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Review Article

Anticancer activity and toxicity of decoction of *Ipomoea batatas* leaves and *Milicia excelsa* roots used in cancer

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Abstract

Medicinal plants are an integral part of the healthcare system in Africa. In traditional medicine, a mixture of Ipomoea batatas leaves and Milicia excelsa roots is used to treat cancer, mostly breast and colon cancer. It can be used on its own or with other common cancer treatments. While popular belief assumes that medicinal plants, being natural, are healthier than conventional medicines, scientific studies have shown that plants can induce serious adverse effects and influence a patient's prognosis. In order to regulate its use, a literature review of the information available on the composition, toxicity and anti-cancer properties of the decoction of Ipomoea batatas leaves and Milicia excelsa roots was carried out in December 2024. To date, there are no scientific publications on the composition, toxicity and anticancer activity of the decoction of extracts of Ipomoea batatas leaves and Milicia excelsa roots. However, the leaves of Ipomoea batatas and the roots of Milicia excelsa, taken separately, are very rich in secondary metabolites which have been shown to be effective against several types of cancer. In terms of toxicity, Ipomoea batatas leaves are best tolerated at doses of 10 to 100 mg/kg. The roots of Milicia excelsa have not been the subject of repeated-dose toxicity studies. This review of the literature revealed a lack of data, particularly in terms of safety, which prevented the formulation of recommendations concerning its use. To find out more about the safety and effectiveness of using a mixture of Ipomoea batatas leaves and Milicia excelsa roots to treat cancer, more research needs to be done.

Keywords: Anticancer activity, toxicity, *Ipomoea batatas*, *Milicia excelsa*.

Introduction

Cancer is one of the leading causes of death worldwide, and the number of cancer-related deaths is rising. In 2024, an estimated 2,001,140 new cancer cases and 611,720 cancer deaths are expected to occur in the United States. By 2050, the number of cancer cases is projected to reach 35 million, according to estimates by the American Cancer Society[1]. Various therapeutic strategies are currently used to treat cancer, including chemotherapy, immunotherapy, surgery, and radiotherapy. Despite the availability of these treatment methods, herbal medicine remains a widely used complementary approach. Medicinal plants are primarily used to reduce the adverse effects of conventional anticancer treatments and for their specific anticancer properties, which stem from their rich bioactive compound content[2]. Rather than serving as alternatives, medicinal plants are generally considered complementary to conventional anticancer drugs[3].In traditional Beninese medicine, the therapeutic arsenal against cancer consists mainly of medicinal plant extracts prepared using various techniques such as maceration, decoction, and infusion. Among these, the decoction of *Ipomoea batatas* leaves and *Milicia excelsa* roots is commonly used. It is still widely used today, either on its own or as a complement to anticancer treatment, as it is believed to be a panacea for breast and colon cancers. However, its use may contribute to adverse effects due to interactions with anticancer drugs and may also influence the patient's recovery[4]. Therefore, it is essential to optimize its use based on efficacy and safety data.

The aim of this review is to present data from the literature on the composition, toxicity, and anticancer properties of this extract, which may justify its use in the prevention and/or treatment of cancer, with the goal of regulating its use.

Materials and Methods

This is a literature review on the leaves of *Ipomoea batatas* and the roots of *Milicia excelsa*. Literature searches were conducted in December 2024 using the ScienceDirect, PubMed, Web of Science, Scopus, and Google Scholar databases with a combination of the following keywords: anticancer activity, antiproliferative, acute, subacute, or chronic toxicity, bioactive compounds, in vivo activity, in vitro activity, *Ipomoea batatas* leaves**,** *Milicia excelsa* roots. All accessible articles published in English or French up to 2024 were included.

There are currently no scientific publications on the composition, toxicity, and anticancer activity of the decoction of *Ipomoea batatas* leaf extracts and *Milicia excelsa* root extracts. However, numerous in vitro and in vivo studies have examined the various plant materials that make up this decoction.

