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Toxicity studies of medicinal plants used in sub-Saharan Africa

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ABSTRACT

In sub-Saharan Africa, traditional medicine is widely used in rural and urban areas also. This is essentially due to the prohibitive cost of pharmaceutical-based medicine and the low incomes of a major part of the population. In addition, the efficacies of many of these traditional and plant-based medicines are proven, but the fact remains that certain plants used in traditional medicine have toxic effects. It is in this perspective that we investigated by bibliographic literature on the toxicity of plants used in traditional medicine. It is crucial to gain knowledge on these plant-based medicines prepared and prescribed by practitioners, particularly in terms of toxicity, composition, specific efficacy of disease and to advise practitioners of this alternative medicine on the protection and security of patients.

1. Introduction

The use of plants is as old as human kind itself. It has always been part of human culture. In Africa, for example, plants are used in traditional medicine to treat different infectious and non-infectious diseases (Diallo et al., 2003; Gurib-Fakim, 2006). These treatments include body-washes, massages, ingestions, *etc.* (Walker and Sillans, 1961). Plants provide a wide variety of biochemicals useful to mankind. Their uses include food, colors, fragrances and agricultural chemicals and pharmaceuticals. According to the World Health Organization (WHO), about 40–90% of people living in developing countries frequently use traditional medicine (van Andel and Carvalheiro, 2013). This situation is the consequence of a limited access to modern health services and also researchers explained the high prevalence of traditional medicine use by massive rural-to-urban migration, the influence of cultural and social surroundings, and the belief that natural products pose no risk (van Andel and Carvalheiro, 2013; Lins Brandão et al., 2006; Bussmann et al., 2007; Oreagba et al., 2011). Though the use of medicinal plants can have deleterious effects on health as reported elsewhere (Fall et al., 2011). Indeed, of about 1,500,000 plants investigated, most of them contain toxic substances (Ishii et al., 1984) like some secondary metabolites. Plants produce a variety of secondary metabolites that are sub-divided by chemists into several classes based on their molecular structure. Among secondary metabolites are saponins, terpenoids, cyanogenic, tannins, toxic amino acids, glycosides, alkaloids (Dai and Mumper, 2010). It has been shown that the toxicity of a given plant depends on various factors, including the strength of secondary metabolites, the quantity consumed, the time of exposure, different parts of the plant (root, oil, leaves, stem bark and seeds), individual body chemistry, climate and soil, and genetic differences within the species (Tülay, 2012). This said it clearly appears that medicinal plants should be used with precautions and toxicology studies conducted to increase the knowledge on the plant or plants preparation given to populations.

For this purpose, *in-vitro* and *in-vivo* models are available to study the toxicity of medicinal plants. Regardless of the type of extract, the parts of plant used, the concentration of the extract, the mode of administration, and the organism under consideration the lethal dose 50 (LD_{50}) who represent the dose who kill 50% of a tested population is used to appreciate the toxicity of the plant (Amy et al., 2002). In addition, for chronic or sub-chronic toxicity histological or genetic modifications are the most relevant indicators.

In this paper, we aimed to review, on the basis of 9 studies, medicinal plant extract induced cellular or organ dysfunction (Table 1) and to show the importance of toxicity studies.

1.1. Hemolytic effect

Chrysophyllum pruniforme (synonym: *Donella pruniformis*) (Pierre ex Engl.) is a tall tree who belongs to the family of Sapotaceae. This plant is widely spread out from West to East Africa and Central Africa. In Gabon and Congo, *C. pruniforme's* bark infusion is used to treat coughs. Phytochemical studies showed that it contains reducing sugars, phenolic compounds, flavonoids,

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Table 1
Recapitulative table of plants and their toxicity.

