraction (MAE), extractions with supercritical carbon dioxide (ScCO₂), hydro fluorocarbon HFC-134a and ionic liquids [6]. The empirical formula of Artemisinin is C₁₅H₂₂O₅. The chemical structure of artemisin is shown in Fig.1.
The demand for new extraction techniques has encouraged the development of alternative extraction techniques and these techniques have enabled automation, shortened extraction time and reduced organic solvent consumption.

2 HISTORY OF ARTEMISIA ANNUA L

Artemisia has been used by Chinese herbalists for more than a thousand years in the treatment of many illnesses, such as skin diseases and malaria. The earliest record dates back to 200 BC, in the "Fifty-two Prescriptions" unearthed from the Mawangdui Han Dynasty Tombs. Its anti-malarial application was first described in Zhouhou Beji Fang ("The Handbook of Prescriptions for Emergencies"), edited in the middle of the fourth century by Ge Hong. In the 1960s a research program was set up by the Chinese army to find an adequate treatment for malaria [7]. In the early 1970s, Chinese scientists screening traditional Chinese medicinal herbs in the search for new anti-malarial isolated artemisinin from the herb known as Qing Hao (generally identified as Artemisia annua L. but may have originally referred to A. apiacea) (Hsu, E., 2006). In 1972, in the course of this research, Tu Youyou (Chinese) discovered artemisinin in the leaves of Artemisia annua [8]. It was one of many candidates then remains tested by Chinese scientists from a list of nearly 200 traditional Chinese medicines for treating malaria. It was the only one that was effective, but it was found that it cleared malaria parasites from their bodies faster than any other drug in history. Artemisia annua is a common herb and has been found in many parts of the world. It remained largely unknown to the rest of the world for about ten years, until results were published in a Chinese medical journal. The report was met with skepticism at first, because the Chinese had made unsubstantiated claims about having found treatments for malaria before [9].

3 ARTEMISIA PLANT AND PRODUCTION

The Plant

Botanically, Artemisia annua is a vigorous weedy annual which is single-stemmed and ranges in height from one to two meters. It grows easily in temperate areas and tropical areas at higher altitudes and is raised in an increasing number of countries. It is well suited to both small-scale and plantation culture. The seed is extremely small and is usually grown to the seedling stage and transplanted. The best quality seed, in terms of production of leaves and yield of artemisinin, is provided by certain forms of purchased seed, which are generally limited in supply. Relatively few inputs are needed, aside from some fertilization, because the plants at present do not seem to have any particular insect or disease problems.
(this could change). Normally, some water is required to establish the crop and dry weather is needed at the harvest and for drying. Artemisinin levels of the plants tend to vary by variety, but the influences of area and growing conditions are not yet clear. It is principally planted early in the calendar year and needs five to six months to mature [10, 11].

Production in Africa
Production was initially largely limited to East Africa - Kenya, Tanzania, and Uganda - and was essentially tied to the activities of one holding company, Advanced Bio-Extracts Ltd (ABE) (www.abextracts.com), and two subsidiaries: East African Botanicals (EAB), Ltd. in Kenya and African Artemisia Ltd. (AA) in Tanzania. In 2007, the name of the firm, reflecting a new investor, was changed to Botanical Extracts Ltd. (BEEPZ) [12]. Contract production was utilized and the firm supplied seed that has proven well adapted to the region; this process also provided a relatively uniform level of artemisinin. The increased demand for artemisinin, starting in 2004, stimulated the efforts to increase the production of Artemisia in East Africa. ABE clearly was in a position to do so. The area subsequently placed under various production arrangements (leased or joint venture efforts) in Kenya, Uganda, and Tanzania (north) expanded to approximately 1,650 ha. (4,100 acres) in 2005. Most of the planting for the calendar year (58.4%) was carried out in the second quarter, followed by lesser amounts in the third (23.8%) and fourth quarters (17.7%). The planted area was principally in Kenya (nearly 65%) followed by Uganda (19%) and Tanzania (north, over 16%) (TechnoServe 2005). Both small and large farms were involved. In 2006, 7,500 farmers were reportedly involved, but area was not revealed. Area estimates for 2007 ranged from 3,500 to 4,000 ha. (8,650 to 9,900 acres) [13]. Currently the plant widely cultivating in many places of Ethiopia.

4 PROPERTIES
Artemisinin is low thermal and chemical stability of the endoperoxide function, low polarity and hence poor solubility in water and good solubility in organic solvents, its extraction with non-polar solvents.

