

## A Review on Traditionally Used Medicinal Plants/Herbs for Cancer Therapy in Ethiopia: Current Status, Challenge and Future Perspectives

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### Abstract

Cancer is a disease which occurs when changes in a group of normal cells within the body lead to uncontrolled growth causing a lump called a tumor; this is true of all cancers except leukemia (cancer of the blood). If left untreated, it leads to death by invading and destroying normal cells. Ethiopia is one of the developing countries which are seriously affected by cancer due to lack of awareness and inaccessible to modern medicine on time. To reduce the severity of this serious problem, about 80% of the population still rely on the traditional medicine as a primary health care modality throughout the country. Even though many plants/herbs have been used by traditional healers of Ethiopian society, many species still await to have scientific evidence of their anticancer activity. The aim of this review is to collect available data about the cancer therapy of medicinal plants/herbs so far studied by ethnobotanical surveys and scientific study in Ethiopia country. It reviews on traditional medicinal plant used by traditional healers within communities of different regional state in Ethiopia country. Out of 65 plants/herbs reviewed in this study, only 30 plants/herbs have been scientifically studied by different researchers at different times for its medicinal value/pharmacological activity against different types of cancer diseases at *in vitro* stage. The rest still needs further investigation to confirm its biological activity for cancer therapy. In general, this review shows the therapeutic potential of many traditional medicinal plants/herbs that can be used in future to treat various types of diseases including cancer.

**Keywords:** Anticancer activity; Medicinal plants/herbs; Ethnobotanical; Cancer; Ethiopia

### Introduction

Cancer is a general term applied to abnormal growth of cells that starts to grow and propagate through uncontrolled cell division and gradually expand throughout body and finally lead to death by invading and destroying normal cells [1-3]. Skin cancer is the most common of all the cancers that affecting peoples due to exposure to uncontrolled ultra violet radiation [4]. Carcinogenic infections are also one of an important cause of cancer, particularly in less developed countries. In 2008, 32.7% of sub-Saharan Africa were affected by cancer through uncontrolled carcinogenic infections [2,5]. According to the World Health Organization (WHO), cancer represents non-communicable diseases responsible for 63% of deaths worldwide, where it is characterized as the second cause of death after cardiovascular disease and was responsible for the death of 7.6 million people in 2005, 12.7 million new cancer cases in 2008, about 14 million new cases and 8 million cancer-related deaths in 2012 [6-10]. However, its severity will be expected to increase to 75 million prevalent cases, 27 million incident cases and 17 million cancer-related deaths by 2030 [9,10].

Recently, Ethiopia is one of the developing countries which are seriously affected by cancer and it has been reported that cancer death accounts for about 4% of all death [11,12]. Only about 15% of all cancers may be inherited from genetic defects and the rest are strongly affected by environmental risk factors such as exposure to ultraviolet ray, aging, diet, lifestyle, smoking cigarette and exposure to harmful substances [13]. So far, cancer treatment is based on surgery,

radiotherapy and chemotherapy. But only 50% of the cancer patients are capable of curing and the rest may have only prolonged survival or even no benefit at all from the treatment and the success of drug therapy is still far from achievement. To overcome this serious problem, a lot of mechanism has been designed to synthesis a potential full anticancer drug. Many hundreds of chemical variants of known class of cancer chemotherapeutic agents have been synthesized but it is not still successfully achieved due to its more side effects. Some recent surveys confirmed that more than 60% of cancer patients use vitamins or herbs as therapy [1]. A successful anticancer drug should kill selectively abnormal or affected cells without excessive damage to normal cells [2,3]. Hence, medicinal plants continue to play an important role in the healthcare system of a large number of the world's population.

Despite the remarkable advancements of the modern medicine, the traditional system of medicine (TSM) still serves as a potential primary health care modality in developing countries. The recent reports suggest that there is a renewed interest has been observed towards TSM even in the developed countries too, because of acute side effects of chemotherapy and radiotherapy can occasionally be life threatening and may affect patient compliance in addition to generating vulnerability to the adoption of herbal medicines use which promise cure [14-16].

According to world health organization, traditional medicine (TM) is the sum total of the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures and nations. It is used in the maintenance of health, prevention, diagnosis, or treatment of disorders. Traditional medicine is popular in the developing world and its use is rapidly spreading in the developed nations. The World Health Organization (WHO) estimates that 80% of

Asian and African populations rely on traditional medicine for their primary health care needs and in the developed countries 70%-80% of the population use some form of complementary and alternative medicine at some stage. In Ethiopia, there is a long history of using medicinal plants to treat a variety of diseases and up to 80% of the population uses it due to the cultural acceptability of healers, local pharmacopeias, the relatively low cost and difficult access to modern health facilities [16-22].

Traditionally, it has been believed that using fruit and leaves from trees/herbs have better potential to heal patients suffering from cancer diseases than modern medicines. Because, these traditional medicinal plants may possess secondary metabolites like polyphenols, terpenes and alkaloids which has anti-mutagenic and anticancer properties. The specific plants to be used and the methods of application for particular ailments were passed down through oral history. Eventually information regarding medicinal plants was recorded in herbals. Right from its beginning, the documentation of traditional knowledge, especially on the medicinal uses of plants, has provided many important drugs of modern day. These traditional medicines initially took in the form of crude drugs such as tinctures, teas, poultices, powders, and other herbal formulations [20,23,24]. Even though many plants/herbs used as a medicine for various diseases including cancer, still it lacks scientific evidence for its therapeutic potential as anticancer agent.

The aim of this review is to collect available data about the cancer therapy of medicinal plants/herbs so far studied by ethnobotanical surveys and scientifically studied in Ethiopia. The information was obtained from scientific research engines Google Scholar between 2000 and 2017.

