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AFRICAN MISTLETOES (LORANTHACEAE); ETHNOPHARMACOLOGY, CHEMISTRY AND MEDICINAL VALUES: AN UPDATE

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Abstract

Mistletoes of the Loranthaceae and Viscaceae are hemiparasitic plants and their preparations in the form of injectable extracts, infusions, tinctures, fluid extracts or tea bags are widely used in various cultures in almost every continent to treat or manage various health problems including hypertension, *diabetes mellitus*, inflammatory conditions, irregular menstruations, menopause, epilepsy, arthritis, cancer, etc. The medicinal values of some species of Mistletoes (Loranthaceae) growing in the West African sub-region have been reviewed along with some considerations of their chemistries and local uses. These have been compared with Mistletoes (Loranthaceae and Viscaceae) growing elsewhere in Europe and Asia. This review has attempted to update our knowledge on the values of these hemi-parasites which belong to the genera – *Globimetula, Phragmanthera, Agelanthus* and *Tapinanthus*, and which have, for years, been seen as only devastating and notorious plants. They are also seen as epiphyting economic, ornamental and medicinal plants. The hemi-parasitic plants (Mistletoes) are not well understood as very little is known about their biology (taxonomy, host/plant relationship, ecology, toxicology, physiological characteristics, etc.) and chemistry (chemical constituents' profile). Some pharmacological studies carried out on the various crude alcoholic extracts and purified fractions have, however, revealed that mistletoes showed hypotensive, hypoglycaemic, antilipidaemic, anti-oxidative, anti-inflammatory, antimicrobial, etc. effects and were non-toxic in experimental animals at the doses used. The findings showed that mistletoes can be very useful as medicinal agents in ameliorating health problems such as *diabetes mellitus*, hypertension, arthritis, pain, cancer and a host of other ailments if properly studied and developed.

Key Words: Mistletoes, Loranthaceae, Viscaceae, Botany, Ethnopharmacology, Chemistry, Pharmacological Effects, Medicinal values

Introduction

Mistletoe, with the common name(s) – bird lime, all heal, devil's fuge, Iscador, etc. – is a general term for woody shoot parasites in several plant families especially Loranthaceae and Viscaceae (Burkill, 1985, Parker and Riches, 1993, Polhill and Wiens, 1998) and most genera of African mistletoes belong to the family Loranthaceae (Polhill and Wiens, 1998).

Seven genera of the Loranthaceae – *Helixanthera, Berhautia, Englerina, Globimetula, Agelanthus, Tapinanthus* and *Phragmanthera* – with about five dozens or more species are recognised in West Africa (Burkill, 1985) and the group term mistletoe is used for all these species. Besides, the host plant is considered as important as the mistletoe since distinction is made between hosts and not between mistletoes, implying that the biology of the Loranthaceae species is not clearly understood. This has implications on the medicinal use of the plant species in the Loranthaceae.

In West Africa, mistletoes are found on many tree crops of economic importance including the shea butter tree (*Vitellaria paradoxa* Gaertn. f.), the neem tree (*Azadirachta indica* L.), citrus species, especially sweet orange (*Citrus sinensis* L.) and grape (*Citrus paradisi* L.), cocoa (*Theobroma cacao* L.) and rubber (*Hevea brasiliensis* Muell Arg) (Bright and Okusanya, 1998; Overfield et al., 1998; Gill and Onyibe, 1990; Begho et al., 2007). Various species of these hemi-parasitic plants growing on other economic, medicinal and cultivated trees such as the hog-plum (*Spondias monbin* L.), the brimstone tree (*Morinda lucida* Benth). the African Rauwolfia (*Rauwolfia vomitoria* Afzel), the kola-nut tree (*Cola nitida* Vent. Schot and Endl.), the sand paper tree (*Ficus exasperata* Vahl), teak (*Tectonia grandis* L. f.), the bread fruit tree (*Artocarpus utilis* Parkinson), forest trees such as *Terminalia glaucescens* Planch ex Benth, *Ficus mucuso* (Welw.) ex Fichalo, etc. have also been found. These findings seem to lend credence and support to the Yoruba adage which sees the Mistletoes as having no roots but that they (mistletoes) are related to all tree hosts.