Chemical Composition of the Different Plant Parts Used in the Preparation

The Leaves of *Ipomoea batatas*

Ipomoea batatas is a creeping plant with perennial vines and adventitious roots, belonging to the Convolvulaceae family. It is cultivated in China, sub-Saharan Africa, Indonesia, Asia, and South America[5]. The leaves of *Ipomoea batatas* are commonly used for both nutritional and medicinal purposes. They serve as a source of nutrition due to their high protein, carbohydrate, mineral, and vitamin content[6,7]. Its medicinal use is attributed to its richness in bioactive compounds that offer significant health benefits. These include phenolic compounds, flavonoids, anthocyanins, and carotenoids[8-12]. Other phytochemical compounds, such as saponins, leucoanthocyanins, tannins, alkaloids, and steroids, have also been detected in smaller quantities[13-15].

The roots of Milicia excelsa

Milicia excelsa is a plant belonging to the Moraceae family, a timber species cultivated in West, Central and East Africa, where it is sold under the trade name Iroko[16]. The roots of Milicia excelsa are used in traditional pharmacopoeia to treat various neurological, cardiovascular and joint diseases[17]. Phytochemical screening of Milicia excelsa roots identified several phenolic compounds and flavonoids[18-24].

The classes of secondary metabolites and phytochemical compounds in Ipomoea batatas leaves and Milicia excelsa roots are presented in Table 1.

Table 1: Phytochemical classes and compounds identified in various plant materials.

Plant material	Classes of secondary metabolites	Isolated bioactive compounds	Ref
Ipomoea batatas leaves	Carotenoids	Lutein, zeaxanthin, β-xanthin, 13 cis β-carotene, all-trans β-carotene, β-9 cis β-carotene	8-12
	Anthocyanins	cyanidin-3-O-(6”-p-hydroxybenzoylsophoroside)-5-O-glucoside [cy-3-O-(6”-p-hydroxybenzoylsoph)-5-O-glc], peo-3-O-(6”-phydroxybenzoylsoph)-5-O-glc, cy-3-O-(6”,6”-dicaffeoylsoph)-5- O-glc, cy-3-O-(6”-caffeoyl-6”-p-hydroxybenzoylsoph)-5-O-glc, cy-3-O-(6”-caffeoyl-6”-feruolylsoph)-5-O-glc, peo-3-O-(6”,6”- dicaffeoylsoph)-5-O-glc, peo-3-O-(6”-caffeoylsoph)-5-O-glc, peo3-O-(6”-caffeoyl-6”-p-hydroxybenzoylsoph)-5-O-glc, and peo-3- (6”-caffeoyl-6”-feruolylsoph)-5-glc)	
	Diterpene	Phytol	
	Flavonoids	Hyperoside, Kaempferol-3-O-glucoside, luteolin-7-O-glucoside, quercetin-3-O-hexoside	
	Phenolic compounds	3,4,5-tri-O-caffeoylquinic acid, 4,5-dri-O-caffeoylquinic acid, caffeic acid	
	Fatty acid	(Z)-9-Octadecenamide	
	Saponins, leucoanthocyanins, tannins and alkaloids	--	13-15
Milicia excelsa roots	Xanthonoids	Cudraxanthone I	18-24
	Flavonoids	Atalantoflavone, neocyclomorusin, 6-geranylnorartocarpetine, 2-(2,4-dihydroxyphenyl)-5-hydroxy-8,8-dimethyl-4H,8H-pyrano[2,3-f]chromen-4-one (2'-hydroxyatalantoflavone)	
	Triterpene	Betulinic acid	

Anticancer Activity of the Different Plant Parts Used in the Preparation

The leaves of Ipomoea batatas

Table 2 shows that the leaves of Ipomoea batatas are rich in secondary metabolites that, through several pharmacological pathways, either prevent or treat cancer[25]. Reactive nitrogen and oxygen species (ROS), released by inflammatory cells during carcinogenesis, can damage DNA and cause mutations[26]. Firstly, flavonoids, particularly quercetin, are natural antioxidants capable of eliminating free superoxide radicals, thereby exhibiting anti-inflammatory properties and reducing the risk of cancer[27]. In vitro and in vivo studies have demonstrated that quercetin exerts anticancer activity on leukemia cells, colon carcinoma cells, and, most notably, human breast cancer cells by inducing apoptosis in tumor cells and alternative cell death processes in epithelial cells, such as autophagy and para-apoptosis. It increases the expression of pro-apoptotic proteins, notably Bax and Bak, while decreasing the expression of Bcl-2. Additionally, it inhibits metastasis by suppressing extracellular matrix remodeling and reduces tumor promotion and progression by inhibiting matrix metalloproteinase activity[28-30].

