Original article

Review of Ethnobotanical and Ethnopharmacological Evidences of some Ethiopian Medicinal Plants traditionally used for the Treatment of Cancer

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Abstract

Background: Ethiopia is endowed with enormous diversity of plants. However, the majority of these plants have not been scientifically investigated. Traditional knowledge on the use of plants as medicinal agents has been transferred from generation to generation, as guarded secrets, through the word of mouth, and scientific studies on these herbs have not been properly compiled.

Objectives: The main objective of this study was to review published ethnobotanical and ethnopharmacological evidences of Ethiopian medicinal plants with anticancer potentials.

Material and methods: A total of 92 articles have been reviewed. They were obtained from search engines such as PubMed, Science Direct and Google Scholar. The following keywords were used to search for the literature inside the databases: plant extract, anticancer, Ethiopia, antioxidant compounds, cytotoxic compounds and *in vivo* toxicity.

Results: The current literature review revealed that about 136 anticancer plants belonging to 57 families have been identified in Ethiopia. Among these, 98 plant species were reported for their traditional use to treat different types of symptomatic cancers. However, only 29 species were scientifically studied for their *in vitro* cytotoxic or free radical scavenging activities. Plant parts commonly used for preparation of anticancer remedies were leaves (41.4%) and roots (32.8%). Among the reported plant species, whilst the crude extracts of *Artemisia annua*, *Acokanthera schimperi* and *Catha edulis* were found to be potent cytotoxic agents (IC_{50}<15 μg/ml), the total extracts of *Cassia arereh*, *Rubus steudneri* and *Thymus schimperi* showed strong radical scavenging activity (IC_{50} <15 μg/ml). Chronic administration of *Syzygium guineense* hydroalcoholic leaf extract, on the other hand, induced pathological changes in liver and kidney of mice.

Conclusions: Although several Ethiopian plants traditionally used for the treatment of cancer were shown to possess cytotoxic and free radical scavenging activities, in most cases compounds responsible for such activities have not been identified. Therefore, activity-guided detailed phytochemical studies coupled with evaluation of the safety particularly on those plant extracts that demonstrated potent activities should be carried out as this may lead to the discovery of safe and cost effective anticancer agents. [*Ethiop. J. Health Dev.* 2017;31 (3):161-187]

Key words: Ethiopian medicinal plants, Antioxidant, Anticancer, Ethnopharmacology, Traditional use

Introduction

Cancer is a complex disease that is variable at the cellular and molecular levels in its presentation, development and outcome. Modern managements of cancer, including surgery and radiation therapy, have been the methods of choice to control non-metastatic cancers (1). Metastatic cancers, on the other hand, are managed better by anticancer chemotherapeutic drugs (2) that usually lack specificity and tend to damage rapidly dividing normal tissues, causing side effects like immunosuppression, neurotoxicity and hair loss (3). Therefore, in view of the side effects and growing incidence of cancer both in developed and developing countries, it is only logical to look for novel compounds in order to treat it.

The use of bioactive compounds of plants as a source of anticancer leads has been a major focus in cancer research. These compounds are synthesized in plants by shikimic acid, salonic acid, mevalonic acid and non-mevalonate (MEP) pathways (4). Among these compounds, alkaloids (5), glycosides (6), flavonoids (7) and terpenoids (8) were reported to have anticancer properties. Between 1994 and 1997, out of 87 approved anticancer drugs, 54 were synthesized from natural products or based on the chemical structures of novel natural bioactive compounds (9). Moreover, there has been world-wide increase in the use of herbal and other natural products among cancer patients (10). This might be due to the lack of access to conventional anticancer drugs, financial difficulties, and ineffectiveness and side-effects of most conventional anticancer therapies (11-13).

Traditional knowledge, chemotaxonomic information and random screening have been the main approaches for selecting plant species in anticancer drug research (14). However, selection of plant species based on traditional knowledge relied on generations of empirical experiences with locally available natural

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resources that can be used to suggest suitable extraction methods for individual plant species (15). In this review, an attempt has been made to summarize reported ethnobotanical and ethnopharmacological studies on Ethiopian medicinal plants that show promising potential for facilitating in-depth investigation of the active constituents, efficacy and safety thereby pave a way for the discovery of anticancer agents.

Methods

Data collection was carried out from November 2014 to December 2015 by analyzing published scientific materials retrieved from online bibliographical databases such as PubMed, Science Direct and Google Scholar; and the book *Illustrated Checklist of Medicinal Plants and Other Useful Plants of Ethiopia* by Dawit Abebe and his colleagues (22). The following keywords were used to search for the literature inside the databases: plant extract, anticancer, antitumor, antioxidant compounds, cytotoxic compounds and Ethiopia. The criteria followed for inclusion of plants which grow in Ethiopia in this review include reported (i) traditional use for treatment of symptoms described by the English word 'cancer' or 'tumor' (ii) *in vitro* and *in vivo* anticancer activities and (iii) pure active anticancer constituents isolated or classes of compounds identified.

Anticancer plants: Due to geographical diversity that favors the occurrence of different habitat and vegetation zones, Ethiopia is considered as the home to many of plant species. More than 60% of Ethiopia's indigenous plant species are believed to have healing potential (16). Among these indigenous species, about 1,000 plants have been used to treat different illnesses for centuries (17). However, ethnomedicinal use of these plants against different diseases was usually kept in Ethiopian Orthodox churches (written in Geez on parchments) or by individual healers and has been passed from generation to generation by word of mouth (18-19).

In this paper, a total of 136 plant species (belonging to 57 families) that grow in Ethiopia are documented (tables 1, 2 and 3). Among these, 98 plant species (belonging to 49 families), traditionally used for treatment of different type of symptomatic cancers in different parts of Ethiopia, only 29 were scientifically investigated for their *in vitro* and *in vivo* cytotoxic or radical scavenging activities (table 3). Similarly, only few plant extracts were evaluated for their *in vivo* toxicity (table 4). The major reason for the small number of pharmacological and toxicological studies may be attributed to the limited number of published ethnobotanical studies and lack of standard laboratory facilities. However, even the available pharmacological studies were seldom based on the traditional use of anticancer medicinal plants.

***Medicinal plants used in traditional symptomatic cancer treatments*:** The etiology and description of cancer in Ethiopian traditional medicinal system is complex and usually tied with socio-cultural and religious beliefs. Ethiopian traditional healers, being technologically challenged, usually find it difficult to accurately diagnose cancer by linking symptoms with underlying pathological changes. According to studies conducted in different parts of Ethiopia, wide range of symptoms like swelling, gland tuberculosis and skin ulcer are described by the same Amharic term 'Nakarsa/Nekersa'. Unfortunately, this term or its other local language equivalents are also used to describe symptomatic cancer/tumor in different parts of the country (35, 46). Among different local language equivalents of 'Nakarsa/Nekersa'; Keledo around Harla and Dengego, Eastern Ethiopia (47), Minshro nekersa around Northern Ethiopia (48) and Naqarsa around Bale Mountains National Park (49) were reported. To avoid possible confusion, in this review paper, medicinal plants that were only reported to be traditionally used to treat symptom described by the English word 'cancer' or 'tumor' are included.

Ethnobotanical studies considered in this paper were mainly reported from the northwestern (32.6%), southern (30.4%) and southwestern parts (15.2%) of Ethiopia. Asteraceae, Fabaceae and Lamiaceae were the dominant botanical families, containing over 6 plant species each used for traditional cancer treatment. Shrubs constituted the largest growth habit (40 species, 41%) followed by herbs (33 species, 34%) and trees (16 species, 17%) (Tables 1and 2). Physical mass reduction methods like chopping, crushing and powdering were commonly applied, and the dominant plant parts used were leaves (41.4%) and roots (32.8%). Fresh plant parts were often extracted by water and sometimes their powder form was mixed with honey (7), butter (2) or other plant species extracts. Accessory additives in herbal recipes like honey and butter are important in improving the taste and decreasing adverse effects like vomiting (50). Bat's blood and hyena feces, though it is difficult to guess the rationale behind their use, were also used as additives to treat symptomatic cancer in some parts of the country (35).

