Pharmacological Activities of African Garcinia Plants

3.1 Introduction

Plants remain rich and potential source of therapeutic compounds for the development of new drugs. Secondary metabolites obtained from plants have been a great source of many drugs for managing various diseases. Even if recent advances in biochemical engineering and other biotechnologies represent alternative sources of drugs, more than 70 % of the current therapeutic drugs derive their structures from plants used in traditional medicine (Chantarasriwong, 2010). Although many and new drugs including antibiotics have been developed in the last three decades, resistance to them by infectious microorganisms has increased. As a result, the search for new bioactive compounds from plants for pharmaceutical purposes has gradually increased worldwide (Kaikabo *et al.*, 2009). Many recent biological studies on medicinal plants used as folklore remedies in the treatment of different ailments have attracted the attention of a number of researchers as possible alternatives to the existing incurable diseases and the problem of drug resistances. Globally, the problems of multiple resistance as well as emergence of new and resurrection of previously eradicated diseases have necessitated the continued effort to search for novel and effective drugs from medicinal plants to complement the existing synthetic drugs.

Recent studies have indicated that *Garcinia* species possess a wide range of biological activities and led to a greater understanding of the pharmacology of various species, particularly in relation to the antimicrobial, anticancer, antiviral, antioxidant, antimalarial and other biological activities. These pharmacological studies supports to the traditional uses of *Garcinia* plants in treating different ailments by many African societies. Hence, reported pharmacological activities on crude extracts and compounds from African *Garcinia* plants indicated

various biological activities, including antibacterial (Ebana *et al.*, 1991), antimalarial (Tona *et al.*, 1999), cytotoxic (Sordat-Diserens et al., 1992), antioxidant (Farombi et al., 2002), antifungal (Kpakote *et al.*, 1998) and antiviral activities (Bakana *et al.*, 1987; Gustafson *et al.*, 1992; Magadula, 2010) and other biological effects (Table 4).

3.2 Antimicrobial Activity

The treatment of infectious diseases has existed for many years and, as a result, many reports of antimicrobial extracts and compounds from *Garcinia* species have been documented from various parts of Africa. Over 20 different crude extracts from more than 10 *Garcinia* plant species found in African flora have been investigated for antimicrobial properties (Table 4).

One of the reports is on the ethanol extract of the dried stem bark of *G. afzelii* collected in Togo. This extract showed significant antibacterial and antifungal activities against *Staphylococcus aureus* and *Asperigillus fumigatus* (Kpakote et al., 1998). In another study from a Congolese plant, *G. huillensis*, the *in vitro* testing of the water extract of the stem bark indicated marked activity against *Cytospora* species (Laine *et al.*, 1985), while the antibacterial activity was noted in the petroleum ether extract of this plant against *Staphylococcus aureus* with the minimum inhibition (MIC) of 62.5 μg/ml (Bakana *et al.*, 1987).

Garcinia kola, collected in Nigeria and Ghana is the most investigated species with all parts studied pharmacologically. Thus, in the study of the ethyl acetate extract of the dried seeds, good antibacterial and antifungal activities were observed against *Bacillus subtilis* and *Aspergillus niger* both at a concentration of 100 μg/ml (Madubunyi, 1995). Another study on the methanolic extract of *G. kola* indicated significant *in vitro* antimicrobial activities against some bacterial isolates comprising both Gram-positive and

Gram-negative organisms tested at a concentration of 20 µg/ml. The zones of inhibition exhibited by the extract against the tested organisms ranged between 10 and 23 mm, while the zones of inhibition exhibited by streptomycin and tetracycline used as standard antibiotics ranged between 15 and 25 mm and, 12 and 25 mm, respectively (Adegboye *et al.*, 2008). Significant antibacterial activities were reported from the water and ethanol extracts of the root bark of *G. kola* in a study conducted by Ebana et al. (1991). Furthermore, the study by Iwu (1993) indicated the plant to have significant antimicrobial and antiiflammatory activities. In the study by Akerele and co-workers on the the crude ethanol extract, aqueous and chloroform fractions of the seeds of *Garcinia kola* showed significant inhibitory activity against a range of clinical isolates of both Gram positive and Gram negative bacteria. The MIC values obtained ranged between 2.5 and 7.5 mg/ml for bacteria and fungi isolates, respectively (Akerele *et al.*, 2008).

Kpakote and co-workers investigated the dried stem barks of *G. ovalifolia* and *G. polyantha* for antibacterial activities. Significant result was obtained against *Pseudomonas aeruginosa* at a concentration of 4.0 mg /ml (Kpakote *et al.*, 1998, Table 4).

The acetone extract of *G. livingstonei* leaves was studied for antibacterial activity using bioautography and by determining the minimum antibacterial concentration against four nosocomial pathogens. Bioautograms showed that two compounds were mainly responsible for the antibacterial activity namely, amentoflavone **(1)** and 4"-methoxyamentoflavone **(2)** (Kaikabo et al., 2009). The antibacterial activity of the isolated compounds was determined against *Escherichia coli, Staphylococcus aureus, Enterococcus faecalis* and *Pseudomonas aeruginosa* with both compounds exhibiting the MIC values ranging from 8-100 µg/ml (Kaikabo *et al.*, 2009). Further studies on the

activities of compounds **1** and **2** were done against fast-growing non-pathogenic *Mycobacterium smegmatis*. In this study, compound **1** was reported to be the most active one with an MIC of 0.60 mg/ml, while the MIC of compound **2** and the positive control isoniazid against *M. smegmatis* were similar at 1.40 and 1.30 mg/ml, respectively. This indicates that some infections caused by *M. smegmatis* may be managed by these compounds (Kaikabo and Eloff, 2011).

On the other hand, *Garcinia* plants used ethnomedically as chewing sticks have been investigated for their antimicrobial potential. Thus, from the antibacterial fraction of the root bark of *G. kola*, biflavanone GB-1 **(3)** was isolated as the major constituent. This compound showed significant antibacterial activities against methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *enterococci* (VRE) with MIC of 32 and 128 μg/ml respectively (Han *et al.*, 2005).

Xanthones is an important class of compounds from *Garcinia* plants due to its diverse biological activities. From the South African *Garcinia* plant, *G. gerradii*, three prenylated xanthones, garcigerrin A **(4)**, B **(5)** and l2b-hydroxy-des-D-garcigerrin A **(6)** were tested for their activity against the plant pathogenic fungus *Cladosporium cucumerinum* using a TLC biossay. Garcigerrins were inactive at 50 μg/ml while compound 6 prevented growth of the fungus at a concentration of 0.2 μg/ml (Sordat-Diserens *et al.*, 1989). From an African mangosteen, compounds **7-9** were tested for their activity against the plant pathogenic fungus *Cladosporium cucumerinum,* using a TLC bioassay with compounds **7** and **8** preventing the growth of the fungus at concentrations of 0.5 and 0.2 μg/ml respectively (Sordat-Diserens *et al.*, 1992). In another study, smeathxanthone A **(10)** and smeathxanthone B **(11)** were isolated from a Cameroonian plant, *G. smeathmannii* and tested for their *in vitro* antibacterial

and antiyeast activities. These compounds showed a mild activity against a range of bacteria and yeasts (Komguem *et al.*, 2005).

