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An ethnopharmacological survey of medicinal plants traditionally used for cancer treatment in the Ashanti region, Ghana

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ABSTRACT

Aims: Cancer represents a major health burden and drain on healthcare resources in the world. The majority of the people of Africa still patronize traditional medicine for their health needs, including various forms of cancer. The aim of the following study is the identification of medicinal plants used for cancer treatment by the traditional healers in the Ashanti area of Ghana and to cross-reference the identified plant species with published scientific literature.

Methodology: Validated questionnaires were administered to 85 traditional healers in 10 communities within Ashanti region. For cross-validation, also 7 healers located outside Ashanti region were investigated to evaluate regional differences. Interviews and structured conversations were used to administer the questionnaires. Selected herbal material dominantly used by the healers was collected and identified.

Results: The ethnopharmacological survey revealed 151 plant species used for cancer treatment. Identified species were classified into different groups according to their frequency of use, resulting in the "top-22" plants. Interestingly group I (very frequent use) contained 5 plant species (*Khaya senegalensis, Triplochiton scleroxylon, Azadirachta indica, Entandrophragma angolense, Terminalia superba*), three of which belong to the plant family Meliaceae, phytochemically mainly characterized by the presence of limonoids. Cross-referencing of all plants identified by current scientific literature revealed species which have not been documented for cancer therapy until now. Special interest was laid on use of plants for cancer treatment of children.

Conclusion: A variety of traditionally used anti-cancer plants from Ghana have been identified and the widespread use within ethnotraditional medicine is obvious. Further *in vitro* and clinical studies will be performed in the near future to rationalize the phytochemical and functional scientific background of the respective extracts for cancer treatment.

1. Introduction

Cancer has a tremendous impact on the healthcare economy and represents a major health burden and drain on healthcare resources worldwide. It is estimated that 70–80% of patients in Africa, and also in Ghana, are treated by traditional healers and herbal practitioners (Nyika, 2007). People in Africa often rely on traditional medicine for their health needs because of the high costs of conventional medicines, inadequate health facilities and healthcare professionals, coupled with a lack of training of health workers for many different diseases (Mahé et al., 2005). Traditional medicines and medicinal plants used for cancer treatments are easily available and affordable, sometimes free of charge. Most of the herbal materials for preparation of the medical formulations have been used for a long time and are assessed to be safer than isolated active compounds (Fabricant and Farnsworth, 2001). Ethnopharmacological investigations on medicinal plants, traditionally used for cancer treatment, have recently been reviewed using scientific data-bases (Tariq et al., 2017), but the identification of unknown plants for this medical use in rural areas is still a hot topic.

Because of the huge reservoir of traditional knowledge on plants used for traditional cancer treatment in West Africa, the following study was performed in central Ghana to obtain validated, quantitative and reliable data on the use of medicinal plants for this therapy in an exactly defined part of the country, the Ashanti region, surrounding the

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regional capital Kumasi. Several reasons have led to the selection of this special study area: the high biodiversity within a typical tropical rainforest area; a mixture of people living in rural as well as in metropolitan areas; the existence of an intact and modern infrastructure, including state-of-the art medical centers and hospitals and a traditional healers community cooperating with the modern medical facilities; the Ashanti community of people from this area with a strong cultural and historical background, preserving own traditional knowledge, but strongly interacting also with modern economy and science. Interstingly, in 2012 this region has also established a population-based cancer registry to collect population-based data on cancer to provide case reports of cancer patients within the city of Kumasi (Laryea et al., 2014). According to this database, the most common cancers among males were diseases of the liver (21%), prostate (13%), lung (5%) and stomach (5%). Among females, the most common cancers were those of the breast (34%), cervix (29%), ovary (11%) and endometrium (5%) (Laryea et al., 2014).

Aims of this study were to find out how traditional healers in this area recognize cancer and how they classify and treat the disease with medicinal plants. Additionally, special emphasize was layed on anticancer plants for treatment of children. It was to be investigated how the respective plants were collected and identified, which part of plants are used, how they are obtained, prepared and applied for the treatment of cancer and what importance these plants have to the healers beside other non-plant based methods within the management of cancer.

2. Material and methods

2.1. Study area and survey

The ethnopharmacological survey was performed in Ashanti region in the central part of Ghana, located between 0.15–2.251W and 5.50–7.461N (Fig. 1). The region shares boundaries with four of the 10 political regions of Ghana. The region covers a total land area of 24,389 km^2, representing 10.2% of the total land area of Ghana. The ethnopharmacological survey was carried out from October 2012 to February 2013 in accordance with the national rights of Ghana and with acceptance and in close co-operation with Ghana Federation of Traditional Medicine Healers Association (GHAFTRAM), an umbrella organization including all traditional healers such as herbal practitioners, fetish priests, divine healers, psychic practitioners and traditional medicine practitioners in Ghana. The selection of the healers for the interviews was based on a list provided by the Ashanti regional branch of GHAFTRAM and we visited them in their homes and herbal or practice centers. All participants were informed about the survey and personal visits were made to their facilities, centers and homes. In respect to the local tradition, some gifts in cash or kinds were given. Interviews and conversations were used to administer the questionnaires. Questionnaires were designed in English and administered to 78 traditional healers and herbal practitioners who represent 60% of all GHAFTRAM members in the region. To compare potential differences between healers from Ashanti and regions outside Ashanti additionally questionnaires from non-Ashanti respondents were investigated to evaluate regional differences.

Responders i.e. healers were asked to provide samples of the plant materials after the administration of the questionnaires and interviews. These samples were identified by the accompanied botanist/taxonomist and his team and the samples of the plant materials were prepared as voucher specimens. Some healers requested that they needed to collect them from the forest or wild sources and hence they got additional time for the subsequent collection.

Voucher specimens (Table 1) of all plants have been deposited in the Ghana Herbarium, Department of Plant and Environmental Biology, University of Ghana, with defined ID-numbers. Plants were identified by Prof. A. Asase, Department of Plant and Environmental Biology, University of Ghana, Legon, Accra, Ghana.

2.2. Literature based validation of the data

Plant species obtained from the questionnaires were cross-checked via The Plant List (www.theplantlist.org) for the accepted name of the species. The databases SciFinder® and PubMed were used to compare

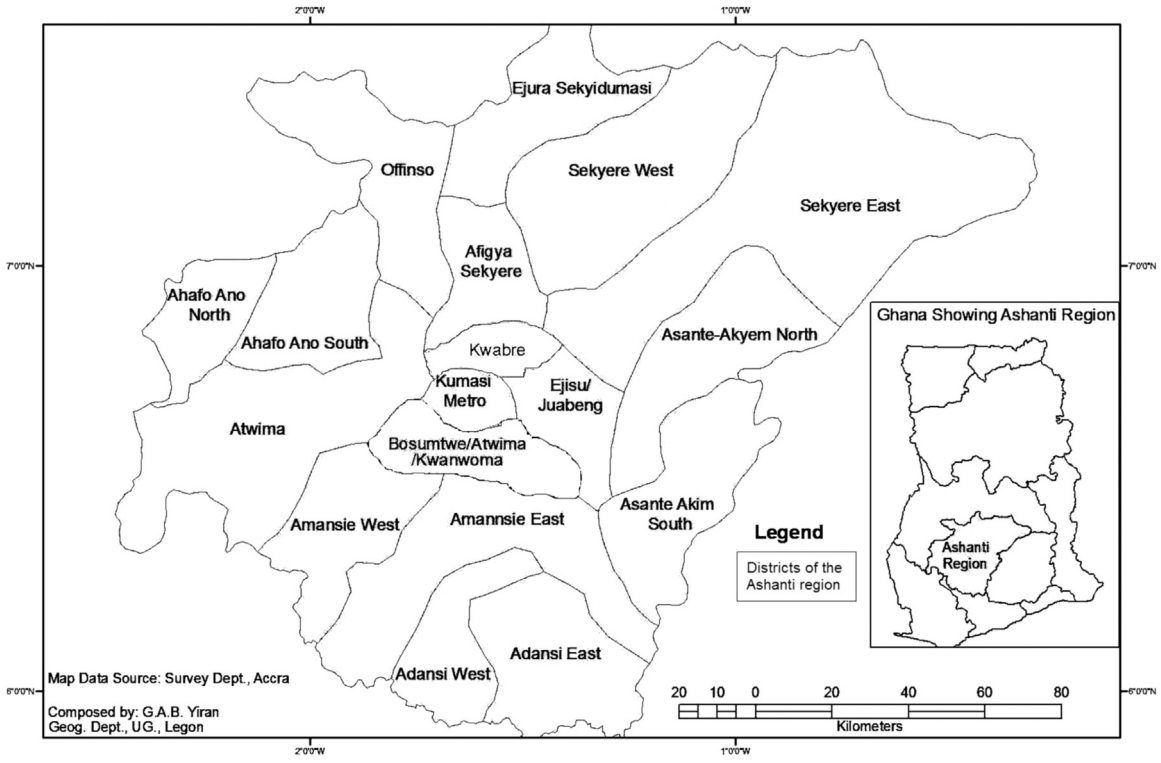

Fig. 1. Map of Ghana with Ashanti region with detailed boundaries of the districts (study area).

