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Opportunities for the discovery of anticancer drugs from traditional herbal medicines in Africa: A Review

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Abstract

Africa is very rich in plant biodiversity which, if fully explored may bring useful drug substances on the world market. Some of the plants have been used by traditional medical practitioners as medicines for curing various ailments and medical conditions. Such knowledge has been conserved within families and has been passed on orally from generation to generation. One major challenge to accessing conventional treatment for cancers in Africa is the cost of treatment hence most cancer patients in Africa use Traditional Medicines (TMs) for primary health care. Some use both conventional treatment and traditional herbal medicines. The incidence and burden for cancer is high with the number of newly diagnosed cancers worldwide expected to reach 24 million by 2035. It is therefore imperative to intensify research and development of anticancer drug substances from previously untapped resources an example being African plants. It is therefore imperative that the herbal medicines which truly cure cancer be prepared following the FDA guidelines for preparation of herbal medicines with efficacy and safety data included.

Keywords: *Discovery, Traditional Medical Practice (TMP), Anticancer, Herbal medicines, Africa*

1. Introduction

Traditional Medicine (TM) is commonly defined as a way of healing founded and comprised of Indigenous Knowledge (IDK) systems that were developed over many generations before the introduction of Western Medicine (WM) (Antwi-baffaur *et al*., 2014). The IDK has been passed on orally from elderly healers to their younger ones through generations and it is jealously protected in certain families or ethnic groups (Antwi-baffaur *et al*., 2014; and Mhane *et al*., 2010). One can view it as a traditional intellectual property protection mechanism similar to the patenting and trade secrets used in conventional business. The practitioners range from herbalists, diviners to midwives and others. Also in traditional medical practice aspects to do with specialization are noted, e.g., some major as spiritualists, some major in herbal medicines and some do both (Antwi-baffaur *et al*., 2014).

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TM has been considered an out of date method of treatment and little effort has been given to investigate the legitimacy and formalization of such practices into the national healthcare systems. This is however, paradoxical given that TM remains key to providing primary healthcare to both rural and urban communities in developing countries, e.g., African countries (Antwi-baffaur *et al.*, 2014). In African traditional health practices, the practitioner personally assesses patients in diagnosis, treatment and prevention of disease using their clinical judgment. The Traditional Health Practitioner (THP)-patient relationship usually begins with interrogations through taking history of the case and basic diagnostic procedures which may involve divination to determine the cause of the patient's problem. After determining the cause of the ailment the THP then prepares medicines which may be derived from medicinal plants, animal parts or minerals. The THP's knowledge would have been derived from the knowledge handed over from the ancestors and their personal experience hence enabling them to offer remedies which are claimed to be effective for treating ailments which may also include diverse types of cancers (Mhane *et al.*, 2010). Conventional scientists have focused their research on the investigation of the potential uses of the plant extracts in the treatment of human diseases including cancer. Many plant species are already being used to treat or prevent cancer. A number of researchers have identified plant species that have demonstrated anticancer properties (Greenwell and Rahman, 2015). There have been many discoveries of potent cytotoxic chemical agents from Asian and Ayurvedic Indian TM but many African medicinal plants have not been explored in the discovery of anticancer lead compounds (Fadeyi *et al.*, 2013). Drug discovery from African plants is of particular interest because Africa has around 57,704 plant species of the world flora. Africans use more than 5,000 of these plants as medicines. The study of African medicinal plants has however, not been accredited or documented as extensively as the Chinese and Indian herbal medicines (Fadeyi *et al.*, 2013).

Cancer patients' survival in Africa has been reported to be far less than that in high income countries. In 2012 it was reported that the 5-year survival rate of women with breast cancer in Europe was 82%, whereas it was 46% in Uganda, 39% in Algeria and 12% in Gambia (Stefan, 2015). One of the factors responsible for this is the unavailability of healthcare facilities and access to treatment. All the 22 chemotherapeutic WHO listed drugs used on the African continent are imported and are not available all the times. The prices of the drugs were found to be between 2.7 and 6.1 times higher in Africa compared to the international reference prices. For most of the drugs it was estimated in Tanzania that the cost for the drugs would be an amount equivalent to between one and seven months of one's income (Stefan, 2015). Africa therefore needs more alternatives to address the limited access to anticancer treatment, either conventional or traditional herbal medicines.