## Ethnobotanical Survey

The ethnobotanical surveys were conducted in different regional state of Ethiopia country. Several commonly used plants/herbs have

been identified by different ethnobotanical surveys as possessing cancer-preventive properties. These include members of various species as mentioned in Table 1 below. Table 1 shows part of the plant/herb used, type of cancer, method of application and therapy type. It includes experimentally studied traditional medicinal plants used by traditional healers in Ethiopia for cancer therapy.

## Medicinal Plants/Herbs with Scientific/Clinical Evidence

Even though many plants/herbs have been used by traditional healers of Ethiopian society, many species do not have scientific evidence of their anticancer activity. Out of 65 plants/herbs reviewed in this study, only 30 plants/herbs have been scientifically studied by different researchers at different times for its medicinal value against different types of cancer diseases. As reviewed in Table 1, some plants/herbs are traditionally in use at community level but not scientifically studied even though it has promise in future to be used as anticancer.

### *Aerva javanica*

*Aerva javanica* is a species of prostrate shrub belonging to the Amaranthaceae family. It is widely distributed in much of tropical Africa, and in the south and south-west of Asia. The plant is deep rooted and used as a soil binder in desert reclamation [12,25].

In Ethiopia, peoples of different religious and ethical group use *A. javanica* as traditional medicine to treat various diseases including cancer [12,26]. The root powder mixed with bat's blood is taken orally early morning before breakfast to treat breast cancer [26]. Scientifically supported study has been reported that the leaf extracts of *A. javanica* showed antiproliferative effect on human breast cancer cell lines (MCF-7). In addition to this, more purified leaf extracts of another species of *A. lanata* genus also showed anticancer, as well as apoptotic activities against different cancer cell lines [12,27].

Scientific name and family	Type of cancer treated	Parts used	Traditional use
<i>Acalypha acrogyna</i> Pax. (Euphorbiaceae)	All types of Cancer/oral	Leaf	First the leaf is grinded with stone mortar; pestle, the resultant paste is mixed with honey, and given orally in morning. The leaf is heated and applied externally over the tumor-affected area until cure [28].
<i>Afroparpus falcatus</i> (Thunb.) C.N (Podocarpaceae)	Cancer	Leaf	The juice of leaf is used to treat cancer [20].
<i>Asparagus africanus</i> (Asparagaceae)	Uterine cancer, Breast cancer	Root	It has been used to treat uterine prolapse and breast tumor [12,29].
<i>Boscia senegalensis</i> Lam.ex.Poiret (Capparidaceae)	Cancer	Root	By crushing and powdering taken orally and dermally [30].
<i>Brucea antidysenterica</i> (Simaroubaceae)	Tumor/cancer	Leaf	pastes made from powered leaves and young twigs with water [11,12].
<i>Bryonia dioica</i> Jacq. (Cucurbitaceae)	Tumor	All parts	Peoples used it traditionally to treat tumor [31].
<i>Calpurnia aurea</i> (Fabaceae)	Tumor/cancer on neck	Leaf	The paste of the leaf applies on the affected area [11,12].
<i>Carissa spinarum</i> L. (Apocynaceae)	Throat/oral cancer, Cancer	Twigs & leaf, fruit	Young twig and fresh leaf is collected, pounded to make paste, and mixed with honey, given orally until cure [28] and fruits can be used for cancer treatment [20].

<i>Cineraria abyssinica</i> (Asteraceae)	Cancer	Leaf, aerial parts	The aqueous decoction of the leaves and aerial parts [32].
<i>Clematis hirsute</i> Per. (Ranunculaceae)	Tumor/cancer on neck	Leaf, stem, bark	The leaves are crushed and applied on the swelling as bandage [11,12,21].
<i>Clematis simensis</i> Fresen. (Ranunculaceae)	Skin cancer	Leaf	Crushing the leaf and apply it to the area of infection [17,18,22].
<i>Cordia fricana</i> Lam. (Boraginaceae)	Cancer	Leaf	The leaf juice and its paste used to treat cancer [20].
<i>Croton macrostachyus</i> Hochst. ex Delile (Euphorbiaceae)	Cancer	Leaf	The leaf juice and its paste used to treat cancer [20].
<i>Dodonaea angustifolia/african</i> (Sapindaceae)	Tumor/cancer on neck	All parts	The paste of its all parts applied directly on the affected area [11,12] (Continued).
<i>Dodonaea viscosa</i> subsp. <i>angustifolia</i> (L.f.) J.G.West (Sapindaceae)	Cancer	Leaf	The leaf juice or its paste used to treat cancer [20].
<i>Dorstenia barnimiana</i> (Moraceae)	Hemorroid-cancer [33] tumor visible on body surface [26,34]	Aerial parts, Root/tubers	The powder of aerial parts made in to paste with butter and applied topically [33], making small opening at affected part and inserting in the opening with fresh or dry root [26,34].
<i>Dovyalis abyssinica</i> (A. Rich.) Warb. (Flacoutiaceae)	Cancer	Fruit	Six to ten fruits are given to eat [35].
<i>Clarke eranthemoides</i> R. Br. ex C.B. (Acanthaceae)	Tumor	Root	Dried or fresh root powder with water is given orally [35].
<i>Erythrina brucei</i> Schweinf.	Cancer	Bark	The juice of the bark drink for cancer treatment [20].
<i>Euphorbia abyssinica</i> (Euphorbiaceae)	Skin cancer	Latex, stem, bark	Decoction and applying the latex to the affected area [17,18,22], the paste of the stem and bark rub to the affected area [11,12,19].
<i>Fagaropsis angolensis</i> (Engl.) Dale (Rutaceae)	Cancer	Fruit	The juice of fruit taken orally and apply externally on affected area [20].
<i>Gladiolus candidus</i> (Iredaceae)	External tumor	Root	The root is powdered and applied on the wound, or the powder is mixed with water and drunk [11,12,21,26].
<i>Impomea</i> sp. (Convolvulaceae)	Cancer	Root	Making small opening and inserting the root to the affected area by cancer [34]
<i>Lycopersicon esculentum</i> ssp (Solanaceae)	Cancer	Fruit	Fresh fruit washed and ate without cooking [12].
<i>Malva verticillata</i> (Malvaceae)	Tumor/cancer on neck	All parts	It is used to treat tumor/cancer on neck [11,12].
<i>Maytenus ovatus</i> (Wight & Am.) Loes., (Celastraceae)	All types of cancer/oral	Leaf	A handful of leaves are minced to make paste and a small quantity of this paste mixed with honey and given orally for morning and evening till cure [28].
<i>Millettia ferruginea</i> (Hochst.) Baker (Fabaceae)	Cancer	Bark	The juice of bark drink for cancer treatment [20].
<i>Myrsine africana</i> L., (Myrsinaceae)	Cancer	Fruit	Dried fruit with dried leaf of <i>Osyrisquatripartita</i> powdered and mixed with little water and given orally [35] (Continued).
<i>Osyris quadripartita</i> Decn., (Santalaceae)	Cancer	Leaf	Dried leaf with dried fruit of <i>Myrsineafricana</i> , powdered, mixed with water is given orally [35].
<i>Pittosporum abyssinicum</i> Delile (Pittosporaceae)	Cancer	Bark	The juice of bark drink for cancer treatment [20].
<i>Ranunculus multifidus</i> (Ranunculaceae)	External tumor/cancer	Root	The paste of root applies externally on affected area [11,12].

