Herbal Medicines in Kenya: A Review of the Toxicity and Quality Control Issues

Maina N[1], Kagira JM[2], Achila O[1], Karanja SM[1], Ngotho M[2]

1. *Department of Biochemistry, Jomo Kenyatta University of Agriculture and Technology, PO Box 62000-00200, Nairobi, Kenya.*

2. *Institute of Primate Research, PO Box 24481*-00502, Nairobi, Kenya;

***Corresponding author**: Dr. Naomi Maina, Department of Biochemistry, Jomo Kenyatta University of Agriculture and Technology, PO Box 62000-00200, Nairobi, Kenya. Email: nmaina@hotmail.com; Tel: +254727726785*

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SUMMARY

In sub-Saharan Africa, it is estimated that 80% of the population depends on indigenous medicines for primary health-care. These herbs often contain highly active pharmacological compounds whose pharmacotherapeutic and toxicity profiles have not been well characterized. Toxicity may be related to several intrinsic and extrinsic factors. Most of the available reports related to the toxic effects of herbal medicines cite hepatoxicity as the most frequently experienced toxicity. However, noxious effects involving kidneys, the nervous system, skin, blood, the cardiovascular system, mutagenicity and carcinogenicity have also been published. This article presents a systematic review on safety and toxicity of herbal medicines used in Kenya.

Keywords: Herbal medicine, herbal preparations, toxicity, Kenya, regulations, complementary and alternative medicine.

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Introduction

Herbal medicine is an important part of the culture and traditions of most African communities. Kenya in particular has a rich and diverse repertoire of flora that has been used by various ethnic communities as medicines for centuries. Ethnobotanical information and usage of traditional herbal medicine by different ethnic communities in Kenya has been investigated by several researchers (Jeruto *et al.*, 2006; Bussman, 2006; Nguta *et al.*, 2010; Njoroge *et al.*, 2010; Kareru *et al.*, 2008; Nagata *et al.*, 2011; Nanyingi *et al.*, 2008). According to some estimates, traditional healers provide the first line of care for 80-90% of the population (Lambert *et al.*, 2011). While herbal usage, especially in rural communities is high, an estimated 23% of the sick do not seek conventional health care (Njoroge *et al.*, 2010; Muthaura *et al.*, 2011). The

importance of herbal medicines in Kenya is further evidenced by the fact that traditional herbal medical practitioners (THMPs) far outnumber conventional or allopathic providers. Given the estimated 40,000 THMPs and assuming a population of 38 million Kenyans, there is a THMP – patient ratio of 1 to 950 (Lambert *et al.,* 2011). Currently, the conventional doctor to patient ratio stands at 1 to 33 000 (Ibid).

The growing popularity of herbal medicines has been attributed to a number of factors including accessibility, affordability, aggressive marketing by THMP and the perception that herbal medicines are natural hence safe (Sahoo *et al.,* 2010). Parallel with the growing popularity is an increasing interest in the scientific rationale for plant usage. Towards this end, several research groups in Kenya have investigated the efficacy of specific herbs. Crude or fractionated extracts of medicinal herbs have been screened in *invitro* and *in vivo* systems for antibacterial (Kareru *et al.,* 2008; Matasyoh *et al.,* 2008); antiviral (Kanyara *et al.,* 2005) and antiplasmodial activity (Kigondu *et al.,* 2011; Wagate *et al.,* 2008). Still, little is known about their mechanisms of actions. Another aspect, which is largely under investigated is the toxicity associated with the use of herbs (Huxtable, 1990). This should raise some concern given the recent warnings by biomedical health practitioners on the potential adverse effects of herbal remedies. In this paper, we evaluate the safety and toxicity herbal medicines used in the country.