2. Status of cancer drug research and traditional medicine for cancer management in Africa

The incidence and burden for cancer is high with the number of newly diagnosed cancers worldwide expected to reach 24 million by 2035. In Zimbabwe the current statistics indicate that there are over 5,000 new diagnosis for cancer and over 1,500 deaths per year (Jemal *et al*., 2012; and Mapara *et al*., 2015). About 715,000 new cancer cases and 542,000 cancer deaths were reported in the African continent in year 2008 and it was projected that these figures were expected to double in the next 20 years because of the ageing and increasing population. The cancers which were reported to have been on the lead were lung, breast cancer in females and prostate cancer in males (Jemal *et al*., 2012). The discovery of new drugs in Africa has generally been considered to have been an almost impossible aspect regardless of the fact that Africa possesses a very rich biodiversity. This has been due to the limited amount of research focused on drug discovery to identify new effective and safe drugs. Some of the major reasons cited to be responsible for this is the poor performance of economies, poor technological infrastructure, lack of appropriate skills in the drug discovery discipline and lack of good management practices (Nyasse, 2012). The Global Strategy and Plan of Action (GSPOA) on Public Health, Innovation and Intellectual property has opened an avenue for a greater attention on supporting developing countries to participate in the discovery, development and delivery of the products that African governments need most (Nyasse, 2012). These products include drugs for both communicable and non-communicable diseases to mention a few. Despite such an opportunity which has been opened by GSPOA, African countries and their responsible institutions did not demonstrate sustainable capacity to transition from basic research into discovery of novel / new chemical entities which can be registered and commercialized as new drug products (Nyasse, 2012). The potential for successful drug discovery has been indicated in the context of Sub-Saharan Africa through possibility for strengthening and utilizing existing capacity and infrastructure, promotion for collaborative efforts with a focus to sustained delivery of affordable health products including those based on natural products and TM (Nyasse, 2012). South Africa, Tunisia and Egypt have been noted to be taking strides towards

drug research and more detailed studies have indicated that South Africa and Egypt take the lead in research on the continent (Nyasse, 2012). The United States National Cancer Institute had formal agreements with four African countries (Gabon, Ghana, Madagascar and Tanzania) for the collection of indigenous African resources for evaluating anticancer effects and exploring the possibilities of anticancer drug discovery. Collections by the Missouri Botanical Gardens (MBG) were also performed in Cameroon and the Central African Republic without the finalization of formal NCI letter for collection (LOC) agreements but with the authorities in these two countries fully aware of the terms of the LOC irrespective of whether the formalities were finalized or not (Beutler *et al*., 2012). These practices have raised concerns on biopiracy of Africa's biodiversity without a framework of shared benefits should successful medicines arise from such material transfers.

In a study on breast cancer treatment in Ghana, it was found out that almost half of woman used alternative medicine before and during hospital treatment. This has been one of the factors leading to delays in conventional treatments. For those patients who stopped hospital treatments, 90% ended up resorting to alternative treatments including TM (O'Brien *et al*., 2014).[10] In a study carried out in Ghana it was shown that most traditional medical practitioners (TMPs) were aware of the causes of cancer and the signs and symptoms which may enable them to appropriately diagnose the diseases. However, it was noted that most of the diagnoses by TMPs is when the cancer is in its late stages (O'Brien *et al*., 2014). From these observations it is quite promising that cancer medicines may be discovered through collaborative work between biomedical scientists and TMPs in Africa. In an ethno-botanical survey carried out in Ghana where 52 species of plants belonging to 28 plant families were documented, it was reported that members of the Fabaceae, Euphorbiaceae, Asteraceae and Sapindaceae were most commonly used as herbal medicines for diverse type of ailments including cancers. Most of the plants being used were said to be trees (O'Brien *et al*., 2014). In the Eastern Cape province of South Africa an ethno-botanical survey conducted revealed that around 17 plant species which belong to 13 families are mainly used by TMPs for treatment of cancer in the province. Of the 13 families the Hyacinthaceae and Hypoxidaceae are the most commonly used. *Solanum aculeastrum* was found to be the most used plant species by TMPs in the province (Koduru *et al*., 2007; and Madhuri and Pandey, 2009). The type of environment including soils types and climate were considered a factor important to traditional healers in Ghana. Most of the TMPs harvested their medicines from lowlands and loamy soils. A small proportion of healers collected medicines from sandy soils and non-collected medicines from clay soils (Boadu and Asase, 2017).

3. Information gaps on treatment of cancer by traditional medicine in Africa

Throughout the world there is a research gap on the testing of herbal medicines at clinical level so as to validate their effectiveness and safety (Rivera *et al*., 2013). Regardless of the benefits of using herbal medicines, areas of concern still remain being the possibility of product contamination or adulteration, potential toxicity, known and unknown drug-herb interactions. Also the mechanisms involved in drug-herb interactions are not fully understood (Rivera *et al*., 2013). In some studies drug-herb interactions were found to occur through the induction or inhibition of drug metabolizing enzymes (Cytochrome P450) or alteration of drug transporters (P-glycoproteins). Herbs that inhibit the metabolism of conventional drugs will result in higher medication levels which can increase efficacy and possible toxicity and the opposite is true for those that stimulate metabolism of drugs. Herbal medicines are not tightly regulated in many countries worldwide including African countries as compared to conventional medicines. There is also lack of consistent terminology of describing whether a product is an herb, food product or a dietary supplement (Rivera *et al*., 2013). The use of herbal medicines is suffering inadequate monitoring and testing for safety and efficacy. In line with poor monitoring of herbal medicines it has been noted that there is lack of suitable quality control, inadequate labelling and absence of appropriate patient information (Ekor, 2014). A common misconception exists in Africa that natural products are non-toxic and safe has often led to the improper use or unrestrained intake and in some case severe poisoning and acute health problems have been noticed (Ekor, 2014). The major challenge in the quality control of finished herbal medicines especially mixture herbal products is the difficulty in ascertaining that all the plant materials have been included due to the complexity of chemicals in herbal preparations as compared to other pharmaceuticals (Ekor, 2014). On the other hand analysis of adverse events related to use of herbal products is much more complex compared to conventional pharmaceuticals (Ekor, 2014).