<i>Rubia/Rubus discolor</i> (Rubiaceae)	Cancer in general	Root	The root can be recommended for all type of cancer [11,12].
<i>Rumex nervosus Vahl.</i> (Polygonaceae)	Breast cancer	Leaf	Leaves are crushed, and its paste applied on affected area disease [36].
<i>Stephania cephalantha</i> Hayata (Menispermaceae)	Cancer	All parts	It's all parts used to treat cancer [23].
<i>Tribulus terrestris</i> L. (Zygophyllaceae)	Cancer	All parts	Plant is recommended as anticancer [31].
<i>Ziziphus spina-christi</i> (L.) Desf (Rhamnaceae)	Tumors	All parts	It is used for the treatment of tumor [31].

**Table 1:** Plants/herbs used by traditional healers for cancer therapy in Ethiopia.

### ***Annona muricata* L.**

*Annona muricata* L. is a small, much branched, perennial tree of Annonaceae family of which is a typical tropical tree with heart shaped edible fruits and widely distributed in most of the tropical countries. Its fruit has been used in traditional medicine in many countries as antiviral, antinociceptive, anti-inflammatory and antihyperglycemic properties. It is also effective against multidrug resistant cancer cell line. It has been demonstrated that leaf extracts of *A. muricata* possess significant anticancer potentials in human cancerous cells [37].

### ***Annona reticulata* L.**

*Annona reticulata* L. is referred as bullock's heart, which is a slender semi-deciduous tree is belonging to Annonaceae family and widely distributed throughout Ethiopia [37,38]. Traditionally peoples have been used *A. reticulata* as insecticides, anthelmintic and are also used externally as suppurate. Experimentally, it has been reported that the ethanol extract of roots showed the presence of antiproliferative activity against cancer cell lines *in vitro* [37,39].

### ***Annona squamosa* L.**

*Annona squamosa* L. known as custard apple, is a family of Annonaceae. It is widely used as traditional medicine in different cultural religious for treating various diseases including antitumor [37,40]. It has been supported with scientific evidence that squamosin which is isolated from *A. squamosa*, inhibited proliferation of HL-60 cells and induced apoptosis by the activation of caspase-3. Ascimicin and acetogenin also exhibited cytotoxic activity against different tumor cells [37,41].

### ***Asparagus racemosus***

*Asparagus racemosus* is species which is belonging to Asparagaceae family. In addition to its traditional medicinal value, it has been documented that asparagamine A which is isolated from *A. racemosus* showed antitumor activity [12].

### ***Asparagus africanus***

*Asparagus africanus* is a species of climbing plant in the family of Asparagaceae [29]. In the practice of Ethiopian traditional medicine, it has been used to treat many diseases including uterine prolapse and breast tumor [12,29]. The roots of the plant have been reported to be used for tumor treatment. Of the compounds isolated from *A.*

*africanus*, gallic acid has been demonstrated to display antineoplastic properties [12].

### ***Bersama abyssinica***

*Bersama abyssinica* is a species belonging to Melianthaceae family and traditionally treat tumor using chewing stem peelings [42]. The fresh roots are pounded and juices [43], infusion prepared from the bark (from stem) were administered to treat some forms of tumor [12]. It has been investigated that bufadienolides-cardiac glycosides compound which was isolated from *B. abyssinica* showed antitumor activity [42]. Hallebergenin-3-acetate and lignin have been isolated and shown to inhibit tumor and certain form of carcinoma respectively [12].

### ***Crinum abyssinicum***

*Crinum abyssinicum* is a species of bulbous plant belongs to Amaryllidaceae family and believed to be native to Ethiopia [44]. Traditionally, the leaves of *C. abyssinicum* have been reported to be used in Ethiopia as a remedy for some forms of tumor [12,34]. The leaf powder mixed with hyena feces and latex applies topically on the affected area and gets relief gradually [26]. It has been scientifically demonstrated that *C. abyssinicum* contain the compounds like lycorine, crimine, narciclasine, 3-epihalmanthidine, crinamine, lycobetaine, preciwelline, crinamide, crinafolidine, criasbetaine, crinasiadine, crinasiatine and crotepoxide, all with antitumor/ anticancer properties [12].

