



An Overview of Ethiopian Traditional Medicinal Plants Used for Cancer Treatment

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ABSTRACT

Traditional medicine plays a significant role in the healthcare of the majority of the people in developing countries, including Ethiopia, and medicinal plants provide valuable contribution to this practice. Emerging evidence indicates that cancer is becoming one of major health problems in Ethiopia. Relying primarily on field surveys, there have been recent efforts to assess the use of Ethiopian traditional medicinal plants for treatment of various diseases including cancer. The present paper is an overview of the literature reporting the use of these plants for cancer treatment. It was reported that 30 species of plants were used for treating human cancer, with most of them belonging to different plant families. In addition to cancer, a large majority of the plants were also used against various types of other diseases. For most of the plants reported (73%), there was some kind of independent experimental/clinical evidence supporting their claimed anticancer activity. A small number of medicinal plants (13%) were mentioned to be used only in Ethiopia for cancer treatment, but no experimental/clinical confirmation was available. Despite certain limitations of the studies reviewed, the present paper provides useful information on the overall status of Ethiopian traditional medicinal plants as used for treatment of cancer. This information can be used for designing and conducting future research on this important subject.

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1. INTRODUCTION

Traditional medicine is defined by the WHO as "...the sum total of all knowledge and practice, whether explicable or not, used in the diagnosis, prevention and elimination of physical, mental or social imbalances, and relying exclusively on practical experience and observation handed down from generation to generation, whether verbally or in writing" [1]. Experts agree that this definition applies to the practice of traditional medicine in Ethiopia. In common with its implementation in many other regions of the developing world, Ethiopian traditional medicine incorporates various "specialties", including spiritual healing, disease prevention measures, surgery/physiotherapy, midwifery, water therapy and herbal therapy. Up to 80% of the Ethiopian population has been reported to rely on traditional medicine as a major provider of health care [2,3].

Of the different forms of specialized areas, herbal therapy appears to play a prominent role in Ethiopian traditional medicine. Ethiopia is considered the home of some of the most diverse plant species in Africa that serve as sources of many traditional medicinal plants. In Ethiopia, medicinal plants contribute, to about 80% of the traditional medicines used in the country (the others being animal and mineral origins) [4,5]. Most of these plants are obtained from local sources in the wild by knowledgeable traditional practitioners.

It has been reported that approximately 800 species of the medicinal plants grown in Ethiopia are used for treating about 300 medical conditions [6]. Among the widely known medicinal plants, some are claimed to be prescribed by traditional healers for cancer treatment [5,7]. There are varying levels of scientific evidence supporting part of this claim.

During the past three decades, there has been increased worldwide interest regarding the use of herbal medicines/supplements, and consistent with this, the use of traditional herbal therapy in Ethiopia has been on the rise. This increase in the use of herbal therapy has produced a greater desire among researchers to conduct studies on traditional Ethiopian medicinal plants [4-22]. The majority of these studies included surveys of utilization of medicinal plants for the treatment

different diseases in different parts of Ethiopia, as recommended by traditional healers / practitioners. Among the various types of plants identified in these surveys were those claimed to be used for cancer treatment. However, while multiple surveys along this line have been conducted, the information collected thus far is largely scattered and unorganized.

In recent years, it has become more apparent that cancer in Ethiopia is on the rise as a major health problem, as it is true in many other developing countries [23,24]. It has been reported that cancer accounts for about 4% of all deaths in Ethiopia, and this number is likely to increase in due course of time unless intervention measures are taken. In view of this concern and in recognition of the importance of having systematically organized information on potential therapeutic agents of natural origin, the present paper provides an overview of the purported use of Ethiopian traditional medicinal plants for cancer treatment by reviewing the available literature in the field. While such a report on Ethiopian medicinal plants is the first of its kind, it can provide a better understanding of the issues under consideration, and facilitate future research direction in this area of knowledge.

Relevant information on the use of Ethiopian traditional medicinal plants for cancer treatment was collected from peer-reviewed journal articles, books, and other online resources from 1980 until the completion of this manuscript. This has been the time during which most of the important and reliable studies on traditional medicinal plants in Ethiopia were conducted. Besides using hard copy materials as information sources, Pub Med/Medline and Google searches were extensively made to access computer-generated information using specific search terms such as "medicinal plants", "traditional medicine", "Ethiopia", "cancer", "tumor", "anticancer effects", and specific plant names, as needed. Hard copy references were identified by searching library collections of Augusta University and from personal collections of authoritative books. The information collected from different sources consisted of pertinent points on individual traditional medicinal plants and was organized under different headings/subheadings in the text and summarized in table.

2. MEDICINAL PLANTS REVIEWED

The traditional medicinal plants reviewed are described below in two separate groups: those supported with scientific/clinical evidence for their claimed anticancer activity and those without such evidence of support. The highlights of the review are summarized in Table 1.

2.1 Medicinal Plants with Documented Experimental / Clinical Evidence for Anticancer Activity

2.1.1 *Aerva javanica*

Aerva javanica is a species of prostrate shrub belonging to the Amaranthaceae family [25]. It is widely distributed in much of tropical Africa, and in the south and south-west of Asia. The plant has been transplanted in Australia where it covers a wide range of the arid regions of the continent. Because it is deep rooted, the plant is used as a soil binder in desert reclamation [25].

In almost all places where it is found, *A. javanica* has a number of uses in traditional medicine. In Ethiopia, it is commonly known as tobia and has been reported to be used for cancer treatment as a traditional medicinal plant [10]. The roots of the plant prepared in the form of powder are used for this purpose. Other than this, no use of any medical relevance has been reported for *A. javanica* in Ethiopia, although this may not be the case in other countries. Reviewing the literature for scientific evidence in support of the claimed anticancer activity revealed that crude leaf extracts of *A. javanica* possess antiproliferative effect on human breast cancer cell lines (MCF-7) [26,27]. Further, more purified leaf extracts of another species in the genus (*A. lanata*) also demonstrated anticancer, as well as apoptotic activities against different cancer cell lines [26,27].