Table 1
Medicinal plants used for the management of various types of cancer in the Ashanti region, Ghana, according to the ethnopharmacological survey.

Plant family	*Species*	*Voucher number*	*Frequency* [a]	*Plant part used*	*Formulation, application*	*Type of cancer*	*Documnted use in literature in regard to cancer* [b]	*Literature references*
Acanthaceae	*Asystasia gangetica* (L.) T.Anderson	CP010/16	2	leaves	decoction	prostate	no	
	Barleria cristata L.	CP005/16	1	leaves	poultice	stomach	no	
	Justicia extensa T. Anderson	CP014/16	1	leaves	decoction	stomach	no	
	***Thunbergia alata* Bojer ex Sims**	CP007/16	1	leaves	tea	stomach	no	
Amaranthaceae	*Alternanthera sessilis* (L.) R.Br. ex DC.	CP001/16	1	leaves	dressing	stomach	no	
	Amaranthus graecizans L.	CP030/16	1	roots	ground roots	brain	no	
	Amaranthus hybridus L.	CP016/16	1	leaves	massage	breast	published literature not relevant	
	Amaranthus viridis L.	CP018/16	2	leaves	wound dressing, decoction (oral)	prostate, breast, brain, stomach	published literature not relevant	
	Dysphania ambrosioides (L.) Mosyakin & Clemants	CP041/16	2	leaves, bark	ground leaves, decoction (oral)	breast, brain, stomach, throat	*in vivo* animal study	(Nascimento et al., 2006; Sousa et al., 2012)
Amaryllidaceae	*Allium cepa* L.	CP003/16	2	bulb	excipient, ground on wounds	stomach, skin	no convincing data	
Anacardiaceae	*Anacardium occidentale* L.	CP020/16	2	leaves, bark	decoction	liver	cytotoxicity by anacardic acid	(Hemshekhar et al., 2012)
	Mangifera indica L.	CP026/16	6	bark, leaves	decoction, poultice topical, tea	lungs, skin, prostate, throat	anticarcinogenic effects of mangostin proven in different preclinical studies; clinical efficacy still not proven. Immunomodulation by mangiferin.	(Zhang et al., 2017), (Núñez Selles et al., 2016)
Annonaceae	*Annona muricata* L.	CP027/16	1	fruit	oral	stomach	yes; acetogenins	(Yang et al., 2015)
	Annona reticulata L.	CP002/16	1	leaves	tea	stomach, prostate	yes; acetogenins	(Roham et al., 2016)
	Annona senegalensis Pers.	CP031/16	4	fruit, leaves, bark	juice, decoction	stomach, throat, skin, breast	yes	(Durodola, 1975)
	Xylopia aethiopica (Dunal) A.Rich.	CP023/16	3	leaves	decoction	stomach, breast	yes, flavonoids, alkaloids	(Kuete et al., 2015)
Apocynaceae	*Alafia multiflora* (Stapf) Stapf	CP050/16	3	leaves, roots	decoction	breast, brain, skin, lungs	published literature not relevant	
	Alstonia boonei De Wild.	CP009/16	3	leaves, bark, roots	ground exudates in lemon for massage, decoction	breast, skin	no	
	Calotropis procera (Aiton) Dryand.	CP025/16	1	leaves	decoction	stomach, skin	yes	(Joshi et al., 2015)
	Funtumia elastica (Preuss) Stapf	CP033/16	2	bark, leaves	decoction	skin, throat, stomach, breast	no	
	Holarrhena floribunda (G.Don) T.Durand & Schinz	CP037/16	2	leaves, bark	decoction	breast, brain, stomach	yes	(Badmus et al., 2015)
	Landolphia owariensis P. Beauv.	CP040/16	1	climber	alcoholic extract for massage	skin	no	
	Picralima nitida (Stapf) T. Durand & H. Durand	CP004/16	2	fruit, bark	topical, decoction, tea	skin	published literature not relevant	
	Pleiocarpa pycnantha (K. Schum.) Stapf	CP019/16	1	roots	decoction	breast	yes, triterpenes	(Omoyeni et al., 2014)
	Rauvolfia vomitoria Afzel.	CP044/16	2	roots	maceration, decoction	genital, skin	yes, β-carbolin alkaloid	(Bemis et al., 2006)
	Saba senegalensis (A. DC.) Pichon	CP045/16	1	stem, climber	tea	stomach	no	
	Strophanthus gratus (Wall. & Hook.) Baill.	CP011/16	1	roots	decoction	skin	no	
	Tabernaemontana crassa Benth.	CP077/16	1	leaves	decoction	lungs	no	
Araceae	*Colocasia* sp. *Colocasia esculenta* (L.) Schott	CP100/16	3	leaves, corn	mix with palm oil (oral), poultice, decoction	throat, prostate, skin, breast	yes, antimetastatic	(Kundu et al., 2012)
	Xanthosoma sagittifolium (L.)	CP065/16	1	leaves	exudate	skin	yes	(Caxito et al., 2015)
Araliaceae	*Cussonia bancoensis* Aubrév. & Pellegr.	CP055/16	1	bark	decoction	brain	no	
Arecaceae	*Cocos nucifera* L.	CP042/16	1	roots	decoction	stomach, lungs	no convincing data	
	Elaeis guineensis Jacq.	CP051/16	1	fruit	extract topical	skin, genital	published literature not relevant	
	Eremospatha macrocarpa H.Wendl.	CP111/16	1	bark	tea	skin	no	
Asclepiadaceae	*Periploca nigrescens* Afzel.	CP028/16	1	leaves	tea	skin, throat, prostate, breast	published literature not relevant	

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Table 1 (*continued*)

Plant family	*Species*	*Voucher number*	*Frequency* [a]	*Plant part used*	*Formulation, application*	*Type of cancer*	*Documnted use in literature in regard to cancer* [b]	*Literature references*
Asteraceae	*Ageratum conyzoides* (L.) L.	CP035/16	5	leaves, roots, bark, whole plant	crushed fresh leaves for juice (oral/topical), decoction, paste	skin, cervical, stomach, breast, lungs	*in vitro* antiproliverative activity against cancer cell lines; contains pyrrolizidine-lkaloids	(Adetutu et al., 2012)
	Aspilia africana (Pers.) C.D.Adams	CP024/16	2	leaves	decoction	lungs	published literature not relevant	
	Bidens pilosa L.	CP056/16	1	whole plant	tea	breast	yes	(Yang et al., 2013)
	Chromolaena odorata (L.) R.M.King & H.Rob.	CP075/16	4	leaves	ground leaves in mixture, maceration, poultice, decoction	skin	*in vitro* antiproliferative activity against cancer cell lines	(Kouamé et al., 2013)
	Emilia sonchifolia (L.) DC. ex DC.	CP061/16	1	whole plant	paste (topical/oral)	stomach, skin	*in vivo* study	(George and Kuttan, 2016)
	Ethulia conyzoides L.f.	CP064/16	2	whole plant	squeezed juice	lungs, skin, breast	published literature not relevant	
	Tridax procumbens (L.) L.	CP029/16	1	roots, leaves	poultice	skin, breast	published literature not relevant	
	Piptocarpha riedelii (Sch.Bip.) Baker	CP101/16	1	leaves	decoction	prostate, lungs, liver	no	
Bignoniaceae	*Kigelia africana* (Lam.) Benth.	CP047/16	2	leaves, bark	ground leaves (topical), decoction	skin, prostate	published literature not relevant	
	Newbouldia laevis (P. Beauv.) Seem.	CP049/16	4	bark, leaves, roots	ground leaves (topical), decoction, tea	prostate, breast, ovarian	antiproliverative activity demonstrated in several reports	(Kuete et al., 2014c)
	Spathodea campanulata P. Beauv.	CP112/16	3	bark, leaves	decoction	stomach, skin, throat	traditionally used widely in Africa	(Ochwang'i et al., 2014)
	Tecoma stans (L.) Juss. ex Kunth	CP104/16	1	leaves	tea	skin, breast	yes, 5-hydroxy-skytanthine	(Marzouk et al., 2006)
Boraginaceae	*Cordia millenii* Baker	CP046/16	1	bark	inhalation	lungs	no	
	Cordia myxa L.	CP052/16	1	leaves	decoction	stomach, brain, breast	published literature not relevant	
	Cordia vignei Hutch. & Dalziel	CP123/16	1	bark	decoction	prostate	no	
	Heliotropium indicum L.	CP115/16	3	leaves	tincture, decoction, maceration, ground leaves (topical)	skin, breast, prostate, stomach, throat	yes; indicine, phase-I study	(Ohnuma et al., 1982)
Brassicaceae	*Sinapis alba* L.	CP105/16	1	seed			published literature not relevant	
Bromeliaceae	*Ananas comosus* (L.) Merr.	CP034/16	3	fruit	juice, decoction, extract	lungs	not convincing data on Bromelain (protease) as chemopreventive agent	
Burseraceae	*Commiphora africana* (A.Rich.) Endl.	CP043/16	1	whole plant	inhalation	lungs	no	
Calophyllaceae	*Mammea africana* Sabine	CP062/16	4	bark resin, stem bark, roots	taped into shea butter, boil/ ground bark for dressing, decoction	cervical, breast, skin, throat	one report on cytotoxic activity of isoprenylated coumarin	(Canning et al., 2013)
Caricaceae	*Carica papaya* L.	CP053/16	2	leaves, seeds, roots	tea	stomach, skin, breast, prostate	not convincing data, conclusion see review	(Nguyen et al., 2013)
Casuarinaceae	*Casuarina equisetifolia* L.	CP063/16	1	bark, kernel	nasal drops	brain	no	
Celastraceae	*Maytenus senegalensis* (Lam.) Exell. (syn. *Gymnosporia senegalensis* (Lam.) Loes.)	CP071/16	1	roots	decoction	prostate	published literature not relevant	
Cleomaceae	*Cleome* sp.	CP073/16	1	leaves	ground for plaster	breast	antiproliverative activity described for several Cleome species	
Clusiaceae	*Garcinia kola* Heckel	CP078/16	1	bark, roots, leaves	decoction, ground	breast, skin	*in vivo* anti-inflammatory activity within cancer treatment	(Popoola et al., 2016)