### ***Cucumis prophetarum/ficifolius***

*Cucumis prophetarum* is a species of tendril bearing herb of Cucurbitaceae family [29]. It is widely grown in Africa, Asia, Australia and Ethiopia [12]. *C. prophetarum* has been used as traditional medicinal plants by community of Oromo in Ethiopia to treat various human ailments including skin cancer. As reported on different ethnobotanical survey, pulverized roots made as pastes/ointments are applied topically on affected areas. In consistent with the traditional use of this plant, scientific studies have also demonstrated potent antineoplastic activity for some compounds of tetracyclic triterpenes isolated from the fruits of the plant [12,29]. The same to this, compounds cucurbitacin D and E obtained from *C. ficifolius* showed potent cytotoxic and antineoplastic agents [12].

### ***Dorstenia barnimiana***

*Dorstenia barnimiana* is a perennial monoecious herb of Moraceae family and it is more unique to East Africa including Ethiopia [12,45]. It is one of the most known traditional medicinal plants in Ethiopia to treat various human ailments including external cancer/tumor visible on the surface of body [12,34]. The powder of areal parts made in to paste with butter and applied topically to treat hemorrhoid-cancer [33]. Making small opening at affected part and inserting in the opening with fresh or dry root is one of the methods used to treat cancer [26,34]. For cancer treatment, the tuber of the plant is directly applied on the affected area. Experimentally, it has been confirmed that styrene is one of the compounds isolated from the tubers of *D. barnimiana* and demonstrated anticancer activity [12,46].

### ***Eucalyptus globulus***

*Eucalyptus globulus* is a species of Fabaceae family. The Sidama communities of Ethiopia are traditionally use *E. globules* leave to rub on skin to reduce fever and use the boiled leave of a mixture of Eucalyptus and "Damakasse" in water to treat common cold. But the scientific study shows that borneol and euglobal-III are compounds isolated from hexane extracts were reported as antitumor, anthelmintic and antihistaminic activity [42,47].

### ***Euphorbia tirucalli***

*Euphorbia tirucalli* is a plant species in the family of Euphorbiaceae and widely distributed in Africa, prominently in the northeastern part of the continent that includes Ethiopia [12]. *E. tirucalli* produces milky vesicant/poisonous latex that partially contributes to its medicinal value. Traditionally, the powder of the roots and/or latex has been used in Ethiopian communities for treatment of different forms of tumors/cancers and other diseases. Experimentally, alcoholic and aqueous extracts of the stems of *E. tirucalli* have been shown significant activity against adenocarcinoma and sarcoma. The esters of the tetracyclic diterpenol phorbol found in the plant act as tumor inhibitors. 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 [12,29]. So, it needs further investigation to confirm whether it has good anticancer activity or not in order to help the community so far use it.

### ***Gindia involucrate***

*Gindia involucrate* is a perennial herb of Thymelaeaceae family [12]. In Ethiopia, *G. involucrate* is used as traditional medicine for treatment of malaria and breast cancer/tumor. The root part is used for cancer treatment. In consistence with traditional value of this plant, it was experimentally proved the anticancer activities of diterpenes, gnidicin, gnididin, gniditrin, gnidiglucin, gnidilatidin and mezerein compounds isolated from *G. involucrate* against cancer cell models [12,29].

### ***Gloriosa superba***

*Gloriosa superba* is a species of perennial trailing/climbing herb belonging to the family Liliaceae [42]. Traditionally, the root part of this plant has been used for the treatment of breast cancer in Ethiopian societies. First, the root part was chewed and applies externally on the affected breast and then get relieve [12,29,34]. Experimentally, it has

been reported that alkaloid colchicines which is a well-known antineoplastic compound was isolated from root of *G. superba* [12,29].

### ***Jatropha curcas***

*Jatropha curcas* is a species of flowering plant belonging to Euphorbiaceae family [12]. *J. curcas* has been used as traditional medicinal plants for the treatment of various diseases including inhibiting some forms of tumor. A paste made from seed powder of the plant with honey is used in the treatment of tumor. In consistence with its traditional value, the extracts of the plant showed significant inhibition against P388 lymphocytic leukemia both *in vitro* and *in vivo*. Triterpenes:  $\alpha$ -amyrin and taraxerol; the diterpenes: jatrophol, jatropholone A, B and phorbols are compounds isolated from this plant and showed significant antitumor activities [12,29].

### ***Kalanchoe petitiiana***

*Kalanchoe petitiiana* is a species of a succulent plant that belongs to the Crassulaceae family [12,48]. In Ethiopia, the leave part of *K. petitiiana* has been used as traditional medicine to treat many diseases including breast tumor and skin cancer [12,29]. Gallic acid which was isolated from leaves of *K. petitiiana* showed significant antitumor activity which confirms the traditional value of the plant [12,29,49].

### ***Lagenaria sicararia***

*Lagenaria sicararia* is a species of climbing plant that belongs to the Cucurbitaceae family [12]. Traditionally, the leaves are crushed and squeezed onto the affected area and relieve from cancerous sores [12,21,29]. In consistence with its traditional value, alcoholic extracts of some triterpinoid compounds isolated from the stems and fruits of *L. sicararia* exhibited significant cytotoxicity and anticancer activities against SKHIP1 cell line and human breast carcinoma cell line (MCF-7) [12].

### ***Maesa lanceolata***

*Maesa lanceolata* is a species belongs to the Myrsinaceae family and is a shrub widely distributed throughout countries in Central Africa, including Ethiopia and Kenya. It's all parts (flowers, leaves, stem, bark, seeds, and roots) has been used as traditional medicinal plants to treat different human ailments but not known its use as anticancer. Experimentally, the quercetin-3-O rhamnose compound isolated from methanolic extracts of seeds of *M. lanceolata* showed significant antitumor activity against HCT116 cells [44].