4. Integration of traditional medicine in cancer treatment in African health care systems

The World Health Organization (WHO) encourages African member states to promote and integrate traditional medical practices in their health delivery system (Mahomoodally, 2013). Scientists have been reported to have

shifted their interest toward traditional knowledge and associated genetic resources in attempts to provide solutions to global health problems such as cancer and human Immunodeficiency syndrome. However, the integration of IDK systems in African countries into the conventional healthcare systems has been facing challenges which include the absence of clinical tests to ascertain the safety and efficacy of some TMs (Mposhi *et al*., 2013). Asian countries, e.g., China, Republic of Korea and Vietnam have an integrated health care system that includes traditional health practices which may serve as models for African countries and other developing nations in the formulation and enactment of national drug policies which recognizes the role of TMPs in the health delivery system while promoting extensive scientific research into TMs to determine safety and efficacy of those medicines (Mposhi *et al*., 2013). The active constituents of most of the TMs in Zimbabwe have not been tested for safety and efficacy in many disease conditions including cancer (Mposhi *et al*., 2013).

5. Regulation and policy on traditional medical practice in Africa

African countries have been reported to be losing out on their IDK systems due to biopiracy and it is imperative for African countries to establish sound legislation and measures which should ensure adequate protection of IDK systems and fair benefit sharing from discoveries whose origin is from African biodiversity (Mposhi *et al*., 2013). Herbal medicines are reportedly being classified as foods or dietary supplements in some countries and this has impacted negatively on the regulatory aspects because with such classification, evidence of quality, efficacy and safety is not a mandatory requirement before marketing (Ekor, 2014). In the United Kingdom a traditional herbal medicine registration scheme was introduced and in this simplified registration scheme herbal medicinal products are required to meet specific standards of safety and quality. On the contrary in Africa and other developing countries many unregistered and poorly regulated herbal products are sold freely on the market with little or no restraint at all (Ekor, 2014).

Table 1: Chemical structures and classification of compounds isolated from herbs/trees with reported anti-cancer properties

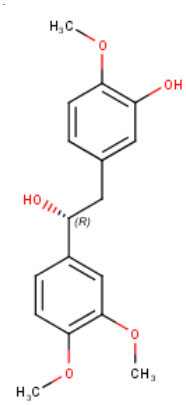
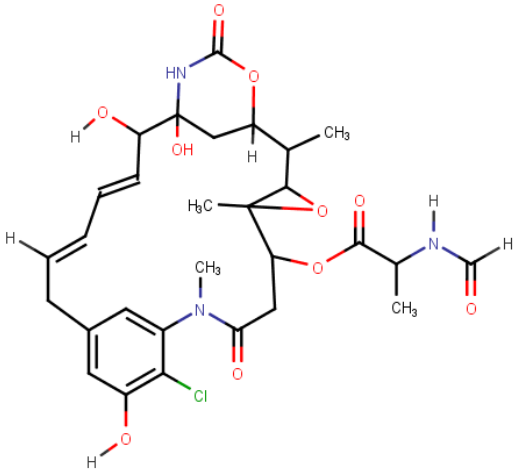
Compound	Chemical structure	Chemical classification
Combretastatins		Natural Phenol
Maytansine		Ansa macrolide

Table 1 (Cont.)