The typical farmer or gardener sees mistletoes as notorious and devastating parasites which pose serious losses to economically-valuable fruit trees like cocoa, rubber, kola-nut, and medicinal plants like *Morinda lucida* and *Rauwolfia vomitoria* whether growing in wild forests, gardens or orchards (Sridhar and Rao, 1978, Zewdie and Eshetu, 1993, Bright and Okusanya, 1998, Overfield et al., 1998 and Jiofack et al., 2010). Very often, host trees that have lots of mistletoes suffer from

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them as the triumph of mistletoes lead to poor growth and productivity and eventual death of such host plants, especially during unfavourable weather conditions and if the host plant is merely a shrub or a small tree.

The problem of correct identification is perhaps a thorny issue as these hemi-parasitic plants are easily affected by weather and ecological factors. The common practice is the use of a group term 'mistletoe' for all these plants just as the Yoruba, for example, refer to them whether they are semi-woody, green, brown, perennial or bushy as '*afomo onisana*,' because the flowers resemble a match stick, sometimes yellow-flowered with red or purple corolla tips such as in *P.capitata* or purple-flowered with yellow corolla tips as in some other mistletoes.

The information here sets to appraise the medicinal values of some species of *Globimetula, Phragmanthera, Agelanthus* and *Tapinanthus (Loranthaceae)* in the West African sub-region, and this is based on the information available in the literature on the subject.

Biology

Spread of Mistletoes

It is widely accepted that the spread of mistletoe species is by seed dispersal and these are usually mediated by birds that thrive on mistletoe fruit or host through faecal excretions or regurgitations (Burkill, 1985, Karunaichamy et al., 1999). In Southern India, Tickel's Flowerpecker, also called the Pale-billed flower pecker, was reported to facilitate seed dispersal of *Dendrophtoe falcata* among neem (Hambali, 1977). This view was corroborated by Weston et al. (2012) who recently studied the dependence on Sunbird pollination for fruit set in three West African montane mistletoe species, *Globimetula braunii, Agelanthus brunneus* and *A. djurensi*s growing in Ngel Nyaki Forest Reserve in Nigeria. Weston and his collaborators observed that all the three mistletoes were self compatible but not capable of autonomous self fertilisation. They noted that the pollination assemblage comprised four species of Sunbirds, *Cyanomitris spp*, *Cinnyris* spp and small social Wasp (Vespinae), and also that whereas none of the mistletoes required birds for flower opening, each mistletoe species required Sunbirds for effective pollination and fruit set.

The above findings and views are supported by the presence of the same species of mistletoe growing on different hosts within the same vicinity. We have identified four different hosts – *Cola nitida, Theobroma cacao, Spondias monbin,* and *Rauwolvia vomitoria* for *Globimetula cupulata* – within the same vicinity and also the occurrence of the same species of mistletoe on the different aerial parts of the same host. We have found and counted about twenty five stands of the mistletoe *Agelanthus brunneus* (syn. *Tapinanthus brunneus*) on a host, *Citrus paradisi* located in Obafemi Awolowo University Teaching and Research Farm Citrus plantation (OAU T&R FARM). That *Tapinanthus bangwensis* had been found on 43 different hosts in 18 plant families (Burkill, 1985) and that *Dendrophthoe falcata* (L. f) Ettingsh (Loranthaceae), the most common of all the mistletoes that occur in India, has about 401 plant hosts and possesses remarkable potentials as a medicinal plant (Pattanayak and Sunita, 2008) showed that some species of the mistletoe may not be selective in the choice of hosts, while other species seem to be restricted to particular hosts, particularly fruit-bearing plants. Otherwise it would appear difficult to explain why the mistletoe, *Agelanthus brunneus,* could be found on only two (one sample each) out of the seven or more stands of *Citrus limon* located in the OAU T&R FARM. An example of this was observed earlier; *Tapinanthus globiferus* was found to parasitise 17 different ornamental, woody and orchard trees in the Middle Awash Valley in Ethiopia while another parasitic plant, *Odontella schimperi*, was found only on two species of trees *Casuarina equistifolia* and *Dobera glabra* (Zewdie and Eshetu, 1993).