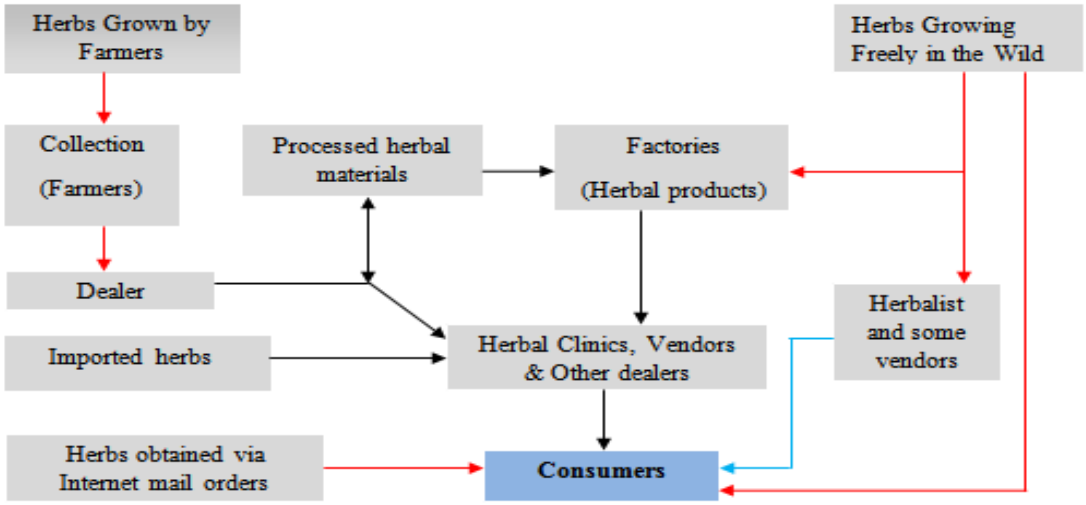
Herbal Medicine in Kenya

Current regulatory status

Herbal medicine practitioners in Kenya are registered by the Ministry of Culture and Social Services. Registration is non-obligatory and is subject to the requirement that herbal medicines used should be should be submitted to national laboratories, namely: Kenya Medical Research Institute (KEMRI), Nairobi University's Mitishamba Drug Research Unit (MDRU) and Government Chemists (GC) for evaluation of safety. However, toxicity tests on the herbal preparations presented are mostly not done. These institutions mainly rely on literature search to predict the efficacy and safety of the herbs. The literature review has some important shortcomings, for instance: most of these studies are directed at the toxicological properties of single plant formulations. However, the labels on most herbal preparations, especially those sold as panaceas for common chronic diseases; indicate that most contain multiple herbs.

For mass produced herbal products, registration is done by the Pharmacy and Poisons Board of Kenya (PPBK) under the Ministry of Health Services. However, PPBK relies, in part, on the same laboratories mentioned earlier and is thus subject to the same challenges highlighted above. In addition, the regulatory scheme by PPBK covers only Good Manufacturing Practices (GMP) and Good Supply Practices (GSP) but not Good Agricultural and Collection Practices (GACP). Figure 1 shows the circulation of herbal medicines in Kenya and how these regulatory regimes apply.

Figure 1: Flow diagram of the circulation of herbal medicines in Kenya.



Red flow lines represent non regulated channels of the flow of herbal medicines or materials; The blue flow lines represent part of the channel regulated by the Ministy of Culture. However, most herbal medicine practitioners are not registered by the Ministry of Culture. Therefore the blue line represents partial regulation. The black flow lines represent part of the channel regulated by the Poisons and Pharmacy Board (PPB).

Safety concerns and challenges in the regulation of herbal preparations are many and include:

- Some practitioners combine herbal treatment with spirituality making regulation difficult (Kokwaro, 1993).
- There are unscrupulous traders/healers who typically use misleading adverts to market their products. This has prompted to the establishment of guidelines for advertisement and promotion of herbal products (Robison, 2011). However, the enforcement of these guidelines remains a challenge.
- There is a general decline in authentic knowledge of traditional remedies; this issue has health implications since sourcing of herbs by non-experts can results in misidentification which may lead to the inadvertent use of toxic herbs.
- There are no forums for exchange of information/knowledge among the herbal medical practitioners (THMPs), and conventional medical practitioners (Lambert *et al.,* 2011).
- Further, the emerging non-traditional use of herbal preparation (e.g., use of sliming products and herbal teas) may lead to prolonged use. Such prolonged usages enhance the likelihood of cumulative toxic consequences (Aronson, 2009).
- Pharmacovigilance for herbal medicines is nonexistent in Kenya (Onyambu, 2011).