Although they lack precision in determination of doses, traditional healers usually establish doses based on age, physical appearance and duration of the illness. Reported unit of measurement used to establish the dose of traditional herbal remedies in Ethiopia were finger length for roots and barks, pinch for powder, water cup for latex/liquid and numbers for leaves, seeds and fruits (35). However, to increase people's trust and compare the clinical effectiveness, pharmacological effects and side-effects with conventional anticancer drugs, therapeutic dose of herbal remedies should be standardized. According to reviewed studies, prepared remedies were commonly taken orally (53.85%), topically (33.85%) and nasally (1.54%). Usually remedies prepared in the form of decoction, infusions and tinctures were taken orally, while remedies in solid or powder form were inserted after incising external tumors (20).

Poly-herbal remedies are products with medicinal properties containing two or more herbal extracts. The

use of poly-herbal therapies might increase or decrease the effectiveness or toxicity of these medicines (51). Synergistic anticancer effect of poly-herbal therapies could be attributed to pharmacologic or biochemical interaction of various active principles of herbs included in the mix. For instance, the combination of curcumin (isolated from *Curcuma longa*) and genistein (isolated from *Glycine max*) was found to increase the potent antiangiogenic effect against human prostate cancer cell line than monotherapy (52). However, herbalists might also use poly-herbal treatment approach, either due to lack of confidence on the curative ability of single remedy or to keep the ingredients secret (46).

Pharmacology: Out of 68 plants reported for their pharmacological activities, 29 were used for symptomatic cancer treatment in Ethiopian folk medicine (table 3). However, ethnobotanical knowledge of the remaining 39 plants was not reported. Large numbers of cytotoxic and/or antioxidant plants were reported from the Asteraceae (9) and Fabaceae (9) families. Reviewed studies used more than 8 solvents to extract the plants and 13 cell lines for cytotoxicity assays. HL-60 cell line was the most commonly used cell line and cytotoxicity studies were conducted using MTT and Alamar Blue assays. For *in vitro* screenings of cytotoxic plant extracts, IC_{50} value of 30 μg/ml represents a cutoff point to be considered for further purification (53). Among reported plant species, crude extracts of *Artemisia annua*, *Acokanthera schimperi* and *Catha edulis* were reported to have an IC_{50} value of less than 15 μg/ml.

Overproduction of free radicals, mainly due to oxidative stress, may cause oxidative damage to biomolecules like DNA, lipids, and proteins leading to many serious diseases, including cancer and diabetes in humans (54). Anticancer medicinal plants may exert their antioxidant effect due to compounds like flavonols that counteract free radicals (55). Bioactive flavonol glycosides such as quercetin-3,7-di-O-glycoside isolated from *Lepidium sativum* were reported to have free radical-scavenging and antioxidant properties (56). Similarly, studies on Ethiopian plants also revealed significant antioxidant activities of *Rubus steudneri*, *Cassia arereh*, *Rumex nepalensis*, *Thymus schimperi*, *Senna singueana*, *Plumbago zeylanica*, *Bersama abyssinica* and *Euclea racemosa* (Table 3).

Compounds with in vitro and in vivo studies: Although 136 Ethiopian medicinal plants are claimed to be used to treat cancer traditionally, a few were checked for their cytotoxic and antioxidant bioactive compounds. Among these compounds, potent cytotoxic activity of knipholone anthrone, a compound isolated from *Kniphofia foliosa*, was reported to have IC_{50} value that ranges between 0.9 ± 0.1 and 3.3 ± 0.4 μg/mL (60). Similarly, quercetin-3-O-diglucosylrhamnoside and rutin from *Chelianthus farinosa*, mangiferin from *Bersama abyssinica* and myricetin-3-O-arabinopyranoside, rutin and myricitrin from *Euclea racemosa* also showed potent radical-scavenging activity (67).

***Toxicity*:** Plants produce biologically active compounds as chemical defense to repel, poison or kill other species. Studies proved the association of active pharmacological ingredients of some herbal remedies with adverse effects that might range from mild allergic reactions to death (75-78). Ethiopian anticancer plants such as *Calotropis procera*, *Croton macrostachyus*, *Euphorbia abyssinica*, *Glinus lotoides*, *Phytolacca dodecandra*, *Plumbago zeylanica*, *Rumex abyssinicus* and *Thymus schimperi* have been reported to cause different types of toxicity (23, 79-82). However, considering the same mechanism shared between toxicity and tumor-regression effects of anticancer plants, only a few toxicity studies have been conducted on these plants (Table 4).

Table 1: **Traditionally used plant species for treatment of cancer/tumor in Ethiopia.**

Family	Botanical name	Vernacular name	Geographical location	Gf	Preparation	Parts used	Ro	Other Ailments treated	References
Acanthaceae	*Justicia schimperiana* (Hochst. ex Nees) T. Anderson	*Kitkit* (Bnc) or *Gulbana* (Kt)	North Bench and Doyo Gena (SNNPR), SE	Sh	Fresh roots are crashed, boiled and the cool decoction is drunk before meal. Fresh leaves are pounded and the juice is applied.	R or L	OR or DR	-	(19)
Aloaceae	*Aloe* sp.	*Gurta waqota* (Kt)	Doyo Gena (SNNPR), SE	Sh	Fresh roots are crashed and the sap is applied on the affected part.	L	DR	-	
Amaranthaceae	*Achyranthes aspera* L.	*Koch ashite* (Bnc)	Mizan Aman (SNNPR), SE	H	Leaves are roasted on metal plate, pounded into powder, mixed with animal butter and smeared on affected part.	L	DR	-	
Amaryllidaceae	*Crinum abyssinicum* Hochst. ex A.Rich.	*Shinkurta*/*boko lo werabessa* (Or)	NA	Bul	NA	NA	NA	Ear ache	(20)
Apiaceae	*Centella asiatica* (L.) Urb.	*Gorongoch* (Sh)	Sheko (SNNPR), SE	H	Young leaves are crashed and the sap sniffed.	L	INS	-	(19)
	Ferula communis L.	*Dog* (Am)	Libo Kemkem, South Gondar, NWE	Sh	Fresh root crushed and drunk with water	R	OR	Impotency, erthroblastosis, evil spirit, aphrodisiac	(21)
	Hydrocotyle mannii Hook.f	*Ye'ti medhanit* (Am)	North Bench (SNNPR), SE	H	Young leaves are crashed and applied.	L	DR	-	(19)
Apocynaceae	*Acokanthera schimperi* (A.DC.) Schweinf.	*Merenz* (Am)	Bahir Dar Zuria, NWE	Sh	Young leaves are crashed and applied.	L	DR	-	
	Carissa spinarum L.	*Agam* (Am), *Hagamsa* (Or)	Gondar and Bahir Dar Zuria, NWE	Sh	Fresh leaf pounded and mixed with honey	L	OR	Malaria, snake bite, aphrodisiac, epilepsy, wounds, impotence, gonorrhea, stomach ache, headache	(13, 19-20, 22-23)
	Catharanthus roseus (L.) G.Don	*Wuluwusha* (Da)	Dawro (SNNPR), SE	H	Pound; cut	Aerial part	OR	Liver infection, wounds, rheumatism	(24)