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Table 1 (*continued*)

Plant family	*Species*	*Voucher number*	*Frequency* [a]	*Plant part used*	*Formulation, application*	*Type of cancer*	*Documnted use in literature in regard to cancer* [b]	*Literature references*
Combretaceae	*Anogeissus leiocarpa* (DC.) Guill. & Perr.	CP124/16	1	roots	tea	skin	no	
	Combretum molle R.Br. ex G.Don	CP107/16	1	leaves	tea	breast	only ethnopharmacological reports	
	Combretum platypterum (Welw.) Hutch. & Dalziel	CP131/16	2	bark	decoction	skin, lungs	no	
	Combretum racemosum P.Beauv.	CP113/16	1	leaves	decoction	throat,breast	no	
	Terminalia catappa L.	CP102/16	9	leaves, bark, fruit, root bark	decoction, tea, nut for oil (topical), distilled oil	stomach, skin, breast	*in vivo* and *in vitro* anti cancer activity proven	(Saroja et al., 2012)
	Terminalia ivorensis A.Chev.	CP057/16	3	leaves, root bark	poultice (topical), decoction	skin, lungs	yes, dimeric triterpens	(Ponou et al., 2010)
	Terminalia superba Engl. & Diels	CP060/16	12	leaves, stem bark, root bark	decoction, ground leaves	stomach, lungs, skin, prostate	no publications related to anti-cancer activity	
Connaraceae	*Rourea coccinea* (Schumach. & Thonn.) Benth. (syn. *Byrsocarpus coccineus* Schumach. & Thonn.)	CP094/16	1	stem bark	decoction	stomach	no	
Connaraceae	*Cnestis ferruginea* Vahl ex DC.	CP099/16	2	roots	ground into powder for dressing (topical)		no	
Crassulaceae	*Bryophyllum pinnatum* (Lam.) Oken	CP145/16	4	leaves, roots	squeezed leaves (topical), decoction	skin, stomach	one report on cytotoxic bufadienolide	(Yan et al., 1992)
Crassulaceae	*Kalanchoe integra* (Medik.) Kuntze	CP134/16	3	bark	decoction	breast	no	
Cucurbitaceae	*Cucurbita maxima* Duchesne	CP116/16	1	leaves	oral	lungs, head	no	
	Momordica angustisepala Harms	CP066/16	1	leaves	tincture (topical)	skin	no	
	Momordica charantia L.	CP059/16	2	fruits, roots	dried ground fruit for dressing wound, decoction	cervical, breast, skin, stomach	yes, for review see	(Nerurkar and Ray, 2010)
Cyperaceae	*Cyperus rotundus* L.	CP048/16	1	bulb, nut	oral	stomach, lungs	data are not convincing; for review see	(Pirzada et al., 2015)
Dioscoreaceae	*Dioscorea alata* L.	CP173/16	1	tubers	ground tubers (topical)	skin	no	
Dioscoreaceae	*Dioscorea bulbifera* L.	CP153/16	2	tuber	paste, decoction	skin, prostate, stomach	yes, *in vivo* mice study	(Wang et al., 2012)
	Dioscorea cayennensis Lam.	CP147/16	2	roots	plaster with lemon, decoction	brain	no	
	Dioscorea cayennensis subsp. *rotundata* (Poir.) J. Miège	CP127/16	2	leaves, roots	drinking boiled extract, cooked roots	breast, skin, prostate,liver	no	
	Dioscorea dumetorum (Kunth) Pax	CP139/16	1	leaves	decoction	breast	no	

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Table 1 (*continued*)

Plant family	*Species*	*Voucher number*	*Frequency* [a]	*Plant part used*	*Formulation, application*	*Type of cancer*	*Documnted use in literature in regard to cancer* [b]	*Literature references*
Euphorbiaceae	*Acalypha ciliata* Forssk.	CP156/16	1	leaves	decoction	breast	no	
	Alchornea cordifolia (Schumach. & Thonn.) Müll.Arg.	CP181/16	2	leaves, bark	decoction	brain, stomach	yes	(Kuete et al., 2016)
	Croton hirtus L'Hér.	CP169/16	2	leaves	decoction (topical/oral)	prostate, skin, breast, throat	no	
	Astraea lobata (L.) Klotzsch (syn. *Croton lobatus* L.)	CP096/16	2	leaves	decoction (topical/oral)	skin	no	
	Euphorbia heterophylla L.	CP129/16	2	leaves	decoction (topical/oral)	throat, prostate, skin, breast	no	
	Euphorbia hirta L.	CP158/16	2	leaves	decoction (topical/oral)	stomach, prostate, skin, breast, throat	no data for this species, but genus Euphorbia in general see review (ingenol?)	(Ernst et al., 2015)
	Euphorbia hyssopifolia L.	CP164/16	2	leaves	decoction (topical/oral)	skin, prostate, breast, throat	No data for this species, but genus Euphorbia in general see review (ingenol?)	
	Jatropha curcas L.	CP172/16	2	leaves, bark, roots	leaves mix with oil, ground bark to plaster, decoction	skin, breast, prostate, stomach, brain	several reports on antiproliverative diterpens	
	Jatropha gossypiifolia L.	CP093/16	2	leaves, roots, bark		stomach (liver)	no	
	Mallotus oppositifolius (Geiseler) Müll. Arg.	CP148/16	7	leaves, roots	decoction (topical/oral), ground (topical)	genital, skin, prostate, breast,throat	*in vitro* antiproliferative activity of dimeric phloroglucinols (mallotophenons) against A2780 ovarian cancer cells.	(Harinantenaina et al., 2013)
	Manihot esculenta Crantz	CP121/16	2	tuber, roots, leaves	grated and squeezed liquid, extract with salt	cervical, skin, genital	anticancer activity of cyanogenic glycosides has not been confirmed in advances studies	
	Phyllanthus sp.	CP017/16	1	leaves	ground leaves	skin		
	Ricinus communis L.	CP168/16	1	leaves	decoction	throat	unclear data, ricin as cytotoxic principle in seeds, but not in leaves	
Fabaceae	*Amphimas pterocarpoides* Harms	CP036/16	1	leaves	decoction	head	no	
	Arachis hypogaea L.	CP058/16	1	leaves	decoction	skin	resveratrol: induction of apoptosis?	(Udenigwe et al., 2008)
	Baphia nitida Lodd.	CP126/16	3	leaves	cold maceration, wound dressing, decoction	breast, skin, prostate, stomach, brain, throat	no	
	Caesalpinia benthamiana (Baill.) Herend. & Zarucchi	CP165/16	1	stem	decoction	liver	no	
	Caesalpinia bonduc (L.) Roxb.	CP076/16	1	roots	topical	genital, prostate	cytotoxic flavonoids	(Ogunlana et al., 2015)
	Desmodium adscendens (Sw.) DC.	CP021/16	5	leaves, stem	internally, wash, decoction, dried leaves tea	prostate, breast, throat, brain	no	
	Dialium dinklagei Harms	CP006/16	2	bark, leaves	decoction	skin	no	
	Entada abyssinica A.Rich.	CP084/16	1	bark	decoction	breast	slight cytotoxic activity	(Kuete et al., 2013)
	Erythrina senegalensis DC.	CP135/16	1	whole plant	nasal drops	head	cytotoxic isoflavonoids	(Kuete et al., 2014a)
	Griffonia simplicifolia (DC.) Baill.	CP038/16	1	roots	decoction	breast	no	
	Mimosa pudica L.	CP074/16	1	leaves	ground (topical)	breast	cytotoxic myricetin derivative	(Jose et al., 2016)
	Parkia biglobosa (Jacq.) G.Don	CP081/16	1	bark, roots, leaves	grinding use (?), wash and massage	breast	no	
	Peltophorum sp.	CP103/16	1	bark	powder	liver		
	Pterocarpus santalinoides DC.	CP095/16	1	leaves	decoction	lungs	no	