Risks associated with herbal medicines.

This may be attributed to a number of quality related issues (Zhang *et al.,* 2011). From cultivation of medicinal herbs to the final product, several factors (internal and external) can influence quality.

External Quality Issues

External quality issues include: contamination, adulteration, substitution and misidentification.

Contamination and substitution of herbal medicines

Contamination of herbal medicines with heavy metals (Lead (Ld), Cadmium (Cd), Mercury (Hg), Arsenic (Ag), misidentified plants, pesticides, excessive levels of microorganisms or their toxins and other noxious organic materials are possible sources of danger in non-regulated use of herbal medicines (Mobusz *et al.,* 2006; Aronson, 2009). Contamination can occur at any stage from harvesting through packaging and storage (WHO, 2005). Experts believe that toxicities associated with herbal medicines are mostly due to these contaminants and clinical reports have vindicated this belief (Robinson et al., 2011). A recent study in Kenya, found that 67% of the herbal samples had bacterial count in the range of 6.00×10^5 to 1.56×10^{10} cfu/ ml and fungal count in the range of 5.30×10^4 to 1.56×10^9 cfu/ ml. Analysis confirmed the presence of microbes including, *Escherichia coli*, *Shigella* spp*, Klebsiella pneumonia* (Onyambu, 2011).

Adulteration of herbal medicines

Another area of concern is the adulteration of herbal medicines with conventional drugs or other plant materials (WHO, 2005). For instance, a study spanning 1990 to 2001 which evaluated 41 products out of 3320 Chinese Proprietary Medicines (CPM) sold in Singapore reported that all these products were contaminated with nineteen synthetic drugs (Sahoo *et al.,* 2010). When 243 proprietary herbal formulations in California were tested, it was revealed that 7% contained undeclared pharmaceuticals (non-steroidal anti-inflammatory drugs (NSAIDs) and antihistamines, among others) (Phua and Heard, 2009). Since some herbs sold in the Country are imported from China, it can be asserted that Kenyans are exposed to the dangers posed by the presence of undeclared pharmaceuticals in TCM. In fact, reports published recently by the PPB indicate that some Chinese herbal contraceptives sold in the country contain high levels of conventional contraceptive (levonorgestrel and quinestrol) (PPB, 2012). Children born to mothers using these concoctions presented with several complications including preconscious sexual maturity, edema, muscular pain and impaired speech (PPB, 2012; Nzioki, 2011; Okwemba 2010).

Internal quality issues

Internal quality challenges are related to the pharmacologically active phytochemicals present in a formulation (Zhang *et al.,* 2011).

Dosage of the active compounds

The concentration of bioactive phytochemicals is determined by several factors including geographical (Matasyoh *et al.,* 2008) and environmental factors (Zhang *et al.,* 2011), species differences, part of the plant used, diurnal and seasonal variations (Saad et

al., 2001; Snodgrass, 2001; Farhat *et al.,* 2001), soil composition and its contaminants and length of storage (Stickel *et al.,* 2005). This means that without proper standardization, the actual dose of bioactive compounds being consumed is often variable, unpredictable or simply unknown. Indeed, batch-to-batch variation of pharmacologically active constituents of herbal formulations presents a major problem when it comes to standardization of herbal medicines (Mobusz *et al*., 2006). While testing the antimicrobial activity of hydro - distilled volatile oils from the leaves of *Ocimum gratissimum* L. (Lamiaceae) of 13 populations of different silvicultural zones in Kenya; a recent analytical study found significant variation in the antibacterial activity of the essential oils sourced from different parts of the country (Matasyoh *et al.,* 2008). Plants sourced from the Meru region had the greatest strength. Such variation in dosage may have greater effects in special group including children, geriatrics, invalids, and malnourished/undernourished, drug users, HIV/AIDS patients, patients with liver or kidney complications and those on long term medications (Snodgrass, 2001).