Secondly, anthocyanins are antioxidant compounds that can neutralise free radicals, also reducing the damage caused to the genome by oxidative stress, thus preventing malignant transformation through genetic mutation[31]. The work of Yoshimoto et al. showed that caffeoylquinic acid derivatives from Ipomoea batatas leaves inhibited the reverse mutation of Salmonella typhimurium TA98 subjected to treatment targeting the mutagen Trp-P-1[32]. These results show that Ipomoea batatas leaves could protect normal human cells from DNA damage caused by free radicals thanks to their antioxidant and antimutagenic properties[32,33]. Chronic inflammation also plays an important role in the process of carcinogenesis. It results from the release of inflammatory factors from abnormal overexpression of these factors[25]. This inflammation can be inhibited by anthocyanins by suppressing the production of nitric oxide and certain pro-inflammatory cytokines such as NFκ-β, TNF-α and IL-6[34]. From a curative perspective, anthocyanins from I. batatas leaves have demonstrated an ability to induce either apoptosis or overexpression of the miR27a gene in breast, cervical and colon cancer cell lines[12,35-37]. Cyanidin-3-glucoside has shown anticancer properties in the ApcMin intestinal cancer model, and on lung tumours in the A549 nude mouse xenograft model[38]. Finally, caffeic acid, 4,5-di-Ocaffeoylquinic acid and 3,4,5-tri-O-caffeoylquinic acid are the main phenolic compounds in Ipomoea batatas leaves[39]. They neutralize free radicals and bind irreversibly to the active sites of Fe+2, rendering it inert and preventing the Fenton reaction from being completed. In combination with flavonoids and anthocyanins, they provide a strong line of defence by reducing ROS levels and DNA fragmentation while increasing cell viability[39-41]. Their curative anticancer properties derive from the synergy of several regulatory mechanisms, especially cell cycle progression, promotion, modulation of enzymatic activities, mitogen-activated protein kinase (MAPK) signalling pathway, induction of apoptosis and metastatic invasion[42-44].

The roots of Milicia excelsa

Milicia excelsa root is also rich in secondary metabolites with anti-cancer activity. Work by Kuete et al. has shown that cudraxanthone I has antiproliferative activity on 09 cancer cell lines (breast, colon, liver, leukaemia and glioblastoma) comprising various phenotypes sensitive and resistant to anticancer drugs (Table 2). The pharmacological mechanisms involved are cell cycle arrest between the G0/G1 and S phases, induction of apoptosis via activation of caspases 3/7, caspase 8, caspase 9 and disruption of mitochondrial membrane potential[18,45]. Oke-Altuntas et al. in 2016 also reported the antiproliferative effect of cudraxanthone I and neocyclomorusin on the HeLa cancer cell line[18,46].

Table 2: **Anti-cancer activities of different plant materials used in the preparation.**

Plant material	Cancer	Cell lines	Pharmacological mechanism	Ref
Ipomoea batatas leaves	Breast	MCF-7	Cell cycle arrest in G0/G1 phase, by direct inhibition of CdK4 and cyclin D1 protein expression. Induction of apoptosis from 100 µg/ml.	12,47
	Liver	ATCC-HB-8065	Inhibition of tumour proliferation	48
	Uterine cervix	HeLa ATCC-CCL-2	Induction of apoptosis Cell cycle arrest	12,48
	Lung	ATCC-CCL-185	Inhibition of tumour proliferation	38, 48
	Colorectal	SNU-C-1 DLD-1 HCT-116	Cell cycle arrest in G0/G1 phase Induction of apoptosis	46-49