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Table 1 (*continued*)

Plant family	*Species*	*Voucher number*	*Frequency* [a]	*Plant part used*	*Formulation, application*	*Type of cancer*	*Documnted use in literature in regard to cancer* [b]	*Literature references*
Lamiaceae	*Clerodendrum capitatum* (Willd.) Schumach. & Thonn.	CP054/16	1	bark, roots, leaves	decoction, ground	breast, skin	no	
	Hoslundia opposita Vahl	CP032/16	2	leaves, root, sap	tea, decoction	lungs, brain, skin	no	
	Hyptis pectinate (L.) Poit.	CP012/16	2	bark, roots	decoction	skin, brain, breast	no	
	Ocimum gratissimum L.	CP091/16	1	leaves	squeezed leaves (topical)	skin, breast, prostate, stomach	no convincing data	
	Ocimum viride Willd.	CP136/16	2	leaves	grind with other plasters, crushed leaves for wash	skin, genital	no convincing data	
Malvaceae	*Abelmoschus esculentus* (L.) Moench	CP015/16	1	seeds	dried ground seeds for powder (topical)	skin	lectin from seeds, cytotoxic polysaccharides	
	Adansonia digitata L.	CP098/16	2	bark	decoction	stomach, breast	no	
	Cola nitida (Vent.) Schott & Endl.	CP068/16	2	bark	decoction	lungs, skin	no	
	Glyphaea brevis (Spreng.) Monach.	CP119/16	1	leaves	decoction	brain, skin	no	
	Gossypium arboreum L.	CP161/16	1	leaves	decoction	stomach, throat	no	
	Mansonia altissima (A.Chev.) A.Chev.	CP142/16	3	bark, roots	cold maceration massage, decoction	breast, skin	no	
	Sida acuta Burm.f.	CP150/16	3	leaves, roots, whole plant	decoction, ground, squeezed juice	skin, breast, colo-rectal	apoptosis induction by cryptolepine	(Ahmed et al., 2011)
	Sida cordifolia L.	CP174/16	1	leaves	decoction	lungs	cell cycle arrest by alkaloid cryptolepine	(Matsui et al., 2007)
	Sterculia tragacantha Lindl.	CP089/16	1	bark	decoction	breast	no	
	Triplochiton scleroxylon K.Schum.	CP092/16	18	stem bark, leaves, root bark	decoction, dressing, grind as lump, squeezed leaves (topical), powder	skin, breast	no reports on proven anti-cancer activity	
	Triumfetta cordifolia A. Rich.	CP071/16	1	leaves and stem bark	poultice	skin and breast	no	
Marantaceae	*Thalia geniculata* L.	CP157/16	2	leaves	tea	skin	no	
Meliaceae	*Azadirachta indica* A.Juss.	CP182/16	17	leaves, stem bark, root bark, fruit	decoction, paste (topical), ground bark, ground fruit	skin, breast, bone	*in vitro* antiproliferative activity of nimbolide	(Hao et al., 2014)
	Carapa procera DC.	CP070/16	1	bark	decoction	breast	cytotoxic tetranortripernoids from the seeds	(Dioum et al., 2016)
	Entandrophragma angolense (Welw.) C.DC.	CP082/16	13	bark, roots, leaves, root bark	decoction, tea	prostate, skin, breast, throat, stomach	no	
	Entandrophragma cylindricum (Sprague) Sprague	CP108/16	3	leaves, bark	decoction	lung, skin	*in vitro* antiproliferative activity of limonoid Entangolensin A against HepG2, MCF-7.	(Zhang et al., 2016)
	Khaya anthotheca (Welw.) C.DC.	CP132/16	1	bark	decoction	breast, prostate	no	
	Khaya senegalensis (Desv.) A.Juss.	CP114/16	19	bark, roots, fruit	decoction, maceration, tincture (massage), percolate (oral), cream (topical), tea, fruit without seeds (topical)	stomach, skin, breast, prostate, lungs	*in vitro* antiproliferative activity of limonoid 3α,7α-dideacetylkhivorin	(Zhang et al., 2007)
	Turraea heterophylla Sm.	CP079/16	4	stem, leaves, roots, fruit	mix with oil (oral), decoction, ground leaves massage, tincture	stomach, prostate, joint, breast, liver, throat	no	
Menispermaceae	*Cissampelos mucronata* A.Rich.	CP085/16	1	leaves	decoction	skin	no	
	Tiliacora funifera (Miers) Oliv.	CP141/16	2	leaves	decoction	breast, throat	no	

(*continued on next page*)

Table 1 (*continued*)

Plant family	*Species*	*Voucher number*	*Frequency* [a]	*Plant part used*	*Formulation, application*	*Type of cancer*	*Documnted use in literature in regard to cancer* [b]	*Literature references*
Moraceae	*Antiaris toxicaria* Lesch.	CP080/16	1	bark	decoction	breast	yes, different reports on cytotoxic cardenolides	
	Ficus asperifolia Miq.	CP149/16	3	roots, bark, leaves, stem	decoction, ground	skin, breast, lungs	no	
	Ficus elastica Roxb. ex Hornem.	CP151/16	2	leaves, roots	decoction (root), tea (leaves)	stomach, prostate, lungs	only reports on cytotoxicity of latex	
	Ficus exasperata Vahl	CP087/16	1	leaves, stem bark	sap	breast	yes, cytotoxicity against ovarial cancer cells	(Bafor et al., 2017)
	Ficus natalensis subsp. leprieurii (Miq.) Hochst. C.C.E.	CP178/16	1	bark	decoction	breast	no	
	Ficus sp.	CP106/16	1	fruits, leaves	exudates,	breast, skin		
	Milicia excelsa (Welw.) C.C.Berg	CP171/16	3	bark, leaves	ground, decoction	skin, prostate	*in vitro* anti-proliferative activity of xanthones	(Kuete et al., 2014b; Oke-Altuntas et al., 2016)
	Milicia regia (A.Chev.) C.C.Berg	CP090/16	9	bark, leaves	decoction, tea	lungs, skin, stomach, throat, heart	no publications for anti-cancer activity (see also *Milicia excelsa*)	
Musaceae	*Musa x paradisiaca* L.	CP120/16	4	leaves, roots	mashed leaves, decoction	stomach, throat, skin, breast	antiangioneteic effects of root extracts?	(Harsha Raj et al., 2017)
Myristicaceae	*Pycnanthus angolensis* (Welw.) Warb.	CP069/16	3	bark	powder (topical), decoction	skin	yes, isoflavones with apotose-inducing effects	(Mansoor et al., 2011)
Myrtaceae	*Psidium guajava* L.	CP166/16	1	fruit, bark, leaves	topical	stomach, skin	radical-inhibiting effects, for review see:	(Correa et al., 2016)
Nyctaginaceae	*Boerhavia diffusa* L.	CP117/16	1	roots	decoction	brain, prostate	yes, alkaloid punarnavine, in vitro and in vivo studies.	(Manu et al., 2007)
Pandaceae	*Microdesmis puberula* Hook.f. ex Planch.	CP067/16	1	fruit	ground fruit (topical)	breast	no	
Papaveraceae	*Argemone mexicana* L.	CP110/16	1	leaves	decoction	throat,breast	yes, cytotoxic alkaloids	(Chang et al., 2003)
Passifloraceae	*Adenia cissampeloides* (Planch. ex Hook.) Harms	CP088/16	1	leaves	decoction	lungs	no	
	Adenia lobata (Jacq.) Engl.	CP179/16	1	bark, roots, leaves	decoction, ground	breast, skin	no	
Phyllanthaceae	*Phyllanthus fraternus* G. L.Webster	CP160/16	1	bark	decoction	skin	no	
	Phyllanthus spp.	CP118/16	1	leaves	ground leaves	skin		
Piperaceae	*Piper umbellatum* L.	CP097/16	2				yes, animal studies, compounds unknown	(Iwamoto et al., 2015)
Plantaginaceae	*Scoparia dulcis* L.	CP013/16	2	roots, bark, leaves	ground roots, decoction	breast, skin	yes, scopadulciol, antiproliferative	(Han et al., 2014)
Poaceae	*Bambusa vulgaris* Schrad.	CP008/16	1	leaves	decoction	stomach	no	
	Brachyachne obtusiflora (Benth.) C.E.Hubb.	CP159/16	1	roots	topical	skin, genital	no	
	Festuca sp.	CP083/16	1	bark, roost, leaves	decoction, nasal	skin, head		
	Zea mays L.	CP176/16	1	corn, grains, leaves	ground grains as poultice	skin	no convincing papers	
Polygalaceae	*Securidaca* sp.	CP109/16	1	bark	cream	breast		
Portulaceae	*Portulaca oleracea* L.	CP170/16	4	roots, leaves	ground on stone plaster as dressing (topical), decoction	prostate, skin, throat, breast	antimetastatic effects documented	(Ji et al., 2015)
Rubiaceae	*Bertiera racemosa* (G.Don) K.Schum.	CP133/16	1	bark, leaves	decoction	breast, skin	no	
	Corynanthe pachyceras K.Schum.	CP128/16	1	leaves	tea	stomach	no	
	Crossopteryx febrifuga (Afzel. ex G.Don) Benth.	CP086/16	1	bark	decoction	prostate	no	