Toxicity of some commonly used herbs in Kenya

Literature on toxicity of herbal medicines used by THMPs in Kenya is generally scant. Therefore, many questions regarding the safety and toxicity of specific herbs used in Kenya cannot be answered definitely by the available scientific data. However, the fact that some of the herbs used by THMPs are toxic cannot be discounted. This is underscored by the fact that some plants used in the country like *Aristocholia sp*. are listed by the European Commission's Committee for Proprietary Medicinal Products (CPMP) as plants which pose serious health risks (Kokwaro, 1993; Hamill *et al.,* 2000). In Table 1 below, we present a list of the toxicological profiles of some commonly used medicinal plants.

Table1: Toxicity of some commonly used herbs

Family	Species	Common Name	Part of plant used	Ethnic Group	Indications and Parts used	Toxicity	Compound	Reference
Amaranthaceae	*Achyranthes aspera*	Chaff Flower	RT, LV:	Nandi(1); Meru,Mbeere(7); Luo(10); Maasai (6);Kamba and Luyha (10)	Amoebiasis, Bleeding wounds and stomach ache. Tooth ache, cough	Antiandrogenic and abortificant property. elevation of thyroid hormone levels†	Unknown	Anuja *et al.*, 2010 Tahiliani and Kar., 2000
Apocynaceae	*Acokanthera longiflora and Acokanthera schimperi*	Common poison bush	RT:	Massai (10)	Syphilis	Cardio toxicity	Cardenolides: (ouabain, acolongifl	Donald., 2008
	Thevetia peruviana	Yellow Oleander	LV	Luo (8), Kikuyu (10)	Skin rash, cuts, burns, Blocked nose	Subendocardial and perivascular hemorrhage, focal	Thevetia A and B, thevetoxin,	Donald., 2008 Bandara *et al.,* 2009
	Nerium Oleander	Rose Laurel		Luo(8);Samburu (10)		Cardiovascular effects†	Cardiac glycosides	Bandara *et al.,* 2009
Aristolochiaceae	*Aristolochia bracteata*		LV	Turkana (10)	chest pain	Nephropathy and Carcinogenicity	Aristolochic acid	Worbs *et al.,* 2011
	Aristolochia petersiana		RT	Swahili (10)	Cough	Nephropathy and Carcinogenicity	Aristolochic acid	Worbs *et al.,* 2011

Aspidiaceae	*Pteridium aquilinum*	Bracken	LV	Nandi (1)	Skin diseases	Immunotoxic (cooked material safe), Carcinogenic	Ptaquiloside, thiaminase	Latorre *et al.,* 2011
Balanitaceae	*Balanites aegyptiaca*	Balanites	LV, BK, FR	Luo (8); Nandi (1)	Itch, bone Problem. Diarrhea, chest pain, cough	Cardiovascular effect †	Unknown	Mohamed *et al.,*1999
Bignoniaceae	*Kigelia africana*	Sausage Tree	BK,FR	Luo (8); Kikuyu (10); Meru (7); Taita and Luyha (10)	Stomach ache, anemia, cold, flu	Potentially mutagenicity	Unknown	Fennell *et al.,* 2004
Brassicaceae	*Heliotropium subulatum*	Heliotrope	RT	Turkana (10)	Post-parturition disease in women	Hepatotoxic and carcinogenic	Pyrrolizidine alkaloids	Donald., 2008
Capparidaceae	*Warbugia salutaris*	Fever Tree	BK	Luhya, Kikuyu, Maasai,	Muscle pain, fever, cough	GIT irritant	Unknown	Donald., 2008
	Capparis tomentosa	African Caper	LV, BK	Kamba and Luo (10)	Asthma and abdominal	Human fatalities reported following root	Stachydrine	Duke *et al .,* 2002
	Maerua edulis		RT	Taita (10)	Syphilis and gonorrhea	Deaths reported	Unknown	Kokwaro 1993
Caesalpiniaceae	*Senna Occidentalis (formerly*	Coffee Senna	RT	Nandi (1).	Stomach ache, diarrhea	Liver and muscle degeneration especially in animals	Unknown	Yadav *et al.*, 2010 Barbosa *et al.* ,2005 Ferreiro *et al.*, 2009