Host/plant relationship

These hemi-parasitic plants have caused the host plants many biological effects, chief among which is salt imbalance. A formulated hypothesis is that these hemi-parasites (Loranthaceae) would contribute to decrease the salt content in parasitized host boughs particularly those bearing fruits (Dibong et al., 2010). To verify this hypothesis, the authors studied and assessed the response of five host species *(Citrus maxima, Manikara zapota, Persia Americana, Psidium guajava* and *Theobroma cacao*) of the hemi-parasite *Phragmanthera capitata* to sodium and potassium distribution in the plant tissues. They found that *P. capitata* reduces the Na^+ concentrations in the aerial parts of infected host trees and maintain the salt level low in photosynthetic organs. High concentrations of K^+ were observed in the leaves of the non infected host branches of three hosts, *Citrus maxima, Manikara zapota* and *Psidium guajava.* On the other hand, the parasite leaves of *Theobroma cacao* had the higher concentrations of K^+ than those of host roots, leaves of non-parasite host branches, the parasitized leaves of the host and the parasite suckers. The authors (Dibong et al., 2010) concluded that Loranthaceae could contribute to decrease the content of salt on parasitized host boughs and then on branches bearing fruits. This phenomenon could explain why the quality of fruits in fruit-bearing plant hosts should decline due to the parasitism of Loranthaceae.

Ethnopharmacology

The ethnomedicinal uses of mistletoes had, for a very long time, been in the hands of very few herbal practitioners who claimed a general use to counter sorcery and magical powers, to treat mental conditions, sterility, and health problems associated with urino-genital system, rheumatism and pain. These hemi-parasitic plants, mistletoes of the Loranthaceae and Viscaceae, are widely used in various cultures in almost every continent to treat various ailments including hypertension, cancer, and diabetes, or used as a diuretic agent (Burkill, 1985; Adodo, 2004; and Jadhav et al., 2010). For example, the tea

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made from Loranthaceae spp. is believed to cure bone fracture and body pain (Ken'ichi, M. et al., 2006). Remedies for tumour (*Tanachaa*) in Southwestern Ethiopia were reported to be prepared by crushing fresh leaves of *Tapinanthus globiferus* (A.Rich.) Tiegh. and mixed with cold water to be administered orally (Yineger and Yewhalaw, 2007). Also in the Ebolowa region of Cameroon, one handful of the fresh leaves of *Tapinanthus globiferus* is usually mixed with one handful of the root bark of *Boswella odorata*, the ingredients are macerated in 5L of local beer and one glassful is taken twice a day for two weeks to cure syphilis (Noumi and Eloumou, 2011). In Saudi Arabia, fresh stems of *Tapinanthus globiferus* (local name, *Hadhal*) are given orally to all types of livestock for the treatment of fever and removal of placenta after parturition (Sher and Alyemeni, 2011).

Various preparations of *Viscum album* (as injectable mistletoe extracts) are already articles of commerce and are sold across Europe with the labels of *Helixor, Iscador, Abnobaviscum* and as fermented *V. album* (Matthes et al., 2005, Urech et al., 2005 and Kienle and Kiene, 2007), and are used to treat epilepsy, infertility, hypertension and arthritis. Powdered leaves of a mistletoe (or mistletoes also identified as *Viscum album*!) and purportedly sourced off cocoa, avocado and citrus - a product of Natural Health Product Services Limited, are sold across Southern Nigeria under the trade name *'NAHEPS' Mistletoe Tea*. *NAHEPS* claims that the tea is traditionally used to promote good health as it enhances natural body immunity.

Mistletoes are now known as "cure all" and have been found beneficial as a drug/remedy for more than twenty health problems (Adodo, 2004). It is usual to prepare the leaves of a single species of mistletoe alone in medicine but more often, the leaves of two or more species of mistletoes which are thought to be the same but are only differentiated by the nature of their hosts are harvested and processed for use together. This is because the efficacy of drug preparations produced are thought to be dependent on the host plant(s) and that mistletoes harvested on certain hosts are suited for the treatment or cure of a particular health problem.