2.1.2 *Asparagus africanus*

Asparagus africanus is a species of climbing plant in the family Asparagaceae [28,29]. It is native to most parts of the Arabian Peninsula, and sub-Saharan and eastern Africa, including Ethiopia. *A. africanus* is a highly adapting species widely naturalized in most other regions of the world. It is commonly found in forests, rainforest margins, open woodlands, urban bushlands, and in vegetations along waterways [28,29].

In many places where it is found, *A. africanus* is used as an ornamental plant, in addition to some

other uses. In Ethiopia, it is commonly known by the local name yeset kest [5]. The plant is used as a remedy for many disease conditions in the practice of Ethiopian traditional medicine. These conditions include infertility, hemorrhoids, migraine, measles, hemorrhages, rectal prolapse, rheumatism, venereal diseases, uterine prolapse and breast tumor [5,7,28]. The roots of the plant has been reported to be used for tumor treatment.

While several bioactive compounds have been isolated from *A. africanus*, gallic acid has been demonstrated to display antineoplastic properties [7]. Moreover, asparaginase, an enzyme from another species in the genus, (*A. officinalis*) has been reported as a potent antileukaemic agent. Antitumor activity has also been documented for asparagine A from yet another species, *A. racemosus*.

2.1.3 *Bersama abyssinica*

Brsama abyssinica is a species of medium-sized evergreen tree belonging to the plant family Melianthaceae [30,31]. It is distributed across sub-Saharan Africa, including Ethiopia, where it is commonly identified as azamirr [16]. In Ethiopia, a liquid preparation from growing shoot tips has been reported to be used as a remedy against dysentery and roundworms, while infusion prepared from the bark (from stem) is administered to treat some forms of tumor [7,16].

To assess the antitumor/anticancer activity of *B. abyssinica*, various types of compounds have been isolated from the plant [7,31]. Among these compounds, hallebergenin 3-acetate and lignin have been shown to inhibit tumor and certain forms of carcinoma, respectively, while six other compounds to display antineoplastic activity.

2.1.4 *Brucea antidysenterica*

Brucea antidysenterica is a species of flowering shrub/tree in the family of Simaroubaceae [7,28,32]. It grows widely in tropical Africa, usually at the edge of semi-humid forests at relatively high altitudes. In Ethiopia, *B. antidysenterica* is commonly known as wagnos or aballo. Preparations made from different parts of the plant are used to treat various conditions in traditional Ethiopian medicine: leprosy, wound, diarrhea, fever, eye disease, rabies and tumor/cancer, among others [28]. For cancer/tumor treatment, pastes made from powered leaves and young twigs with water are reported to be employed topically [7].

Table 1. Summary of review of Ethiopian traditional medicinal plants reported to be used for cancer treatment

Botanical name, with family name in parenthesis	Local name	Part used	Cancer type reported to be treated by medicinal plants	Reported scientific evidence for anticancer effect
<i>Aerva javanica</i> (Amaranthaceae)	Tobia	Roots	Cancer in general [10].	Antiproliferative effect of crude leaf extract against human breast cancer cell lines (MCF-7) [26,27].
<i>Asparagus africanus</i> (Asparagaceae)	Yeset kest	Roots	Uterine cancer, breast cancer [5,7,29].	Antineoplastic and antileukaemic activities of gallic acid and l-asparaginase, respectively, isolated from plant [7].
<i>Brsama abyssinica</i> (Melianthaceae)	Azamirr	Bark	Tumor in general [7,17].	Antitumor and anticarcinoma effect of hallebergenin 3-acetate and lignin, respectively; antineoplastic activity of six other compounds [7,31].
<i>Brucea antidysenterica</i> (Simaroubaceae)	Waginos/aballo	Leaves	Tumor/cancer in general [29].	Antitumor, antileukemic and antineoplastic activity of bruceantin and bruceantinol in cells and animals [7,29]
<i>Cucumis prophetarum/ficifolius</i> (Cucurbitaceae)	Yemdir embuay	Roots	Skin cancer [7,29].	Antineoplastic activity of tetracyclic triterpens [7].
<i>Crinum abyssinicum</i> (Amaryllidaceae)	Yegibb shinkurt	Leaves	Tumor in general [7,11].	Antitumor/anticancer activity of lycorine, crimine, narciclasine, 3-epihalmanthidine, crinamine, lycobetaine preciweliline, crinamide, crinafolidine, criasbetaine, crinasiadine, crinasiatine and crotepoxide [7].
<i>Dorstenia barnimiana</i> (Moraceae)	Worq bameda	Roots/tubers	Tumor visible on body surface [11].	Anticancer activity of styrenes [37].
<i>Gindia involucrate</i> (Thymelaeaceae)	Mejrit/yezingero	Roots	Breast cancer/tumor [7].	Anticancer activity of diterpenes, gnidicin, gnididin and gniditrin; gnidiglucin; gnidilatidin, and mezerein in cancer cell lines [7].
<i>Euphorbia tirucalli</i> (Euphorbiaceae)	Kinchib	Roots, latex	Tumor/cancer in general [7,11].	Antiadenocarcinoma and antisarcoma activity of aqueous/alcohol extracts stems; tumor inhibition by esters of tetracyclic diterpenol phorbol [7]
<i>Gloriosa superba</i> (Liliaceae)	Etse Lebona	Roots	Breast cancer [7,8].	Anticancer activity of colchicine isolated from roots [7].
<i>Jatropha curcas</i> (Euphorbiaceae)	Controversial name	Seeds	Tumor in general [7].	Inhibition of P388 lymphocyte leukemia by plant extracts; antitumor activity of triterpenes, α -amyrin and taraxerol; and the diterpenes, jatrphol, and jatropholone A, B, phorbols [7].
<i>Kalanchoe petitiiana</i> (Crassulaceae)	Indahula	Leaves	Breast cancer, skin cancer [7,29].	Antitumor activity of gallic acid isolated from leaves [7,43].
<i>Lagenaria sicararia</i> (Cucurbitaceae)	Qil/kil	Leaves	Cancerous sores [21,29].	Cytotoxic and anticancer effect of alcohol extract and triterpenoid compounds isolated from stems and fruits against SK-HIP 1 and MCF-7 cell lines [44,45].