	Cassia occidentalis)							
Celastracea	*Catha edulis*	Khat	RT	Used nationally	As a recreational drug. RT: Amebas, gonorrhea, sexually transmitted infections	Cardiovascular effects	Cathinone	Getahun *et al*., 2010 Duke *et al* ., 2002 Aronson *et al.,* 2009
	Tithonia diversifolia	Tithonia	LV, RT	Luo (7); Kikuyu, Meru, Mbeere (7), Eastern	Stomach ache, headache	Hematological and acute toxicity of liver and kidney †	Unknown	Elifioye *et al*., 2009 Duke *et al* ., 2002
	Bidens pilosa	Spanish Needles	LV	Luo (1), Meru and . Mbeere	Stomach ache,	Genotoxicity	Unknown	Elifioye *et al.,* 2009
	Senecio sp. (S.discifolius, S.lyratipartitus, S.syringifolius)		RT, LV	Meru, Luo, Digo (10)	Emetic, cold, stomach ache in pregnant women	Genotoxicity (veno–occlusive disease)	Pyrrolizidine alkaloids	Ernest and Pittler 2003
Euphorbiaceae	*Euphorbia tirucalli*	Pencil Tree	LV	Luo (8); Kalenjin (2); Marakwet (10)	(Chira) Unexplained weight loss.	Kerato – conjunctivitis , uveitis carcinogenic	Ingenane – and tigliane – type	Donald., 2008
	Europhobia candelabrum	Candelabra Cactus	ST	Luo, Kipsigis, Maasai (10)	Pregnant women	Kerato – conjunctivitis, dermatitis, uveitis	Diterpene hydrocarbon	Donald., 2008

	Croton macrostachyus		LV	Luyha, Meru, kikuyu and Kamba (10)	LV: Anti-helminthic, Malaria and	Phorbol esters	Diterpene hydrocarbons	Kokwaro, 1993
	Jatropha circus	Bubble Bush or Purging	LV, ST	Giriama (10)	Kidney disease	Amnesia, convulsions, delirium, diarrhea, nausea, vertigo and	Curcin	Donald., 2008
	Ricinus communis	Castor	LV	South Coast (4); Kikuyu ; Akamba (5); Samburu (10); Meru and Luo (10)	Malaria, Fever	Ribosome inactivation, hypersensitivity reactions , Genotoxic†	Ricin (mostly in seeds)	Aronson *et al.*, 2009 Fennell *et al.,* 2004
Fabaceae	*Abrus precatorius*	Jequirity	LV, BK, RT	Luo (8); Eastern Kenya (5)	Cough, cold, Gonorrhea, stomach ache	Ribosome inhibitor†	Abrin (mostly in seeds)	Ferreiro *et al.,* 2009
Meliaceae	*Azadirachta indica*	Neem	LV	Luo (8); Akamba (5); Meru, Mbeere (7), Kikuyu (10), Maasai (6)	Malaria, skin, rashes, Rashes	Nausea, diarrhea vomiting, drowsiness, tachypnea†	Azadiratchin compounds	Boeke *et al.*, 2004
	Melia azedarach	Chinaberry	LV	Luo (8); Kikuyu (10)	Measles,	Muscle, contractions, weakness, ataxia, paresis, abdominal distress, dyspnea,	Tetranortriterpene limonoid compounds(mel	Ferreiro *et al.*, 2009