Asclepiadaceae	*Calotropis procera* (Aiton) Dryand.	*Kobo* (Am), *Ginda* (Ti)	Gewane, NEE	Sh	NA	Fl, R, Ltx	NA	Rough skin, leprosy, venereal diseases, kidney stone, Haemorrhoids, Wart, Tuberculosis	(18-20, 26)
	Pentarrhinum insipidum E.Mey.	*Barohula* (Af)	Gewane, NEE	Sh	Fresh roots are crashed and the sap is applied.	R	DR	-	(19)
	Echidnopsis dammanniana Sprenger	*Mureli* (Af)	Gewane, NEE	H	Stems are cut and the sap is applied.	Sm	DR	-	
Asparagaceae	*Asparagus africanus* Lam.	*Seriti/Kestench a* (Or & Am)	NA	Cl	Powder	R	OR	Gonorrhea, measles, diarrhea, arthritis	(20)
Asphodelaceae	*Kniphofia foliosa* Hochst.	*Shushube*(Or)	Bale Goba, SEE	Sh	Dry roots are pounded and the powder is mixed with honey.	R	OR	-	(19)
Asteraceae	*Acmella caulirhiza* Delile	*Kust asht* (Bnc)	Mizan Aman (SNNPR), SE	Sh	Young leaves are chewed by the healer and spit on.	L	DR	-	
	Artemisia absinthium L.	*Natrara* (Wl)	Sodo Zuria (SNNPR), SE	H	Dried leaves are ground and macerated in coffee or tea.	L	OR	-	
	Artemisia afra Jacq. ex Willd.	*Agufa* (Kt)	Doyo Gena (SNNPR), SE	H	Dried leaves are ground and macerated in coffee or tea.	L	OR	-	
	Artemisia annua L.	*Artemisia* (En)	Sodo Zuria (SNNPR), SE	T	Dried leaves will be ground and decocted in hot water.	L	OR	-	
	Bidens macroptera (Sch.Bip. ex Chiov.) Mesfin	*Adey Abeba* (Am)	Libo Kemkem, South Gondar, NWE	H	Dried and powdered	Fl	Ns	-	(21)
	Cineraria abyssinica Sch.Bip. ex A.Rich.	Unknown	Bale Robe, SEE	H	Fresh leaves are pounded and the sap is applied.	L	DR	-	(19)
	Guizotia scabra (Vis.) Chiov.	*Sheshota* (Kt)	Doyo Gena (SNNPR), SE	Sh	Fresh leaves are pounded and the sap is applied.	L	DR	-	
	Solanecio gigas (Vatke) C. Jeffrey	*Arbaba* (Kt)	Doyo Gena (SNNPR), SE	Sh	Fresh leaves are pounded and the sap is applied.	L	DR	-	
	Vernonia amygdalina Delile	*Girawa* (Am)	Bale, SEE	Sh	NA	L	NA	Wound dressing	(20, 26)

	Vernonia auriculifera Hiern	*Barawa* (Kt)	Doyo Gena and Wendo Genet (SNNPR), SE	Sh	Fresh leaves are pounded and the sap is applied.	L	DR	-	(19)
	Baccharoides filigera (Oliv. & Hiern) "Isawumi, El-Ghazaly & B.Nord."	*Qilxuu* (Or), *Weynagift* (Am)	Nekente, WE Jimma, SWE	T	Decocted leaf is drunk	L	OR	Ear lesion, wounds	(26-28)
Capparidaceae	*Cleome brachycarpa* (Forssk.) Vahl ex DC.	*Berbere* (Af)	Gewane, NEE	H	Fresh leaves are pounded and the sap is applied.	L	DR	-	(19)
Celastraceae	*Gymnosporia buchananii* Loes.	*Atat* (Am), *kambolcha* (Or)	Gondar, NWE	Sh	Leaves are minced to make paste and mixed with honey	L	OR	-	(23)
	Gymnosporia senegalensis (Lam.) Loes.	*Atat* (Am)	Denbi, NWE	Sh		L	OR	Snake repellent	(24, 29)
Colchicaceae	*Gloriosa superba* L.	NA	NA	H	Powdered	R	DR	-	(20)
Commelinaceae	*Commelina benghalensis* L.	*Laluncha* (Kt)	Doyo Gena (SNNPR), SE	H	Fresh roots are pounded and the sap is applied.				(19)
Convolvulaceae	*Ipomoea* sp.	*Filatsut* (Am)	Zegie Peninsula, NWE		Making small opening and inserting	R	DR	-	(30)
Crassulaceae	*Kalanchoe petitiana* A. Rich.	*Endahula* (Am) *Anchura* (Or)	Bale, SEE	H	Fresh leaves are roasted for 2 minutes and applied.	L	DR	Gonorrhea, syphilis, trachoma, tapeworm infection	(19-20)
	Kalanchoe lanceolata (Forssk.) Pers.	*Bosoke* (Or)	Nekemte, WE	H	The juice of freshly squeezed roots and leaf is drunk	R/L	OR	-	(28)
Cucurbitaceae	*Lagenaria siceraria* (Molina) Standl.	*Qil* (Am), *Basu baqula* (Sid)	Hawassa city (SNNPR), SE	Cl	Pounded, powdered, and drink	R	OR	Gonorrhea, haemorrhoids, ascaris, mental illness	(20, 31)

Euphorbiaceae	*Croton macrostachyus* Hochst. ex Delile	*Masincho* (Sid), *Bisana* (Am)	Hawassa city (SNNPR), SE	T	Crushed and inserting to the wound	L/Sd	DR	Malaria, Wound, Gonorrhea, Diarrhea, stomach ache	(19-20, 24, 31-32)
	Euphorbia schimperiana Scheele	*Gendalelata* (Kt)	Doyo Gena (SNNPR), SE	Sh	Fresh roots are pounded and the sap is applied.	R	DR	-	(19)
	Euphorbia tirucalli L.	*Kinchib* (Am) *Anano* (Or)	Fiche, CE	Sh	Mixed with bean powder and eat; apply on the skin	Ltx/R	OR/DR	Wound	(33-34)
	Ricinus communis L.	*Qenbo'o* (Sid), *Kobo* (Or), *Gulo* (Am)	Hawassa city (SNNPR), SE	Sh	Chew and swallow/apply	R	OR/ DR	Constipation, as contraceptive	(20, 24, 31-32)
	Jatropha curcas L.	*Ayderke* (Am)	NA	Sh	Honey paste of the seed powder	Sd	OR	Gonorrhea, hypertension, tape worm, clotting blood, wound healing	(20, 24)
	Acalypha acrogyna Pax	*Gullo* (Am)	Gondar, NWE	Sh	Leaves are grinded and mixed with honey	L	OR	-	(23)
Fabaceae	*Acacia seyal* Delile	*Wacho* (Sid)	Bensa (SNNPR), SE	T	Chewing and swallowing	L	OR	Evil eye, swelling	(31)
	Albizia lebbeck (L.) Benth.	NA	Adekfurdu, Tigray, NE	T	Wheat dough paste of root powder	R	DR	Oral hygiene	(25)
	Calpurnia aurea (Aiton) Benth.	*Digita*(Am)	Bahir Dar Zuria, NWE	Sh	Dry leaves or seeds are ground, macerated in cold water and drunk.	L/Sd	OR	-	(19)
	Crotalaria agatiflora Schweinf.	Unknown	Bale Goba, SEE	Sh	Dry seeds are ground, mixed with honey and applied.	Sd	DR	-	
	Crotalaria incana L.	*Chelke* (Kt)	Doyo Gena (SNNPR), SE	Sh	Fresh leaves are crashed and the sap applied.	L	DR	-	
	Lonchocarpus laxiflorus Guill. & Perr.	*Amera* (Am)	Bahir Dar Zuria, NWE	T	Grounded together with onion and honey	R, L, Bk	DR	-	(23)
	Senna singueana (Delile) Lock	*Gefa*(Am)	Bahir Dar Zuria, NWE	Sh	Fresh leaves are crashed, macerated and drunk.	L	OR	-	(19)
Flacourtiaceae	*Dovyalis abyssinica* (A.Rich.) Warb.	*Koshim* (Am)	Fiche, CE	Sh	Eating 6 – 10 fruits a day	Fr	OR	Abdominal pain	(27, 34)
Iridaceae	*Gladiolus candidus* (Rendle) Goldblatt	*Milas Golgul* (Am)	Dega Damot and Deq island, NWE	H	Powdered and drunk or applied	R	OR/ DR	-	(22, 35)