<i>Maytenus senegalensis</i> (Celastraceae)	Kebkebe	Bark	Cancer in general [16,29].	Anticancer/antitumor activity of maytansin in mice [33].
<i>Plumbago zeylanicum</i> (Plumbaginaceae)	Amerra	Leaves	Tumor/cancer in general [11,15].	Anticancer/antitumor activity of chitranone, isozeylanicone, zeylanicone, elliptinone, droserone and plumbagin (isolate from roots) in prostate gland [48,49].
<i>Prunus africana</i> (Rosaceae)	Tikur enchet	Roots	Cancer in general [7,8].	Inhibition of prostate hyperplasia by the bark extract, pygeum; antineoplastic activity of tenuifolin and ferulic acid (isolated from roots and leaves) [7,8,51].
<i>Rumex abyssinicus</i> (Polygonaceae)	Meqmeqo	Roots	Breast cancer [52].	Anticancer activity of root extract in tumor cell lines of prostate, brain and breast, and in leukemia cell cultures [52,53]
<i>Solanum nigrum</i> (Solanaceae)	Embuayzerech embuay	Leaves, stems, roots	Cancerous sores [14,17,19].	Inhibition of growth of cervical cancer in mice by plant leaf preparation; antineoplastic activity by solasodine [7].
<i>Stephania abyssinica</i> (Menispermaceae)	Yeayet hareg/itse-eyesus	Roots	External tumor/cancer [7].	Antineoplastic activity by stephanine and stephavanine [7].
<i>Vernonia spp.</i> (Compositae)	Grawa	Leaves	Tumor/cancer in general [7].	Inhibition of Erlich ascites carcinoma cells by plant extracts; inhibition of carcinoma cells of nasopharynx by vernoid, vernodaline and vernomygdin; antitumor and cytotoxic activity by verinolepin in Walker 256 carcinosarcoma in a rat model [7].
<i>Verbascum sinaiticum</i> (Scrophulariaceae)	Yeferes zeng	Roots	Tumor in general [7,8].	Anticancer activity against breast and prostate cancer cells by sinaitien isolated from plant [7,11,18].
<i>Withania somnifera</i> (Solanaceae)	Gezawa	Not reported	External tumor/swelling [7,17,29].	Anticancer activity of plant extract in animal and cell culture cancer models; tumor inhibitory/antimitotic activity of withaferin and withanolides isolated from plant [7,17,29].
<i>Clematis hirsute per</i> (Ranunculaceae)	Yazo hareg	Leaves, stems, bark	Tumor/cancer on neck [8,18,21].	Not reported
<i>Calpurnia aurea</i> (Fabaceae)	Degeta	Leaves	Tumor/cancer on neck [8,11,15-18].	Not reported
<i>Dodonaea angustifolia/viscosa</i> (Sapindaceae)	Ketketa	Not reported	Tumor/cancer on neck [29].	Not reported
<i>Euphorbia abyssinica</i> (Euphorbiaceae)	Kulkuwal	Latex	Skin cancer [8,11,12,19,29].	Not reported
<i>Gladiolus candidus</i> (Iridaceae)	Milas golgul	Roots	External tumor [21].	Not reported
<i>Malva verticillata</i> (Malvaceae)	Lut	Not reported	Tumor/cancer on neck [15,17].	Not reported
<i>Rubia/Rubus discolor</i> (Rubiaceae)	Encheber	Roots	Cancer in general [8,15,29].	Not reported
<i>Ranunculus multifidus</i> (Ranunculaceae)	Etse siol	Roots	External tumor/cancer [8].	Not reported

In connection to the anticancer effect of *B. antidysenterica*, two potential quassinoid compounds (bruceantin and bruceantinol) were isolated from the plant by the US National Cancer Institute (NCI) during its search for anticancer drugs from natural sources [33]. These compounds were found to possess strong antileukemic, anti-tumor and/or antineoplastic activity in cell and/or animal models. However, further investigations in phase 2 clinical trials did not display expected results to continue the trials. Nonetheless, since studies on the anticancer activity of *B. antidysenterica* have not been performed as reported by Ethiopian traditional healers, it is not clear whether or not similar effects are produced by adoption of the traditional protocol.

2.1.5 Cucumis prophetarum/ficifolius

Cucumis prophetarum is a species of tendril-bearing herb in the Cucurbitaceae family [28]. It has variously colored fruits that attract children and some animals. It is widely grown in Africa, Asia and Australia. It is commonly known by the name yemdir embuay in Ethiopia, where it is often seen in pastures [34].

Cucumis prophetarum (same genus as cucumber) is used in traditional Ethiopian medicine as a remedy for a number of conditions including coughing, rabies in dogs, stomach pain, to induce abortion, toothache, bad breath, diarrhea, eye diseases, gonorrhoea, TB, and skin cancer [7,28]. While different parts of the plant are used for treating the different conditions, for skin cancer, pulverized roots made as pastes/ointments are reported to be applied directly onto affected areas. Consistent with the reported anticancer claim in Ethiopia, scientific studies have also demonstrated potent antineoplastic activity for some compounds isolated from the fruits of the plant [7]. Moreover, compounds obtained from the related species, *C. ficifolius* (cucurbitacin D and E), have been found to be potent cytotoxic and antineoplastic agents.