	Trichilia emetica	Trichilia	BK, SP	Meru and Mbeere (7)	Kidney problems, skin rashes	Genotoxicity	Unknown	Fennell *et al.,* 2004 Duke *et al* ., 2002
Myrtaceae	*Psidium guajava*	Guava	LV	Kikuyu(10); Luo (8)	ENT infections, Diarrhea, gingivitis	Hypersensitivity reaction. Should not be used for a period exceeding 30 days†	Hydrosable tannins, essential oils, terpenes and Estragole	WHO 1999
Lamiaceae	*Ocimum basilicum*	Sweet Basil	LV	Kikuyu(10); Akamba(5); Maasai (3); Miji Kenda (4)	ENT infections (Bronchial Cattarh), Malaria	Potentially carcinogenic	Estragole	Duke *et al* ., 2002
Leguminosae	*Cassia didimobotrya*		LV,ST, RT	Kamba, Luyha, Meru, Luo (10)	purgative	GIT irritation	Sennosides	Donald., 2008
Liliaceae	*Aloe vera*	Aloe	LV	Used nationally	Swelling, boils, diarrhea, burns. Forms part of a large number of formulations sold nationally.	Overdose is associated with diarrhea †. Interaction with other drugs is also suspected	Anthraquinone compounds	Rodriguez-Fragoso *et al.,* 2008
Poaceae	*Cymbopogon*	Lemon	LV	Luo (8); Kikuyu	Headache,	Associated with GIT	Unknown	Fandohan *et al.,* 2008

	citratus	Grass		(10)	purify blood, clean pores	irritation, potentially neurotoxic †		
Rhamnaceae	*Rahmnus prinoides*			Kikuyu (10)	Malaria	Potentially genotoxic	Unknown	Fennell *et al.*, 2004
Rosaceae	*Prunus africana*	Pygeum	BK	Meru and Mbere (6); Maasai (6)	Cancer. Typhoid	Potentially Genotoxic	Docosanol, β-sitosterol,	WHO 2002
	Hagenia abyssinica	Kouso	LV	Nandi (1); Meru (7); Kikuyu (10)	Eye infections	Retinotoxicity	Unknown	Arbo *et al.,* 2009
Solanaceae	*Datura stramonium*	Jimsonweed	ST	Kikuyu (10). Swahili (10)	Tonsillitis	Acute psychosis. May cause peripheral Anticholinergic toxicity (decreased salivation,	Tropane belladonna alkaloids	Phua *et al.*, 2009
	Withania somnifera (Physalis somnifera)	Ashwagandha	DR	Kikuyu (10); Masaai (6).	ENT infections, Malaria	May potentiate barbiturates, berries may cause severe GIT pain. †	Withanolides I-XI, Withasomnifer ols A-C, Alkaloids	Duke et al ., 2002
Verbenaceae	*Lantana camara*	Wild Sage	LV, RT	Kikuyu(10);South coast (4); Luo (8); Maasai (6).	Measles, sore throat, cough, Malaria	Cholestasis, hepatotoxicity and photosensitization†	Lantadene A, B	Donald., 2008 Jordan et al., 2011

(a) Ethno medical information was obtained from Jeruto *et al.,* 2006[1]; Okello *et al.,* 2010[2]; Bussman *et al.,* 2006[3]; Nguta *et al.,* 2010[4]; Njoroge *et al.,*2010[5]; Kigondu *et al.,* 2011[6]; Kirira *et al* , 2006[7]; Nagata *et al.,* 2011[8]; Kokwaro, 1993[10].

(**b**). LV: leaves; RT: root; WP: Whole plant; BK: bark; SE: seed; ST: stem; FR: fruit; SP: sap; ENT, Ear nose and throat

(**c**). † No health hazards known at proper dosage levels.