Lamiaceae	*Ajuga leucantha* Lukhoba	*Tiks asht* (Bnc)	North Bench (SNNPR), SE	H	Fresh leaves are crushed and the sap is applied.	L	DR	-	(19)
	Leonotis ocymifolia (Burm.f.) Iwarsson	*Armagusa* (Am)	Bale Goba, SEE	H	Fresh leaves are crashed, macerated overnight and drunk.	L	OR	-	
	Ocimum gratissimum L.	*Mekedesisa* (Sid)	Wendo Genet (SNNPR), SE	H	Fresh roots are crushed boiled and drunk.	R	OR	-	
	Premna schimperi Engl.	*Xullangee* (Or)	Bule Horra, SWE	Sh	Pounding and making s/n	L	OR/DR	Eye diseases, wounds, toothache, haemorrhoids, hypertension	(30, 37)
	Pycnostachys abyssinica Fresen.	*Tontona* (Kt)	Doyo Gena (SNNPR), SE	H	Fresh leaves are crushed and the sap is applied.	L	DR	-	(19)
	Rotheca myricoides (Hochst.) Steane & Mabb.	*Mardhisiis Aa* (Or), *Malasincho* (Bn)	1. Bule Hora, SWE 2. Bensa (SNNPR), SE	Sh	1. Crush the root mix it with butter and apply 2. Chop leaf and eat or apply;	L; R	OR/DR	Evil eye, stomach bloating, vomiting, urine retention	(32, 35-36, 38)
	Salvia nilotica Juss. ex Jacq.	*Barnbanch* (Bnc) or *Hulegeb/Keskeso* (Am)	North Bench,(SNNPR), SE; Gonder, NWE	H	Fresh leaf is grounded with water to make a paste	L	DR	Wounds, bleeding, Herpes simplex, tonsillitis, constipation	(19, 23-24, 27, 39)
	Thymus schimperi Ronniger	*Tosigne* (Am)	Bale Goba, SEE	H	Dry leaves are decocted and drunk.	L	OR	-	(19)
Malvaceae	*Sida schimperiana* Hochst. ex A. Rich.	*kote jebessa* (Sid)	Wendo Genet (SNNPR), SE	Sh	Fresh leaves and roots are crashed, macerated and drunk.	L and R	OR	-	
Melianthaceae	*Bersama abyssinica* Fresen.	*Azamir* (Am)	Bahir Dar Zuria, NWE	Sh	Dry bark is ground, macerated and drunk before meal.	Bk	OR	-	
Menispermaceae	*Stephania abyssinica* (Quart.-Dill. & A.Rich.) Walp.	*Kalala* (Or)	Nekemte, WE	Cl	The juice of freshly squeezed root is mixed with honey	R	OR	Cholera, gonorrhea, syphilis, wounds, anthrax	(20-21, 28)
Meliaceae	*Lepidotrichilia volkensii* (Gürke) J.-F.Leroy	*Tabecho* (Bn)	Bensa (SNNPR), SE	T	Chopped leaf and fruit mixed with water	L/Fr	OR	-	(40)

Moraceae	*Ficus carica* L.	*Beles* (Am)	NA	T/ Sh	NA	Bk	NA	Cough, ascariasis, eye diseases, leprosy	(20)
	Dorstenia barnimiana Schweinf.	*Work Bemeda* (Am)	Bahir Dar Zuria, Dek island and Zegie Peninsula, NWE	H	- Dry roots are ground, mixed with water and honey and drunk; - Dry roots are ground, mixed with honey and applied; or - Incise and insert into the affected part	R	DR	Diarrhea, goiter, heart failure, gonorrhea, diabetes	(19-20, 30, 35)
Oxalidaceae	*Oxalis corniculata* L.	*Qinta* (Sid)	Wendo Genet (SNNPR), SE	H	Fresh leaves and roots are crashed and applied with a bandage.	L and R	DR	-	(19)
Phytolaccaceae	*Phytolacca dodecandra* L'Hér.	*Endod* (Am)	Bensa and Dawro (SNNPR), SE	Sh	Chopped; pound	L and R	OR	Dandruff, gonorrhea, rabies, amoebic dysentery	(20, 24)
Plantaginaceae	*Plantago lanceolata* L.	*Qorxobi* (Or) *Yebeglat* (Am)	Hawassa city (SNNPR), SE	H	Crushed, powdered and apply	Sd	DR	Diarrhea, trachoma, cough, scorpion bite, wound, Tinea corporis	(20, 22, 27, 31, 41)
Plumbaginaceae	*Plumbago zeylanica* L.	*Martus* (Or); *Amira* (Am)	Ghimbi, SWE; Zegie Peninsula, NWE and Kilte Awulaelo, Tigray, NE	H	Leaf squeezed and taken orally; root powder mixed with sulphur and applied topically; crushed and drunk with boiled coffee or tea	L; R	OR; DR	Gonorrhea, leprosy, lung tuberculosis, syphilis, Tinea corporis and Tinea nigra, cutaneous leishmaniasis, wounds, rheumatism, toothache, abdominal colic	(13, 20, 30, 38)
Podocarpaceae	*Afrocarpus falcatus* (Thunb.) C.N.Page	*Bribira* (Am)	Dek island, NWE	T	Powdered dry root mixed with water	R	OR/DR	-	(35)
Polygonaceae	*Rumex abyssinicus* Jacq.	*Mokemoko* (Ti)	Seharti Samre, Tigray, NE	H	Root powder is mixed in spicy stew	R	OR	Gonorrhea, leprosy, lung tuberculosis, fever	(20, 41)
	Rumex nepalensis Spreng.	*Goecho* (Kt)	Doyo Gena (SNNPR), SE	H	- Dry roots are ground and taken with food; or - Fresh bark is crashed,	R/Bk	OR/DR	-	(19)

					squeezed and the sap is applied.				
	Rumex nervosus Vahl	*Huhot* (Ti)	Seharti Samre, Tigray, NE	Sh	Crushed and paste applied on affected area	L	DR	-	(19-20, 41)
Punicaceae	*Punica granatum* L.	*Roman* (Am)	Libo Kemkem, South Gondar, NWE	T	Crushed and ate	Fr	OR	Gonorrhea, cough, biliharziasis, diarrhea	(20-21)
Ranunculaceae	*Clematis virginiana* L.	*Fidy* (Or)	Bale, SEE	Cl	Pounding the leaves, making s/n or mix with butter	L	OR/ DR	-	(42)
	Clematis simensis Fresen.	*Yeazo Hareg* (Am)	Libo Kemkem, South Gondar, NWE	Cl	Crushed and applied	L	DR	-	(19, 21)
Rosaceae	*Prunus africana* (Hook.f.) Kalkman	*Homii* (Or), *Tikur enchet* (Am), *Gebrcho* (Bn)	Bensa (SNNPR), SE	T	Powdered bark	Bk, L	OR/DR	Swelling	(19, 39, 43)
Rubiaceae	*Pavetta gardeniifolia* Hochst. ex A.Rich.	*Qadiidaa* (Or)	Bule Horra, SWE	Sh	Pounded and applied	R	DR	Liver disease, common cold	(36, 44)
Rutaceae	*Clausena anisata* (Willd.) Hook.f. ex Benth.	*Limich* (Am)	Abay Gorge, NWE	Sh	Dry leaves are ground, mixed with honey and eaten.	L	OR	-	(19)
	Zanthoxylum chalybeum Engl.	*Ga'da* (Sid)	Hawassa city (SNNPR), SE	T	Powdered and drunk	L	OR	Toothache, common cold	(31-32, 44)
Sapindaceae	*Dodonaea viscosa* subsp. *angustifolia* (L.f.) J.G.West	*Kitkita* (Am)	Bahir Dar Zuria, NWE	T	- Dry roots are ground, mixed with honey and applied or - Dry roots are ground, decocted and drunk.	R	DR/OR	-	(19)
Simaroubaceae	*Brucea antidysenterica* J.F.Mill.	*Abalo* (Am, Or)	1. Jimma, SWE 2. SEE	Sh /T	Dry bark is ground, macerated and drunk before meal.	Sm; Bk	NA	Amoebiasis, Tinea corporis, malaria	(19, 43, 26)