2.1.6 Crinum abyssinicum

Crinum abyssinicum is a species of bulbous plant that belongs to the family of the Amaryllidaceae [35]. This plant prefers a sunny condition on fresh to moist soil to grow well. It is believed to be native to Ethiopia, although it also grows in the adjacent places in the north and southeast. *Crinum abyssinicum* is recognized in Ethiopia by the local name yegibb shinkurt [7].

As a traditional medicinal plant, the leaves of *C. abyssinicum* have been reported to be used in Ethiopia as a remedy for wound, chancroid and some forms of tumor [7,11]. Corroborating with its anticancer effect, studies have revealed that this species and other members of the Amaryllidaceae family contain the compounds lycorine, crimine, narciclasine, 3-epihalmanthidine, crinamine, lycobetaine preciweline, crinamide, crinafolidine, criasbetaine, crinasiadine, crinasiatine and crotepoxide, all with antitumor/anticancer properties [7].

2.1.7 Dorstenia barnimiana

Dorstenia barnimiana is a perennial monoecious herb in the family of Moraceae [36]. It consists of a tuber usually with a small swelling above, accompanied by a relatively large aerial stem. The plant grows well in warm and moist environment. While there is not much literature information on this particular species, it has been reported to be more unique to East Africa, including Ethiopia [36]. However, the genus *Dorstenia* is known to contain as many as 170 species worldwide, most of which are used in traditional medicine for treating various types of diseases in many regions in Africa, and Central and South America [36]. In Ethiopia, *D. barnimiana* is commonly known as worq bameda and is considered to be an important traditional medicinal plant [11]. Among the diseases reported to be treated using this plant are found rabies in dog, syphilis, dysentery, fever, leprosy, coughing and external cancer/tumor visible on the surface of body [11]. For cancer treatment, preparations made from the tuber of the plant are usually applied directly/locally on suspected area of the body. Supporting this claim, in the tubers of *D. barnimiana*, researchers have shown the presence of several closely related anticancer compounds known as styrenes [37].

2.1.8 Gindia involucrate

Gindia involucrate is a perennial herb in the family Thymelaeaceae [38]. It is an erect woody plant with a slender stem and woody rhizomes. It is widely found in tropical Africa in open and/or wooded grassland, and stony hills. In Ethiopia, *G. involucrate* is known by the local name mejrit or yezingero telba and it is used in traditional medicine for treating malaria and breast cancer/tumor [7]. Preparations made from the roots are preferred to be used for cancer treatment. In support of this contention, various

anticancer compounds (evaluated using cancer cell models) have been isolated from this and other species of the genus [7]. These compounds include the diterpenes, gnidicin, gnididin and gniditrin; gnidiglucin; gnidilatidin, and mezerein [7].

2.1.9 Euphorbia tirucalli

Euphorbia tirucalli, is a plant species in the family Euphorbiaceae, which is widely distributed in Africa, prominently in the northeastern part of the continent that includes Ethiopia [39]. It is commonly identified as kinchib in Ethiopia [7]. The plant grows well in semi-arid tropical climates.

Like *E. abyssinica*, *E. tirucalli* produces milky vesicant/poisonous latex that partially contributes to its medicinal value (see also 2.2.4. below). *E. tirucalli* finds multiple uses in traditional medicine in many cultures. Accordingly, the powder of the roots and/or latex has been used in Ethiopia for treating different forms of tumors/cancers and some other conditions such as amoebiasis [7,11]. Experimentally, alcoholic and aqueous extracts of the stems of *E. tirucalli* have been shown to be active against adenocarcinoma and sarcoma. Also, esters of the tetracyclic diterpenol phorbol found in the plant, act as tumor inhibitors [7]. However, even though *E. tirucalli* has been promoted and traditionally used as an anticancer agent, under certain circumstances it also suppresses the immune system and promotes tumor growth [7]. Whether this holds true when the plant is used in accordance with the practice of Ethiopian traditional medicine, remains to be further investigated.

2.1.10 Gloriosa superba

Gloriosa superba is a species of perennial trailing/climbing herb belonging to the family Liliaceae [40]. Although it is believed to be native to tropical Africa and Asia, the species is found widely distributed worldwide. It is commonly recognized as an ornamental as well as a poisonous plant in some parts of the world, *Gloriosa superba* is also used as a traditional medicinal plant for treating various types of diseases [7]. In Ethiopia, this plant species is called Etse Lebona [8]. Although *G. superba* is not widely used in the practice of Ethiopian traditional medicine, there are documents indicating the roots of the plant being used as a remedy for stomachache and breast cancer

when chewed and applied externally on location, respectively [7,8]. Consistent with the anticancer effect, the alkaloid colchicine and related compounds have been isolated from the roots of the plant. Colchicine is a well-known antineoplastic compound which is commonly used in veterinary medicine. It has been shown to work by arresting mitosis at metaphase [7]. Colchicine is also commonly used in medicine to treat acute attacks of gout by the same mechanism of action.

2.1.11 Jatropha curcas

Jatropha curcas is a species of flowering plant in the Euphorbiaceae family [41]. It is cultivated in tropical and subtropical regions worldwide. Its ability to resist a high degree of aridity enables it to grow in deserts.

It has been documented that *J. curcas* is used in traditional Ethiopian medicine for skin infection, wound healing and to inhibit some forms of tumor, among others [7]. A paste made from seed powder of the plant mixed with honey is used in the treatment of tumor. Consistent with this, extracts of the plant has been shown to inhibit P388 lymphocytic leukaemia both *in vitro* and *in vivo* [7]. Several bioactive compounds have also been isolated from the *J. curcas* plant with antitumor properties: the triterpenes, α -amyrin and taraxerol; and the diterpenes, jatrophol, jatrophenolone A, B, phorbols, among others [7].