Hepatotoxicosis

Hepatotoxicity is one of the biggest concerns raised by the indiscriminate use of herbal medicines. Ephedra and pyrrolizidine containing plants including *Crotalaria*, *Heliotropium and Senecio* spp. are commonly used in Kenya and have been associated with hepatoxicity (Huxtable, 1990; Stickel *et al.,* 2005; Willet *et al.,* 2004; Ernst and Pittler., 2003; Seeff *et al.,* 2001). The reported liver pathologies range from mild elevation of liver enzymes to fulminant liver failure requiring liver transplantation (Pak *et al.,* 2004). According to Steenkamp and colleagues, the excessive exposure to pyrrolizidine alkaloids may be responsible for the high rates of liver cancer, veno-occlusive disease (VOD) and cirrhosis seen in Africa (Steenkamp, *et al.,* 2000). In Kenya, *Senecio* species used by the Luo (Kokwaro, 1993) Meru, Mbeere (Kareru *et al*., 2008), Nandi (Jeruto *et al.,* 2006) and the Miji Kenda (Nguta *et al.,* 2010) are known to contain pyrrolizidine alkaloids. Research in animal's studies indicates that unbound pyrroles are highly reactive hepatocarcinogens (Stickel *et al.,* 2005). Another commonly used plant which may cause liver toxicity is *Lantana camara* which grows in most of the agro-ecological zones in Kenya. While the exact mechanism of toxicity is unknown, animal studies have demonstrated that extracts from the plant can cause widespread changes in mitochondrial, microsomal, and membrane enzymes resulting in cholestasis, hepatotoxicity, and photosensitization (Bevilacqua *et al.,* 2011; Ernst and Pittler, 2003). Human fatalities have been attributed to ingestion of green berries (Duke *et al.,* 2002).

Gastro-intestinal tract toxicities

Several herbs including *Aloe sp., Cinnamomum caphora*, *Cassia didimobotrya, Warbugia salutaris, Melia azedarach, Turraea mombassana, Cocculus hirsutus, Olinia rochetiana, Pittosporum viridiflorum* are known to contain toxins which are detrimental to the gastrointestinal tract (Duke *et al.,* 2002). Toxalbumins, which are toxic to gastro-intetsinal tract, have been isolated from plants such as *Ricinus communis, Abrus precatorius*, *Jatropha curcas* and *Jatropha multifida* (Levin *et al.,* 2000). Some studies have shown that administration of the fruit of *Jatropha curcas* increases fetal resorptions when administered soon after implantation (Donald, 2008). Other toxins such as ricin and abrin which are derived from *Ricinus communis and Abrus precatorius,* respectively, feature highly on the list of substances which might be used in bioterrorism (Fennell *et al.,* 2004). The compounds are highly toxic, heterodimeric type II ribosome inactivating proteins. Ingestion of meliatoxins, a toxin from ripe berries of *Melia azedarach,* has also been associated with vomiting and diarrhea in children (Ferreiro *et al.,* 2010). *Aloe Vera*, a herb which has found widespread commercial application, contains several biologically active constituents including emodin and anthrone (Duke *et al.,* 2002). Emodin anthrones act as GI tract irritant. Therefore, it is generally contraindicated for patients with inflammatory intestinal diseases such as Crohn disease, ulcerative colitis, and irritable bowel

syndrome or to children less than ten years of age (Ibid).

Cardiovascular system

A number of cardenolide-containing garden plants are used in traditional herbal formularies in Kenya. Over 400 cardiac glycosides have been isolated from the plant kingdom. In Kenya, commonly used plants containing cardiac glycoside include *Thevetia peruviana* and *Nerium oleander* (Nagata *et al.,* 2011; Nanyingi *et al.,* 2008; Kirira *et al.,* 2006). High concentrations of cardiac glycosides are found in seed, stems, and roots, followed by the fruit (Donald, 2008). Overdosage of *Nerium Oleander* may cause arrhythmia, bradycardia, cardiodepression, confusion, cyanosis, diarrhea, headache, hyperkalemia, nausea, neurodepression, stupor and vomiting (Duke *et al.,* 2002). Another herb that is grown in Kenya and used as stimulant is *Catha edulis* (Khat). Habitual consumption of khat may enhance the risk of acute myocardial infarction and hypertension (Getahun et al., 2010). Myocardial necrosis in rabbits fed on *Senna occidentalis* has also been reported (Yadav et al., 2010).