The biology of the Loranthaceae remains largely unclear. The relationships between Loranthaceae and their hosts have been a subject for study in the past and will continue to be for the lesser-known African mistletoes particularly. The sucker ensures the continuity of the major elements, Na^+, K^+, Ca^{2+}, Mg^{2+} etc., of the two plants and enables the diversion of water and nutritive substances from the plant to the parasite (Bannister et al., 2002). Apart from minerals, organic acids and pigments, how much of the host plant constituents may be transported to the mistletoe and vice versa? It was once observed, for instance, that medicinal properties of *Dendrophthoe falcata* may vary in effects respective to different hosts it establishes a relation with (Mallavadhani et al., 2006). Wang et al. (2008) reported that *Taxillus spp* Loranthaceae exhibited potent inhibition on fatty acid synthase and that the difference in host plants did not affect markedly on the inhibitory ability of the parasite. In practical terms, herb sellers and herbalists have always recommended mistletoes harvested on particular hosts in the management or treatment of certain health problems (Adodo, 2004; Burkill, 1985). This may not have a scientific backing as constituents of *Korthalsella japonica* did not change or disappear irrespective of its host trees (Fukunaga et al., 1989).

A recent ethnopharmacological study (Dibong et al., 2009) carried out on the hemi-parasites growing in Cameroon sought information on the biology, ecology and the medicinal uses of the Loranthaceae. The authors used a structured questionnaire to interview 150 active traditional healers and reported that the herbalists recognised the existence of only one species which they later identified as *Phragmanthera capitata*. (This species, the authors identified as "cancer" in the French language). The authors also reported that 82% of the healers recommended *P. capitata* for the treatment of some 22 different diseases, including hypertension, hypotension, irregular menstruations, menopause, convulsions, diabetes, rheumatism related pains, epilepsy, kidney and chronic muscular pains. Fresh leaves are usually used in infusion or macerated, and the dosage is not usually standardised. It is noteworthy from available reports that the uses of *P. capitata* were similar to those reported for European mistletoes, particularly *Viscum album* and that the Loranthaceae is generally recognised in ethnomedicine.

The Chemistry of the Mistletoes

Not much information is readily available on the chemistry of many African mistletoes. The two chemical information readily available include (1), the structural identification of a polysaccharide in *Phragmanthera capitata* leaf cell wall and (2), the isolation, purification and the study of metabolic activities of a peptide from the fresh leaves of *Phragmanthera incana* . Apart from the above chemical reports, the information given in Table 1 below on the Loranthaceae and the Viscaceae relates to some information available in the literature for *Viscum album* and other European and Asian mistletoes.

The most distinctive constituents of most European and Asian mistletoes are proteins, the viscotoxins, lectins and carbohydrates. The small molecular weight compounds include flavonoids and phenylpropanoids of varying structural types, and they contribute to the anti-oxidative properties of the various Loranthaceae extracts examined. There have been two reports listed here of a peptide and a carbohydrate from the genus *Phragmamthera* in the African Loranthaceae. Many reports of the presence of smaller molecular weight compounds, alkaloids, flavonoids, tannins and other plant constituents in the African Loranthaceae have not been substantiated by isolation and proper identification. There is, therefore, a lot more to be done to fully appreciate the chemical constituents' profile of the African mistletoes.

Pharmacological Effects of Mistletoe Extracts

The biological effects of the extracts of *Viscum album* and other mistletoes and their influence on quality of life in cancer patients are well known (see Table 2). Wang et al. (2008) found that the reversible inhibitory ability of the extracts

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from *Taxillus chinensis* (DC) Dancer Loranthaceae was nearly 400-fold stronger than that from the Viscaceae and that the medicinal herb with high inhibitory ability on fatty acid synthase (FAS) significantly reduced the body weight and food intake of mice by oral administration. The medicinal herbs from the family Loranthaceae were thus found suitable as botanical sources of parasitic loranthus for weight control and that herbs from the genus *Taxillus* Tieghem were the best in both reversible and irreversible inhibition.