Momo and co-workers investigated the methanol crude extract from *G. lucida* for its antimicrobial activity against *Escherichia coli*, *Pseudomonas aeruginosa, Salmonella typhi, Staphylococcus aureus,* and *Candida albicans.* The result of the crude extract indicated a good inhibitory activity with a MIC value of 64 μg/ml on *Candida albicans* and it was inactive for other tested organisms (Momo *et al.*, 2011). The isolated compounds from the CH_2Cl_2 fraction of *G. lucida* were not active except cycloartenol **(12)** which exhibited moderate and selective antimicrobial activity with IC_{50} of 512 μg/ml against *E. coli* and *P. aeruginosa* (Momo *et al.*, 2011).

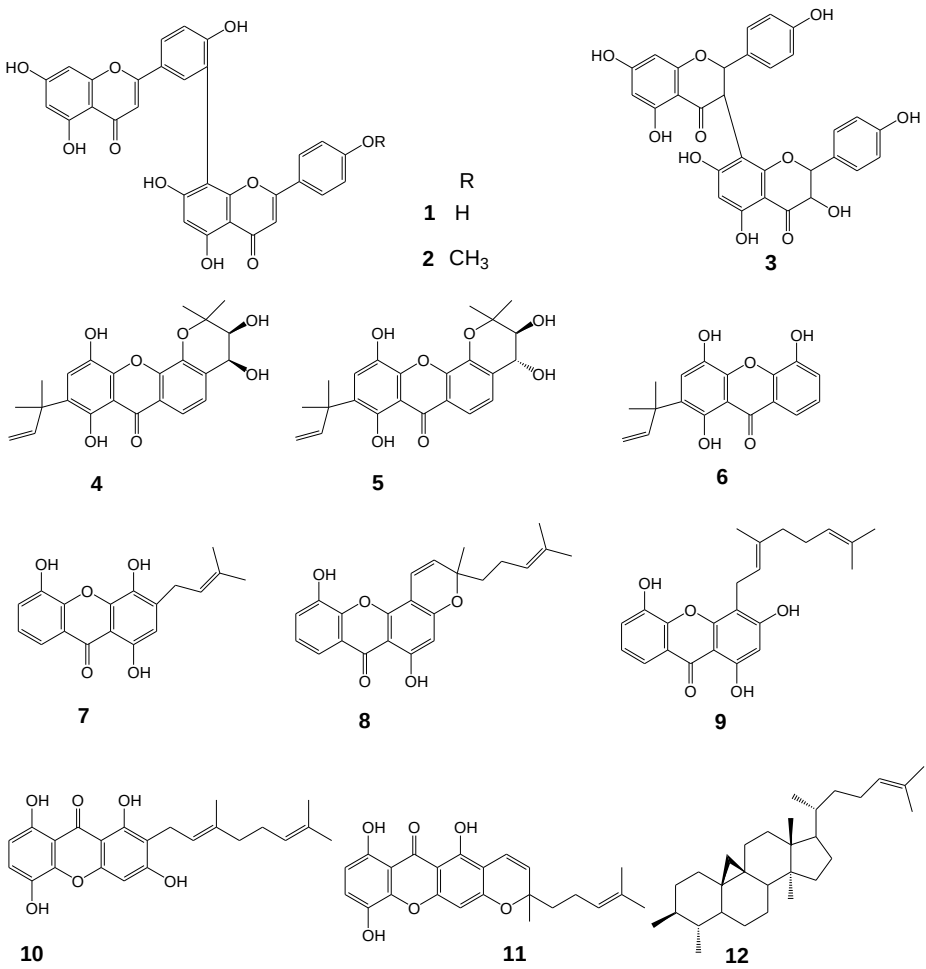

Fig. 20. *Structures of bioactive compounds isolated from some African Garcinia plants.*

Table 4. *Biological activities of extracts from African Garcinia species.*

Plant species (Country)	**Effects (Organism tested)**	**Part used (Extracting solvent)**	***In vivo***	***In vitro***	**Reference**
G. afzelii (from Togo)	Antibacterial (*Pseudomonas aeruginosa*)	Dried Stem (EtOH)		Inactive- at a conc of 4.0 mg /ml	Kpakote *et al.* (1998)
	Antibacterial (*Staphylococcus aureus*)	Dried Stem (EtOH)		Active- at a conc of 4.0 mg /ml	Kpakote *et al.* (1998)
	Antifungal (*Asperigillus fumigatus*)	Dried Stem (EtOH)		Active- at a conc of 4.0 mg /ml	Kpakote *et al.* (1998)
	Antiyeast (*Candida albicans*)	Dried Stem (EtOH)		Inactive- at a conc of 4.0 mg /ml	Kpakote *et al.* (1998)
G. edulis (from Tanzania)	Antiviral (HIV-1 protease)	Stem bark (Ethanol)		Active with IC_{50} value of 9.2 µg/ml	Magadula (2010)
	Cytotoxicty (*Artemia salina*)	Root bark (Ethanol)		Active with LC_{50} value of 2.36 µg/ml	Magadula (2010)
G. gerradii (from South Africa)	Larvicidal (*Aedes aegypti*)	Dried Leaf (CH_2Cl_2)		Active- at a conc of 500.0 mg /ml	Cepleanu *et al.* (1994)
	Anticrustacean (*Artemia salina*)	Dried Leaf (CH_2Cl_2)		Active- with LC_{50} value of 53.0 µg /ml	Cepleanu *et al.* (1994)
	Molluscicidal (*Biomphalaria glabrata*)	Dried Leaf (CH_2Cl_2)		Inactive- at a concentration of 400 ppm	Cepleanu *et al.* (1994)
	Antifungal (*Cladosporium cucumerinum*)	Dried Leaf (CH_2Cl_2)		Inactive- at a concentration of 100 µg/plate	Cepleanu *et al.* (1994)
	Cytotoxicty (CA-COLON-SW 480)	Dried Leaf (CH_2Cl_2)		Active- with IC_{50} value of <5.0 µg /ml	Cepleanu *et al.* (1994)
	Cytotoxicty (CA-HUMAN-COLON-CO-115)	Dried Leaf (CH_2Cl_2)		Weak activity- with IC_{50} value of 7.0 µg /ml	Chapuis *et al.* (1988)
	Antifungal (*Cladosporium cucumerinum*)	Root bark		Active- at a concentration of 100 µg/plate	Sordat-Diserens, *et al.* (1989)
G. huillensis (from DR	Antifungal (*Cytospora* sp)	Dried stem bark (H_2O)		In an agar plate, active at a conc of 1-10	Laine *et al.* (1985)