Solanaceae	*Discopodium penninervium* Hochst.	*Chechanga* (Kt)	Doyo Gena (SNNPR), SE	Sh	Fresh leaves are crashed and applied.	L	DR	-	(19)
	Solanum americanum Mill.	*Tikur awut* (Am)	NA	Sh	Leaves are boiled thoroughly and eaten	L; R; Sm	OR/DR	Gonorrhea, leprosy, syphilis, rheumatism, toothache, abdominal colic, epistaxis, bleeding after delivery	(20, 41, 45)
Thymelaeaceae	*Gnidia involucrata* Steud. ex A.Rich.	*Mejrit*, *demerarit*, *yezingero telba* (Am)	NA	H	Powdered and paste with honey	R	OR	Gonorrhea, leprosy, syphilis, toothache, heart pain, rheumatism	(19-20, 24)
Verbenaceae	*Lantana trifolia* L.	*Hanshebello* (Sid)	Wondo Genet (SNNPR), SE	Sh	Fresh leaves are ground, macerated in cold spring water and drunk.	L	OR	-	(19)
	Lippia adoensis Hochst.	*Kessie* (Am)	Abay Gorge, NWE	Sh	Dry leaves are ground, macerated in cold water and drunk.	L	OR	-	
Vitaceae	*Cyphostemma serpens* (Hochst. ex A.Rich.) Desc.	*Eiriti* (Af)	Gewane, NEE	Cl	Dry roots are ground, pasted with honey and eaten and applied.	R	OR and DR	-	

Key:- **Growth form** (Gf): H= herb, Cl=climber, Sh=shrub, and T: tree;
Parts: Bk=bark, L= leaves, Ltx= Latex, Sd=seed, Fr=fruit, Fl= Flower, Sm=stem and R=root;
Geographical locations:CE=central Ethiopia, EE= East Ethiopia, WE= West Ethiopia, SE= South Ethiopia, NE= North Ethiopia, NWE= North West Ethiopia, NEE= North East Ethiopia, SWE= South West Ethiopia, SEE= South East Ethiopia and SNNPR= Southern Nations, Nationalities and People regional state;
Vernacular Names: Af=Afarigna, Am=Amharigna, Bnc=Benchigna, Bn=Bensa, Da= Dawrigna, En= English, Kt=Kembatigna, Or=Oromigna, Sid=Sidamigna, Sh=Sheko, Ti= Tigrigna and Wl=Wolayitigna;
Preparation: s/n= Solution;
Route of application (Ro): OR=Oral, INS=Intranasal and DR=dermal; and
NA = Not available

Table 2: **Traditional anticancer medicine with multiple plants prescription**

No	Family	Botanical name	Vernacular name	Geographical location	Gf	Preparation	Parts used	Ro	References
1	Cucurbitaceae	*Cucumis ficifolius* A.Rich.	*Yemidir Embuay* (Am)	Debre Libanos, NWE	H	Powder mixed with water	R	OR	(13, 22, 27, 30, 31, 41)
	Euphorbiaceae	*Euphorbia abyssinica* J.F.Gmel.	*Qulqwal* (Am)		T		La		
		Euphorbia tirucalli L.	*Kinchib* (Am)		Sh		La		
	Fabaceae	*Calpurnia aurea* (Aiton) Benth.	*Digita* (Am)		Sh		L		
	Malvaceae	*Malva verticillata* L.	*Lut* (Am)		H		R		
	Sapindaceae	*Dodonaea viscosa* subsp. *angustifolia* (L.f.) J.G.West	*Kitkita* (Am)		T		L		
2	Amaranthaceae	*Aerva javanica* (Burm.f.) Juss. ex Schult.	*Tobia* (Am)	Dek island, NWE	H	Powder mixed with bat's blood	NA	OR	(35)
	Brassicaceae	*Lepidium sativum* L.	*Fetto* (Am)		H		NA		
	Plumbaginaceae	*Plumbago zeylanica* L.	*Amira* (Am)		H		NA		
3	Amaryllidaceace	*Crinum abyssinicum* Hochst. ex A.Rich.	*Gibb Shinkurt* (Am)		Bl	Powder mixed with hyena feces and latex	NA	DR	
	Crassulaceae	*Kalanchoe petitiana* A. Rich.	*Endehuahula* (Am)		H		NA		
	Euphorbiaceae	*Euphorbia abyssinica* J.F.Gmel.	*Qulqwal* (Am)		T		La		
	Scrophulariaceae	*Verbascum sinaiticum* Benth.	*Qetetina* (Am)		Sh		NA		
4	Asclepiadaceae	*Caralluma speciosa* (N.E.Br.) N.E.Br.	*Ya'ii Bera* (Or)	Harla and Dengego valleys, EE	H	Crushed and put on the tumor	Sm	DR	(30, 35, 47)
	Colchicaceae	*Gloriosa superba* L.	*Harmel Kubra* (Or)		H		L		
5	Santalaceae	*Osyris quadripartita* Salzm. ex Decne.	*Queret* (Am)	Fiche, CE	Sh	Powder dried leaves of *O. quadripartita* with dried fruits of *M. africana*	L	OR	(20, 34)
	Myrsinaceae	*Myrsine africana* L.	*Kechemo* (Am)		Sh		Fr		
6	Apocynaceae	*Carissa spinarum* L.	*Agam* (Am)	Bahir Dar Zuria, NWE	Sh	The mixture of fresh leaves of *A. schimperiana* and *C. spinarum* are macerated in cold water for 2 days and the macerated liquid is drunk.	L	OR	(19)
	Fabaceae	*Albizia schimperiana* Oliv.	*Sessa* (Am)	Abay Gorge, NWE	T		L		

7	Myrtaceae	*Syzygium guineense* (Willd.) DC.	*Dokima* (Am)	Bahir Dar Zuria, NWE	T	Dry leaves and roots of *S. guineense* and dry leaves of *O. quadripartita* are ground, mixed, decocted and drunk.	R & L	OR	
	Santalaceae	*Osyris quadripartita* Salzm. ex Decne.	*Queret* (Am)	Abay Gorge, NWE	Sh		L		
8	Moraceae	*Dorstenia barnimiana* Schweinf.	*Work Bemeda* (Am)	Bahir Dar Zuria, NWE	H	Fresh roots of *D. barnimiana* mixed with fresh leaves of *C. simensis*pounded and applied.	R	DR	
	Ranunculaceae	*Clematis simensis* Fresen.	*Yeazo Hareg* (Am)		Cl		L		

Key:- **Growth form** (Gf): H= herb, Sh=shrub, Bl=bulbous, Cl= climber and T= tree;
Parts: L= leaves, La=latex, Fr=fruit, Sm=stem and R=root;
Geographical locations: CE=central Ethiopia, EE= East Ethiopia and NWE= North West Ethiopia;
Vernacular Names: Am= Amharigna and Or= Oromigna; and
Route of application (Ro): OR= Oral and DR=dermal;

Table 3: ***In vitro*** **cytotoxicity and radical scavenging evaluation of Ethiopian plants**

Family	**Botanical name**	**Plant part**	**Extract/drug**	**IC_{50} (**µg/mL)		**Cell line**	**Test substance**	**Method**	**References**
				Cytotoxicity	Radical scavenging activities				
Acanthaceae	*Justicia schimperiana* (Hochst. ex Nees) T. Anderson	Fl	MeOH	219.8	-	HL-60	Crude	Resazurin reduction test	(57)
			CH_2Cl_2	135.6	-				
Apiaceae	*Ferula communis* L.	Al	MeOH	236.6	-				
			CH_2Cl_2	99.9	-				
	Foeniculum vulgare Mill.	L	HD	-	133.3 ± 9	-	Oil	DPPH assay	(58)
	Coriandrum sativum L.	Sd		-	21.22 ± 2.43				
Apocynaceae	*Acokanthera schimperi* (A.DC.) Schweinf.	L	MeOH	-	7.1	HL-60	Crude	Resazurin reduction test	(57)
			CH_2Cl_2	-	28.8				
	Carissa spinarum L.	R	80% EtOH	-	97.2 ± 4.9	-	Crude	DPPH assay	(59)
Asphodelaceae	*Kniphofia foliosa* Hochst.	-	-	3.3 ± 0.4	-	B16	knipholone anthrone	Alamar Blue assay	(60)
				1.6 ± 0.3	-	RAW 264.7			
				0.5 ± 0.1	-	U937			
				0.9 ± 0.1	-	THP-1			
					22 ± 1.5	-		DPPH assay	(61)