Table 1: The Chemistry of Mistletoes

Plant	Active constituents	Parts used	References
Phragmanthera capitata	Pectin and hemicellulosic polysaccharides	Leaf	Aboughe Angone et al., 2009
Phragmanthera incana	Phragmanthin	Fresh leaf	Fasanu and Oyedapo, 2008
Viscum album	Glycoproteins; mistletoe lectins I, II, and III, proteins; viscotoxins and polysaccharides; galacturonan, arabinogalactan	Leaf	Obata, 1941 Samuelsson and Pettersson, 1971 Schaller et al.,1998 Margaret Loeper, 1999 Deliorman et al., 2000
V .articulatum and *Helianthus elastica* (Ders.)	Triterpenoids and polyphenolics	Leaf	Jadhav et al., 2010
V. angulatum	Phenolic glycosides (pinocembrin 7-O-apiosyl(1→5) apiosyl(1→2)-ß-D-glucopyranoside, 2´,3´,4´,3´-tetramethoxy-1,3-diphenylpropane 5´,4´-di-O-ß-D-glucopyranoside and rhamnocitrin 3-O-apiosyl(1→5) apiosyl(1→2)-[α-L-rhamnopyranosyl(1→6)]-ß-D-glucopyranoside). Viscumneoside, naringenin and homoeriodictyol	Leaf	Lin et al., 2002
Loranthus tanakae Fr. Et Sav.	Four anti-tumour flavonoid rhamnopyranosides identified as rhamnetin 3-O-α-L-rhamnoside, quercetin 3-O-α-L-rhamnoside, rhamnocitrin 3-O-α-L-rhamnoside and kaempferol 3-O-α-L-rhamnoside.	Leaf	Kim et al., 2004
Scurrula ferruginea Danser .	Three cyto-toxic natural flavonols-quercetin, quercitrin and 4″-O-acetyl-quercitrin	Leaf	Lohézic-Le Dévéhat et al., 2002
Taxillus yadoriki Danser,	Hyperin and quercitrin with fatty acids, phytosterol and phytosterol glucoside.	Leaf	Fukunaga et al., 1989
Taxillus kaempferi Danser	Fatty acids, phytosterol, phytosterolglucoside, quercetin, avicularin and taxillusin; also quercitrin and hyperin	Leaf	Fukunaga et al., 1989
Korthalsella japonica Engler	Chrisoeriol-4´-O-glucoside, fatty acids, phytosterol, oleanolic acid and phytosterolglucoside. Chrysoeriol-4´-O-glucoside was a common constituent of this mistletoe irrespective of the host.	Leaf	Fukunaga et al., 1989
Dendrophthoe falcate (L. f) Ettingsh (Loranthaceae)	Three new triterpenes -(3ß-acetoxy-1ß-(2-hydroxy-2-propoxy)-11α-hydroxy-olean-12-ene (1), 3ß-acetoxy-11α-ethoxy-1ß-hydroxy-olean-12-ene (2), and 3ß-	Leaf	Mallavadhari, 2006 Pattanayak et al., 2008, 2012,

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	acetoxy-1ß-hydroxy-11α-methoxy-0lean-12-ene), five known triterpenes,two flavonols and gallic acid were reported.		

Metabolic studies of *Phragmanthin* isolated from *Phragmanthera incana* (Loranthaceae) in Sprague-Dawley rats showed that it caused significant reduction in the levels of plasma inorganic phosphate, haemoglobin, activities of L-alanine aminotransferase and alkaline phosphatase, muscle glycogen and blood sugar. It also exhibited a slight elevation of the levels of plasma L-aspartate amino-transferase activity and creatinine (Fasanu and Oyedapo, 2008).These pharmacological effects and other biological assets of mistletoe extracts are summarised in the Table 2 below:

Table 2: Pharmacological Effects of Mistletoe Extracts

PLANTS	PARTS USED	PHARMACOLOGICAL USES	REFERENCES
Viscum album	Leaf	Anti-cancer	Zee-Cheng, 1997; Mahfouz et al., 1998; Mengs et al., 2002; Cebović et al., 2008; Kienle et al., 2009; Kienle and Kiene, 2007, 2010
	Leaf	Anti-diabetic and hypotensive	Lutomski, 1986, Swanson-Flatt et al, 1989; Adsersen and Adsersen, 1997, Gray and Flatt, 1999 and Orhan et al, 2005.
Taxillus chinensis	Leaf	Herb with high inhibitory ability on fatty acid synthase (FAS)	Wang et al., (2008)
Phragmanthera incana.	Leaf	Leaf extract exhibited a slight elevation of the levels of plasma L-aspartate amino-transferase activity and creatinine. Phragmanthin caused a reduction in the levels of plasma inorganic phosphatase, haemoglobin, muscle glycogen and blood sugar.	Fasanu and Oyedapo, 2008
Globimetula braunii	Leaf	Oxytocic properties: Leaf extract showed oxytocic properties compared with that of a standard uterine stimulant oxytocin and uterine smooth muscle antagonists, atropine and salbutamol	Le and Zam, 2008
Globimetula braunii	Leaf	Laxative properties: Fresh leaf extract of the plant exhibited laxative properties compared with a reference substance (Senna)	Fred-Jaiyesimi et al., 2008
Globimetula braunii	Leaf	Anti-oxidative Properties: Ethyl acetate fraction caused a significant increase ($p< 0.05$) in the activities of superoxide dismutase, catalase, glutathione peroxidase and malonydialdehyde (MDA) levels, while the level of triacylglycerol decreased ($p < 0.05$) compared to control.	Okpuzor et al., 2009
Globimetula cupulatum	Leaf	*Globimetula cupulatum* was reported to have the highest hydroxyl radical scavenging activity of $63.84 \pm 0.97\%$ in a screening process. The extracts demonstrated high lipid peroxidation inhibitory activity and possessed significant antioxidant and radical scavenging activities.	Akinmoladun et al., 2010
Globimetula cupulata	Leaf	Hypoglycaemic properties: The authors concluded that their result supported the traditional use of the leaf of the plant in the	Ojewole and Adewole, 2007

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	Leaf Leaf	management of *diabetes mellitus* when compared with streptozotocin and metformin as reference drugs. Hypoglycaemic properties. Histopathological studies showed a restorative effect of the extract on pancreatic islet cells. *G. cupulata* was listed as an anti-hypertensive and hypoglycaemic plant	Edem, 2009 Talha et al, 2011.
Tapinanthus bagwensis	Leaf Leaf	Anti-diabetic properties Anti-inflammatory Properties: The authors found that the extract from the butanol fraction possessed anti-inflammatory effects in experimental animals	Ekhaise et al, 2011 Patrick-Iwuanyanwu et al., 2010
Tapinanthus sessilifolius	Leaf	Antimalarial Activities: Leaf methanol extracts of *Tapinanthus sessifolius* showed a mild to weak antiplasmodial activity in the *in vitro* assay while it had intrinsic antimalarial properties that were doe dependent *in vivo*)	Okpako and Ajaiyeoba, 2004
Tapinanthus dodoneifolius	Leaf	Antimicrobial Properties; the authors found a wide spectra of antimicrobial activities against certain multiple drug resistant bacterial and fungal isolates of farm animals including the inhibition of the growth of *Bacillus* sp.. *Agrobacterium tumefaciens, Escherichia coli, Salmonella* sp., *Proteus* sp., and *Pseudomonas sp*	Deeni and Sadiq, 2002
Tapinanthus globiferus	Leaf Leaf	Anti-oxidant activities Antimicrobial activities; the authors found that the crude methanolic and chloroform extracts had growth inhibitory effects on *B. aureus, P. stautii, E. coli, P. aeruginosa, S. aureus* and *K. pneumonia* but did not inhibit the growth of *S. typhi, A. niger* and *C. albicans*. The authors also found the methanol extract bacteristatic and bactericidal, it also compared well with standard drugs, gentamycin and rifanpicin used as reference drugs in the study.	Cook et al, 1998 Ndukwe et al., 2001
Globimetula braunii	Leaf	Lipid Lowering Activities**:** The authors concluded that the results obtained indicated antilipemic and hypocholesteremic activities of *G. braunii*, indicative of possible cardio-protective potential in normo and hypercholesteremia situations.	Erukainure et al., 2010
Tapinanthus globiferus	Leaf	The authors concluded that the leaf extract lowered total cholesterol, LDL-cholesterol and triglycerides, and suggested its use in the management of hypertension.	Akanji et al., 2009