Plant species (Country)	**Effects (Organism tested)**	**Part used (Extracting solvent)**	***In vivo***	***In vitro***	**Reference**
Congo)				mg /ml	
	Antiviral (Virus-Herpes Simplex 1)	Dried stem bark (PetEther)		Inactive-the conc was not given	Bakana *et al.* (1987)
	Antiviral (Virus-Coxsackie)	Dried stem bark (PetEther)		Inactive-the conc was not given	Bakana *et al.* (1987)
	Antiviral (Virus-Poliovirus 1)	Dried stem bark (PetEther)		Inactive-the conc was not given	Bakana *et al.* (1987)
	Antibacterial (*Staphylococcus aureus*)	Dried stem bark (PetEther)		In an agar plate, seen active with MIC value of 62.5 µg /ml	Bakana *et al.* (1987)
G. huillensis (from Tanzania)	Antitrypanosomal (*Trypanosoma brucei*)	Dried stem + root (CH_2Cl_2)		Active- with IC_{50} value of 4.4 µg /ml	Freiburghaus *et al.* (1996)
G. kingaensis (from Tanzania)	Antiviral (HIV-1 protease)	Root bark (Ethanol)		Active with IC_{50} value of 15.2 µg/ml	Magadula (2010)
G. kola (from DR Congo)	CNS stimulant	Dried stem bark (H_2O)	Not active in rat and the dose was not stated		Sandberg and Cronlund (1977)
	CNS depressant	Dried stem bark (H_2O)	Not active in rat, the dose was not stated		Sandberg and Cronlund (1977)
G. kola (from Nigeria)	Antioxidant	Dried fruit (H_2O)	Active in rat liver at a conc of 2.5 mg/ml		Adegoke *et al.* (1998)
	Bronchodilator (Human adult, male)	Fresh fruit (H_2O)	19 healthy volunteers aged 17-25 years were used for this study. Decoction was taken orally at a dose of 15.0 gm/person. Weak activity was observed in 1 hour after treatment with results been		Orie and Ekon (1993)

Plant species (Country)	**Effects (Organism tested)**	**Part used (Extracting solvent)**	***In vivo***	***In vitro***	**Reference**
			significant at $p < 0.05$ level		
	Hepatoprotective	Saline Ext	Active at a dose of 10 ml/kg. The rats were given partial hepatectomy and enzyme (glucose-6-phosphatase) activity was inhibited by 31%.		Adegoke *et al.* (1998)
	Hepatoprotective	Commercial sample of kernel (H_2O)	Protein & DNA synthesis inhibition at a dose of 5 ml/kg Rats were given partial hepatectomy		Oruambo (1989)
	Molluscicidal (*Biomphalaria pfeifferi, Lymnaea natalensis & Bulinus globosus*)	Dried leaf (MeOH)		Strong activity at a conc of 100 ppm leading to 100% mortality	Okunji and Iwu (1988)
	Antibacterial (*Streptococcus-beta hemolytic*)	Dried root bark (EtOH)		Active but the concentration was not given	Ebana *et al.* (1991)
	Antibacterial (*Proteus mirabilis*)	Dried root bark (H_2O)		Active but the concentration was not given	Ebana *et al.* (1991)
	Antibacterial (*Klebsiella pneumoniae*)	Alkaloid fraction		Active but the concentration was not given	Ebana *et al.* (1991)
	Antibacterial (*Pseudomonas aeruginosa*)	Glycoside mixture		Active but the concentration was not given	Ebana *et al.* (1991)
	Antibacterial (*Escherichia coli*)	Dried root bark (H_2O)		Active but the concentration was not given	Ebana *et al.* (1991)
	Hypotriglyceridemia	Dried seed (flavonoid fraction)	Active in rat at a dose of 500 mg/kg with inhibition of enzyme increase versus CCl_4-Induced hepatotoxicity		Braide (1991a)
	Antihepatotoxic	Dried seed (flavonoid	Active in rat at a dose of 500 mg/kg		Braide (1991a)

Plant species (Country)	**Effects (Organism tested)**	**Part used (Extracting solvent)**	***In vivo***	***In vitro***	**Reference**
		fraction)	with inhibition of enzyme increase versus CCl_4-Induced hepatotoxicity		
	Glutathione depletion inhibition	Dried seed (flavonoid fraction)	Active in rat at a dose of 500 mg/kg with inhibition of enzyme increase versus CCl_4-Induced hepatotoxicity		Braide (1991a)
	Barbiturate potentiation	Commercial sample of seed	The dose used in n rat 200 mg/kg. The hexobarbitol-induced sleeping time increased on days 1-7		Braide (1991b)
	Antibacterial (*Bacillus subtilis, Escherichia coli, Bacillus megaterium, Staphylococcus aureus*)	Dried seed (EtOAc)		In agar plate, it was active at a conc of 100 µg/ml	Madubunyi (1995)
	Antifungal (*Aspergillus niger*)	Dried seed (EtOAc)		In agar plate, it was active at a conc of 100 µg/ml	Madubunyi (1995)
	Spasmolytic	Dried seed (flavonoid fraction)	Active in an ileum & duodenum of Guinea pig at a conc of 12.5 µg/ml vs Histamine-induced contractions.		Braide (1989)
	Spasmolytic	Dried seed (alkaloid fraction)	Active in an ileum & duodenum of Guinea pig at a conc of 12.5 µg/ml vs Histamine-induced contractions.		Braide (1989)
	Molluscicidal (*Bulinus globosus*)	Dried seed (H_2O)		Active against *Bulinus globosus* at a	Okunji and Iwu (1988)

Plant species (Country)	**Effects (Organism tested)**	**Part used (Extracting solvent)**	***In vivo***	***In vitro***	**Reference**
				conc of 100 µg/ml	
	Molluscicidal (*Bulinus globosus*)	Dried seed (MeOH)		Strong activity against *Bulinus globosus* at a conc of 100 µg/ml	Okunji and Iwu (1988)
	Molluscicidal (*Lymnaea natalensis*)	Dried seed (MeOH)		Strong activity against *Lymnaea natalensis* at a conc of 100 µg/ml	Okunji and Iwu (1988)
	Antidiarrheal	Seeds	Active in a male rat at a conc of 10% of diet vs castor oil-induced diarrhea.		Okunji and Iwu (1988)
	Antiobesity	Seeds	Active in a male rat at a conc of 20% of diet. Feeding for 6 weeks decreased body weight from 134 to 110 gm/rat		Braide (1990)
	Dietary intake	Seed powder	The seed powder incooperated on animal feed was studied on serum levels of electrolytes and heavy metals on male albino rats. The pair-fed controls received basal feed diet daily for six weeks. Results showed a significant ($P< 0.05$) dose dependent elevation of serum Cl^-, HCO_3, Ca2+,Mg^{2+}, Cu^{2+}, Zn^{2+} and Mn^{2+}		Agada and Braide (2009)