(*continued on next page*)

Table 1 (*continued*)

Plant family	*Species*	*Voucher number*	*Frequency* [a]	*Plant part used*	*Formulation, application*	*Type of cancer*	*Documnted use in literature in regard to cancer* [b]	*Literature references*
Rutaceae	*Citrus aurantiifolia* (Christm.) Swingle	CP140/16	4	fruit, leaves, bark	juice mix with latex of *Alstonia boonei* for plaster, squeezed, boiled bark	breast, skin, throat	Citrus flavonoids are regarded to be cancer-preventive. No final conclusion until now.	
	Citrus limon (L.) Osbeck	CP162/16	1	fruit	juice massage	breast, prostate	Citrus flavonoids are regarded to be cancer-preventive. No final conclusion until now.	
	Citrus sinensis (L.) Osbeck	CP152/16	6	fruit, leaves	juice, wash, decoction	cervical, brain, throat, prostate, stomach	Citrus flavonoids are regarded to be cancer-preventive. No final conclusion until now.	For review see: (Chidambara Murthy et al., 2012; Khan et al., 2014)
	Zanthoxylum gilletii (De Wild.) P.G.Waterman	CP125/16	1	bark	cold maceration	liver	yes, anticancer activity of the genus Zanthoxylum see review:	(Epifano et al., 2011)
	Zanthoxylum zanthoxyloides (Lam.) Zepern. & Timler	CP039/16	7	stem bark, root bark	decoction	stomach, skin, brain, breast	*in vitro* anti-proliferative activity of acridone alkaloids, chalcones against different cell lines; inhibition of aromatase and glycosyltransferases.	(Choumessi et al., 2012; Fiorito et al., 2013; Misra et al., 2013; Vyry Wouatsa et al., 2013; Wouatsa et al., 2013)
Salicaceae	*Oncoba spinosa* Forssk.	CP023/16	1	bark	decoction	skin	no	
Sapindaceae	*Blighia sapida* K.D.Koenig	CP167/16	10	roots, bark, leaves, fruit, root bark	poultice, decoction, raw fruit, maceration (topical), tea	lungs, breast, stomach, colo-rectal, skin	unspecific anticancer activity plausible	
	Blighia unijugata Baker	CP138/16	2	leaves	decoction	breast,throat	no	
	Paullinia pinnata L.	CP175/16	3	climbers, stem	decoction, cold maceration	stomach, skin, liver, breast	no	
Solanaceae	*Capsicum annuum* L.	CP154/16	1	leaves	decoction	throat	yes, anticancer activity of capsaicin	(Clark and Lee, 2016)
	Capsicum frutescens L.	CP137/16	1	leaves	decoction	breast	yes, anticancer activity of capsaicin	(Clark and Lee, 2016)
	Lycopersicon esculentum Mill.	CP144/16	4	fruit, leaves, roots	squeezed fruit for drink, ground leaves (topical), boiled roots (oral)	throat, lungs, prostate, breast, skin	growth-inhibitory effects documented	(Gupta et al., 2013)
	Physalis angulate L.	CP180/16	1	leaves	massage	breast	yes, cytotoxic withanolides	(Gao et al., 2017)
	Solanum torvum Sw.	CP130/16	2	fruit	tea, soup	stomach, breast	yes, cytotoxic methyl caffeate, steroidal glycosides	(Balachandran et al., 2015)
	Solanum verbascifolium L. Species unresolved (www.theplantlist.org)	CP163/16	2	leaves	crushed leaves (topical)	skin, genital, breast		
Solanaceae	*Withania somnifera* L. Dunal	CP155/165	1	roots	ground root as plaster	genital		
Verbenaceae	*Stachytarpheta indica* (L.) Vahl	CP122/16	1	leaves	decoction	breast, skin	no	
Zingiberaceae	*Aframomum melegueta* K.Schum.	CP143/16	3	fruit, roots	excipient for poultice/lump	brain, stomach	no convincing data	
	Zingiber officinale Roscoe	CP177/16	2	roots, rhizome	ground as plaster excipient oral or massage	stomach, brain	divers and inconsistent data	
Zygophyllaceae	*Balanites aegyptiaca* (L.) Delile	CP146/16	1	bark	oral	stomach	yes, cytotoxic activity of diosgenyl saponins	(Issa et al., 2015)

[a] : Frequency – indicates how many times a given species was mentioned and recorded by the 85 healers.

[b] : "no" – indicates absence of literature for the plant species regarding the search terminus "cancer"; "no convincing data" indicates that the test systems or the outcome of the respective studies concerning cancer are doubtful and not necessarily related to state-of-the-art science; "published literature not relevant" is an asessement that the available data cannot be used to rationalize the use of the plant species for cancer.

the plant species mentioned by the healers with available literature concerning *in vitro* or *in vivo* activity against cancer or cancer cell lines.

3. Results and discussion

3.1. Survey on plants used for cancer treatment

An ethnopharmacological survey was carried out in 10 different locations the Ashanti region in Ghana (Fig. 1). This region comprises a dense rainforest area in the central part of Ghana with rural villages besides a metropolitan area around the main capital Kumasi. The Ashanti region reflects both, the traditional and the modern West Africa, with modern Western-style healthcare and traditional, culture-based medical care. For cross-validation, data were additionally collected from locations outside Ashanti region, mainly from the Eastern region of Ghana, which shows a similar botanical vegetation, but predominantly rural population. This cross-validation was performed to investigate potential regional and cultural differences within the cancer treatment strategies.

86 professional healers contributed to the survey. All of them treated cancer patients, in average 3.4 patients per year (minimum 1, maximum 20). About 31% of the respondents were in the age between 21 and 30 years, 9% between 31 and 40 years and 40% between 41 and 60 years. This age distribution reflects an interesting finding as similar surveys in the same study region in 2009 have documented a significant dominance of elder or very aged healers (Agyare et al., 2009). This indicates changes in the age distribution of the healers within about one decade, which has also been documented recently in another study from the same region (Agyare et al., 2014), were a trend for younger people in this profession has been reported. In total, this trend indicates that the profession “Healer” is becoming increasingly popular in the Ashanti region and reflects that more and more young people choose this profession. About half of the healers are men, the other half are women.

Also the level of education of healers has changed over the last decade: while in 2008 only 1% of them had a university degree and the majority (40%) had no education, in the present study -performed in the same study area – 9% held an university degree, 42% a high school degree, 19% went to middle school, 21% to primary school and only 5% were illiterate or without any formal education (8% did not answer this question). Also, this finding reflects a shift in demographic properties in the healer community in the Ashanti region in Ghana, which should be connected to the immense activity of the Ghana Federal Government to increase the education level. It might be speculated that the level of education could determine the level of readiness of healers to apply scientifically proven methods of preparation of their medicines and treatment of the respective ailments. Therefore, it will be also very interesting to see if it will be possible to integrate scientific facts from medical research into the daily routine of the traditional healers in the study region in the near future. At least clear shifts towards younger and better educated professionals are becoming obvious.

This shift is also reflected by the time of practice: 17% of the healers have worked in this profession for 5 years, 29% for up to 10 years, 26% for up to 20 years and 13% for up to 40 years and only 2% for more than 40 years. Again, a trend to younger healers can be seen.

On the other side it became obvious during the study that the profession “Healer” is interpretated not necessarily in the same way. Herbal practitioners constitute the majority (56%) of the healers. Divine healers and traditional healers constitute 30% and 8% respectively. It is important to note however, that there is no clear distinction of practice between the three kinds of healers. Each could play the role of the other, and this is common amongst traditional medical practice.