	Stomach	SNU-1 Kato III	Induction of apoptosis Fragmentation of genomic DNA	47,49
	Prostate gland	LNCaP, DU145, PC-3, C4-2, C4-2B	Induction of apoptosis Cell cycle arrest	50
	Pancreas	PANC-1	Induction of apoptosis Fragmentation of genomic DNA	51
	Leukaemia	NB4 HL-60	Induction of apoptosis Fragmentation of genomic DNA	49, 52
Milicia excelsa roots	Breast	MDA-MB-231 pcDNA MDA-MB-231 BCRP	Inhibition of tumour proliferation	45,46
	Colorectal	HCT116 (p53+/+) HCT116 (p53−/−)		
	Glioblastoma	U87MG U87MG.EGFR		
	Liver	HepG2		
	Leukaemia	CCRF-CEM CEM/ADR5000	Cell cycle arrest between G0/G1 and S phases, Induction of apoptosis Disturbance of mitochondrial membrane potential	
	Uterine cervix	HeLa	Inhibition of tumour proliferation	

Toxicity data relating to the different parts of plants in the preparation

The leaves of Ipomoea batatas

Assessment of the in vitro cytotoxicity of anthocyanins from Ipomoea batatas leaf using the Hoechst 33342 live cell staining method had revealed no cellular toxicity at several concentrations (100-400 µg/mL)[12,53]. Furthermore, in vivo Ipomoea batatas leaf extracts did not induce behavioural changes and mortality during acute oral toxicity assessment in rats[54,55]. Similarly, the subacute toxicity study showed that Ipomoea batatas leaf is relatively safe at doses of 10-100 mg/kg. However, at doses above 1000mg/ kg and 2500mg/kg, Ipomoea batatas leaf can cause hepatic cytolysis and renal failure respectively[54,56].

The roots of Milicia excelsa

Very few toxicity studies have been carried out on Milicia excelsa roots. Adébayo et al. reported that the LD50 of the methanolic extract of Milicia excelsa roots was greater than 5000mg/kg and considered unlikely to induce acute toxicity according to the WHO risk classification system[57,58]. Table 3 summarizes the toxicity studies of the different plant materials making up the preparation.

Table 3: Toxicity studies on the various plant materials used in the preparation.

Plant material	Toxicity study			Ref
	Extract type	Acute toxicity	Subacute toxicity	
Ipomoea batatas leaves	Aqueous extract	DL50 : l2.0 ± 1.2 g/kg	- Decreased liver weight at 120 mg/kg, - Increased spleen weight at 240 mg, - Hepatic cytolysis at 1.2 g/kg.	54,55
	Ethanolic extract	DL50>5000mg/kg	-Hepatic cytolysis from 1000mg/kg, -Renal insufficiency from 2500mg/kg.	54,56
Milicia excelsa roots	Methanolic extract	DL50>5000mg/kg	--	57

In sum, the leaves of Ipomoea batatas and the roots of Milicia excelsa, taken individually, are very rich in secondary metabolites which exert preventive and curative anti-cancer effects. Their combination, as in the case of this preparation, could have an additive or synergistic effect on the regulation of metabolic and signalling pathways, angiogenesis, microtubule assembly and induction of apoptosis[59,60]. However, given that the extraction methods used (aqueous, methanolic, ethanolic, etc.) are not the same, it is unlikely that the composition of the decoction of Ipomoea batatas leaves and Milicia excelsa roots is a compendium of compounds isolated from the different plant materials. In addition, the toxicity profile of the decoction of Ipomoea batatas leaves and Milicia excelsa roots may not be equivalent to those of the two plant materials due to the variation in composition. Thus, the absence of conclusive data on the efficacy and safety of the decoction of Ipomoea batatas leaves and Milicia excelsa roots in cancer does not allow recommendations to be made regarding its use in this indication. Nevertheless, given the therapeutic potential of Ipomoea batatas leaves and Milicia excelsa roots, the traditional use of a decoction of Ipomoea batatas leaves and Milicia excelsa roots could be justified in the treatment of cancer and is an anti-cancer therapeutic option worth exploring.

Conclusion

This literature review revealed a lack of scientific data on the decoction of Ipomoea batatas leaves and Milicia excelsa roots and, in particular, on its toxicity profile. It is therefore urgent to carry out toxicity studies on the decoction of Ipomoea batatas leaves and Milicia excelsa roots in order to assess the toxicity risks incurred by users.

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