Plant scientific name	Family name	Botanical description	Parts used	Adverse effect	Model of experimentation	References
Chrysophyllum pruniforme (Pierre ex Engl.)	Sapotaceae	Tall tropical tree growing to 10–20 m or more in height. The leaves are oval, 3–15 cm long, green above, densely golden pubescent below.	Barks	Hemolytic	Human blood samples	Aboughe et al., 2013
Semecarpus anacardium Linn.	Anacardiceae	Medium-to-large size tree, 15–25 m in height with gray bark exuding an irritant secretion on incising and exfoliating in small irregular flakes. Leaves are simple alternate, obviate – oblong, 30–60 cm long and 12–30 cm broad, rounded at the apex coriaceous glabrous above and more or less pubescent, beneath.	Leaves	Neurotoxic	Intraperitoneal administration on mice	Chaudhary et al., 2010
Quassia amara L. Radlk.	Simaroubaceae	Small tropical tree, growing only 2–6 m in height. It has beautiful red flowers and fruits that turn red as they mature.	Stem bark	Spermatotoxic	Oral administration of rats	Obembe and Raji, 2012
Artemisia maciverae Linn.	Asteraceae	Small herbaceous.	Whole plant	Nephrotoxic	Intraperitoneal administration on *Swiss albinos* rats	Atawodi et al., 2013
Nerium oleander L.	Apocynaceae	An evergreen shrub reaching 4 m in height. Leaves are 10–22 cm long, narrow, untoothed and short-stalked, dark or gray-green, white or yellow. All leaves have a prominent mid rib, are leathery in texture and usually arise in groups of three from the stem.	Leaves	Toxic for lung and heart	Oral administration on mice	Ali Hussien, 2010
Aphania senegalensis (Juss. Ex Poir.)	Sapindaceae	A forest tree to 55 ft high, with short bole and dense drooping foliage. The flowers are greenish-white and fragrant. The ripe fruits are red and edible.	Leaves	Hepatotoxic	Oral administration on *Wistar* rats	Fall et al., 2011
Cupressus sempervirens L.	Cupressaceae	A medium-sized coniferous evergreen tree to 35 m tall, with a conic crown. The foliage grows in dense sprays, dark green in color. The leaves are scale-like, 2–5 mm long, and produced on rounded (not flattened) shoots.	Leaves	Toxic for spleen	Intraperitoneal administration on mice	Nusaibah, 2012.
Herniaria cinerea DC.	Caryophyllaceae	A yellowish green, prostrate, hairy, spreading herb. Stem and branches with 3–9 mm long internodes, with short spreading hairs. Leaves are opposite, sessile, hirsute, blade narrow elliptic to lanceolate or oblanceolate, usually 4–7 mm long and 1.5–2.3 mm wide, acute, margins entire with straight spreading hairs.	Whole plant	Toxic for gastrointestinal tract	Oral administration on *Wistar* rats	Sokar et al., 2003
Inula viscosa L. Aiton.	Asteraceae	Small shrub. The stem is dark brown. The leaves have an elongated lanceolate shape with a pointed tip. The larger leaves measure about 70 mm × 18 mm.	Leaves	Genotoxic	On *Alium cepa*	Tulay and Ozlem, 2010

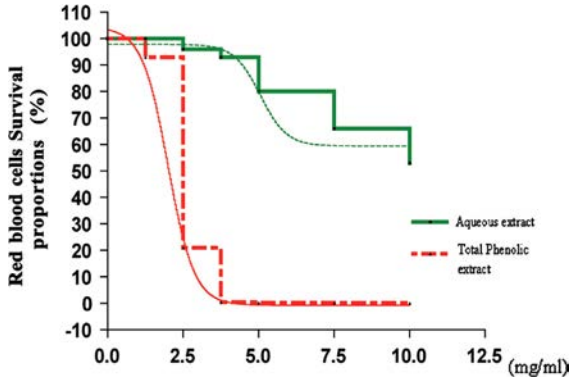

Fig. 1. Hemolytic activity of aqueous and phenolic extracts on human erythrocytes (Aboughe et al., 2013).

saponins, and catechic tannins (Aboughe et al., 2013). In this study the author shows that *in vivo* studies, the LD_{50} was 90 mg/kg in mice by oral administration of the aqueous extract, what according to the scale of toxicity of Hodge ant Sterner classifies it among the moderately toxic ones. In addition, aqueous and total phenolic extract of *C. pruniforme* show a hemolytic effect on human erythrocytes obtained from healthy donors. At the end of the experimentation, the aqueous extract showed hemolytic activities about 0%, 3%, 7%, 20%, 33%, and 47% in 1.25; 2.5; 3.75; 5; 7.5; and 10 mg/mL, respectively. At the same time total phenolic extract showed hemolytic activities about 7%, 79%, 99.6%, 99.9%, and 100% for the same plant concentrations. The hemolytic activity of total phenolic extracts was significantly higher compared to the one of aqueous extracts (Fig. 1) (Aboughe et al., 2013). Hemolytic activity is an indicator of general cytotoxicity towards normal, healthy cells (Da Silva et al., 2004).

1.1.1. Hepatotoxic effect

Aphania senegalensis (Juss. Ex Poir.) (Sapindaceae) is a medicinal plant widely used in Senegal in folk medicine. But, this tree can be found in several other African countries and in Asia. A phytochemical screening of leaves revealed that, they contain flavonoids, tannins and saponins (Faye, 2008). Its pharmacological activity was described mainly for the leaves and relied on anti-parasitical, analgesic and anti-inflammatory activities (Fall et al., 2009). Tests of acute and sub-acute toxicity were carried out in male and female *Wistar* rats. The LD_{50} could not be determinate because of no deaths or observable clinical signs occurred after acute oral administration of a dose of 5.000 mg/kg. For sub-acute toxicity was carried out for a 28-day period with the administration of increasing doses of 500, 1000 and 2000 mg/kg of aqueous extract of plants. Biochemical analyses revealed a significant increase in aminotransferase activity. Levels of aminotransferase in treated animals were found to be twice higher than normal values. Further histological examination of liver of treated animals confirmed the existence of various liver lesions like degenerated hepatocytes with pyknotic nuclei, congestion, the central veins and the surrounding sinusoids in some lobules were filled with blood and fatty body (Fig. 2) (Fall et al., 2011), (Figs. 3 and 4).

1.1.2. Neurotoxic effect

Semecarpus anacardium Linn. Belonging to the family of Anacardiaceae is a moderate-sized deciduous tree found in found in abundance in Assam, Bihar, Bengal and Orissa, Chittagong, central