Plant species (Country)	**Effects (Organism tested)**	**Part used (Extracting solvent)**	***In vivo***	***In vitro***	**Reference**
	Hepatoprotective	Kolanut (H_2O)	Studied on mice with 10 mg/kg methamphetamine used to induce neurotoxicity and 200 mg/kg of extract was taken orally. Results indicated the serum levels of some of the marker enzymes and bilirubin to decrease significantly ($P < 0.05$).		Oze et al. (2010)
	Antibacterial (*Escherichia coli*)	Seed			Adegboye *et al.*, (2008)
G. kola (from DR Congo)	Antimalarial (*Plasmodium falciparum*)	Dried seed (CH_2Cl_2)		Active against *P. falciparum* at a concentration of 6 µg/ml	Tona *et al.* (1999)
	Antimalarial (*Plasmodium falciparum*)	Dried seed (EtOH)		Active against *P. falciparum* at a concentration of 6 µg/ml	Tona *et al.* (1999)
	Antimalarial (*Plasmodium falciparum*)	Dried stem bark (CH_2Cl_2)		Active against *P. falciparum* at a concentration of 6 µg/ml	Tona *et al.* (1999)
	Antimalarial (*Plasmodium falciparum*)	Dried stem bark (EtOH)		Active against *P. falciparum* at a concentration of 6 µg/ml	Tona *et al.* (1999)
	Antiamebic (*Entamoeba histolytica*)	Decoction		Weak activity was observed at a MIC of 125 µg/ml	Tona *et al.* (1999)
	Antibacterial (*Klebsiella pneumoniae*)	Dried stem bark (Tannin fraction)		Active at a concentration of 120 µg/ml	Lutete (1994)

Plant species (Country)	**Effects (Organism tested)**	**Part used (Extracting solvent)**	***In vivo***	***In vitro***	**Reference**
	Antibacterial (*Citrobacter diversus*)	Dried stem bark (Tannin fraction)		Active at a concentration of 95 µg/ml	Lutete (1994)
	Spasmolytic	Dried trunk bark (Butanol ext)	Active in the Ileum of Guinea pig at a conc of 0.2 mg/ml. Oberved 70.3% reduction incontraction vs KCl-Induced contractions		Kambu (1990)
G. livingstoneii (from South Africa)	Cytotoxicty (CA-HUMAN-COLON-CO-115)	Dried Leaf (MeOH)		Inactive-the conc was not given	Chapuis *et al.* (1988)
	Cytotoxicty (CA-HUMAN-COLON-CO-115)	Dried root bark (CH_2Cl_2)		Inactive-the conc was not given	Sordat-Diserens *et al.* (1992)
	Cytotoxicty (Human Cancer cell line HT 29)	Dried root bark (CH_2Cl_2)		In a cell culture, it was active with IC_{50} value of 10.0 µg /ml	Sordat-Diserens *et al.* (1992)
	Cytotoxicty (Human Cancer cell line, HT 620)	Dried root bark (CH_2Cl_2)		Active with IC_{50} value of 8.0 µg /ml	Sordat-Diserens *et al.* (1992)
	Antitumor (CA-COLON-SW 480)	Dried root bark (CH_2Cl_2)		Active with IC_{50} value of 8.0 µg /ml	Sordat-Diserens *et al.* (1992)
	Antifungal (*Cladosporium cucumerinum*)	Dried root bark (CH_2Cl_2)		Active- at a concentration of 100 µg/plate	Sordat-Diserens *et al.* (1992)
	Anticrustacean (*Artemia salina*)	Dried root bark (CH_2Cl_2)		Active- with LC_{50} value of 17.0 µg /plate	Cepleanu *et al.* (1994)
	Molluscicidal (*Biomphalaria glabrata*)	Dried root bark (CH_2Cl_2)		Seen inactive at a concentration of 400 ppm	Cepleanu *et al.* (1994)
	Antifungal (*Cladosporium cucumerinum*)	Dried root bark (CH_2Cl_2)		Active- at a concentration of 100 µg/plate	Cepleanu *et al.* (1994)
G. livingstoneii	Cytotoxicity (A549, DU145, KB and	Fruit (Ethanol)		Active with an average CC_{50}	Magadula and

Plant species (Country)	**Effects (Organism tested)**	**Part used (Extracting solvent)**	***In vivo***	***In vitro***	**Reference**
(from Tanzania)	Kbivin)			value of 5.7-12.0 μg/ml	Suleiman (2010)
	Antiviral (HIV-1 viral replication in MT4 cells)	Fruit (Ethanol)		Inhibited the HIV-1 viral replication of MT4 cells with EC_{50} value of 2.25 μg/mL)	Magadula and Suleiman (2010)
G. lucida (from Cameroon)	Antimicrobial (*E. coli, P. aeruginosa, S. typhi, S. aureus, C. albicans*).	Stem bark (Methanol)		Active only to *C. albicans* with MIC value of 64 μg/mL	Momo *et al.* (2011)
G. lucida (from Cameroon)	Tripanosomal (*T. b. brucei)*	Stem bark (1:1 CH_2Cl_2:MeOH mixture)		Activity value at IC_{50} 4.9 μg/mL)	Fotie *at al.* (2007)
G. lucida (from Cameroon)	Antileishmanial (promastigote *L. donovani)*	Stem bark (1:1 CH_2Cl_2:MeOH mixture)		Crude extract (100 μg/mL) was able to clear the parasites (100% inhibition)	Fotie *at al.* (2007)
G. ovalifolia (from Central African Republic)	Antiviral (Virus-HIV)	Dried Leaf ($CHCl_3$-MeOH)		In a 1:1 conc under cell culture, it was reported to be active but the conc was not given	Gustafson *et al.* (1992)
G. ovalifolia (from Togo)	Antiyeast (*Candida albicans*)	Dried Stem bark (EtOH)		Inactive at a concentration of 4.0 mg/ml	Kpakote *et al.* (1998)
	Antibacterial (*Staphylococcus aureus*)	Dried Stem bark (EtOH)		Active at a concentration of 4.0 mg/ml	Kpakote *et al.* (1998)
	Antibacterial (*Pseudomonas aeruginosa*)	Dried Stem bark (EtOH)		Inactive at a concentration of 4.0 mg/ml	Kpakote *et al.* (1998)
	Antifungal (*Aspergillus fumigatus*)	Dried Stem bark (EtOH)		Active at a concentration of 4.0 mg/ml	Kpakote *et al.* (1998)