Chemical Constituents of Artemisia Annua
Several secondary metabolites characterize the chemical composition of the genus Artemisia. According to surveyed literature, almost all classes of compounds are observed to be present in the genus with particular reference to terpenoids and flavanoids [14]. A large number of mono terpenoid compounds have been characterized from the essential oil of Artemisia annua. The derivative compound is shown in Fig. 2. The yield of the oil generally varies between 0.3% and 0.4% (v/w). The chemical constituents of Artemisia annua oil varied from country to country for example principal of Chinese oil were 63.9% Artemisia Ketone, 7.5% Artemisia alcohol 5.1%, 4.7% guaine and 3.3% comphor. The Vietnamese oil contained camphor (21.8%), germacerene D (18.3%) and 1.8-cineole (3.1%) etc, in this plant were given much attention is artemisinin, which is responsible for anti-malarial activity. Artemisinin is by lack of nitrogen containing heterocyclic ring system which is found in most anti-malarial drugs. A large number of flavonoids have been reported from the plant and also few compounds like triterpenoids and steroids have been reported [15].
A large variation in artemisinin content has been observed in the leaves of different samples of Artemisia annua. Contents varying from 0.01 to 1.38% in the dry leaves have been reported (Table 1). The variation in the content of artemisinin might be because of several reasons. In addition to the use of different methods for extraction and analysis, the time of collection and preparation of the samples, contributes a lot to the variation among different samples. Moreover, an environmental factor such as temperature and availability of nutrient has also much to do with the variations.

Table 1. Artemisinin content in different samples of Artemisia annua (% dry weight)

<table>
<thead>
<tr>
<th>S.No</th>
<th>Origin of the plant</th>
<th>Artemisinin content (%)</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Europe</td>
<td>0.01</td>
<td>1998</td>
</tr>
<tr>
<td>2</td>
<td>(Connecticut) USA</td>
<td>0.06</td>
<td>1990</td>
</tr>
<tr>
<td>3</td>
<td>Argentina</td>
<td>0.1</td>
<td>1986</td>
</tr>
<tr>
<td>4</td>
<td>China</td>
<td>0.14</td>
<td>1990</td>
</tr>
<tr>
<td>5</td>
<td>Dakota (USA)</td>
<td>0.21</td>
<td>1990</td>
</tr>
<tr>
<td>6</td>
<td>Spain</td>
<td>0.24</td>
<td>1993</td>
</tr>
<tr>
<td>7</td>
<td>China</td>
<td>0.79</td>
<td>1980</td>
</tr>
<tr>
<td>8</td>
<td>Vietnam</td>
<td>0.86</td>
<td>1994</td>
</tr>
<tr>
<td>9</td>
<td>China</td>
<td>1.07</td>
<td>1993</td>
</tr>
<tr>
<td>10</td>
<td>Hybrid (Switzerland)</td>
<td>1.38</td>
<td>1996</td>
</tr>
</tbody>
</table>

Physical properties of Artemisia annua
It has fern-like leaves, bright yellow flowers, and a camphor-like scent. Its height averages about 2 m tall, and the plant has a single stem, alternating branches, and alternating leaves which range 2.5 cm in length. It is in flower from August to September, and the seeds ripen from September to October [16]. The scientific classification is listed in Table 2 and image of leaves is shown in Fig.3.
Table 2. Scientific classifications

<table>
<thead>
<tr>
<th>S.No</th>
<th>Specification</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>kingdom</td>
<td>Plantae</td>
</tr>
<tr>
<td>2</td>
<td>division</td>
<td>Magnoliophyta</td>
</tr>
<tr>
<td>3</td>
<td>Class</td>
<td>Magnoliopsida Plantae</td>
</tr>
<tr>
<td>4</td>
<td>Order</td>
<td>Asterales</td>
</tr>
<tr>
<td>5</td>
<td>Family</td>
<td>asteraceae</td>
</tr>
<tr>
<td>6</td>
<td>Genus</td>
<td>Artemisia</td>
</tr>
<tr>
<td>7</td>
<td>species</td>
<td>Artemisia annua</td>
</tr>
</tbody>
</table>

Formula: $C_{15}H_{20}O_{5}$

Density: $1.24 \pm 0.1$ g/cm$^3$

Melting point: 152–157 °C

Molecular mass: 282.332 g/mol

Fig. 3. Artemisia Annua with physical and chemical property

**Over view of Artemisinin oil**

Artemisinin is a drug used to treat multi-drug resistant strains of falciparum malaria. The compound (a sesquiterpene lactone) is isolated from the plant Artemisia annua. Not all plants of this species contain artemisinin. It can be synthesized from artemisinic acid. Use of the drug by itself as a monotherapy is explicitly discouraged by the World Health Organization as there have been signs that malarial parasites are developing resistance to the drug. The drug is also being studied as a treatment for cancer [17]. The major compound found in essential oil is listed in Table.3.
Table 3. Major compound found in essential oils of Artemisia annua

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Compounds</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Camphor</td>
<td>44</td>
</tr>
<tr>
<td>2</td>
<td>Germacrene D</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
<td>trans-pinocarveol</td>
<td>11</td>
</tr>
<tr>
<td>4</td>
<td>beta-selinene</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>beta-caryophyllene</td>
<td>9</td>
</tr>
<tr>
<td>6</td>
<td>Artemisia ketone</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>alpha-pinene</td>
<td>0.032</td>
</tr>
<tr>
<td>8</td>
<td>camphene</td>
<td>0.047</td>
</tr>
<tr>
<td>9</td>
<td>beta-pinene</td>
<td>0.882</td>
</tr>
<tr>
<td>10</td>
<td>myrcene</td>
<td>3.8</td>
</tr>
<tr>
<td>11</td>
<td>1,8-cineole</td>
<td>5.5</td>
</tr>
<tr>
<td>12</td>
<td>Artemisia ketone</td>
<td>66.7</td>
</tr>
<tr>
<td>13</td>
<td>linalool</td>
<td>3.4</td>
</tr>
<tr>
<td>14</td>
<td>Camphor</td>
<td>0.6</td>
</tr>
<tr>
<td>15</td>
<td>borneol</td>
<td>0.2</td>
</tr>
<tr>
<td>16</td>
<td>beta-caryophyllene</td>
<td>1.2</td>
</tr>
</tbody>
</table>