Concerning the treatment of cancer by the respondents, only 44% treat the disease, whereas 53% stated in the interviews that they do not take care for these patients, which implies that they will send them to local physicians or hospitals associated with conventional medicine. On the other side all of the interviewed healers gave information on anti-cancer plants they either use or which they think could be used. Most of the cancer diagnoses are done by the traditional healers based on their long years of experience and apprenticeship. In few cases, the patient will be diagnosed at a hospital, health center or facility but prefers to use herbal preparations or remedies for the treatment.

Concerning the different types of cancer treated in daily routine by the healers, breast and skin cancer dominated the activities, followed by lung, throat, prostate and stomach cancer. The detailed cancer list is presented in the Supplementary Data File (Table S2) together with details how the heales try to diagnose the respective cancer type.

The respondents were also asked about the main causes of cancer in humans in their area based on their experience. Interestingly, more than 75% claimed food-related causes for cancer, followed by smoking, waste water, lifestyle, pollution, drugs, chemical substances, lack of sanitation, radiation, genetics etc. The detailed comments to this question are presented in the Supplementary Data File (Table S3) as these data reflect a quite good, and in principle more or less modern understanding on oncogenesis.

Concerning the herbal medicines, 151 plant species from 137 genera, belonging to 57 families were recorded as anticancer agents (Table 1). Plants are mostly obtained from the forest areas (79 counts), much less from farms or gardens (13 counts), from commercial collectors or from the market (12 counts) or from a special farm (only 1 case). Also the collection in national parks, around the own home or within the living community is rather common (21 counts).

Identification of the herbal material is ensured in most cases as the healers state to have long experience with the respective plant (55%). Also the habitat and the location of the plant is used to prove the identity (36%), while odour, morphology etc. as identifying criteria are named only to a low extent. Asking the respondents directly if they have problems with the identification, 61% clearly answered “no”, while 34% claimed to be sometimes not sure due to similarity to other plants and environmental changes, e.g. extinction, afforestation, etc.

More than 83% of all healers reported that they sometimes have problems with the collection of the plant material due to seasonal unavailability, long distances, lack of money or vehicles to transport the collectors and plant materials, extinction of the plants, bad equipment, difficulties in transportation and storages, and no access to remote locations. This information seems interesting as it could be useful to implement specialized collectors or to install more wholesale traders to overcome these problems in availability in the future.

Interstingly, about one third (30%) of the healers claimed that they mix plant-based preparations also with chemical cancer drugs; 61% of the respondents claimed not to do this (9% did not answer on this question). The information on the combination of herbal preparation and drug/anticancer provided here is what is being practiced by the healers in the region and hence as researchers, we are reporting the issue as provided by the respondents. The regulation and monitoring of medications or drugs in Ghana and other developing countries is not all that strict compared to that of the developed countries and hence we have situations where prescription drugs or medications can end up in the hands of unauthorized persons.

Similar to the cancer statistics of Ghana (Laryea et al., 2014), for cross-referencing, healers were also asked what plants they use specifically to treat cancer of liver, prostate, stomach breast and female genital cancer, which are the malignant diseases comprising the most common cancer types in this region. Table 3 summarizes these data, which are more or less in congruence with the information displayed in Table 1.

Patients who always need special care in respect to cancer are children. The incidence of these patients in Kumasi and details on the specific types of the different diseases is documented by the Kumasi Cancer Registry (Laryea et al., 2014), and therefore the traditional healers have been interviewed about special plants used for children. The respective results are displayed in Table 4, indicating that 5 of the

Table 2
Plants used for cancer treatment from group I (very frequent use, recorded more than 10 times by the 85 healers), group II (frequent use, recorded 7–9 times) and group III (less frequent use, recorded 4–6 times).

Group I		Group II		Group III	
Plant species	Frequency	Plant species	Frequency	Plant species	Frequency
Khaya senegalensis	18	*Blighia sapida*	10	*Mangifera indica*	6
Triplochiton scleroxylon	18	*Milicia regia*	9	*Citrus sinensis*	6
Azadirachta indica	17	*Terminalia catappa*	9	*Ageratum conyzoides*	5
Entandrophragma angolense	13	*Mallotus oppositifolius*	7	*Desmodium adscendens*	5
Terminalia superba	12	*Zanthoxylum zanthoxyloides*	7	*Lycopersicum esculentum*	5
				Bryophyllum pinnatum	4
				Chromolaena odorata	4
				Citrus × aurantiifolia	4
				Mammea africana	4
				Musa paradisiac	4
				Newbouldia levi	4
				Portulaca oleracea	4

identified plants (*P. oleracea*, *A. conyzoides*, *C. aurantifolia*, *M. regia*, *B. pinnatum*) represent species which are generally used for cancer treatment, but 16 plants seem to be specifically used for treatment of children (Table 4).

Most recorded species (14 species / 9.3%) were from the family Fabaceae, followed by Euphorbiaceae (13 species / 8.6%), Apocynaceae (12 species / 7.9%), Malvaceae (11 species / 7.3%), Asteraceae (8 species / 5.3%), and Combretaceae (7 species / 4.6%) which is not congruent with the main plant families from the overall available flora of the Ashanti region.

Obviously no differences were found among the answers of the healers from Ashanti region compared to healers from other areas in central and East Ghana (no statistical evaluation was performed, but from the plants named it is clear that similar plants are used by healers from outside the Ashanti region), which indicates that there is not necessarily a region-specific treatment culture in Ghana.

In order to investigate which of these plants have already been reported in scientific literature for cancer treatment, cross-referencing was performed by entering of the botanical name in combination with the search term “cancer” into the database PubMed (Table 1).

Medicinal plants recorded during the survey were clustered into 3 groups according to their frequency of use (Table 2): group I (very frequently used plants, named by healers more than 10 times), group II (frequently used plants, recorded between 7 and 9 times), and group III with plants recorded 3–7 times. Table 2 comprises all species found for group I (5 plants / 3.3% of all species recorded, 78 hits / 22% of 348 hits in total during the survey) and group II (5 plants / 3.3% of all species recorded, 42 hits / 12% of 348 hits in total during the survey) and group III (12 plants / 7.9% of all species recorded, 55 hits / 16% of 348 hits in total during the survey). This means that 22 medicinal plants comprise 15% of all records from the healers.

In order to investigate whether the “top-22″ plants are already known plants for cancer treatment, cross-referencing was made to scientific literature using SciFinder® data base (Tables 1, 2). Interestingly, in group I three (out of five!) plant species were from the Meliaceae family (*Azadirachta indica*, *Entandrophragma angolense* and *Khyaya senegalensis*,) and for all three plants anti-proliferative activity against different cancer cell lines under *in vitro* conditions have been described. This bioactivity has been correlated to the presence of limonoids, biosynthetically deduced from tetracyclic triterpenes (structural features of Nimbolide from *A. indica*, Entangolensin from *E. angolense* and 3α,7α-dideacetylkhivorin from *K. senegalensis*, Fig. 1). It has to be mentioned that additionally to these plants in group I, two other species (*K. anthoteca* and *E. cylindricum*) from the genus Khaya and Entandrophragma are used by the healers (Table 1), but with less frequency. From the phytochemical point of view, the presence of similar limonoid derivatives might be possible, which again could rationalize the use of these plants for cancer treatment.

Another plant species from group I (*Triplochiton scleroxylon*) has been named by the healers as the most commonly used plant. Interestingly, no data concerning functional studies of extracts from this plant against cancer have been published until now and details on the phytochemical composition of this Malvaceae species are also very rare. For this, further studies on this plant might be a promising subject.

Within group I, *Terminalia superba* has been listed as anti-cancer species; the existing literature does not verify antiproliferative activity of this plant. On the other side, other Terminalia species have been mentioned by the healers, especially *T. catappa* which can be found in group II of this study, but also *T. ivorensis* which is used in traditional medicine. For *T. catappa*, *in vitro* as well as *in vivo* data are available on antiproliferative activity of a flavonoid-enriched fraction against Ehrlich ascites carcinoma. As the genus Terminalia belongs to the plant family Combretaceae and many members from this family are characterized by the presence of the tubulin inhibiting combretastatines (stilbene and dihydrostilbe derivatives, structural features of Combretastatin A and B see Fig. 2), it can be speculated that these antimitotic compounds are also present in Terminalia extracts. That such stilbenes can indeed be detected in the genus Terminalia has recently been shown for *T. sericeae* (Joseph et al., 2007).

Plant species from group II are frequently used by healers. Besides *Terminalia catappa*, for which the activity again could be due to the presence of combretastatines, *Blighlia sapida*, a member of the Sapindaceae, was named frequently. This plant is widely used as a food source in many tropical and subtropical areas, especially in the Caribbean area, and is better known as Ackee fruit. All parts of the plant, except for the arrilus, are toxic (Blake et al., 2006) probably due to the content of the cyclic amino acid hypoglycin (Fig. 2), a potent fatty acid inhibitor. It can be speculated that the use of hypoglycin-containing extracts might indeed stop uncontrolled cell proliferation in cancer cells, but the unspecifity and the high toxicity of Ackee has to be taken into account (Oke-Altuntas et al., 2016; Surmaitis, 2017). If other natural products from *B. sapida* can also contribute to a potential antiproliferative activity should be investigated by bioassay-guided fractionation of extracts. Especially the high content of triterpene saponins of the plant should be taken into account.