Plant species (Country)	**Effects (Organism tested)**	**Part used (Extracting solvent)**	***In vivo***	***In vitro***	**Reference**
G. polyantha (from Togo)	Antifungal (*Aspergillus fumigatus*)	Dried Stem bark (EtOH)			Kpakote *et al.* (1998)
G. verrucosa ssp orientalis (from Madagascar)	Cytotoxicity (Murine P388 cell line)	Stem bark (EtOAc)		Exhibited 99 % inhibition of the P388 cell growth at a concentration of 10 µg/ml	Rajaonarivelo *et al.* (2009)
G. semseii (from Tanzania)	Cytotoxicity (A549, DU145, KB and Kbivin)	Fruit (Ethanol)		Active with CC_{50} value range of 7.8-9.1 µg/mL)	Magadula and Suleiman (2010)
	Antiviral (HIV-1 viral replication in MT4 cells)	Fruit hulls (Ethanol)		Inhibited the HIV-1 viral replication of MT4 cells with EC_{50} value of 0.93 µg/mL)	Magadula and Suleiman (2010)
G. volkensii (from Tanzania)	Antimicrobial, antioxidant and Cytotoxicity	Stem bark (Ethanol)		Antibacterial activity with MIC values ranging of 0.049->2.50 mg/ml. The BST exhibited LC_{50} value >100 µg/ml.	Mbwambo *et al.* (2011)

3.3 Antimalarial Activity

Malaria is one of the most serious protozoal diseases in man and ranks number one in terms of morbidity in the tropical countries. It is estimated that at least 40% of the world's population live in endemic areas, among which 90% are distributed in Africa south of Sahara desert (Bruce-Chwatt *et al.*, 1981). The use of plant secondary metabolites as a cure and/or leads for the development of

potential antimalarial compounds is a well known approach (Philipson and Wright, 1990). Currently many medicinal plants, including *Garcinia* plants from Africa have been investigated *in vitro* and/or *in vivo* testing for their potential antimalarials.

Tona and co-workers investigated 20 extracts from different parts of some African medicinal plants used in Congolese traditional medicine for the treatment of malaria. Of these, the dichloromethane and ethanol extracts of the dried seeds of *G. kola* exhibited more than 60% inhibition of the *Plasmodiun falciparum* growth *in vitro* at a test concentration of 6 μg/ml (Tona *et al.*, 1999), (Table 4).

In another study from *G. polyantha*, which is an important medicinal plant of Cameroonian traditional medicine, phytochemical analysis of its different parts gave xanthones, flavonoids, benzophenones and triterpenoids (Lannang *et al.*, 2008). The isolated compounds were tested for their *in vitro* antimalarial potential. In this assay, only isoxanthochymol **(13)** showed strong chemosuppression of *P. falciparum* when tested *in vitro* (Lannang *et al.*, 2008).

In a study from *G. livingstoneii*, a series of xanthones and flavonoids was isolated and tested for antiparasitic activity against *P. falciparum*. One of the isolates, a biflavonoid *ent*-naringeninyl-(I-3α,II-8)-4'-*O*-methylnaringenin **(14)**, showed a remarkable *in vitro* activity against *P. falciparum* with the IC_{50} value of 6.0 μg/ml (Mbwambo *et al.*, 2006). Other xanthones and biflavonoids isolated from this plant were not active in this assay.

3.4 Anticancer Activity

Cancer is rapidly becoming a major health problem with a global burden of about 8 million deaths worldwide (WHO, 2007). This problem is correlated

with the emergence of HIV/AIDS, in which malignancies occur as part of opportunistic diseases due to depressed immune system and other life styles. Since many people in Africa live in rural areas, treatment of cancer-related illnesses has mostly involved plant extracts, since most of people can not afford the costs of currently available anticancer drugs. This necessitates the need for continued search for anticancer compounds from medicinal plants. Currently, several anticancer extracts and compounds from African *Garcinia* plants have been characterized and their activities against different types of human cancer cell-lines established (Rajaonarivelo *et al.*, 2009; Magadula & Suleiman, 2010; Mbwambo *et al.*, 2006).

A recent study from *Garcinia* plants collected in Tanzania; reported the evaluation of ethanol extracts for their *in vitro* cytotoxicity against four human cancer cell lines. Among the tested extracts, the fruit extract of *G. livingstoneii* and fruit hulls of *G. semseii* showed moderate to mild cytotoxic activities against A549, DU145, KB and Kbivin human cell lines, with 50 % cytotoxic (CC_{50}) values ranging from 5.7-20.0 µg/ml (Magadula and Suleiman, 2010), whereby taxol was used as a positive control. Rajaonarivelo and co-workers investigated the cytotoxicity of the ethyl acetate extract of the stem bark of *G. verrucosa* ssp *orientalis*, collected from the Eastern rain forest of Madagascar. In this study the EtOAc extract exhibited 99 % *in vitro* inhibition of the P388 cell growth at a concentration of 10 µg/ml (Rajaonarivelo *et al.*, 2009). In another study on anticancer activity, a dichloromethane extract of the root bark of *G. livingstoneii*; collected in South Africa exhibited *in vitro* growth inhibitory activities against four human colon carcinoma cell lines. The human cell lines tested were CO 115, SW 480, SW 620 and HT 29 with the IC_{50} values of 10, 8, 8 and 10 µg/ml, respectively (Sordat-Diserens *et al.*, 1992).

Flavonoids possess various pharmacological properties including anticancer activities (Iriti and Varoni, 2013). Two anticancer flavonoids have been reported from the leaves of *G. livingstoneii*, namely; amentoflavone **(1)** and 4"-methoxy amentoflavone **(2)** (Kaikabo *et al.*, 2009). The cytotoxicity of these compounds was assessed using Vero monkey kidney cells. The authors showed low toxicity against the cell line with LD_{50} values of 386 µg/ml and >600 µg/ml, respectively (Kaikabo *et al.*, 2009). In this test, berberine (CC_{50} = 170 µg/ml) was used as a positive control. In a different study from the root bark of *G. livingstoneii*, two dimeric xanthones, garcilivins A **(15)** and C **(16)** were isolated and tested for *in vitro* cytotoxicity against MRC-5 cells. Compound 15 showed a higher and nonselective cytotoxicity (IC_{50} = 2.0 µg/ml), than its diastereoisomer, compound 16 (IC_{50} = 52.3 µg/ml) (Mbwambo et al., 2006). Further investigation from the root bark of *G. livingstoneii* gave two xanthones, 6,11-dihydroxy-2,2-dimethyl-pyrano[3,2-c]xanthone **(17)** and 4- (3', 7'-dimethylocta-2', 6'-dienyl)-1,3,5-trihydroxy-9*H*-xanthone **(18)**. These compounds inhibited the growth of SW 480 and CO 115 human colon carcinoma cells with compound 18 (IC_{50} = 0.6 µg/ml) showing comparable activity to the synthetic drug, 5-fluorouracil (IC_{50} = 0.4 µg/ml) (Sordat-Diserens *et al.*, 1992).