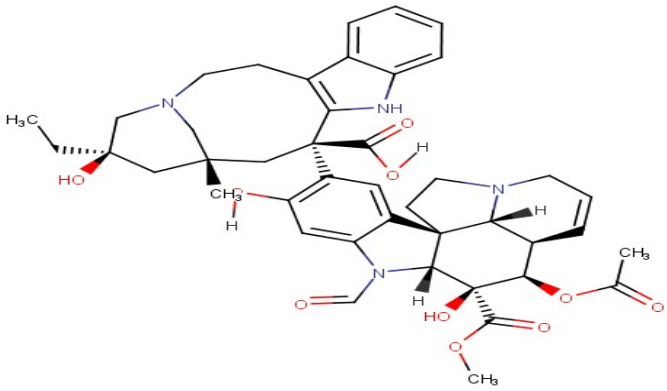
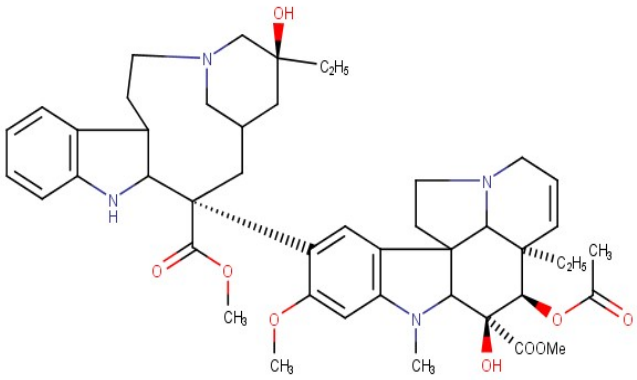
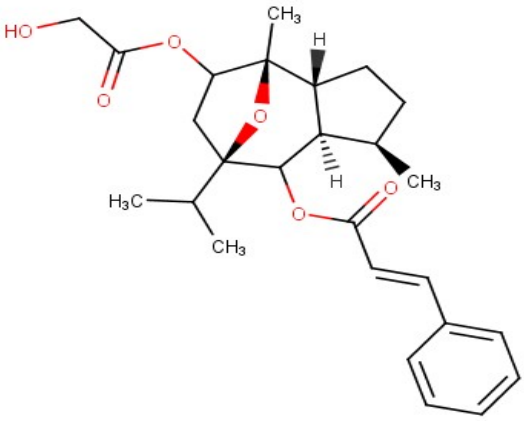
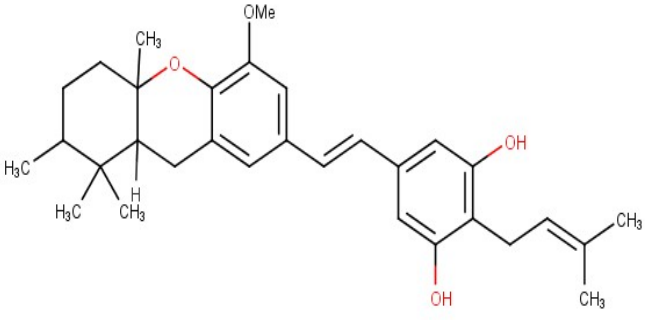
Compound	Chemical structure	Chemical classification
Vincristine		Plant Alkaloid
Vinblastine		Plant Alkaloid
Englerins		Guanine Sesquiterpenes
Schweinfurthins		Flavonoid

Table 1 (Cont.)

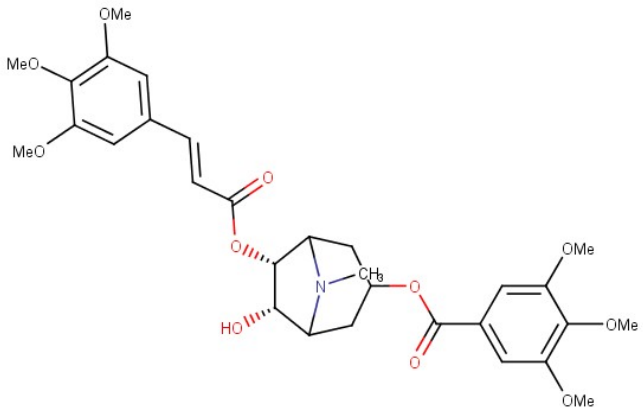
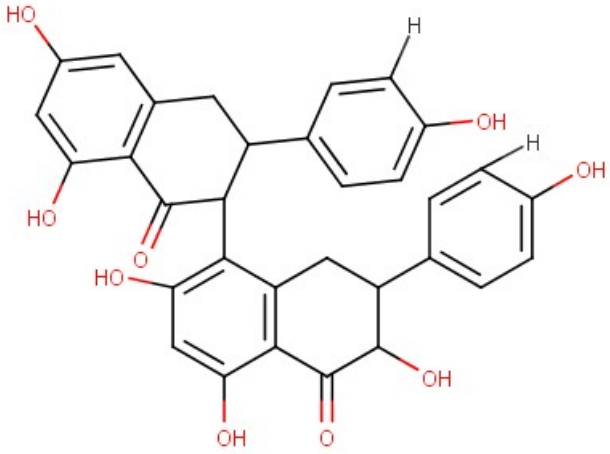
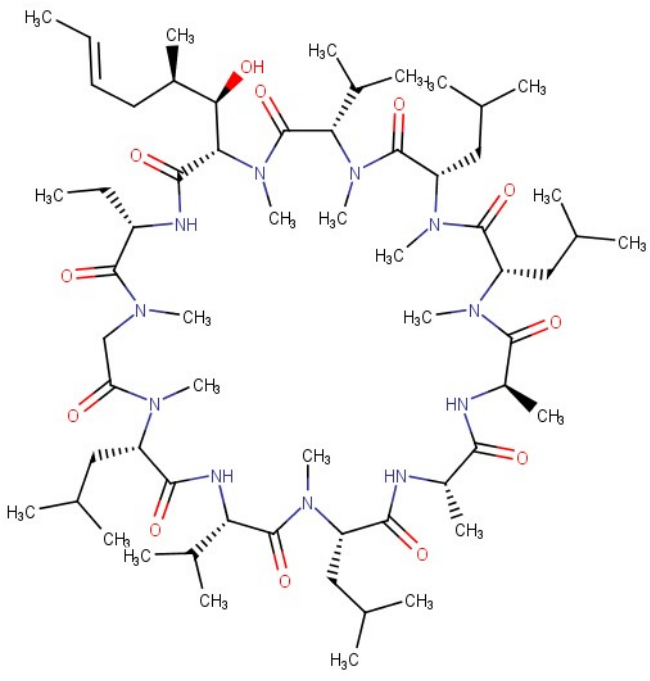
Compound	Chemical structure	Chemical classification
Pervilleines		Alkaloid
Kolaviron		Flavonoid
Cyclosporins		Cyclic undecapeptide