### ***Maytenus senegalensis***

*Maytenus senegalensis* is a shrub species belonging to Celastraceae family [12]. In the community of Ethiopia, traditional medicinal plants/herbs are widely used for the remedial solution of different human ailments. As reports of ethnobotanical surveys indicates, *M. senegalensis* is used to treat cancer [12,50]. Ansamacrolide which was isolated from *M. senegalensis* showed significant inhibition against tumor in mice but, like the quassinoids from *B. antidysenterica*, did not show sufficient activity in phase 2 clinical trials [12].

### ***Ostostegia integrifolia***

*Ostostegia integrifolia* is an herbaceous plant belongs to Lamiaceae family [14,51]. Some research has been indicated that stigmasterol



which is one of the chemical constituents of *O. integrifolia* showed to some extent anticancer activities against certain cancers, including ovarian, prostate, breast and colon cancers [14,52]. Its traditional use for the treatment of cancer is not yet known.

### ***Plumbago zeylanicum***

*Plumbago zeylanicum* is a species of evergreen shrub with long tuberous roots and straight stems belongs to the Plumbaginaceae family [53]. It is used in Ethiopian traditional medicine for the treatment of different types of diseases, including cancer/tumor [12,34,54]. The juicy product of squeezed fresh leaves is taken orally to treat cancer/tumor. In consistency with its traditional value, chitranone, isozeylanicone, zeylanicone, elliptinone, droserone and plumbagin were isolated from *P. zeylanicum* have shown anticancer activities. Of the compounds mentioned above, plumbagin which is a class of quinoid inhibit tumor by controlling hormone-refractory invasive prostate cancer (PC-3, LNCaP, and C4-2) [12,53,55-58] with apoptosis induction, which was accompanied by ROS generation and depletion of intracellular GSH levels [55-58]. It is also strong enough to inhibit molecular targets such as PKC, STAT-3, AKT and PI-3K [12]. Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) is a promising anti-cancer agent. Plumbagin enhances TRAIL-mediated apoptosis through up-regulation of death receptor in human melanoma A375 Cells. It activates ERK1/2 and inhibits Akt activity in cancer cells. It activates NAD(P)H oxidase, Src, and PI3K and that the activated PI3K or PDK1 subsequently stimulate Akt and Ras-Raf-MEK1/2-ERK1/2 in 3T3-L1 cells. The antiproliferative and apoptotic activity of plumbagin by using two human colonic cancer cell lines, HT29 and HCT15 showed the IC50 of plumbagin for HCT15 and HT29 cells (22.5  $\mu$ M and 62.5  $\mu$ M, respectively) were significantly different through activation of NF $\kappa$ B, Caspases-3, elevated levels of TNF- $\alpha$ , cytosolic Cytochrome C were seen in both HCT15 cells HT29 treated with plumbagin, aberrant apoptosis with decreased level of pEGFR, pAkt, pGsk-3 $\beta$ , PCNA and Cyclin D1 was observed only in 15  $\mu$ M and 30  $\mu$ M plumbagin treated HCT15 and 75  $\mu$ M plumbagin treated HT29 cells. It has been used to inhibit ultraviolet radiation (UVR)-induced development of squamous cell carcinomas (SCC). It (5-20  $\mu$ mol/L) induces apoptosis of SGC-7901 cells and potentiated the sensitivity of SGC-7901 cells to chemotherapeutic agent TNF- $\alpha$  and cisplatin. The naphthoquinones, juglone and plumbagin could be promising chemopreventive agents for human intestinal neoplasia [55-58]. Ethanolic extract of root has anticancer activity against male Swiss albino mice and Wistar albino rats induced with cancer [53,59].

### ***Prunus africana***

*Prunus africana* is an evergreen tree belongs to Rosaceae family [12]. Traditionally, the root of *P. africana* is used to treat a number of diseases including cancer. In addition to its traditional medicinal value, tenuifolin and ferulic acid those were isolated from the roots and leaves of *P. africana* have been demonstrated antineoplastic properties [12,29].

### ***Rumex abyssinicus***

*Rumex abyssinicus* is a perennial weed plant in the family Polygonaceae. Traditionally, Ethiopian women use the roots of the plant as cosmetic to beauty their palms hands and feet. Like others traditional medicinal plants, its roots also used for treating various types of diseases including breast cancer. The literature report shown that the anticancer activity of the crude extracts of the roots of *R.*

*abyssinicus* seen against tumor cell lines of prostate, brain, breast and in leukemia cell cultures [12].

### ***Solanum nigrum***

*Solanum nigrum* is a species of perennial shrub belongs to the Solanaceae family [29]. The different parts (leaves, roots and stem) of *S. nigrum* are reported to be used as both food and medicinal plants in different rural communities of Ethiopia. It has been used as medicinal plant for the treatment of cancerous sores [12,31,60]. In support with its anticancer effects, experimentally the leaves of the plant have shown significant inhibition against growth of cervical carcinoma in mice. *S. nigrum* and other species in the genus have been shown to contain the compound solasodine which has potent antineoplastic activity and supporting at least the claimed anticancer activity of the plants used in Ethiopia [12,29]. Acetic acid, solanine, solanidine are some of the isolated compounds from leave part of *S. nigrum* showed significant antioxidant, hepatoprotective, anti-tumor cytostatic and anti-convulsant [42,61].

### ***Verbascum sinaiticum***

*Verbascum sinaiticum* is a perennial plant species belongs to Scrophulariaceae family [12]. As a traditional medicinal plant, the community of Ethiopia uses the root part of *V. sinaiticum* for different types of diseases including tumor. In consistent with the reported use of *V. sinaiticum* as antitumor, the bioactive compound sinaiticin has been isolated with proven anticancer activity against breast and prostate cancer cells [12,29].