**Essential oil characteristic**

Essential oil is a concentrated, hydrophobic liquid containing volatile aroma compounds from plants. Essential oils are also known as volatile or ethereal oils or simply "oil off" the plant from which they were extracted. Oil is "essential" in the sense that it carries a distinctive scent, or essence, of the plant. Essential oils do not as a group need to have any specific chemical properties in common, beyond conveying characteristic fragrances. An essential oil is a liquid that is generally distilled, most frequently by steam, from the leaves, stems, flowers, bark, roots, or other elements of a plant and they contain the true essence of the plant it was derived from. Essential oils are generally extracted by distillation. Other processes include expression, or solvent extraction [18]. They are used in perfumes, cosmetics, soap and other products, for flavoring food and drink, and for scenting incense and household cleaning products. Various essential oils have been used medicinally at different periods in history. Medical application proposed by those who sell medicinal oils range from skin treatments to remedies for cancer, and are often based on historical use of these oils for these purposes. Such claims are now subject to regulation in most countries, and have grown vaguer to stay within these regulations. Interest in essential oils has revived in recent decades with the popularity of aromatherapy, a branch of alternative medicine which claims that the specific aromas carried by essential oils have curative effects [19].

5 APPLICATION OF ARTEMISIA ANNUA L

Medicinal use: Artemisia annua essential oil is beneficial for anti-bacteria, anti-periodic, anti-septic and anti-cancer properties. It has the following medicinal uses

**Parasite treatment**

It is commonly used in tropical nations which can afford it, preferentially as part of a combination-
cocktail with other anti-malarials in order to prevent the development of parasite resistance.

**Malaria treatment**

Artemisinin is an unusual sesquiterpene lactone incorporating an endoperoxide group. It has potent anti-plasmodial activity and was shown in clinical trials to be highly effective against malaria, including patients with cerebral malaria and patients with malaria parasites resistant to chloroquine [20-23]. In contrast to other antimalarials such as quinine, (used for treating chloroquine-resistant malaria), artemisinin was found to be remarkably non-toxic and the importance of its discovery against the background of a rising incidence of multidrug-resistant malaria parasites cannot be underestimated.

Several semi-synthetic artemisinin derivatives including artemether, arteether and sodium artesunate are now in clinical use worldwide for the treatment of malaria [24-26]. However, antimalarial drugs such as the artemisinin derivatives are expensive and are not accessible to the majority of people who are at risk of malaria, especially in Africa with the result that approximately 1 million people, mostly children, die from malaria each year [22]. The life cycle Plasmodium falciparum is shown in Fig. 4.

![Life cycle of Plasmodium falciparum](image-url)

**Fig. 4.** Life cycle of *Plasmodium falciparum*
Cancer treatment
The plant has also been shown to have anti-cancer properties. It is said to have the ability to be selectively toxic to some breast cancer cells and some form of prostate cancer, there have been exciting preclinical results against leukemia, and other cancer cells [28]. Artemisinin is the active component of the herb Artemisia annua. (www.allergyresearchgroup.com) The Artemisinin extract provides approximately 300 times more of the active ingredient than the whole herb itself. Artemisinin is non-toxic, so treatment can continue indefinitely with no expected side effects. The World Health Organization recommends Artemisinin in the treatment of Malaria in areas where resistance to Malaria drugs has developed [11]. Artemisinin has a unique chemical structure that prevents cancer resistance. The active molecule in artemisinin reacts with free iron, releasing highly-reactive free radicals that destroy cells harboring free iron. (The iron in our red blood cells is not free iron. Rather, it is strongly bonded to resist the effects of Artemisinin.) Most cancer cells have high rates of iron intake, due to their greedy appetite for blood to support their rapid growth [29]. Thus, if cancer developed resistance to Artemisinin, its blood supply would diminish resulting in tumor death (www.allergyresearchgroup.com).

Edible use
In modern-day central China, specifically Hubei Province, the stems of this plant are used as food in a salad-like form. The food product "cold-mixed wormwood" is a slightly bitter salad with strong acid overtones from the spiced rice vinegar used as a marinade. It is considered a delicacy and is typically more expensive to buy than meat. It is also used as flavorings.

6 CONCLUSION
Ethiopia import medicines from outside that are made from Artemisia annua with expensive prices, but Artemesia annua and other natural medicines growing in our country. The reason for entering the on extraction market at this time is produce Artemisinin in large for our country due to this decrease the death rate by malaria
- Health, societal and economic Benefit
- Environmental Benefit
- Employment Benefit: local economies benefit from job creation in agricultural and manufacturing sectors.

REFERENCE