Table 2: Some of the physico chemical properties of the compounds in table 1 above

Compound name	pKa	LogP non ionized and LogD at isoelectric point	Molecular polariz-ability	Van der Waals volume (Å^3)	Polar surface area (2D)	Molecular surface area (3D)	Hydrogen bond donors	Hydrogen bond acceptors
Combretastatins	9.9 and 14.36	Log P Chem axon = 2.27 Log P Consensus =2.50 No Isoelectric point	32.31	280.69	93.06	439.55	Donor count = 2 Donor sites = 2	Acceptor count = 5 Acceptor sites = 9
Maytansine	11.33 14.01 11.66 7.67 -1.55 12.29	LogP Chemaxon = 1.48 LogP Consensus = 1.72 LogD not given	61.93	537.68	187.26	839.23	Donor count = 5 Donor sites = 5	Acceptor count = 8 Acceptor sites = 16
Vincristine	8.50 14.40 10.88 7.93 3.41 9.08	LogP Chemaxon =1.82, Log D at PI = -1.73 LogP Consensus = 2.28 Log D at PI = -0.83	82.58	699.57	198.40	1099.66	Donor count = 5 Donor sites = 5	Acceptor count = 10 Acceptor sites = 18
Vinblastine	-14.41 10 2.92 -1.57 8.57 10.93	LogP Chemaxon = 3.44, Log D at PI = 3.05 LogP Consensus = 3.67 Log D at PI = 3.27	90.03	757.42	152.74	1220.27	Donor count = 3 Donor sites = 3	Acceptor count = 10 Acceptor sites = 16
Englerins	13.13	LogP Chemaxon = 4.34 LogP Consensus = 4.38 No isoelectric point	48.86	422.54	82.06	685.43	Donor count = 1 Donor sites = 1	Acceptor count = 4 Acceptor sites = 8

Table 2 (Cont.)

Compound name	pKa	LogP non ionized and LogD at isoelectric point	Molecular polariz-ability	Van der Waals volume (Å³)	Polar surface area (2D)	Molecular surface area (3D)	Hydrogen Bond donors	Hydrogen bond acceptors
Schweinfurthins	8.46 9.91	LogP Chemaxon = 7.96 LogP Consensus = 8.04 No isoelectric point	57.30	474.02	58.92	774.83	Donor count = 2 Donor sites = 2	Acceptor count = 4 Acceptor sites = 8
Pervilleines	13.53 7.71	LogP Chemaxon = 2.97 LogP Consensus = 2.78 LogD not given	62.24	528.60	132.65	866.01	Donor count = 1 Donor sites = 1	Acceptor count = 10 Acceptor sites = 19
Kolaviron	9.31 8.02 8.91 13.15 7.4 15.50 10.09 9.66	LogP Chemaxon = 5.51 LogP Consensus = 5.79 No isoelectric point	55.58	473.40	178.58	701.16	Donor count = 7 Donor sites = 7	Acceptor count = 9 Acceptor sites = 18
Cyclosporins	14.31 12.96 11.83 12.56 12.23	LogP Chemaxon = 3.38LogP Consensus = 3.64 No isoelectric point	132.77	1216.35	278.80	2033.47	Donor count = 5 Donor sites = 5	Acceptor count = 12 Acceptor sites = 24

6. Some of the anticancer plant compounds that have been discovered in African traditional medicines

6.1. Combretastatins

Combretastatins were isolated from the bark of the South African tree *Combretum caffrum* (Eckl. and Zeyh.) Kuntze (Combretaceae). Combretastatin A is active against colon, lung and leukemia cancers and it was expected that this molecule was the most cytotoxic phytomolecule isolated by that time (Shoeb, 2006). Combretastatins are a family of compounds which primarily act as anti-angiogenic agents which inhibits the formation of blood vessels supplying tumors leading to tumor necrosis (Beutler *et al*., 2012). A number of

clinical trials were done for different cancers using combretastatins and their analogues and promising results were obtained (Beutler *et al*., 2012). Combretastatin A4 phosphate was granted orphan drug designation by FDA in year 2006 for the treatment of ovarian cancer. Treatment of patients with platinum-resistant ovarian cancer with a combination of CA4P, carboplatin, and paclitaxel was reported to have produced a higher response rate in the patient population compared to chemotherapy given without CA4P (Cragg and Pezzuto, 2016).