2.1.12 Kalanchoe petitiiana

Kalanchoe petitiiana is a species of a succulent plant that belongs to the family Crassulaceae [42]. For optimum growth, the plant prefers a sunny to partly-shady condition on fresh to moist soil, with a temperature above 1°C.

Kalanchoe petitiiana is native to Ethiopia and here it is commonly called indahula [28,42]. Different parts of the plant are used for treating a number of disease conditions in Ethiopian traditional medicine. These conditions include epilepsy, trachoma, allergy, intestinal parasites, gonorrhoea, malignant wounds, breast tumor and skin cancer [7,28]. The leaves of the plant have been reported to be used for treating both forms of cancer. Confirming the anticancer effect reported, gallic acid with potent antitumor activity has been isolated from the leaves *K. petitiiana* [7,43]. Similarly, leaf extracts of another species in the genus, *K. tubiflora*, have been shown to inhibit cell proliferation by disrupting centrosome

integrity and chromosome alignment in mitotic cells [7,43].

2.1.13 Lagenaria sicararia

Lagenaria sicararia is a climbing plant that belongs to the Cucurbitaceae family [44]. It is believed to be indigenous to Africa and the first plant to be domesticated by humans [44]. It is now widely distributed almost throughout the world. However, it is mostly cultivated in the tropics and subtropics in a wide range of soil types and at variable altitudes below 2,500 m. The plant has been used for many purposes, primarily to provide food, medicine and utility objects [44]. In Ethiopia, *L. sicararia* is widely found around human settlement areas and it is commonly called qil/kil [21,28]. It is reported to be used as a traditional medicinal plant for treating otitis media, mental illness and cancerous sores [21,28]. To treat cancer, the leaves are crushed and squeezed onto the affected body part. Complying with this, there is scientific evidence that alcohol extracts and some triterpenoid compounds isolated from the stems and fruits of *L. sicararia* exhibit significant cytotoxicity and anticancer activities against SK-HIP1 cell line and human breast carcinoma cell line (MCF-7) [44,45].

2.1.14 Maytenus senegalensis

Maytenus senegalensis is a shrub species belonging to the Celastraceae family [46]. It is widely distributed, but most notably in the savannah regions of tropical Africa, east Africa, Middle East, Arabian Peninsula and India. The species occupies a wide range of habitats, including woodland, undergrowth areas, wooded grassland, river banks and swamp margins. In Ethiopia, *M. senegalensis* goes under the common name Kebkeb [16,29].

Although *M. senegalensis* has been reported to be used in many other traditional medical cultures for the treatment of various non-cancerous ailments, such as respiratory diseases, inflammation, microbial infections and topically for healing wounds, in Ethiopia, interestingly, it is only reported to be used as an anticancer remedy [16,28]. Preparations mostly made from the bark of the plant are used for this purpose.

While a number of bioactive compounds have been isolated from the *Maytenus* genus, maytansin (an ansa macrolide) was isolated

from *M. senegalensis* by the US NCI as a potential anticancer compound [33]. This compound was indeed found to be a potent inhibitor of various forms of tumor in mice but, like the quassinoids from *B. antidysenterica*, it did not show sufficient activity in phase 2 clinical trials [33]. However, it appears relevant to assess the anticancer property of *M. senegalensis* preparation(s) as used by traditional healers.

2.1.15 Plumbago zeylanicum

Plumbago zeylanicum is a species of evergreen shrub with long tuberous roots and straight stems [29,47]. It belongs to the Plumbaginaceae family. It is distributed as a weed throughout tropical and subtropical regions of the world, thriving in well-drained soil. In Ethiopia, it is believed to grow widely and in most places it is known by the local name Amerra [28]. It is used in Ethiopian traditional medicine for the treatment of different types of diseases, including tonsillitis, abdominal colic, eye disease, TB, toothache and cancer/tumor [11,15]. As a remedy for cancer/tumor, the juicy product of squeezed fresh leaves is taken orally by patients suspected of having the disease. In support, the scientific literature also reveals that certain compounds isolated from the plant (chitranone, isozeylanicone, zeylanicone, elliptinone, droserone and plumbagin) have some anticancer effects [48,49]. More notable in this regard is the strong anticancer activity of plumbagin which was isolated from the root of *P. zeylanicum* [48,49]. Plumbagin is a quinoid that has been shown, among other effects, to inhibit tumor by controlling hormone-refractory invasive prostate cancer. Reported molecular targets inhibited by this compound include PKC, STAT-3, AKT and PI-3K. Besides inhibiting cancer cell growth, plumbagin induces apoptosis in these cells [48,49].

2.1.16 Prunus africana

Prunus africana is an evergreen tree within the Rosaceae family [50]. It is native to some regions of sub-Saharan Africa and Indian Ocean islands. The plant requires a moist climate to flourish and it grows well in many parts of Ethiopia, where it is commonly known by the local tikur enchet. Traditionally, *P. africana* is used to treat a number of diseases, the major ones being respiratory disorders, bad breathe, diarrhea, gonorrhoea, rabies in dogs, TB, wounds, ear problems and cancer [7,8]. The root of the plant is preferred for treating cancer.

Supporting the traditionally claimed anticancer activity of the plant, there are some lines of evidence from scientific studies. An extract prepared from the bark of *P. africana* (commonly known as pygeum), has been shown to have anti-inflammatory property and to improve urinary symptoms associated with prostate hyperplasia [7,8,51]. In addition, the compounds, tenuifolin and ferulic acid, isolated from the roots and leaves of *P. africana*, have been demonstrated to be antineoplastic [7,8,51].