Asteraceae	*Guizotia scabra* (Vis.) Chiov.	Fl	MeOH	246.8	-	HL-60	Crude	Resazurin reduction test	(57)
			CH_2Cl_2	25.5	-				
	Vernonia amygdalina Delile	Al	MeOH	158.9	-				
			CH_2Cl_2	22.4	-				
	Vernonia hochstetteri Sch.Bip. ex Walp.	Fl	MeOH	230.2	-				
			CH_2Cl_2	140.9	-				
	Artemisia annua L.	L	95% MeOH	3	-	LNCap	Crude	WST-1 assay	(62)
	Artemisia abyssinica Sch.Bip. ex A.Rich.	L	HD	350±5	-	THP-1	Oil	-	(63)
	Xanthium strumarium L.	L	-	7.09	-	HL-60	Squalene	Alamar Blue assay	(64)
				52.50	-		Xanthatin		
				50.07	-		Stigmasterol		
				24.91	-		β-Sitosterol-O-glucoside		
	Solanecio angulatus (Vahl) C.Jeffrey	L	MeOH	130.77	-	HL-60	Crude	Alamar Blue assay	(65)
		Fl	MeOH	27.39	-				
			Alkaloid extract	133.72	-		Monocrotaline		
	Senecio hadiensis Forssk.	Fl	MeOH	217.65	-	HL-60	Crude	Alamar Blue assay	
	Cineraria abyssinica Sch.Bip. ex A.Rich.	L	80% MeOH	-	5.78	-	Crude	DPPH assay	(66)
				-	3.53	-	Rutin		
Boraginaceae	*Cordia monoica* Roxb.	L	MeOH	53.2	-	HL-60	Crude	Resazurin reduction test	(57)
			CH_2Cl_2	219.9	-				
	Cordia sinensis Lam.	L	MeOH	169.3	-				
			CH_2Cl_2	206.4	-				
	Cynoglossum coeruleum var. *mannii* (Baker & C.H.Wright) Verdc.	L	MeOH	183.95	-			Alamar Blue assay	(65)
			CH_2Cl_2	312.62	-				
		Fl	MeOH	360.20	-				
	Heliotropium cinerascens DC. & A.DC	Tw	MeOH	247.91	-				
			CH_2Cl_2	161.31	-				
Celastraceae	*Catha edulis* (Vahl) Endl.	L	95% MeOH	2.4	-	LNCap	Crude	WST-1 assay	(62)
Chenopodiaceae	*Dysphania ambrosioides* (L.) Mosyakin & Clemants	Al	MeOH	44.8	-	HL-60	Crude	Resazurin reduction test	(57)
			CH_2Cl_2	219.0	-				

Combretaceae	*Combretum molle* R.Br. ex G.Don	Bk	MeOH	>250.0	-				
			CH_2Cl_2	>250.0	-				
Ebenaceae	*Euclea divinorum* Hiern	L	MeOH	>250.0	-				
			CH_2Cl_2	187.7	-				
	Euclea racemosa L.	L	Acetone	-	11.3	-	Crude	DPPH assay	(67)
				-	26.8		Quercetrin		
				-	14.2		Myricitrin		
				-	9.5		Rutin		
				-	15.8		Myricetin-3-O-arabino-pyranoside		
Euphorbiaceae	*Croton macrostachyus* Hochst. ex Delile	Al	MeOH	108.2	-	HL-60	Crude	Resazurin reduction test	(57)
			CH_2Cl_2	150.8	-				
Fabaceae	*Albizia schimperiana* Oliv.	L	MeOH	184.1	-				
			CH_2Cl_2	225.6	-				
	Calpurnia aurea (Aiton) Benth.	L	MeOH	147.5	-				
			CH_2Cl_2	244.3	-				
	Millettia ferruginea (Hochst.) Baker	Al	MeOH	248.4	-				
			CH_2Cl_2	87.5	-				
	Cassia arereh Delile	Pd	Petroleum Ether	-	113.2	-	Crude	DPPH assay	(68)
			EtOH	-	8.84				
			H_2O	-	16.76				
	Senna singueana (Delile) Lock	L	80% MeOH	-	18.75	-	Crude	DPPH assay	(69)
		Bk		-	6.16				
	Crotalaria agatiflora Schweinf.	Sd	MeOH	> 500	-	HL-60	Crude	Alamar Blue assay	(65)
			CH_2Cl_2	> 500	-				
	Crotalaria abbreviata Baker f.	L	MeOH	489.77	-				
			CH_2Cl_2	191.16	-				
	Crotalaria emarginella Vatke	L	MeOH	266.69	-				
			CH_2Cl_2	380.69	-				
	Crotalaria incana L.	Tw	MeOH	404.61	-				
		L		232.22	-				
	Crotalaria laburnifolia L.	L	CH_2Cl_2	332.39	-				
		Pd	MeOH	468.75	-				
		Tw	MeOH	401.58	-				
			CH_2Cl_2	173.70	-				
	Lonchocarpus laxiflorus Guill. & Perr.	-	-	-	-		Rotenone	-	(20)

Flacourtiaceae	*Dovyalis abyssinica* (A.Rich.) Warb.	L	MeOH	167.2	-		Crude	Resazurin reduction test	(57)
			CH_2Cl_2	174.9	-				
Lamiaceae	*Leonotis ocymifolia* (Burm.f.) Iwarsson	Al	MeOH	207.9	-				
			CH_2Cl_2	61.0	-				
	Ocimum gratissimum L.	L	MeOH	231.6	-				
			CH_2Cl_2	156.2	-				
	Thymus schimperi Ronniger	L	MeOH	-	45.8±3	-	Crude	DPPH assay	(70)
			Acetone	-	19.8±1.3				
			80% MeOH	-	11.1±1				
	Rosmarinus officinalis L.	L	HD	-	28.08 ± 1.97	-	Oil	DPPH assay	(58)
	Micromeria imbricata (Forssk.) C.Chr.	L	HD	0.013 ± 0.002	-	THP-1	Oil	-	(63)
Meliaceae	*Ekebergia capensis* Sparrm.	L	MeOH	186.8	-				(57)
			CH_2Cl_2	179.5	-				
Melianthaceae	*Bersama abyssinica* Fresen.	L and Tw	80% EtOH	-	26.0 ± 3.9	-	Crude	DPPH assay	(59)
		L	MeOH	-	7.5	-	Crude	DPPH assay	(67)
				-	23.7		Isoquercetrin		
				-	22.6		Hyperoside		
				-	20.7		Quercetin-3-O--arabinopyranoside		
				-	> 50		Kaempferol-3-O-arabino-pyranoside		
				-	15.9		Mangiferin		
Molluginaceae	*Glinus lotoides* L.	Sd	*n*-Hexane	74.6±1.2	-	Caco-2	Crude	MTT assay	(71)
			CH_2Cl_2	140.3±1.3	-				
			MeOH	69.7±1.2	-				
			H_2O	268.4±1	-				
			n-Hexane	79.8±1.3	-	Calu-3			
			CH_2Cl_2	112±1.3	-				
			MeOH	29.7±1.3	-				
			H_2O	262.2±1.2	-				
Myrsinaceae	*Maesa lanceolata* Forssk.	Sd	MeOH, fractionation	72.3	-	HCT116	Quercitrin	Clonogenic assay	(40)