6.2. Maytansine

Maytansine was isolated from the Ethiopian plant *Maytenus serrate* (Hochst. Ex A. Rich.) Wilczek (Celastraceae family) for the NCI as part of a random collection program performed through a collaboration with the US Department of Agriculture (USDA) (Beutler *et al*., 2012; and Nwankwo, 2017). The yield of the maytansine from the Ethiopian plant was very low and a sevenfold yield was obtained from Kenyan *Maytenus buchanii* (Loes) R. Wilczek (Celastraceae family) (Beutler *et al*., 2012). *Putterlickia verrucosa* (E. May ex Sonder) Szyszyl collected in South Africa proved to be the richest source, with a yield eight times that from *Maytenus buchanii* (Beutler *et al*., 2012). *Maytenus senegalensis(syn. Gymnosporia senegalensis), (Celestraceae)* is a *Maytenus species* indegenous to west Africa and is commonly found in Nigeria has the potential to yield maytensanoids upon further investigations on the plant (Nwankwo, 2017). It was unfortunate that though maytansine had very promising preclinical animal testing, the drug failed to have significant efficacy in human clinical trials and it was dropped from further study in the early 1980s. However, closely related compounds to maytansine, the ansamitocins were subsequently isolated from a microbial source of actinomycete *Actinosynnema pretiosum*. This led to questions as to whether the maytansines are actually plant metabolites or are produced through a plant microbe-symbiotic association. The microbial production of the ansamitocins enabled production of larger quantities of this class of compounds and motivated by their extreme potency their development was pursued. The maytansanoid derivatives, DM1 and DM4 were conjugated to monoclonal antibodies (mAbs) in targeting a variety of cancers. Some of the cancers which were targeted included but not exclusively pancreatic, biliary, colorectal and gastric cancers (Beutler *et al*., 2012). The maytansines were conjugated to mAbs like the trastuzumab to combine the bilological activity of trastuzumab with the targeted delivery of a highly potent antimicrotubule agent DM1 (N-methyl-N-[3-mercapto-1-oxopropyl]-L-alanine ester of maytansinol), which is a maytansine derivative against HER2-overexpressing breast cancer cells (Beutler *et al*., 2012; and Barginear *et al*., 2012). The antibody conjugated emtansine (Kadcyla) has been approved by the FDA in 2013 as a new therapy for patients with HER2-positive, late stage(metastatic) breast cancer (Cragg and Pezzuto, 2016).

6.3. Englerins

Englerins A and B were isolated from the Tanzanian plant *Phyllanthus engleri* Pax Collected by Z. Mbwambo and Moussori botanical gardens in 1989. Englerins were shown to have selective inhibition of growth on renal cancer cell lines. Englerin A showed 1000-fold selectivity on six of the eight renal cancer cell lines with IC50 values in the range of 1 to 87 nM. Christmann group from Dortmud Germany, Nicolaou, Echavarren, Ma and Chain are the groups which explored chemical synthesis of englerin A and different strategies were reported. The strategy developed by Chain was considered more efficient in which englerin A was prepared in eight steps with 20% overall yield from readily available starting materials (Beutler *et al*., 2012). Replacement of the cinnamate ester with a naphthoate moiety led to improved selectivity in structure activity relationship studies carried out by both Chen and Christmann groups (Beutler *et al*., 2012).

6.4. Schweinfurthins

Schweinfurthins A, B and F were isolated in 1996 from a Cameroonian plant *Macaranga shweinfurthii* Pax, which was collected by the Missouri Botanical garden in 1987. These compounds showed remarkable selectivity against central nervous system, renal, and breast cancer cell lines in the NCI 60 cell line anticancer assay (Beutler *et al*., 2012). There has been considerable interest and effort in developing schweinfurthins and their analogs because of their unique selectivity profile on cancer types. However, the efforts have been obstructed by the lack of understanding of the mechanisms involved in their inhibition on cancer cells. Xingfeng Bao and colleagues in year 2015, reported the specific arresting effect on TGN trafficking as a key cellular mechanism which results in potent inhibition of mTOR / AKT signaling and induction of ER stress for selective anti-proliferative schweinfurthin class of natural compounds (Bao *et al*., 2017).

6.5. Pervilleines

Pervilleines which demonstrated multidrug resistance(MDR) inhibition through activity on P-glycoprotein were isolated from *Erythroxylum pervillei* Baillon and was collected from Madagascar in 2003 showed MDR inhibition both in vitro and in vivo (Beutler *et al*., 2012).

6.6. Other Anticancer agents isolated under the NCI collaboration with African countries

Sensevistatins 1 and 2 and spirostanol saponins, were isolated from *Sansevieria ehrenbergii* which was collected in Kenya in 1966. Agarofuran sesquiterpenes, reissantins A-E were isolated from *Reissantia buchananii* collected in 1989 from Tanzania. Rautandiols A and B and pterocarpans were isolated from *Neorautanenia mitis* which was collected in 1993 from Tanzania. Two diterpenes, (3alpha, 12alpha)-dihydroxy-ent-8(14), 15-isopimaradien-18-al and trans-9-acetyl-4,9'-di-O-methyldehydrodiconiferyl alcohol were isolated from Tanzanian plant *Euphorbia quinquecostata* by Z. Mbwambo in 1999. In the same year 1999 flavonoid (3S)-discoloranone was isolated from *Berchemia discolor* collecetd from Tanzania (Beutler *et al*., 2012).