The bioassay-guided fractionation of the EtOAc extract of the stem bark of *G. verrucosa* led to the isolation of a new cytotoxic polycyclic prenylated acylphloroglucinol, named garcicosin **(19)**. This compound was observed to inhibit P388 cell growth at a concentration of 10 µg/ml with an IC_{50} value of 3.0 µg/ml. (Rajaonarivelo *et al.*, 2009).

The study by Dibwe and co-workers on the chloroform extract of *Garcinia huillensis* indicated a preferential cytotoxicity (PC_{50} = 17.8 µg/mL) against human pancreatic cancer PANC-1 cells under nutrient-deprived conditions.

Further investigation of the active constituents revealed 12 known anthraquinones together with a damnacanthal **(20)**. Compound **20** caused preferential necrotic cell death of PANC-1 and PSN-1 cells under nutrient-deprived and serum-sensitive conditions of $PC_{50} = 4.46$ μm and 3.77 μm, respectively (Dibwe *et al.*, 2012).

3.5 Antioxidant Activity

Antioxidants such as dietary flavonoids work by scavenging free radicals, chelation of metal ions, and decomposition of peroxides such as lipid peroxides (Dufresne and Farnsworth, 2001). It is well established that; phenolic compounds are known to be antioxidants with excellent hydrogen or electron donor capacity (Chiang *et al.*, 2003). It has been suggested that the antioxidant effect of *Garcinia* plants is ascribed mostly to biflavonoids (Farombi *et al.*, 2002). Thus, they are thought to play important role in the prevention of various human disorders as free radical scavengers.

Garcinia kola, a tropical plant which grows in moist forest, has found to have many applications in traditional medicine, especially in the West and Central African sub-region. This plant is the highly investigated among all *Garcinia* species growing in Africa. Farombi and co-workers investigated the antioxidant and scavenging properties of a flavonoid extract of *G. kola* seeds. The *in vitro* assay involved the free radicals and reactive oxygen species from which the flavonoid extract, commonly known as kolaviron, exhibited noticeably reducing power and antioxidant activity by inhibiting the peroxidation of linoleic acid. It further exhibited 57% scavenging effect on superoxide at a concentration of 1 mg/ml and 85% scavenging activity on hydrogen peroxide at a concentration of 1.5 μg/ml. Similarly, flavonoid extract, at a concentration of 2 mg/ml, showed a 89% scavenging effect on a,a-diphenylb-picrylhydrazyl radical (DPPH),

indicating that the extract has effective activities as a hydrogen donor and as a primary antioxidant to react with lipid radicals (Farombi *et al.*, 2002). The protective effects of kolaviron, a Garcinia biflavonoid extract from the seeds of *G. kola* widely consumed in some West African countries, was tested against oxidative damage to molecular targets *ex-vivo* and *in vitro*. Treatment with hydrogen peroxide (H_2O_2) at a concentration of 100 μg/ml increased the levels of DNA strand breaks and oxidized purine and pyrimidine bases in both human lymphocytes and rat liver cells using alkaline single cell gel electrophoresis (COMET assay). Kolaviron was protective at concentrations between 30-90 μg/ml and decreased H_2O_2-induced DNA strand breaks and oxidized bases (Farombi *et al.*, 2004). Furthermore, kolaviron exhibited protective effects against oxidative damage to molecular targets via scavenging of free radicals and iron binding (Farombi *et al.*, 2004).

In another study by Farombi and co-workers, the antioxidant and radical scavenging activities were investigated from the flavonoid fraction of the seeds of *G. kola*. The extract was fed to the male rats for six weeks and their body weights decreased from 134 to 110 gm/rat (Table 3) (Farombi *et al.*, 2002). Further studies from the seeds of *G. kola* indicated the methanolic extract to show many activities. Methanol extract was subjected to column chromatography under silica gel to give five fractions, and each fraction was tested for the free radical scavenging activities and antioxidant potentials for various *in vitro* models (Okoko, 2009). Results indicated that the fourth fraction possessed the highest antioxidant and radical scavenging activities as compared with the rest of fractions. It was also established that the fourth fraction strongly inhibited nitric oxide production in lipopolysaccharide activated macrophage U937 cells (Okoko, 2009). The CH_2Cl_2/MeOH (1:1) extract of the stem bark of *G. afzelii* was found to exhibit significant anti-oxidant effects, based on the scavenging of the stable DPPH free radical showing the IC_{50} value of 20.5

μg/100 ml (Waffo *et al.*, 2006). Two novel prenylated xanthones, afzeliixanthones A **(21)** and B **(22)**, were isolated and tested for their antioxidative properties. The two compounds showed high antioxidant activity with the IC_{50} values of 17.7 and 14.0 μg/100 ml comparable to α-tocopherol **(23)** (IC_{50} 13.5 μg/100 ml) as a standard (Waffo *et al.*, 2006).

In another study by Okoko on the methanol extract of the seeds of *G. kola*, column chromatographic fractionation under silica gel and spectroscopic analysis of the active fraction revealed the presence of four compounds namely garcinia biflavonoids GB1 **(3)** and GB2 **(24)**, garcinal **(25)** and garcinoic acid **(26)**. These four compounds were reported to be responsible for the great antioxidant potential of *Garcinia kola* seeds (Okoko, 2009). Further work by Terashima and co-workers investigated the structure-antioxidative activity relationships of derivatives based on garcinoic acid **(26)** from *Garcinia kola*, which led to the discovery of a powerful antioxidative agent of a chromen moiety (compound **27**) that showed activity of 18.7 higher than standard compound, **23** (Terashima *et al.*, 2002).