Myrtaceae	*Syzygium guineense* (Willd.) DC.	L	MeOH	>250.0	-	HL-60	Crude	Resazurin reduction test	(57)
			CH_2Cl_2	119.8	-				
Oleaceae	*Jasminum abyssinicum* Hochst. ex DC.	L	80% EtOH	-	26.3 ± 6.5	-	Crude	DPPH assay	(59)
Plumbaginaceae	*Plumbago Zeylanica* L.	R	EtOH, $CHCl_3$	-	100	-	F_8P– 006	DPPH assay	(72)
				-	93.47		F_7P– 006		
				-	196.53		F_CP– 006		
				-	634.21		F_3P– 006		
Polygonaceae	*Rumex nepalensis* Spreng.	L and Tw	80% EtOH	-	10.7 ± 1.7	-	Crude	DPPH assay	(59)
		R		-	5.7 ± 0.9				
	Rumex abyssinicus Jacq.	L	95% MeOH	29	-	THP-1	Crude	WST-1 assay	(62)
Pteridaceae	*Cheilanthes farinosa* (Forssk.) Kaulf.	Al	MeOH	-	52.5	-	Crude	DPPH assay	(67)
				-	9.5		Rutin		
				-	15.1		Quercetin-3-O--diglucosyl-rhamnoside		
				-	>58.1		Kaempferol-3-O-diglucosyl-rhamnoside		
				-	>78		Kaempferol-3-O-gluco-rhamnoside		
				-	23.3		Caffeic acid		
				-	22.6		Chlorogenic acid		
Rosaceae	*Hagenia abyssinica* (Bruce ex Steud.) J.F.Gmel.	Female Fl	MeOH	196.6	-	HL-60	Crude	Resazurin reduction test	(57)
			CH_2Cl_2	32.3	-				
	Rosa abyssinica Lindley	L	MeOH	153.3	-				
			CH_2Cl_2	58.7	-				
	Rubus steudneri Schweinf.	R	80% EtOH	-	5.8 ± 1.1	-	Crude	DPPH assay	(59)
		L	80% MeOH	-	6.5	-	Crude	DPPH assay	(73)
			Acetone	-	9.8				
			MeOH	-	9.9				
	Rubus apetalus Poir.	L	80% MeOH	-	12.3				
			Acetone	-	8.8				
			MeOH	-	8.4				

	Rubus niveus Thunb.	L	80% MeOH	-	19.0				
			Acetone	-	14.5				
			MeOH	-	14.4				
Rubiaceae	*Pavetta gardeniifolia* Hochst. ex A.Rich.	L	MeOH	>250.0	-	HL-60	Crude	Resazurin reduction test	(57)
			CH_2Cl_2	133.7	-				
Rutaceae	*Clausena anisata* (Willd.) Hook.f. ex Benth.	Al	MeOH	118.5	-				
			CH_2Cl_2	225.4	-				
Sapindaceae	*Dodonaea viscosa* subsp. *angustifolia* (L.f.) J.G.West	L	80% EtOH	-	22.2 ± 1.2	-	Crude	DPPH assay	(59)
Solanaceae	*Datura stramonium* L.	L	MeOH	120.4	-	HL-60	Crude	Resazurin reduction test	(57)
			CH_2Cl_2	106.4	-				
	Solanum incanum L.	L	MeOH	227.2	-				
			CH_2Cl_2	82.0	-				
	Withania somnifera (L.) Dunal	Al	MeOH	221.5	-				
			CH_2Cl_2	187.1	-				
Verbenaceae	*Verbena officinalis* L.	WP	MeOH	225.6	-				
			CH_2Cl_2	175.8	-				
	Lippia adoensis Hochst.	Al	MeOH	>250.0	-				
			CH_2Cl_2	-	-				
	Lippia adoensis var. *koseret*	L	HD		10.08 ± 0.94	-	Oil	DPPH assay	(58)
Violaceae	*Viola abyssinica* Steud. ex Oliv.	Al	60% MeOH in H_2O	7.6	-	U-937 GTB	Comp. 1 (Cyclotide)	Flourometric microculture cytotoxicity assay	(74)
				2.6	-		Comp. 2 (Cyclotide)		

Key:- **Plant part**: Al=Aerial part, Bk=bark, L= leaves, Sd=seed, Fl=Flower, Tw=Twig, Pd=Pod, R=root and WP=Whole part;
Extraction solvents/Extraction methods: H_2O= Distilled water, MeOH=Methanol, EtOH= Ethanol, CH_2Cl_2= Dichloromethane, $CHCl_3$= Chloroform and HD= Hydrodistillation;
Cell lines: HL-60= Human promyelocytic leukemia, THP-1= Human leukemic monocyte, HCT116= Human colorectal carcinoma, Calu-3= Human lung adenocarcinoma, Caco-2= Human colorectal adenocarcinoma, LNCap= Human Prostate carcinoma, U-937= Human histiocytic lymphoma, RAW 264.7= Murine monocyte macrophage, B16= Murine melanoma; and
Assays: ABA= Alamar Blue assay, DPPH=1, 1-diphenyl-2-picrylhydrazyl, RRT=Resazurin reduction test, WST-1= 4-[3-(4-iodophenyl)-2-(4-nitrophenyl)- *2H*-5-tetrazolio]-1,3-benzene disulfonate and MTT=3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphemyl-tetrazolium bromide

Table 4: ***In vivo*** **toxicity evaluation of Ethiopian plants**

Family	Botanical name	Plant part	Solvent	Experimental animal	Toxicity study (experimental periods), Dose (mg/kg, b.w.), route of administration and LD_{50} (mg/kg) b.w. or NOEL	Result	References
Acanthaceae	*Justicia schimperiana* (Hochst. ex Nees) T. Anderson	L	H_2O	-	Acute toxicity (24 hr), LD_{50}>2000	No mortality or signs of toxicity within the 14-day observation period.	83
Apiaceae	*Ferula communis* L.	-	-	-	-	-	-
	Foeniculum vulgare Mill.						
	Coriandrum sativum L.	Sd	H_2O	Swiss albino mice	15000 mg/kg (Or)	No mortality or signs of toxicity within the 14-day observation period.	84
					LD_{50}=2177.5 (Ip)	Low mortality and signs of toxicity.	
Apocynaceae	*Acokanthera schimperi* (A.DC.) Schweinf.	L	H_2O and MeOH	Swiss albino mice	Acute toxicity (24 hr), 2000 mg/kg (Or)	No mortality or signs of toxicity within the 14-day observation period.	85
					Subacute toxicity (96 hr), 2000 mg/kg (Or)		
	Carissa spinarum L.	-	-	-	-	-	-
Asphodelaceae	*Kniphofia foliosa* Hochst.						
Asteraceae	*Guizotia scabra* (Vis.) Chiov.	R	H_2O	Swiss albino mice	Acute toxicity (24 hr), Ip, LD_{50}= 783.4	Mortality and signs of toxicity.	86
			HA		Acute toxicity (24 hr), Ip, LD_{50}= 1023		
	Vernonia amygdalina Delile	L	MeOH		LD_{50}>5000	No mortality or signs of toxicity within the 14-day observation period.	87
	Vernonia hochstetteri Sch.Bip. ex Walp.	-	-	-	-	-	-
	Artemisia annua L.						
	Artemisia abyssinica Sch.Bip. ex A.Rich.						
	Xanthium strumarium L.						
	Solanecio angulatus (Vahl) C.Jeffrey						
	Senecio hadiensis Forssk.						
	Cineraria abyssinica Sch.Bip. ex A.Rich.	L	H_2O	Wistar albino mice	Acute toxicity (24 hr), 3000 mg/kg (Or)	No mortality or signs of toxicity within the 14-day observation period.	88
			HA				

Boraginaceae	*Cordia monoica* Roxb.	-	-	-	-	-	-
	Cordia sinensis Lam.						
	Cynoglossum coeruleum var. *mannii* (Baker & C.H.Wright) Verdc.						
	Heliotropium cinerascens						
Celastraceae	*Catha edulis* (Vahl) Endl.	L	$CHCl_3$ and $(C_2H_5)_2O$	Sprague Dawley rats	Sub-acute toxicity (24 hr), 400 mg/kg (Or)	Mild to moderate kidney damage.	89
Chenopodiaceae	*Dysphania ambrosioides* (L.) Mosyakin & Clemants	-	-	-	-	-	-
Combretaceae	*Combretum molle* R.Br. ex G.Don						
Ebenaceae	*Euclea divinorum* Hiern						
	Euclea racemosa L.						
Euphorbiaceae	*Croton macrostachyus* Hochst. ex Delile	L	H_2O and MeOH	Swiss albino mice	Acute toxicity (24 hr), 1000 mg/kg (Or)	No mortality or signs of toxicity within the 14-day observation period.	85
			H_2O		Sub-acute toxicity (96hr), 1000 mg/kg (Or)	Weight loss	
		R	-	-	Acute toxicity (24hr), 5000 mg/kg (Or)	No mortality or signs of toxicity within the 14-day observation period.	83
Fabaceae	*Albizia schimperiana* Oliv.	L	MeOH and CH_2Cl_2	Albino mice	Acute toxicity (24 hr), 2000 mg/kg (Or)	No mortality or signs of toxicity within the 14-day observation period.	90
	Calpurnia aurea (Aiton) Benth.	L	MeOH	Swiss albino mice	Acute toxicity (24hr), 2000 mg/kg (Or)	No mortality or signs of toxicity within the 14-day observation period.	91
	Millettia ferruginea (Hochst.) Baker	Sd	HA	Albino wistar rats	Acute toxicity (24 hr), Or, LD_{50}= 3500	Low mortality rate and signs of toxicity.	92
	Cassia arereh Delile	-	-	-	-	-	-
	Senna singueana (Delile) Lock	L	HA	Swiss albino mice	Acute toxicity (24 hr), 2000 mg/kg (Or)	No mortality or signs of toxicity within the 14-day observation period.	93
	Crotalaria agatiflora Schweinf.	-	-	-	-	-	-
	Crotalaria abbreviata Baker f.						
	Crotalaria emarginella Vatke						