2.1.17 *Rumex abyssinicus*

Rumex abyssinicus is a perennial weed plant in the family Polygonaceae [51]. It grows in tropical Africa, particularly in central and Eastern Africa, more commonly in cultivated lands. It is widely known as meqmeqo in Ethiopia [8,11,15-17]. The roots of the plant are commonly used as cosmetic by Ethiopian women in northern Ethiopia for dyeing the palms of the hands and feet. As a traditional medicinal plant, the roots of *R. abyssinicus* are also claimed to be used for treating various types of diseases including hypertension, hepatitis, malaria, gonorrhea, constipation, neuralgia, rheumatism, migraine, ear problems, rabies, scabies, wound, typhus, diabetes and breast cancer [52]. However, concerning the anticancer effect of the plant asserted traditionally, no detailed information is available as to how it is used. On the other hand, there is scientific evidence supporting this activity of the plant. In this regard, it has been shown that extracts of the roots of *R. abyssinicus* displayed cancer inhibitory activity when evaluated in tumor cell lines of prostate, brain and breast, and in leukemia cell cultures [52,53]. As part of the mechanism for this action, COX-2 inhibition by anthraquinones present in the extract has been proposed. It is thus clear that scientific evidence supports the value of traditional knowledge as a possible source of information for developing therapeutic agents [52,53].

2.1.18 *Solanum nigrum*

Solanum nigrum is a species of perennial shrub that belongs to the Solanaceae family [54]. It is believed to be native to Eurasia, but it is unclear when it was introduced into Ethiopia. There are several species of the genus in Ethiopia which share the same local name- embuay/zerech embuay [17,19]. *Solanum nigrum* usually grows in wooded areas and disturbed habitat.

The different parts of *S. nigrum* are reported to be eaten as food in different rural communities of Ethiopia. In addition, the leaves, roots and stems of the plant are used for the treatment of various diseases including stomachache, skin allergy, anthrax, gonorrhea, rabies, cancerous sores [14,17,19]. In support of the reported anticancer effects, the leaves of the plant have been demonstrated experimentally to inhibit growth of cervical carcinoma in mice [7]. *Solanum nigrum* and other species in the genus have been shown to contain the compound solasodine which has potent antineoplastic activity, supporting at least the claimed anticancer activity of the plants used in Ethiopia [7].

2.1.19 *Stephania abyssinica*

Stephania abyssinica is a climbing shrub within the family Menispermaceae [55]. It is found widely distributed in tropical Africa, including Ethiopia. Its natural habitat includes grassland, abandoned fields and road sides, at elevations up to 3500 m. The plant is obtained from the wild for local use as a source of medicine and dyeing material. In Ethiopia, it is commonly called yeayet hareg or itse-eyesus [11,17,28]. As a traditional medicinal plant, it is used in Ethiopia as a remedy against multiple conditions, including anthrax, stomach problems, miscarriage, rabies, syphilis and external tumor/swelling [7]. For treatment of tumor/swelling, the root of the plant is crushed, squeezed and then spread on affected part of the body. In confirmation of the antitumor activity reported, stephanine and stephavanine isolated from *S. abyssinica* have been shown to exhibit antineoplastic activity [7]. Other compounds with anticancer properties have also been isolated from several other members of the genus [7].

2.1.20 *Vernonia* spp. (*V. amygdalina* and *V. hymenolepis*)

Vernonia is a genus of about 1000 species of relatively small plants in the Compositae family [56,57]. There are numerous distinct subgenera and subsections in this genus that are known for having intense purple flowers. In Ethiopia, at least two species of *Vernonia* have been reported to grow widely and be used in the practice of traditional medicine as a remedy for different types of disease conditions. These are *V. amygdalina* and *V. hymenolepis*, with overlapping medicinal uses in some aspects [7,28].

Vernonia amygdalina is the species that grows more widely in tropical Africa [56-58]. In its natural habitat, it grows more commonly in overgrazed areas, forest edges and in secondary scrub, 1700-3000 m above sea level. Because of its bitter taste, the species is called bitter leaf. However, the cooked leaves are eaten as vegetable in different forms in tropical Africa. In Ethiopia, *V. amygdalina* is commonly known by the local name grawa [7,19,21,28]. Its leaves are often used to prepare a local drink called tella. On the other hand, *V. hymenolepis* (with the same local name) is less popular in Ethiopia. The nutritional composition of *V. hymenolepis* leaves is generally believed to be comparable to that of *V. amygdalina*, but the former is less bitter [19,21,56-58]. Compared to *V. amygdalina*, there is less information on *V. hymenolepis* regarding its use in Ethiopia.

As a traditional medicinal plant, different parts of *V. amygdalina* are used in Ethiopia for treating ascariasis, excessive menstrual bleeding, wound, gastrointestinal disorder, malaria, and cancer/tumor [7]. On the other hand, *V. hymenolepis* is more recognized for its use as an antitumor. Confirming the anticancer effects claimed for both plants in Ethiopian traditional medicine, extracts from both species were found to be active against Erlich ascites carcinoma cells under in vitro condition [7].

As a follow up to the above anticancer effects, different potentially bioactive compounds have been isolated from both *V. amygdalina* and *hymenolepis* and other species of *Vernonia*. Among the many compounds isolated, vernoid, vernodaline and vernomygdin have been shown more convincingly as effective cytotoxic and antitumor in multiple tests [7]. More specifically, both compounds exhibited inhibition of carcinoma cells of nasopharynx *in vitro*, among other effects. Another compound identified as verinolepin was also reported to act as cytotoxic as well as antitumor against Walker 256 carcinosarcoma in a rat model [7].

2.1.21 *Verbascum sinaiticum*

Verbascum sinaiticum is a biennial plant species in the family Scrophulariaceae [59]. It is commonly found in eastern Africa and the Arabian Peninsula. It grows in a wide range of geographic areas in Ethiopia and is commonly known by the local language yeferes zeng [8,11,18,28]. In traditional Ethiopian medicine, it is used for treating a number of ailments including ascites, anthrax, diarrhea, fever, heart

disease, impotence, infertility and tumor [7,8,11,18,28]. The roots have been implicated for tumor treatment. Consistent with the reported use of *V. sinaiticum* as antitumor, the chemical compound sinaitiein has been isolated with proven anticancer activity against breast and prostate cancer cells [7].