Genotoxicity

A large proportion of plants which are used in traditional medicine in Kenya have *in vitro* mutagenic effects (Elgorashi et al., 2003; Fennell et al., 2004). A recent study in South Africa, which screened more than 50 plants sourced from different parts of the continent for genotoxicity showed that both polar and apolar extracts of some plants maybe genetoxic. Plants used locally which were shown to be to be highly toxic (caused both DNA damage and chromosomal aberrations) are *Prunus africana*, *Rhamnus prinoides L'Hér*, *Ricinus communis* and *Trichelia emetica* (Fennell *et al.,* 2004). Extracts derived from *Euphorbiaceae sp*. have also been linked to tumorigenesis (Norhanom and Yadav, 1995). According to some scholars, the high prevalence of Burkitt lymphoma in East Africa maybe associated with the commonplace use of these plants in folk medicine (Ibid). The observation is premised on the findings that extracts from some *Euphorbiaceae sp*. have Epstein Barr virus (EBV) – activating capacity (Ibid). Other locally used plants which have been linked to carcinogenesis include anthrone – containing laxatives from Aloe *spp*. While Aloe has been identified as a possible risk factor in colorectal cancer, the claim is still controversial since studies in rats suggest that Aloe can have antitumorigenic effects (Duke *et al.,* 2002).

Toxicities associated with herb-conventional drug interactions

The concurrent use of herbal preparations alongside conventional drugs raises concerns about possible adverse reactions due to drug–herbal interactions. Some constituents of herbal medicines can induce or inhibit enzymes involved in drug metabolism (Sahoo *et al.,* 2010). Evaluating how phytochemicals and cytochrome P450 interact has been proposed as a possible way of predicting both the therapeutic outcome of herbal medicines and possible side effects (Ibid). Competitive inhibition at the P450 active site

has been proposed as the putative point of herb-drug interaction in these reactions (Ulbright *et al.,* 2008).

At present, the number of studies on this subject is scant. However, several warnings have been issued on the strength of these studies. In Kenya, studies have shown that African potato (*Hypoxis hemerocallidea*) extracts which are sold to HIV patients may inhibit HAART drug metabolism and transport (Mills *et al.,* 2006). Therefore, some experts are of the opinion that the concomitant use African potato extracts and HAART by HIV patients should be discouraged (Izzo, 2004). In addition, studies have shown that use of *Allium sativum* (garlic) supplements may reduce the plasma concentrations of the antiretrovirals (indinavir and saquinavir) (Williamson *et al.,* 2009). Other studies have suggested that *Aloe vera* extracts, (Aloe gel) might have additive effects when used with anti-diabetes drugs (Anuja *et al.,* 2010). Preliminary evidence suggests that aloe gel might lower blood glucose levels and may interact with conventional anti-diabetic drugs (Rodriguez-Fragoso *et al.,* 2008) and increase the risk of hypoglycemia in some patients. Other studies suggest that excessive use of *Aloe* and cardiac glycoside drugs might potentiate diuretic induced potassium loss, increasing the risk of hypokalaemia. Since *Aloe* inhibits thromboxane A2 and prostaglandins; concomitant use with anticoagulants might prolong bleeding time (Ibid).

Conclusion

The toxicity associated with the use of herbs is largely under-investigated and only a few studies have looked at toxicity of some herbs used in Kenya. At the same time, very few studies have focused on chronic toxicity or interactions with concurrently administered drugs. Therefore, toxicological investigations remain a high priority area. In recognition of this, we suggest that evaluation of toxicity should be included in the registration process. In addition, research has shown that the dangers associated with the use of herbal medicines are not necessarily inherent in the herbs themselves. Contamination (deliberate or otherwise), adulteration with conventional drugs, substitution, misidentification and concomitant herb-drug usage have also been cited as possible sources of danger. In view of this, enforcement of regulation including GMP, GACP and GSP should be prioritized. In addition, continuous monitoring of the quality of herbal medicines sold in the local market should be established and the public should be sensitized to the dangers of indiscriminate use of herbal medicines.

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