	Crotalaria incana L.						
	Crotalaria laburnifolia L.						
	Lonchocarpus laxiflorus Guill. & Perr.						
Flacourtiaceae	*Dovyalis abyssinica* (A.Rich.) Warb.	L	MeOH and CH_2Cl_2	Swiss albino mice	Acute toxicity (24 hr), Or, LD_{50}= 1265	Low mortality rate and signs of toxicity.	94
Lamiaceae	*Leonotis ocymifolia* (Burm.f.) Iwarsson	L and R	H_2O	Pregnant rats	*In vivo* anti-implantation and anti-fertility study (19 days), 300 mg/kg (Or)	Anti-implantation effect.	95
	Ocimum gratissimum L.	-	-	-	-	-	-
	Thymus schimperi Ronniger	L	H_2O	Wistar rats	Acute toxicity (24 hr), Or, LD_{50}>10,000	No mortality or signs of toxicity within the 14-day observation period.	96
					Sub-chronic toxicity (90 days), 200 mg/kg (Or)	Significant increase in body weight.	
	Rosmarinus officinalis L.	-	-	-	-	-	-
	Micromeria imbricata (Forssk.) C.Chr.						
Meliaceae	*Ekebergia capensis* Sparrm.						
Melianthaceae	*Bersama abyssinica* Fresen.	R	HA	Albino mice	Acute toxicity (24 hr), Or, LD_{50}= 5044	Mortality and signs of toxicity.	97
Molluginaceae	*Glinus lotoides* L.	Fr	H_2O	Swiss albino mice	Acute toxicity (24 hr), Ip, LD_{50}= 532.6	Mortality and signs of toxicity.	86
			HA		Acute toxicity (24 hr), Ip, LD_{50}= 1811		
Myrsinaceae	*Maesa lanceolata* Forssk.		H_2O		Acute toxicity (24 hr), Ip, LD_{50}= 4847		
			HA		Acute toxicity (24 hr), Ip, LD_{50}= 3218		
Myrtaceae	*Syzygium guineense* (Willd.) DC.	L		Wistar albino rats	Acute toxicity (24 hr), Or, LD_{50}>5000	No mortality or signs of toxicity within the 14-day observation period.	98
			H_2O	Swiss albino mice	Chronic toxicity (6 weeks), Or, 600 mg/kg	Structural damage of the liver and kidney tissues.	99
Oleaceae	*Jasminum abyssinicum* Hochst. ex DC.	R			Acute toxicity (24hr), Ip, LD_{50}= 428.4	Mortality and signs of toxicity.	86
			HA		Acute toxicity (24 hr), Ip, LD_{50}= 673.3		

Plumbaginaceae	*Plumbago Zeylanica* L.	R		Rabbits	Skin irritation test using 9.45% of the crude extract.	Moderate irritation	100
Polygonaceae	*Rumex nepalensis* Spreng.	-	-	-	-	-	-
	Rumex abyssinicus Jacq.	Rh	H_2O and HA	Albino mice	Acute toxicity (24 hr), Or, LD_{50}>5000	No mortality or signs of toxicity within the 15-day observation period.	101
Pteridaceae	*Cheilanthes farinosa* (Forssk.) Kaulf.	Fro	MeOH	Wistar rats	Acute toxicity (24 hr), Or, 800 mg/kg	No mortality or signs of toxicity within the 10-day observation period.	102
Rosaceae	*Hagenia abyssinica* (Bruce ex Steud.) J.F.Gmel.	Fl	H_2O	Albino rats	Single dose toxic effect (5000mg/kg), Or, LD_{50}>5000	No mortality or signs of toxicity within the 14-day observation period.	103
					Repeated dose toxic effect (350, 750, and 1500 mg/kg), Or, NOEL>1500		
	Rosa abyssinica Lindley	Fr	HA	Albino Swiss mic	Acute toxicity (24 hr), Or, limited dose at 2000 mg/kg, LD_{50}>2000	No mortality or signs of toxicity within the 14-day observation period.	104
	Rubus steudneri Schweinf.	-	-	-	-	-	-
	Rubus apetalus Poir.						
	Rubus niveus Thunb.						
Rubiaceae	*Pavetta gardeniifolia* Hochst. ex A.Rich.						
Rutaceae	*Clausena anisata* (Willd.) Hook.f. ex Benth.						
Sapindaceae	*Dodonaea viscosa* subsp. *angustifolia* (L.f.) J.G.West	L	H_2O	Swiss albino mice	Acute toxicity (24 hr), Ip, LD_{50}= 285.5	High mortality rate and signs of toxicity.	86
			HA		Acute toxicity (24 hr), Ip, LD_{50}= 322.3		
Solanaceae	*Datura stramonium* L.	-	-	-	-	-	-
	Solanum incanum L.	R	H_2O	Swiss albino mice	Acute toxicity (24 hr), Or, LD_{50}>15,000	No mortality or signs of toxicity within the 14-day observation period.	105
	Withania somnifera (L.) Dunal	L	$CHCl_3$ and MeOH		Acute toxicity (24 hr), Or, LD_{50}>1000	No mortality or signs of toxicity within the 14-day observation period.	106

Verbenaceae	*Verbena officinalis* L.	-	-	-	-	-	-
	Lippia adoensis Hochst.	L	H_2O and EtOH	Swiss albino mice	Acute toxicity (24 hr), Or, 50, 100 and 200 mg/kg	No mortality or signs of toxicity within the 14-day observation period.	75
	Lippia adoensis var. *koseret*	-	-	-	-	-	-
Violaceae	*Viola abyssinica* Steud. ex Oliv.						

Key:- **LD_{50}**=Lethal Dose 50; **NOEL**=No Observed Effect Level; **Hr= Hour, b.w.= body weight**
Plant part: L= leaves, Sd=seed, Fr=Fruit, Fl=Flower, Rh=Rhizomes, Fro=Fronds and R=root;
Extraction solvents/Extraction methods: H_2O= Distilled water, MeOH=Methanol, EtOH=Ethanol, CH_2Cl_2= Dichloromethene, $(C_2H_5)_2O$=Diethyl ether, $CHCl_3$=Chloroform and HA=Hydroalcololic; and **Route of administration**: Or= Oral and Ip= Intraperitoneal

Conclusions:
The most frequently cited anticancer plants identified by at least four different ethnobotanical studies were *Carissa spinarum* L., *Croton macrostachyus* Hochst. ex Delile, *Dorstenia barnimiana* Schweinf., *Plantago lanceolata* L., *Plumbago zeylanica* L.,*Ricinus communis* L., *Rotheca myricoides* (Hochst.) Steane & Mabb and *Salvia nilotica* Juss. ex Jacq. (table 1). This might suggest better efficacy of these plants and make them candidate for further scientific studies. However, information regarding specific type of cancer treated, doses of the remedies, methods of preparation and toxicity were not documented by the majority of reviewed ethnobotanical studies. Moreover, a limited number of ethnopharmacological studies, seldom based on the locally available ethnomedicinal knowledge, were conducted on plants that grow in Ethiopia. Therefore, it is imperative to do more detail and comprehensive ethnobotanical studies and carry out mechanistic studies, using different cancer cell lines and tumor models, with the aim of promoting the use of traditional anticancer herbal remedies and discovering novel anticancer agents.

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