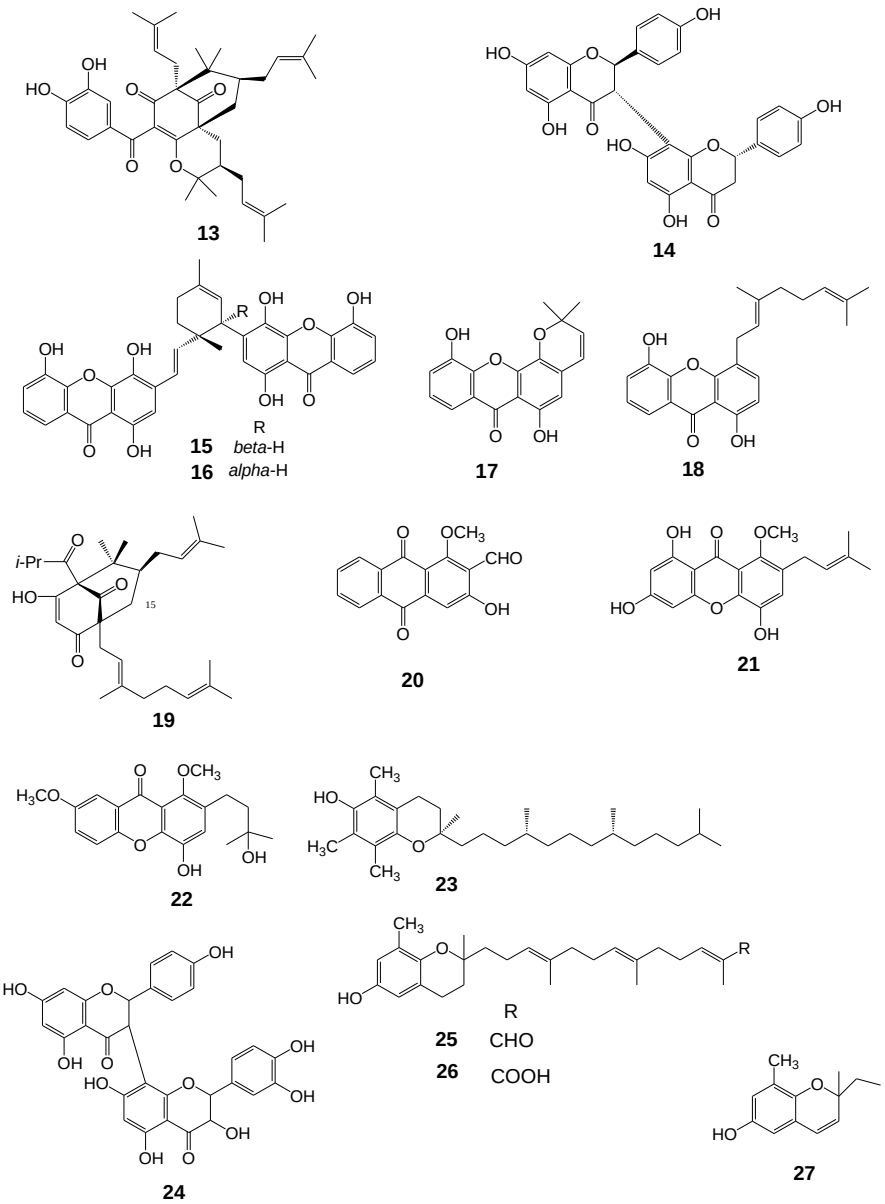

Fig. 20. *Structures of bioactive compounds isolated from some African Garcinia plants (Cont).*

Phytochemical analysis from the chloroform extract of the stem bark of *G. polyantha* resulted in the isolation of four prenylated xanthones, bangangxanthones A **(28)** and B **(29)**, 1,5-dihydroxyxanthone **(30)** and 2-hydroxy-1,7-dimethoxyxanthone **(31)** that were screened for DPPH radical scavenging activity (Lannang *et al.*, 2005). Compound **28** showed significant activity with IC_{50} value of 87.0 µg/ml relative to the standard, 3-*t*-butyl-4-hydroxyanisole (IC_{50} = 42.0 µg/ml). Likewise, compound **29** showed weak activity with IC_{50} of 482.0 µg/ml, while compounds **30** and **31** showed 47.8% and 39.5% of inhibition respectively, at the concentration of 1 µg/ml (Lannang *et al.*, 2005).

In the search for antioxidant compounds from *G. buchananii*, Stark *et al.* (2012), isolated and identified three 3,8″-linked biflavanones and two flavanone-C-glycosides biflavonoids using hydrogen peroxide scavenging and oxygen radical absorbance capacity (ORAC) assays. The compounds included a biflavanone GB-2 **(24)**, manniflavanone **(32)**, taxifolin- 6- C- β- D-glucopyranoside **(33)**, aromadendrin-6-C-β-D-glucopyranoside **(34)** and buchananiflavanone **(35)**. Manniflavanone **(32)** and GB-2 **(24)** showed high H_2O_2 scavenging activity with EC_{50} values of 2.8 and 2.2 µM, respectively and the ORAC activities of 13.73 and 12.10 µmol TE/ µmol, respectively, (Stark *et al.*, 2012).

3.6 Antiviral Activity

In the absence of a vaccine and efficient treatment, HIV/AIDS continues to be a growing public health problem in the world. The rising number of HIV/AIDS cases in Africa has raised the demand for medical care and consequently has created a burden to the available limited health budgets.

Consequently, this has raised the interest of screening crude plant extracts for anti-HIV activity, while little research has been done on pure compounds.

Two *Garcinia* plants growing in Tanzania has been evaluated for their *in vitro* anti-HIV activity against HIV-1 viral replication in MT4 cells. The ethanol extracts of the fruits of *G. livingstonei* and *G. semseii* revealed significant anti-HIV-1 activity with EC_{50} values of 2.25 ± 0.51 and 0.93 ± 0.67 μg/mL respectively (Magadula & Suleiman, 2010). Furthermore, another study from ethanol extracts of some *Garcinia* species collected in Tanzania were investigated for their HIV-1 protease (HIV-1 PR) inhibitory activities using high performance liquid chromatography (HPLC). Among the tested extracts, the fruit hulls of *G. semseii* showed the most potent inhibitory activity against HIV-1 PR with an IC_{50} value of 5.7 μg/ml, followed by the stem bark extracts of *G. edulis* and *G. kingaensis* with IC_{50} values of 9.2 and 15.2 μg/ml, respectively (Magadula & Tewtrakul, 2010). In another study, the chloroform-methanol (1:1) extract of the dried leaf of *G. ovalifolia*, collected from Central African Republic, showed significant anti-HIV activity when tested *in vitro* (Gustafson *et al.*, 1992).

Benzophenones are phenolic compounds which are reported to display antiviral activity. For instance, a polyisoprenylated benzophenone, guttiferone A **(36)** isolated from the fruits of *G. livingstonei* was found to inhibit the cytopathic effects in human lymphoblastoid CEM-SS cells *in vitro*, with EC_{50} values of ≤ 10 μg/ml (Gustafson et al., 1992). Phytochemical investigation of the root bark of *G. edulis* gave a new isoprenylated xanthone, 1, 4, 6-trihydroxy -3-methoxy-2- (3-methyl-2-butenyl)-5-(1,1-dimethyl-prop-2-enyl)xanthone **(37)** that showed significant *in vitro* anti-HIV-1 protease activity with IC_{50} value of 11.3 μg/ml (Magadula, 2010).