2.1.22 *Withania somenifera*

Withania somnifera is a shrub in the Solanaceae family [60]. It is common in open grasslands and it is widely found in Ethiopia, where it is more commonly known by the local name gezawa [8,15,17,18,29]. As a traditional medicinal plant, *W. somnifera* is used in Ethiopia as a remedy for malaria, arthritis, and tumor/swelling [7,17,29]. Supporting the reported antitumor effect, extracts of the plant have been reported demonstrating anticancer activity in animal and cell culture models [7]. Further, the compounds, withaferin A and withanolides isolated from *W. somnifera* have also been shown to possess tumor inhibitory effect [7]. Withaferin A was also shown to have antimetabolic action.

2.2 Medicinal Plants with no Documented Experimental / Clinical Evidence for Anticancer Activity

2.2.1 *Clematis hirsute perr*

Clematis hirsute perr is a species of woody climbing plant among more than 250 species in the family of Ranunculaceae [61]. It usually grows in galleried forest and in open or wooded areas. It is found widely spread in tropical Africa and in regions of intermediate altitudes, including Ethiopia. *Clematis hirsute*, in Ethiopia, is commonly known as yeazo hareg, and as a traditional medicinal plant it has been reported to be used for treating edema, leishmaniasis, herpes, hemorrhoids and tumor on the neck, among others [8,18,21]. Powder made from barks, leaves and stems of the plant are applied directly to affected tumor sites. However, there is no experimental or clinical evidence supporting or rejecting this claim, thus awaiting future investigations.

2.2.2 *Calpurnia aurea*

Calpurnia aurea is a species of a small multi-stemmed tree in the family Fabaceae [62]. It occurs widespread in bushland and grassland in sub-Saharan Africa and India. In Ethiopia, it is commonly recognized as degeta, which is often

found in overgrazed areas [28]. *Calpurnia aurea* is used in traditional Ethiopian medicine to treat diverse medical conditions and parasitic infestations, both in humans and animals. In humans, these conditions include scabies, syphilis, tinea capitis, rectal prolapse and cancer on the neck [8,11,15-18]. For cancer, leaf powder of the plant mixed with water is applied externally on site. Although the compounds calpurmenin, virgiline and lupanine have been isolated from *C. aurea* as biologically active ingredients in several aspects, their role as anticancer compounds has not yet been specifically determined/established.

2.2.3 Dodonea (V. angustifolia and D. viscosa)

Dodonaea angustifolia is an evergreen slender shrub belonging to the Sapindaceae family [63]. It is commonly found in scrub, mountain and in rocky soils. Although it is considered to be native to Australia, it is widely distributed throughout the tropics and subtropics. Growing in Ethiopia, it is commonly known by the local name ketketa [8,11,15,16,19,21,28]. It has a wide range of traditional therapeutic applications in Ethiopia, including treatment of multiple infectious and non-infectious disease conditions, such as snake bite, taeniasis, gastrointestinal disorders, and cancer on neck [28]. However, no information is available in the literature as to how the plant is used traditionally for cancer treatment nor is there scientific evidence for its claimed anticancer activity.

2.2.4 Euphorbia abyssinica

Euphorbia abyssinica is a succulent, leafless tree belonging to the family Euphorbiaceae [64]. It is a plant that survives well in moist montane forest, humid woodlands and scrub savannah, mostly in East Africa. In Ethiopia, it grows in dry, moist and wet agroclimatic zones, usually above 1,900 m. Locally, it is widely known by the name kulkuwal [28]. *Euphorbia abyssinica* produces milky vesicant/poisonous latex which in part contributes to its traditionally claimed medicinal property. Although *E. abyssinica* finds some use as a traditional medicinal plant in Ethiopia, it is mostly used by the local population for live fencing, firewood and timber.

There is no published information on the use of *E. abyssinica* as a traditional medicinal plant outside Ethiopia. On the contrary, it is classified as a poisonous plant by the US Food and Drug Administration (FDA) [65]. In Ethiopia, the plant has been reported to be used in traditional

medicine for the treatment of a number of diseases including ascariasis, gonorrhoea, leprosy, rabies, 'mitch' (allergy), toothache, syphilis, tinea infestation, TB, and skin cancer [8,11,12,19,28]. For skin cancer treatment, pulverized roots and plant latex prepared as pastes/ointments are applied onto the affected area. However, the effectiveness this treatment has not been verified scientifically for this particular species. On the other hand, reports on two other related species of Euphorbia, namely, *E. tirucalli* and *E. prolifera*, have described their use as anticancer/antitumor remedies in traditional medicine outside Ethiopia [7]. In addition, compounds isolated from these species have also been shown to possess anticancer activities. Based on the reported information, it is justifiable to scientifically evaluate *E. abyssinica* for what it is used in Ethiopia by traditional medicine practitioners.

2.2.5 Gladiolus candidus

Gladiolus candidus is one of the more than 300 species that belongs to the family Iridaceae [66,67]. It mostly grows in moderately moist soil in a sunny condition. The genus is found in Asia, southern Europe, sub-Saharan Africa and South Africa. *Gladiolus candidus* is considered by some authorities to be native to eastern Africa, which includes Ethiopia. In Ethiopia, the species is popularly known as milas golgul, which has been used in traditional medicine for treatment of some diseases, among which are included edema and cancerous tumor [21]. As to cancer treatment, powdered root is either applied directly on the tumor or it is taken orally by mixing it with water. However, there is no experimental or clinical evidence reported in the literature supporting this claim.