6.7. Kolaviron

Kolaviron was isolated from Bitter kola (*Garcinia kola*) seed obtained from southern Nigeria. Kolaviron has a chemopreventive potential in inhibition of human alflatoxin B1-induced genotoxicity and possibly carcinogenecis (Nwankwo, 2017).

6.8. Cyclosporin B

Phakellistan 10 and Phakellistan 11 are two peptide alkaloids which were isolated from the marine sponge *Phalellia ssp* and both compounds had significant cytotoxic activity against P-388 leukemia cell line with ED50 of 2.1 and 0.2 micrograms / ml respectively. Cyclosporin B which is structurally related to Phakellistans was isolated from latex of *Jatropha gossypifolia*(Euphobiaceae) from Senegal and Togo and was expected to display some cytotoxic activity though it was not confirmed at that time (Nwankwo, 2017).

7. Methodologies and approaches in the discovery of drugs from herbal medicines

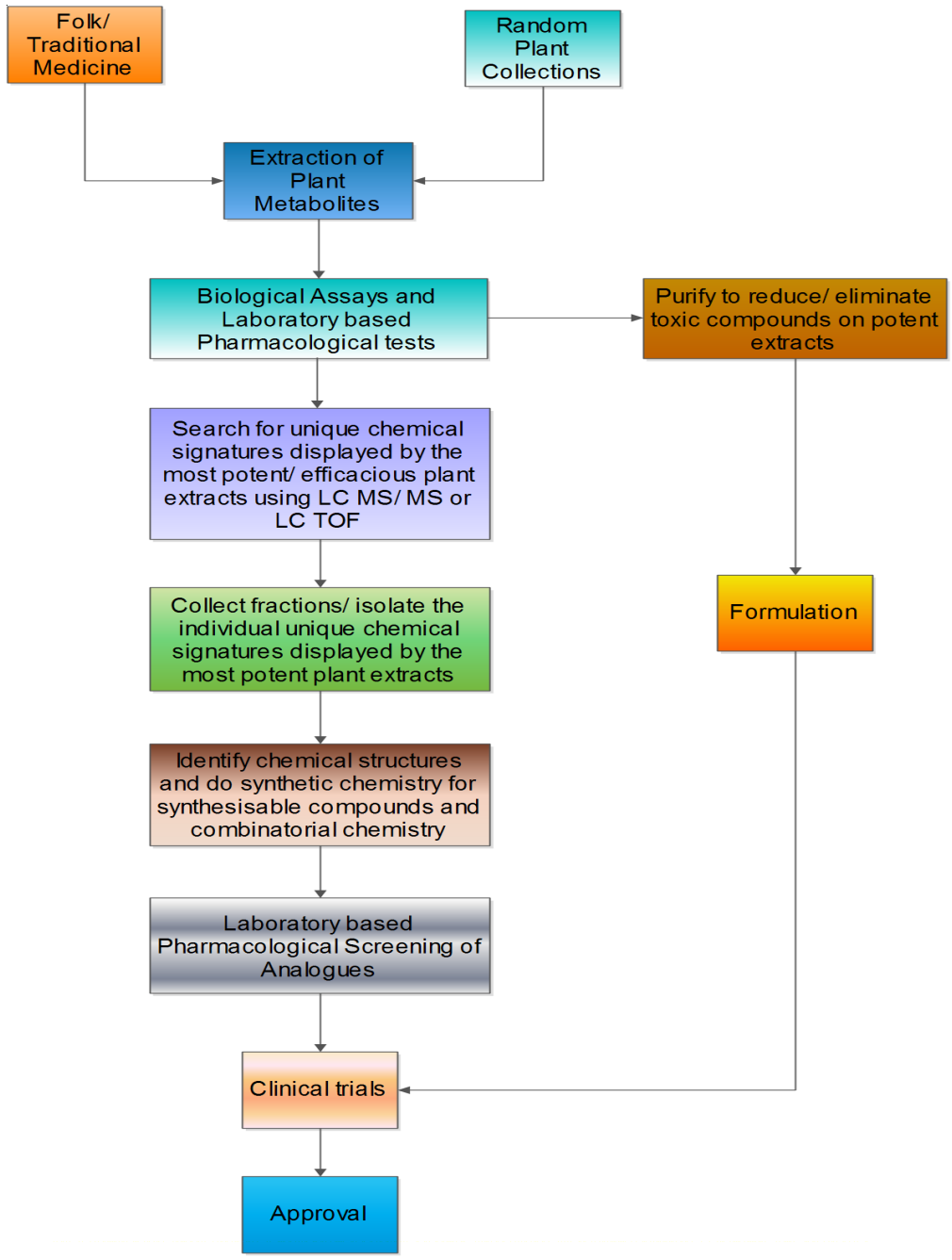
The World Health Assembly (WHA) has put emphasis on the need to ensure the quality of medicinal plant products through use of modern control techniques and standards (Shinde *et al*., 2009). Basically the WHO guidelines for quality and standardization of herbal formulations are based on the following parameters: (1) Quality control of crude drug material, preparations and finished products, (2) Shelf life and stability evaluations, (3) Safety aspects and (4) efficacy (Shinde *et al*., 2009). The WHO guideline for assessing quality of herbal medicines with reference to contaminants and residues categorized herbal medicines to comprise the following: herbs, herbal materials, herbal preparations and finished herbal products (WHO, 2007). Herbs include crude plant material such as leaves, flowers, fruit, seeds, stems, wood, bark, roots, rhizomes or other plant parts which may be entire, fragmented or powdered. Herbal materials were defined as either whole plant or parts of medicinal plants in the crude state including herbs, fresh juices, gums, fixed oils, essential oils, resins and dry powders of herbs. Herbal preparations are produced with the aid of extraction, distillation, expression, fractionation, purification, concentration, fermentation or other physical and biological processes. Finished herbal products or herbal medicines contain as active substances exclusively herbal drugs or herbal drug preparations and they may consist of herbal preparations made from one or more herbs. They may contain excipients in addition to the active ingredients (WHO, 2007). Drug discovery can employ different approaches which may range from: (1) Random selection followed by chemical screening, (2) Random selection followed by one or more biological assays, (3) Follow up of biological activity reports and (4) Follow up of ethno-medical (traditional medicine) uses of plants (Okigbo *et al*., 2009). Developing countries have faced challenges in the discovery of novel drugs for various medical conditions for a long time, the main reason being the high capital that is needed in this endeavor. Basically there are two main approaches to drug discovery which are the classical approach and the reverse pharmacological approach. The classical approach is costly as it begins with synthetic chemistry and then testing for the new chemical entities. The reverse pharmacological approach involves starting with known use of medicinal compounds, e.g., from traditional medicinal plants and then investigating for their pharmacological properties. This reverse pharmacological approach is the hope for developing countries to develop new novel drugs for disease conditions because it is less costly compared to