### ***Vernonia amygdalina***

*Vernonia amygdalina* is a species of relatively small plants belongs to Compositae family [12]. As a traditional medicinal plant, different parts of *V. amygdalina* are used in Ethiopia for relieving from cancer/tumor. In agreement with its traditional value, vernoid and vernomygdin were isolated from *V. amygdalina* and shown inhibition of carcinoma cells of nasopharynx *in vitro*. Another compound identified as verlnolepin was also reported to act as cytotoxic as well as antitumor against Walker 256 carcinosarcoma in a rat model [12,29]. Sesquiterpene lactones, flavonoids (luteolin), coumarins and phenolic acids are among the cancer chemoprevention, free radical scavenging and induce detoxification compounds isolated from leaves and tender shoots of *V. amygdalina* [42,62].

### ***Withania somnifera***

*Withania somnifera* is a shrub species belongs to Solanaceae family [12]. It is Ethiopian traditional plants used to treat different ailments including tumor/swelling. It is experimentally supported that the crude extract as well as compounds (withaferin A and withanolides) isolated from *W. somnifera* shown antitumor properties against animal and cell culture models [12,29].

### ***Zingiber officinale***

*Zingiber officinale* is a species herbal plants belonging to Zingiberaceae family. It is traditionally used as spice and used for motion sickness and gastrointestinal distress. Experimentally, some compounds such as monoterpenoids: gingerols and shogaols are among the isolated compounds from *Z. officinale* act as immuno-

modulatory, antitumorogenic, anti-inflammatory and antiapoptotic [42,63].

## Conclusion

Ethiopia is one of the developing countries which is seriously affected by cancer and it has been reported that cancer death accounts for about 4% of all death. To overcome this serious problem, about 80% of the population uses traditional medicine due to the cultural acceptability of healers and local pharmacopeias, the relatively low cost and difficult access to modern health facilities. Traditionally, it has been believed that using fruit and leaves from trees/herbs have better potential to heal patients suffering from cancer diseases than modern medicines.

This review shows the therapeutic potential of many traditional medicinal plants/herbs that can be used as anticancer agents in future. The extensive study on the anticancer activity of traditional medicinal plants/herbs in Ethiopia highlighted their potential for future chemotherapeutic agents, especially *Annona muricata*, *Bersama abyssinica*, *Crinum abyssinicum*, *Eucalyptus globules*, *Euphorbia tirucalli*, *Gindia involucrate*, *Jatropha curcas*, *Maesa lanceolata*, *Plumbago zeylanicum*, *Prunus Africana* and *Vernonia amygdalina* are among the species which have more phytochemical constituents that showed anticancer properties at *in vitro* stage. Even though many plants/herbs have been used by traditional healers of Ethiopian society, many species still do not have scientific evidence of their anticancer activity. So, it needs scientific study to know whether it has therapeutic potential for cancer treatment or not. In addition to *in vitro* analysis, it needs further investigation at *in vivo* and in clinical trials to know its anticancer potential more for future use. Furthermore, it needs better knowledge and skills on the mechanism of action in order to establish rational phototherapeutic approaches.