2.2.6 Malva verticillata

Malva verticillata is a species of plant within the family Malvaceae [68]. It is reported to be widely found in east Asia. It mostly inhabits woodland areas of different soil types. The genus is widespread throughout the different climatic regions of Africa, Asia and Europe.

In Ethiopia, *M. verticillata* is commonly known as lut and it is used in the practice of the local traditional medicine for treating various diseases including vomiting, dysentery, and tumor of the neck [15,17]. However, there is no report on the use of *M. verticillata* as an anticancer medicinal plant in any other known traditional medical

practice elsewhere, nor is there scientific evidence confirming or refuting this claim. The lack of evidence awaits further investigations based on the traditional knowledge reported.

2.2.7 Rubia/Rubus discolor

Rubia discolor is a perennial species of blackberry in the family Rubiaceae, which occurs widely in different parts of the world [69]. While the plant is cultivated for its berries in some places, growing as a wild plant in most other places has given it the reputation of being considered an invasive species. In Ethiopia, *R. discolor* is found in different altitude zones and it is commonly known by the local name encheber [28].

In Ethiopian traditional medicine, *R. discolor* is used to treat cough, gastrointestinal disorders and cancer [8,15,28]. The root of the plant has been reported to be used for cancer treatment. The claimed anticancer effect of *R. discolor* in Ethiopia is the first report of its kind, as this has not as yet been documented elsewhere nor has it been investigated scientifically. This observation, once again, provides evidence for the possible role that plant-based natural resources play in the discovery of novel anticancer remedies. It should, however, be noted that experimentally *R. discolor* has been shown to be a powerful antioxidant, a property that could be linked to anticancer activity, despite absence of direct evidence [7]. Moreover, root extracts of a closely related species, namely, *R. cordifolia*, and compounds isolated from the root of this plant have been found to be inhibitory to tumor and neoplasm [7].

2.2.8 Ranunculus multifidus

Ranunculus multifidus is a species of a perennial herb in the family Ranunculaceae [70]. It is found throughout much of sub-Saharan Africa, including Ethiopia, where it is considered a native plant. It often grows in wet ground, near rivers, streams, ditches and swampy places. In Ethiopia, *R. multifidus* is commonly known as etse siol [8,21]. While no documented evidence is available for the medicinal use of this species anywhere else, in Ethiopia, the roots are reported to be used traditionally for cancer treatment externally [8]. However, there is neither experimental nor clinical evidence to support or refute this report. This observation indicates the uniqueness of this species of plant, drawing

greater attention to further investigate the potential for developing anticancer drug therapy.

3. DISCUSSION

Traditional medicine plays an important role in the healthcare of the majority of the people in developing countries, including Ethiopia, and medicinal plants serve as valuable sources of natural therapeutic agents. In recent years, there has been greater awareness that cancer in Ethiopia has become an increasing health problem [23,24]. In view of these important observations, the present paper is designed to give an overview of the purported use of Ethiopian traditional medicinal plants for treatment of cancer based on the review of the available published literature.

Reviewing the literature, it has become apparent that only 30 species of plants have been reported to be used in Ethiopian traditional medicine for the treatment of cancer. Most of these plants belong to a wide variety of unrelated plant families. The following general observations were made regarding the use of these purported anticancer plants.

- (1) For 73% of the plants reported to be used for cancer treatment, there was some kind of independent experimental/clinical evidence supporting their claimed anticancer activity, while this was not the case for the rest (27%) of the plants.
- (2) In addition to cancer, about 93% of the plants were also reported to be used for treating various types of other diseases, while the rest (7%) were used only for cancer treatment.
- (3) Nearly 13% of the plants were reported to be used for treatment of cancer only in Ethiopia, but without documented scientific evidence.

The availability of scientific evidence (experimental and/or clinical) for most of the traditional medicinal plants reviewed, justifies the importance of ethnopharmacological knowledge as a source of information for drug discovery and/or development using scientific methods. This positive correlation between the two experiences provides support for continued scientific research on purported anticancer activity of plants that have not yet been experimentally/clinically tested. Such an effort may lead to the discovery of therapeutic substances through scientifically validated

methods. Since 27% of the medicinal plants reviewed (about 13% used only in Ethiopia) fall in this category, this observation is too important to be ignored.

The fact that many plant species (93%) were reported to be used for treating different types of diseases (some of them unrelated), besides cancer, suggests that each of the plants in this category may contain different bioactive constituents with different biological and therapeutic effects. Alternatively, the possibility exists that one constituent may have different effects on different systems. However, a more likely scenario would be a combination of both effects. To have a better understanding of the processes involved, and exploit the opportunity that may be available, it is relevant to conduct further research geared towards addressing this particular issue. Such research may enable to come up with a more targeted treatment modality, with a likelihood of reduced adverse consequences.

4. LIMITATION

It should be noted that, aside from the relatively limited number of publications reported on Ethiopian traditional medicinal plants, at least some of the surveys reviewed for the current paper were associated with one or more of the following shortcomings: (1) lack of proper documentation of the identity of plant species; (2) collection of information based on self-reporting that may be associated with recall bias and misinformation; (3) lack of reporting of documented experimental/clinical evidence along with the rest of the survey information; and (4) lack of collection of some other key information in survey studies, such as specifics/details on diseases and methods of use of plant materials for treatment.

5. CONCLUSION

In spite of the above noted limitations on the reviewed papers, the present overview provides, for the first time, valuable compilation of information on Ethiopian traditional medicinal plants claimed to be used for cancer treatment. While most of the information presented is supported by various types of scientific evidence, with justifications for further exploration, the rest of the information still awaits initial evaluation. In short, the present work on purported anticancer medicinal plants can be a valuable initial source of information for overall understanding of the

subject and for designing and conducting future research by identifying areas of weaknesses and formulating research approaches that need be pursued.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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