Within group II, the use of bark and leaves from *Milicia regia* has been recorded. No data have been published on this species regarding a potential use for cancer. On the other side, a further Milicia species, *M. excelsa*, has been pinpointed by the healers (Table 1) but with less frequent use. Interestingly, for this species several reports have been published on *in vitro* antiproliferative activity against several cancer cells due to the presence of the cytotoxic xanthones Cudraxanthone I and Neocyclomorusin (Fig. 2) (Kuete et al., 2014b; Oke-Altuntas et al., 2016). Phytochemical and functional studies should be performed on

Table 3
Herbal remedies used for cancer treatment for the most common types of cancer.

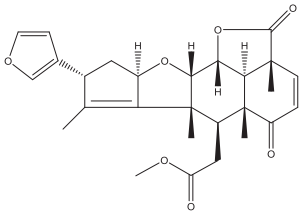
Cancer type	Plant (local name)	Botanical name	Part of the plant used
Liver	Mahogani/ Odupong	*Khaya senegalensis*	bark
	Akwafanu	*Desmodium adscendens*	leaves
	Ɔyaa	*Zanthoxylum zanthoxyloides*	bark
	Mango	*Mangifera indica*	bark
	Ankaa	*Citrus sinensis*	fruit
	Sapele	*Entandrophragma angolense*	root bark, bark
	Akakaduro	*Zingiber officinale*	rhizome
	Asase ne aboo	*Portulaca oleracea*	leaves
	Nkrangyedua	*Jatropha gossypiifolia*	leaves
	Nunum	*Ocimum gratissimum*	leaves
	Akonfem tikro	*Heliotropium indicum*	seed
	Awudifoo kɛte	*Vernonia conferta*	leaves
	Beat root	*Solidago spp.*	upper part
	Ntoosi	*Lycopersicum esculentum*	fruit
	Ahunu anyankwa	*Turraea heterophylla*	leaves
	Bese (Kola)	*Cola nitida*	bark
	Famwisa	*Aframomum melegueta*	fruit
	Nyanyaforowa	*Mallotus oppositifolius*	roots
	Odum	*Milicia regia (Chlorophora regia)*	bark, leaves
	Ofema	*Microdesmis puberula*	fruit
	Baakɔɔ	*Saba comorensis*	climbers
Prostate	Tuantini	*Paullinia pinnata*	climbers
	Ahabayere	*Dioscorea dumetorum*	underground tubers
	Samanbayere	*Dioscorea bulbifera*	tubers
	Adwera	*Portulaca oleracea, Portulaca spp.*	leaves, roots
	Oyea	*Zanthoxylum gilletii*	roots
	Odum	*Milicia excelsa (Chlorophora excelsa)*	bark
	Nyamedua	*Alstonia boonei*	bark, leaves
	Gyeene	*Allium cepa*	bulb
	Nunum	*Ocimum gratissimum*	leaves
	Akonfem tiko	*Heliotropium indicum*	leaves
	Awudifoo kɛte	*Vernonia conferta*	leaves
	Asosomasa	*Nerbouldia laevi*	bark
	Ahunu anyankwa	*Turraea heterophylla*	leaves
		Euphorbia heterophylla	leaves, flowers
	Wawa	*Triplochiton scleroxylon*	bark
	Mahogany/ Odupong	*Khaya senegalensis*	bark
	Ofram	*Terminalia superba*	leaves
	Ofema	*Microdesmis puberula*	fruit
	Yaa kankan	*Ethulia conyzoides*	whole plant
	Mofra bayere	*Boerhavia diffusa*	bark
Stomach	Gyeene	*Allium cepa*	bulb
	Mahogany/ Odupong	*Khaya senegalensis*	bark
	Mango	*Mangifera indica*	
	Nyanya	*Momordica angustifolia*	leaves, climbers
	Ɔyaa	*Zanthoxylum zanthoxyloides*	stem bark
	Ankaa	*Citrus sinensis*	fruit
	Ahabayere	*Dioscorea spp.*	tuber
	Nunum	*Ocimum gratissimum*	
	Akonfem tikro	*Heliotropium indicum*	leaves
	Awudifoo kɛte	*Vernonia conferta*	
	Gyama	*Alchornea cordifolia*	leaves
	Mmatwa	*Strophanthus gratus*	roots
	Ahunu anyankwa	*Turraea heterophylla*	stem
	Nkasare kasare	*Alternanthera repens*	leaves
		Euphorbia heterophylla	leaves
	Guakro	*Ageratum conyzoides*	leaves
	Ofema	*Microdesmis puberula*	fruit
Breast	Gyeene	*Allium cepa*	bulb
	Ahabayere	*Dioscorea dumetorum*	underground tubers
	Akwafanu	*Desmodium adscendens*	leaves
	Akyee	*Blighia sapida*	roots, bark
	Amunamuna	*Mimosa pudica*	leaves
	Tɛtɛ	*Cleome sp.*	leaves
	Aburo	*Zea mays*	leaves, grains
	Egoro	*Bryophyllum pinnatum*	leaves
	Nunum	*Ocimum gratissimum*	
	Akonfem tikro	*Heliotropium indicum*	leaves
	Awudifoo kɛte	*Vernonia conferta*	
	Mahogany/ Odupong	*Khaya senegalensis*	
	Kyirituo	*Securidaca sp.*	
	Ofuntum	*Funtumia elastic*	bark
	Mmatwa	*Strophanthus gratus*	roots
	Ahunu anyankwa	*Turraea heterophylla*	roots, climbers
	Nyanyafurowa	*Mallotus oppositifolius*	roots
	Wawa	*Triplochiton scleroxylon*	bark, leaves
	Aburofo nkateɛ	*Terminalia catappa*	bark, fruit
	Yaa kankan	*Ethulia conyzoides*	whole plant
Genital cancer (women)	Akuokuoninsuo	*Spathodea campanulata*	bark
	Mahogany/ Odupong	*Khaya senegalensis*	bark
	Ankaa	*Citrus sinensis*	fruit
	Nyanyaforowa	*Mallotus oppositifolius*	leaves
	Pepediewuo	*Solanum verbascifolium*	leaves
	Ɛme	*Ocimum viride*	leaves
	Nunum	*Ocimum gratissimum*	
	Akonfem tikro	*Heliotropium indicum*	
	Awudifoo kɛte	*Vernonia conferta*	
	Mmatwa	*Strophanthus gratus*	roots
	Odwono	*Baphia nitida*	stem bark
	Odum	*Milicia regia (Chlorophora regia)*	bark
	Nyanya	*Momordica charantia*	fruits
	Ahunu anyankwa	*Turraea heterophylla*	roots, climbers
	Yaa kankan	*Ethulia conyzoides*	whole plant

Table 4
Specific herbal materials or therapies in the daily work of traditional healers used for therapy of cancer of children.

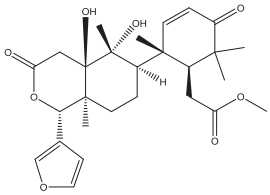
Botanical name	*Plant (local name)*	*Part of the plant*
Jatropha gossypiifolia		
Portulaca oleracea	Adwera	leaves, root
Dioscorea dumetorum	Ahabayere	underground tubers
Alternanthera sp.	Asaase ne abos	leaves
Allium cepa	Bulb	bulb
Allium sativum	Garlic	bulb
Zingiber officinale	Ginger	rhizome
Ageratum conyzoides	Guakro	whole plant
Citrus aurantifolia	Lemon fruit	fruit
Colocasia sp.	Mankani	leaves, tuber
Alternanthera repens	Nkasae kasare	leaves
Milicia regia (Chlorophora regia)	Odum	leaves
Pycnanthus angolensis	Otie	seeds
Bryophyllum pinnatum	Taumeawu	leaves
Paullinia pinnata	Tuantini	aerial part

M. regia in order to gain more information on this species and the respective xanthon derivatives.

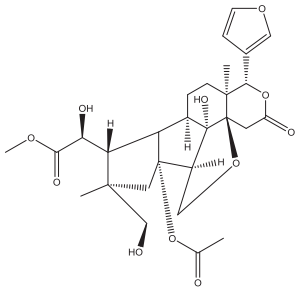
Mallotus oppositifolius, a member of the Euphorbiaceae in group II, is characterized by a high amount of phloroglucinols and phloroglucionol dimers. These compounds, named Mallotophenon and Mallotojaponins (Fig. 2), from this species have been described for anticancer activity against ovarian cancer cells in the low micromolare range and also antiplasmodial activity is documented (Harinantenaina et al., 2013). No data on the respective mode of action of these compounds have been