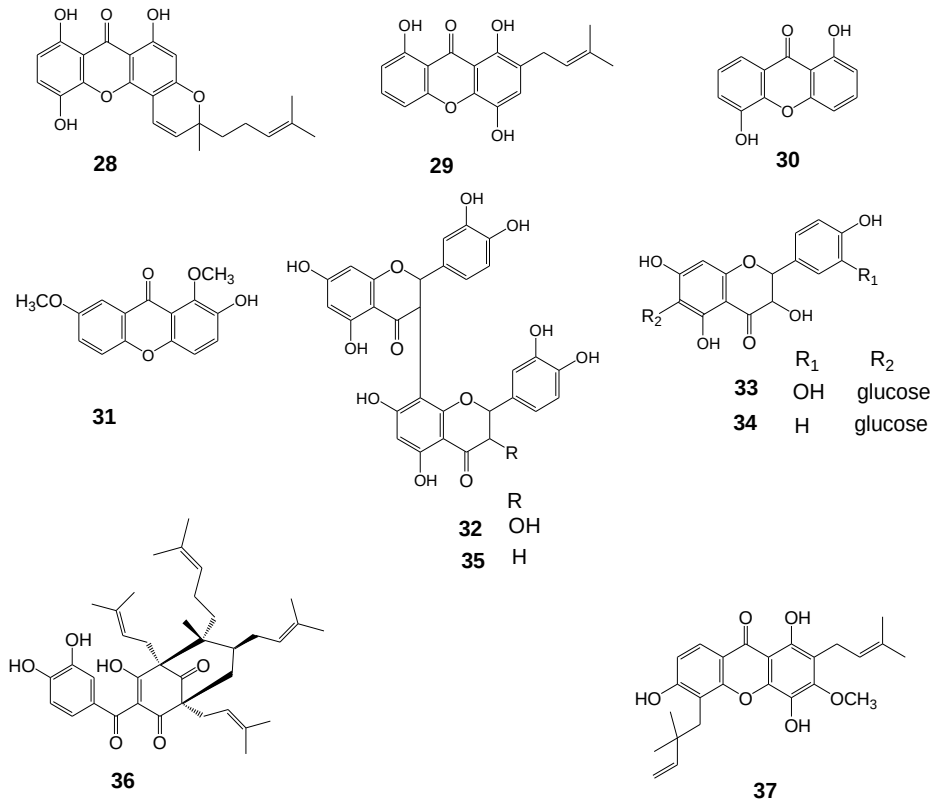

Fig. 20. *Structures of bioactive compounds isolated from some African Garcinia plants (Cont).*

3.6 Other Biological Activities

The phytochemical study on the methanol extract of the wood trunk of *G. polyantha*, gave a series of oxygenated xanthones that were screened for their anticholinesterase potentials on acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes (Louh *et al.*, 2008). Polyanxanthones A-C **(38-40)**, 1,3,5-trihydroxyxanthone **(41)**, 1,5-dihydroxyxanthone **(30)** and 1,6-dihydroxy-5-methoxyxanthone **(42)** showed noteworthy inhibitory activities. Compounds **30**, **40** and **41** showed significant inhibition against BChE with an

IC_{50} value of 93.0, 2.54 and 74.4 μg/ml, respectively, while compound **39** showed significant inhibition against both AChE (IC_{50} = 46.3 μg/ml) and BChE (IC_{50} = 25.5 μg/ml) compared to the standard, galantamine (IC_{50} = 0.5 and 8.5 μg/ml, respectively). Compound **38** indicated 41.8% and 7.0% inhibition against AChE and BChE, respectively, at the concentration of 0.2 mg/ml (Louh *et al.*, 2008).

Kolaviron, the predominant constituent in *G. kola*, is a biflavonoid complex [containing biflavanones GB-1 **(3)** and GB-2 **(24)** and kolaflavanone **(43)**] that has been reported to prevent hepatotoxicity mediated by several toxins (Iwu *et al.*, 1987). Similarly, kolaviron exhibited hypoglycemic effects in normal and alloxan- and streptozotocin-induced diabetic animals (Adaramoye *et al.*, 2006). In another study for kolaviron, the protein expression levels of cyclooxygenase (COX-2) and inducible nitric oxide synthase (iNOS) were evaluated by western blotting, while DNA-binding activities of nuclear factor kappa B (NF-κB) and activator protein-1 (AP-1) were determined by electrophoretic mobility shift assay. The results indicated kolaviron to have an ability to inhibit COX-2 and iNOS expression through down regulation of NF-κB and AP-1 DNA binding activities, which could be a mechanism for the hepatoprotective properties of kolaviron (Farombi *et al.*, 2009).

In the study by Balemba and co-workers, the stem bark of *G. buchananii* inhibited propulsive motility and fast synaptic potentials in the guinea pig distal colon. The result indicated a concentration-dependent manner, with an optimal concentration of about 10 mg/ ml. In this study, no any active principle was isolated from the active fractions (Balemba et al., 2010). Further study from the same plant investigated the potential of the constituents on reducing gastrointestinal peristaltic activity *via* 5-HT(3) and 5-HT(4) receptors. Phytochemical screening of the crude extract indicated the presence of

flavonoids, steroids, alkaloids, tannins and phenols. The results revealed that the anti-motility effects of the aqueous extract of *G. buchananii* are significantlly mediated by compounds that affect 5-HT(3) and 5-HT(4) receptors. However, no single compound was characterized or identified from the active components (Boakye et al., 2012). Furthermore, the *G. buchananii* extract and its anti-motility fractions were studied to be effective remedies against lactose-induced diarrhea. Results indicated that the active extract contained compounds that are responsible for reducing the body weight and supporting the upward intake of food and water (Boakye *et al.*, 2012).

Depsidones isolated from *Garcinia* plants are reported to possess many biological activities (Ito *et al.*, 2001). In a phytochemical study from the stem bark of *G. brevipedicellata* collected in Cameroon, four new depsidones named brevipsidones A-D **(44-47)** were isolated and evaluated for their possible glycosidase enzyme inhibitory activity against α-glucosidase. These compounds showed moderate α-glucosidase inhibition with IC_{50} values of 21.2, 27.8, 59.6 and 7.04 µg/ml respectively (Ngoupayo *et al.*, 2008).

The crude extract of the stem bark of the *G. lucida* indicated a significant trypanocidal and antileishmanial activities. The bioassay guided isolation of the constituents of the stem bark led to the isolation of three benzo[*c*]phenanthridine alkaloids, dihydrochelerythrine **(48)**, 6-acetonyldihydrochelerythrine **(49)** and lucidamine A **(50)**. The isolated compounds as well as the crude extract displayed poweful antiprotozoal activity against *Trypanosoma brucei brucei* and *Leishmania donovani*, with little toxicity to Vero cells and the host cells (Fotie *et al.*, 2007). The crude extract of *G. lucida* displayed significant activity against *T. b. brucei* (IC_{50} 4.9 μg/mL) with no toxicity on the Vero cell. The isolated compounds, the dihydrochelerythrine derivatives **(48-50)** exhibited interesting activity, with IC_{50}

values in the range 0.8–14.1 μM. Dihydrochelerythrine **(48)** was the most potent compound (IC_{50} 0.8 μM), with more than 44-fold selectivity for *T. b. brucei* parasites over Vero cells (Fotie *et al.*, 2007). When tested on promastigote *L. donovani*, the crude extract (100 μg/mL) and compounds 48-50 (100 μM) were able to clear the parasites (100% inhibition), whereas at 10 μM, these compounds achieved about 89, 87, and 76% inhibition, respectively.