## References

1. Kaur R, Singh J, Singh G, Kaur H (2011) Anti-cancer plants: A Review. *Journal of Natural Product and Plant Resource* 1: 131-136.
2. Chavan SS, Damale MG, Shamkuwar PB, Pawar DP (2013) Traditional medicinal plants for anticancer activity. *International Journal of Current Pharmaceutical Research* 5: 50-54.
3. Jaikumar B, Jasmine R (2016) A Review on a few medicinal plants possessing anticancer activity against human breast cancer. *International Journal of Pharm Tech Research* 9: 333-365.
4. Tabassum N, Hamdani M (2014) Plants used to treat skin diseases-A Review. *Pharmacognosy* 8: 52-60.
5. Plummer M, Martel C, Vignat J, Ferlay J, Bray F, et al. (2016) Global burden of cancers attributable to infections in 2012: a synthetic analysis. *Lancet Global Health* 4: 609-616.
6. Alwan A, MacLean DR, Riley LM, Espaignet ET, Mathers CD, et al. (2010) Monitoring and surveillance of chronic non-communicable diseases: progress and capacity in high-burden countries. *The Lancet* 376: 1861-1868.
7. Ferlay JDM, Parkin E, Steliarova F (2010) Estimates of cancer incidence and mortality in Europe in 2008. *European Journal of Cancer* 46: 765-781.
8. Kashfi K (2013) Dysfunctional cell signaling dynamics in oncology: diagnostic, prognostic and treatment opportunities. *Biochemical Pharmacology* 85: 595-596.
9. Forman D, Ferlay J (2014) The global and regional burden of cancer. In: Stewart BW, Wild CP (eds.), Lyon: International Agency for Research on Cancer, pp. 7250-7257.
10. Alves-Silva JM, Romane A, Efferth T, Salgueiro L (2017) North African Medicinal Plants Traditionally Used in Cancer Therapy. *Frontiers in Pharmacology* 8: 1-24.
11. Bruni A (2012) Non-communicable diseases. Cancer - a growing public health concern for Ethiopia. Activities of the genus *Aerva*: a desert plant. *Acta Poloniae Pharm Drug Research* 69: 67-77.
12. Abebe W (2016) An Overview of Ethiopian Traditional Medicinal Plants Used for Cancer Treatment. *European Journal of Medicinal Plants* 14: 1-16.
13. Abu-Rabia A (2015) Key Plants in Fighting Cancer in the Middle East. *Chinese Medicine* 6: 124-135.
14. Karunamoorthi K (2014) Tinjute [*Labiatae*; (*Otostegia integrifolia*)]: A versatile Ethiopian ethnomedicinal plant a systematic review of the scientific evidences. *Tang Humanitas Medicine* 4: 1-6.
15. Pal SK, Fatima SH (2014) Cancer Treatment with the Alternative Herbal Medicine HUMA: Two Case Reports. *Middle East Journal of Cancer* 5: 41-46.
16. Thomford NE, Dzobo K, Chopera D, Wonkam A, Skelton M, et al. (2015) Pharmacogenomics Implications of Using Herbal Medicinal Plants on African Populations in Health Transition. *Pharmaceuticals* 8: 637-663.
17. Kebede D, Alemayehu A, Binyam G, Yunis M (2006) A historical overview of traditional medicine practices and policy in Ethiopia. *Ethiopian Journal Health Development* 20: 128-134.
18. Dejene T (2011) An overview of the role of traditional medicine in Ethiopia. *Journal of Research Arts Education* 2: 34-40.
19. Wabe NT, Mohammed MA, Raju NJ (2011) Ethnobotanical survey of medicinal plants in the Southeast Ethiopia used in traditional medicine. *Spatula DD* 1: 153-158.
20. Kewessa G, Abebe T, Demessie A (2015) Indigenous Knowledge on the Use and Management of Medicinal Trees and Shrubs in Dale District, Sidama Zone, Southern Ethiopia. *Ethnobotany Research and Applications* 14: 171-182.
21. Limenih Y, Umer S, Wolde-Mariam M (2015) Ethnobotanical study on traditional medicinal plants in Dega Damot Woreda, Amhara Region, North Ethiopia. *International Journal of Research in Pharmacy and Chemistry* 5: 258-273.
22. Wubetu M, Abula T, Dejenu G (2017) Ethnopharmacologic survey of medicinal plants used to treat human diseases by traditional medical practitioners in Dega Damot district, Amhara, Northwestern Ethiopia. *Bio Medicinal Central* 10: 1-13.
23. Amuamuta A, Na-Bangchang K (2015) A review of ethnopharmacology of the commonly used antimalarial herbal agents for traditional medicine practice in Ethiopia. *African Journal of Pharmacy and Pharmacology* 9: 615-627.
24. Kasa T (2016) Uses of medicinal plants in Ethiopia: A Review. *International Journal of Advanced Research* 4: 242-248.
25. Kamalanathan D, Natarajan D (2013) Anticancer potential of leaf and leaf-derived callus extracts of *Aerva javanica* against MCF-7 breast cancer cell line. *Journal of Cancer Therapy Research* 9: 215-226.
26. Teklehaymanot T (2009) Ethnobotanical study of knowledge and medicinal plants use by the people in Dek Island in Ethiopia. *Journal of Ethnopharmacology* 124: 69-78.
27. Kamalanathan D, Natarajan D (2014) Antiproliferative and antioxidant potential of leaf and leaf derived callus extracts of *Aerva lanata* (L.) against human breast cancer (MCF-7) cell lines. *Journal of Natural Product* 4: 271-279.
28. Rangunathan M, Solomon M (2009) The study of spiritual remedies in orthodox rural churches and traditional medicinal practice in Gondar Zuria district, Northwestern Ethiopia. *Pharmacognosy Journal* 1: 178-183.
29. Fullas F (2001) Ethiopian traditional medicine: common medicinal plants in perspective. Sioux City, IA: USA.
30. Birhanu A, Haji F (2017) Ethnobotanical Study of Medicinal Plants Used for the Treatment of Human and Livestock Ailments in Dawe Kachen