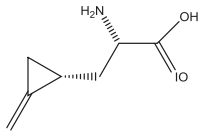
Nimbolide *Azadirachta indica*



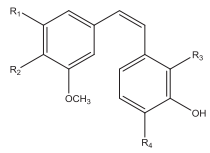
Entangolensin *Entandrophragma angolense*



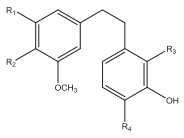
3α,7α-Dideacetylkhivorin *Khyaya senegalensis*



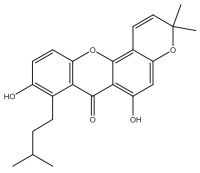
Hypoglycin *Blighlia sapida* (Ackee)



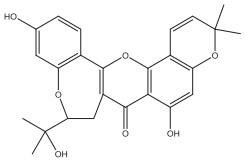
Combretastatine A



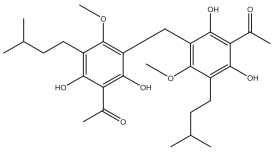
Combretastatine B



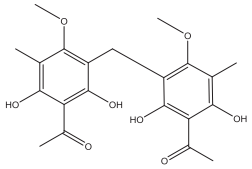
Cudraxanthone I *Milicia excelsa*



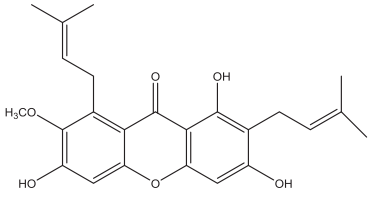
Neocyclomorusin *Milicia excelsa*



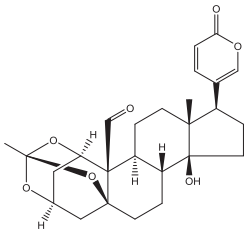
Mallotojaponin C *Mallotus oppositifolius*



Mallotophenon *Mallotus oppositifolius*



α-Mangostin *Mangifera indica*



cytotoxic bufadienolide *Bryophyllum pinnatum*

Fig. 2. Structural features and origin of selected cytotoxic compounds from the "top-22" plant species used in traditional medicine against cancer.

published.

A further member from group II was *Zanthoxylum zanthoxyloides*, a member of Rutaceae family, for which antiproliverative activity has been described in detailed, which can be correlated to the presence of acridone alkaloids and chalcones, probably due to an inhibition of aromatase (Wouatsa et al., 2013).

Plant species listed within group III represent herbal drugs which are used less frequently (Table 2). On top of this list, the bark and leaves from Mango tree (*Mangifera indica)* are named. The use of mangosteen extracts (mostly from the pericarp) in cancer is well known all over the world. Despite the numerous publications on preclinical data, only very limited clinical data have been communicated. The main hypothesis nowadays is that the prenylated xanthon α-mangostin (Fig. 2) acts as a chemopreventive agent, interacting with initiation and progression of carcinogenesis (Núñez Selles et al., 2016). A recent review on this subject highlights the respective knowledge on this potential anticancer species (Zhang et al., 2017).

Within group III, several Citrus species have been listed. The use of Citrus extracts for cancer prevention and treatment is part of numerous publications, and especially the monoterpenes are used to explain a potential anticancer activity (Chidambara Murthy et al., 2012). For review see (Khan et al., 2014). On the other side, truly convincing *in vitro* data and clinical studies have not been presented until now on this subject.

Ageratum conyzoides, a member of the Asteraceae family, contains quite high amounts of pyrrolizidine alkaloids, including the highly toxic Δ1,2-unsaturated derivatives, which can easily be toxified by cellular metabolism into compounds strongly interfering with bionucleophiles like DNA or proteins. This of course will lead to antiproliferative effects, which have already been described by an *in vitro* study for extracts from *A. conyzoides* (Adetutu et al., 2012). The use of this plant in humans should be abandoned completely as the pyrrolizidine alkaloids are well known to exert strong mutagenic, carcinogenic and liver toxic properties (Fu, 2017). From this point of view it seems essential to inform traditional healers about these facts and within health education, people should receive the information not to use this plant species in daily life any more.

A further species from group III is *Desmodium adscendens*, for which no data on anti-cancer activity have been published in scientific literature until now.

Fruit, leaves and roots from tomato (*Lycopersicum esculentum*) are listed as group III plant for several kinds of cancer. A clear asessement on functionality of this use is difficult as no convincing data on tomato extracts are published, while numerous studies have been performed with the carotenoid lycopene from tomato which could interfere with cell proliferation (Hazai et al., 2006). On the other side it has to be kept in mind that the carotenoids are part of the ripe fruits and will not occur in higher amounts in roots or leaves, which are the main plant parts used in traditional medicine. It can be hypothesized that a theoretical anti-cancer activity of such extracts could be due to the content of steroid alkaloids (e.g. tomatine) in roots and leaves for which anticancer activity *in vitro* and *in vivo* in mice has been documented (Tomsik et al., 2013) (Shieh et al., 2011). As these alkaloids are formed biosynthetically in the roots and can accumulate in green fruits and leaves a potential bioactivity of tomato against cancer could be due to the presence of these steroid alkaloids. On the other side a quite high toxicity of tomatine and related alkaloids to humans after ingestion has been documented and should be taken into account for a rationalized risk-benefit assessment.

For *Bryophyllum pinnatum* which has been listed as a group III plant, anti-cancer activity has been documented only in one report against several cancer cells due to its content of a strongly cytotoxic bufadienolide (Fig. 2) (Yan et al., 1992). It has to be mentioned that *B. pinnatum* has been reported to be a remedy against nematode infections in West Africa, which again could be related to cytotoxic effects (Agyare et al., 2014).

Chromolaena odorata, commonly known as Siam weed, is commonly used in many countries, also in Asia, against cancer. This Asteraceae species is phytochemically characterized by the presence of a huge variety of flavonoids, chalcones and triterpens with proven *in vitro* antiproliferative activity against different cell lines (Hung et al., 2011; Kouamé et al., 2013). Clinical data are not available.

Also, extracts from *Mammea africana*, used as herbal remedies against cancer as listed in group III, have been reported in literature to exert cytotoxic effects against two cancer cell lines due to the presence of a prenylated coumarin called Mammea A/AA (Fig. 2) with strong antibacterial effects (Canning et al., 2013). Selectivity of this plant should be investigated in future studies as the antibacterial and anticancer effects of the coumarin might be a hint for a rather unspecific mode of action.

Despite manifold publications on the potential use of leaves and roots from *Musa paradisiaca* as herbal remedy for cancer, the potential rationalization of this use seems doubtful. An anti-angiogenic effect of Musa extracts has been documented (Harsha Raj et al., 2017), but in total, the available literature on this subject does not seem to justify the use of *M. paradisiac* as anti-cancer drug.

Harder facts have been reported for extracts from *Newbouldia laevi*, also a group III species, for which cytotoxic activity against leukemia cells has been shown within a screening of African plants (Kuete et al., 2014c). This antiproliverative activity was not very pronounced and exerted less than 50% inhibition of cellular proliferation at a concentration of 40 μg/mL. For this reason, the authors of this study did not follow up this plant species.

From *Portulaca oleracea*, listed in group III, the cerebroside portulacerebroside A (Fig. 2) has been isolated for which antimetastatic and antiinvasive activity in liver cells has been documented (Ji et al., 2015). Also polysaccharides from the plant seem to have immunomodulating effects (Zhao et al., 2017). Follow up studies might be useful to clarify the clinical significance of these findings.

Correlation of the above findings to clinical efficacy has to be evaluated by controlled clinical studies in the future. On the other side, it has to be clarified if the efficacy-risk ratio is positive for some of the identified plants. For example, the use of pyrrolizidine alkaloid containing plants for liver cancer might reduce cancer progression, but also toxicity and mutagenicity of these compounds against non-cancer cells has to be kept in mind. Further on, there is a strong need to characterize the plant material concerning quality aspects, but also in regard to phytochemical aspects to isolate the compound(s) responsible for functional activity. Therefore, structured follow-up studies are needed to clarify the clinical impact and the risk potential of these traditionally used plants as well as projects for preparation of high-quality, but still affordable medications by use of standardized extracts or isolated compounds. Taken together, the present study indicates a good and reliable base for the development of a rational phytotherapy based on the traditional herbal medicine of Ghana.

4. Conclusion

From the above results there is a strong indication that the traditional use of plant materials for cancer treatment as it is used by Ghanaian healers, is assessed to be a valuable phytotherapeutic tool, which in many cases can be rationalized by *in vitro* investigations. The ethnopharmacological and traditional selection of plants from the Ashanti area in Ghana can be rationalized, as most of the “top-22” plant species antiproliferative and anticancer effects have been documented in the recent literature, mostly by *in vitro* cell based assays.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jep.2017.10.019.

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