Toxicological studies on Mistletoe Leaf Extracts

Mistletoes are generally considered to be toxic probably because some of their constituents such as lectins are cytotoxic to certain organisms. Crude mistletoe fruit or herb is used to make tea to treat hypertension at a dosage of 10g/day (*Drugs.com*). Toxicity could be a function of the specie of mistletoe; whereas the fruit of *D. falcata* tasted sweet and was consumed as food (Mallavadhani et al., 2006), the fruits of most African mistletoe were described as toxic berries (Adodo, 2004) which could lead to vomiting, hypotension, cerebral dysfunctions and death by a heart attack if ingested in large numbers (Dibong et al., 2009). The results of the various feeding experiments as well as the toxicity tests carried out suggest that the crude mistletoe leaf extracts were non-toxic to laboratory animals.

Okpuzor et al. (2009) investigated the safety of *Globimetula braunii* leaf extracts in rats. It was evaluated for possible hepatic and haematological effects. The rats were fed with various extracts of the plant at a dose of 200 mg/kg body weight for 14 days. They observed significant increases ($p \leq 0.05$) in packed cell volume (PCV) and haemoglobin (Hb) in the rats treated with $CHCl_3$, EtOAc and Water fractions. The red blood cell (RBC) count increased ($p < 0.05$) after the administration of $CHCl_3$ and EtOAc fractions, while white blood cell (WBC) count increased ($p < 0.05$) in the crude and all its fractions except BuOH.

Liver function enzymes were also assessed. Significant decreases ($p < 0.05$) in the activities of aspartate amino transferase (AST) and alanine amino transaminase (ALT) enzymes were observed in rats treated with $CHCl_3$ fraction, while there was elevation in the activity of ALT in the BuOH group. Though they recorded no difference ($p > 0.05$) in enzyme activities in the MeOH fraction, the administration of other fractions to the rats, led to increases ($p < 0.05$) in the activities of both enzymes. Total and direct bilirubin showed increases ($p < 0.05$) in EtOAc and hexane fractions, while only direct bilirubin increased ($p < 0.05$) in the crude fraction. They concluded that *G.braunii* $CHCl_3$ fraction had an influence on haematological functions and liver enzyme levels in rats.

In another study, the crude MeOH extracts of *Tapinanthus bangwensis* and its various fractions were evaluated for their hepatoprotective potential against CCl_4-induced hepato-toxicity in Wistar albino rats (Patrick-Iwuanyanwu et al., 2010). The activities of the marker enzymes, ALT, AST and ALP and bilirubin were highest in rats treated with CCl_4 alone. The administration of the extract (400mg/kg BW) for 7 days, significantly ($p \leq 0.05$) decreased the activity of marker enzymes and bilirubin. Total protein concentration increased significantly ($p \leq 0.05$). These extracts also decreased the concentration of thiobarbituric acid reactive substances (TBARS) which indicated a reduction in lipid peroxidation. Histopathological examination of hepatocytes of rats that received the extracts showed normal architecture, whereas rats treated with CCl_4 alone were characterised by necrosis of the liver. The crude MeOH extract did not show any mortality even at a dose of 2000mg/kg BW. They concluded that the title plant possessed strong anti-oxidant properties and hepatoprotective potentials against CCl_4-induced hepatotoxicity in rats

Conclusion

Mistletoes possess many ethnomedicinal assets. The importance of the mistletoes in ethnopharmacology is now well known and this is supported by the scientific information recorded in the pharmacological studies of some of the crude or purified extracts. In addition to the above, it is now appreciated that mistletoes are therapeutically useful in oxidative stress induced health problems, are potential sources of natural anti-oxidants, and have great potentials as medicinal agents.

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