- District of Bale Zone, Southeast Ethiopia. *International Journal of Emerging Trends in Science and Technology* 4: 5043-5055.
31. Yadav RH (2013) Medicinal plants in folk medicine system of Ethiopia. *Journal of Poisonous and Medicinal Plants Research* 1: 007-011.
32. Meresa A, Gemechu W, Basha H, Fekadu N, Teka F, et al. (2017) Herbal Medicines for the Management of Diabetic Mellitus in Ethiopia and Eretria including their Phytochemical Constituents: A review. *American Journal of Advanced Drug Delivery* 5: 040-058.
33. Birhanu Z, Endale A, Shewamene Z (2015) An ethnomedicinal investigation of plants used by traditional healers of Gondar town, North-Western Ethiopia. *Journal of Medicinal Plants Studies* 3: 36-43.
34. Teklehaymanot T, Giday M (2007) Ethnobotanical study of medicinal plants used by people in Zegie Peninsula, Northwestern Ethiopia. *Journal of Ethnobiology and Ethnomedicine* 3: 1-11.
35. Enyew A, Asfaw Z, Kelbessa E, Nagappan R (2014) Ethnobotanical Study of Traditional Medicinal Plants in and Around Fiche District, Central Ethiopia. *Current Research Journal of Biological Sciences* 6: 154-167.
36. Araya S, Abera B, Giday M (2015) Study of plants traditionally used in public and animal health management in Seharti Samre District, Southern Tigray, Ethiopia. *Journal of Ethnobiology and Ethnomedicine* 11: 1-25.
37. Saripalli HR, Dixit PK (2014) Studies on Morphological Features and Biological Activities of the Genus *Annona* of Ethiopia, N. E. Africa with a Special Emphasis on *Graviola*: A Review. *International Journal of Science and Research* 5: 821-827.
38. Zegeye H, Teketay D, Kelbessa E (2011) Diversity and regeneration status of woody species in Tara Gedam and Abebaye forests, northwestern Ethiopia. *Journal of Forestry Research* 22: 1-315.
39. Suresh HM, Shivakumar B, Hemalatha K, Heroor SS, Hugar DS (2011) In vitro anti proliferative activity of *Annona reticulata* roots on human cancer cell lines. *Pharmacogony Research* 3: 9-12.
40. Kachhawa JBS, Sharma N, Tyagi S, Sharma KK (2012) Screening of Stem Bark Methanol Extract of *Annona squamosa* for Antibacterial Activity. *International Journal of Current Pharmaceutical Research* 4: 48-50.
41. Biba VS, Amily A, Sangeetha S, Remani P (2014) Anticancer, Antioxidant and Antimicrobial Activity of *Annonaceae* Family. *World Journal of Pharmacy and Pharmaceutical Sciences* 3: 1595-1604.
42. Busse H, Tefera G (2013) *Handbook of Sidama Traditional Medicinal Plants*. University of Wisconsin-Madison School of Medicine & Public Health, Madison, WI: USA.
43. Misha G, Yarlagaadda R, Wolde-Mariam M (2014) Knowledge, Attitude, Practice and Management of Traditional Medicine among People of Shopa Bultum, Southeast Ethiopia. *Research Journal of Pharmaceutical, Biological and Chemical Sciences* 5: 152-170.
44. Shin SY, Dekebo A, Dinku W, Terfa A, Lee YH, et al. (2014) Identification of an Anticancer Compound Contained in Seeds of *Maesa lanceolata*, a Medicinal Plant in Ethiopia. *Journal of Korean Society for Applied Biological Chemistry* 57: 519-522.
45. Zhang EH, Wand RF, Guo SZ, Liu BU (2013) An update on antitumor activity of naturally occurring chalcones. *Evidence Compulsory and Alternative Medicine* 6: 15-29.
46. Bhandurgesa P, Rajarajeshwari NB, Ganapatya S, Pattanshettib S (2013) The *Gnidia* genus: A review. *Asian Journal Biomed and Pharmaceutical Science* 3: 1-3.
47. Kumar HD, Laxmidhar S (2011) A Review on Phytochemical and Pharmacological of *Eucalyptus Globulus*: A Multipurpose Tree. *International Journal of Research in Ayurveda and Pharmacy* 2: 1527-1530.
48. Hsieh YJ, Leu YL, Chang CJ (2013) The anticancer activity of *Kalanchoe tubiflora*. *Alternative Medical* 1: 18-19.
49. Lim KT (2012) *Lagenaria siceraria*. Edible medicinal and non-medicinal plants. *Journal Pharmacogony and Phytochemistry* 1: 117-124.
50. Birhanu Z (2013) Traditional use of medicinal plants by the ethnic groups of Gondar Zuria District, North Western Ethiopia. *Journal of Natural Remedies* 13: 2320-3358.
51. Sadaf HM, Bibi Y, Riaz I, Saboon MAS, Bibi F (2016) Pharmacological aptitude and profiling of active constituent from *Otostegia limbata*-Comprehensive review. *Asian Pacific Journal of Tropical Disease* 6: 918-924.
52. Gabay O, Sanchez C, Salvat C, Chevy F, Breton M, et al. (2010) Stigmasterol: a phytosterol with potential anti-osteoarthritic properties. *American Journal Clinical Nutrition* 18: 106-116.
53. Chauhan M (2014) A review on Morphology, Phytochemistry and Pharmacological activities of medicinal herb *Plumbago Zeylanica* Linn. *Journal of Pharmacogony and Phytochemistry* 3: 95-118.
54. Gebeyehu G, Asfaw Z, Enyew A, Raja N (2014). Ethnobotanical study of traditional medicinal plants and their conservation status in Mecha Woreda, West Gojjam Zone of Ethiopia. *International Journal of Pharmaceutical Heal Care Research* 2: 137-154.
55. Jain S, Dwivedi J, Jain PK, Satpathy S, Patra A (2016) Medicinal Plants for Treatment of Cancer: A Brief Review. *Pharmacogony Journal* 8: 87-102.
56. Powolny AA, Singh SV (2008) Plumbagin-induced Apoptosis in Human Prostate Cancer Cells is Associated with Modulation of Cellular Redox Status and Generation of Reactive Oxygen Species. *Pharmaceutical Research* 25: 2171-2180.
57. Checker R, Sharma D, Sandur SK, Subrahmanyam G, Krishnan S, et al. (2010) Plumbagin inhibits proliferative and inflammatory responses of T cells independent of ROS generation but by modulating intracellular thiols. *Journal of Cell Biochemistry* 110: 1082-1093.
58. Chen CA, Chang HH, Kao CY, Tsai TH, Chen YJ (2009) Plumbagin, Isolated from *Plumbago zeylanica*, Induces Cell Death through Apoptosis in Human Pancreatic Cancer Cells. *Pancreatology* 9: 797-809.
59. Hiradeve S, Kishor D, Vijay K, Bibhilesh M (2010) Evaluation of anticancer activity of *Plumbago zeylanica* L. leaf extract. *International Journal of Biomedical Research* 1: 1-9.
60. Mesfin F, Demissew S, Teklehaymanot T (2009) An ethnobotanical study of medicinal plants in Wonago Woreda, SNNPR, Ethiopia. *Journal of Ethnobiology and Ethnomedicine* 5: 28-39.
61. Atanu FO, Ebiloma UG, Ajayi EI (2010) A review of the pharmacological aspects of *Solanum nigrum* Linn. *Biotechnology and Molecular Biology* 6: 01-07.
62. Farombi EO, Owoeye O (2011) Antioxidative and Chemopreventive Properties of *Vernonia amygdalina* and *Garcinia biflavonoid*. *International Journal of Environmental Research and Public Health* 8: 2533-2555.
63. Badreldin HA, Blunden G, Tanira MO, Nemmar A (2008) Some phytochemical, pharmacological and toxicological properties of ginger (*Zingiber officinale* Roscoe): A Review. *Food and Chemical Toxicology* 48: 409-420.