the classical approach (Vaidya, 2014). It has been reported that the success rate for discovering drugs using the reverse pharmacology approach from herbal medicines should in theory be very high compared to the classical approach of chemical synthesis and collection from chemical libraries of already existing compounds and their analogues. On the contrary it has been noted that drug discovery from herbal medicines is more of experience driven and very challenging because of the complexity of chemical entities which comprise herbal extracts (Fong *et al*., 2014; and Pan *et al*., 2010).

8. Future prospects

Generally most of the researches in African countries are based on the activity of plants extracts against selected cancer cell lines but not much has been documented on the specific compounds that those plant

Figure 1: Proposed model for drug discovery incorporating the reverse pharmacology approach



species have with regards to anticancer / cytotoxic effects. Also not much has been said about the purification and extraction of the lead compounds from the African indigenous plant resources (Fadeyi *et al.*, 2013; and Maroyi, 2012). Plants have been known to have secondary metabolites which are a mixture of different phytochemicals which may act individually, additively or in a synergistic way to improve health. The combined effects of the phytochemicals surpass the total activity of individual constituents. The combined actions of the chemical entities may influence the activity of the main constituent by either speeding up or slowing down its assimilation or elimination from the body. It has been postulated that secondary metabolites from plants origins might increase the stability of the active compound(s) or phytochemicals, reduce the rate of undesirable adverse side effects and may have an additive, potentiating or antagonistic effect (Mahomoodally, 2013). There is therefore need to evaluate the synergistic effects of compounds within herbs that show activity for particular diseases an example being cancer. This may bring another dimension to the way herbal medicines are targeted for possible drug discovery (Rivera *et al*., 2013; and Mahomoodally, 2013). A threat on natural biodiversity was pointed out to be the result of the promotion of incorporation of TMs into healthcare systems. This should then be complemented by tightly regulated biodiversity national and regional / continental biodiversity policy (Mposhi *et al*., 2013). Figure 1 above is therefore being proposed as an approach which may lead to accelerated drug discovery from folk medicine and safe utilization of traditional medicines in their crude form.

9. Conclusion

It is therefore concluded that Africa has a lot of potential in the discovery of useful drug substances as noted by the promising compounds which have been obtained through collaborative researches between some African countries and the American National Cancer Institute. African governments may need to give priority to researches involving IDK systems in the pursuit to discovering medically useful drug substances. African countries may need to further work on policy which may enhance recognition of traditional medical practice and find ways through which TMPC be an integral part of conventional training of medical practitioners. This may help reduce adverse effects which may occur due to drug-herb interactions because herbal medicines are still one of the major primary health care in Africa. There is also need to set quality assurance measures in the harvesting, processing and commercialization of herbal medicines in African countries so as to realize commercial advantage from IDK systems.

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