REVIEW ARTICLE



INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Published by JK Welfare & Pharmascope Foundation

Journal Home Page: <u>www.ijrps.com</u>

An overview on Ethnopharmacologicals studies carried out on *Lannea microcarpa* Engl. & K. Krause (Anacardiaceae): a medicinal plant used in Burkina Faso for the treatment of hypertension

Salfo Ouédraogo^{1,2}, Mathieu Nitiéma¹, Lazare Belemnaba¹, Tata Kadiatou Traoré^{*2}, Bavouma C Sombié², Hermine Zime Diawara², Sylvin Ouédraogo¹, Rasmané Semdé²

¹Department of Traditional Medicine and Pharmacopoeia-Pharmacy (MEPHATRA-PH), Health Science Research Institute (IRSS/CNRST), 03 BP 7047 Ouaga 03, Burkina Faso ²Drug Development Laboratory (LADME), Doctoral School of Health, Joseph Ki-Zerbo University, 03 BP 7021 Ouaga 03, Burkina Faso

Article History:	ABSTRACT
Received on: 01 Mar 2021 Revised on: 04 Apr 2021 Accepted on: 07 Apr 2021 <i>Keywords:</i>	<i>Lannea microcarpa</i> , is one of the species of medicinal plants used in medicine and traditional pharmacopoeia for the treatment of human pathologies in Africa. This review focuses on the ethnobotanical and ethnopharmacological previous studies of <i>Lannea microcarpa</i> . Some information on phytochemical makeup and its effects on human health are already documented. However,
Lannea microcarpa,	information concerning its ethnopharmaceutical and phytopharmaceutical
Medicinal Plants,	potential is scarce and poorly documented. These data were obtained by docu- mentary researches using different scientific sites such as Google Scholar, Sci-
Hypertension, Formulation	ence Direct, Scopus, ResearchGate, PubMed, and SCIENCEDOMAIN, from the-
Formulation, Phytomedicine	ses, dissertations and scientific articles. Additional information was obtained from classic books about herbal medicine and others scientific databases. Eth- nobotanical surveys carried out have indicated their uses in the management of arterial hypertension. It appears from bibliographic research that <i>Lannea</i> <i>microcarpa</i> has vasorelaxant, hypotensive and antihypertensive effects, etc. Other studies have shown the presence of phytochemicals of interest for the management of high blood pressure. However, their use in traditional forms does not make it possible to guarantee the stability of medicinal preparations. Quality control and standardization studies were carried out in order to define the optimal conditions for guaranteeing effectiveness. This article gives an overview of previous studies carried out on the plant in order to have data for the improvement of its use.

*Corresponding Author

Name: Tata Kadiatou Traoré Phone: 00226 71642608 Email: tatakady@yahoo.fr

ISSN: 0975-7538

DOI: <u>https://doi.org/10.26452/ijrps.v12i3.4812</u>

Production and Hosted by

IJRPS | www.ijrps.com

@ 2021 | All rights reserved.

INTRODUCTION

High blood pressure (hypertension) is a severe condition, called by some epidemiologists for five decades "the silent killer" (WHO, 2013; Bell *et al.*, 2015). Over the past decade, hypertension has become the main contributor to the global burden of disease and at the same time causes an increasing number of deaths and disabilities linked to poorly controlled blood pressure (Murray and Lopez, 2013). Besides, studies have shown as early as the 2000s that 26.4% of the world's adult population was hypertensive, and this proportion is

expected to reach 29.2% by 2025 (Kearney et al., 2005). In Africa, the African Union estimates that more than 40% of adults have hypertension (UA, 2013). In 2005, the prevalence of hypertension was 11% in Togo, 13% in Benin, and in Côte d'Ivoire and 16.3% in Mali (Coulibaly et al., 2005). In Burkina Faso, the overall prevalence of hypertension is 17.6% (19.4% in men and 16% in women) (MS, 2017; Bell et al., 2015). However, the treatment cost remains expensive in modern medicine and challenging to access for most developing countries, particularly in black Africa. Research results show that there is a lot of herbal data supporting the development of therapeutic grade herbal medicines. Indeed, the rich and varied African pharmacopoeia can contribute to the geographical and economic accessibility of the majority of populations to effective drugs essential for the management of pathologies of priority concern such as hypertension. In Burkina Faso, the Department of Traditional Medicine and Pharmacopoeia of the IRSS has acquired notoriety in the field of traditional medicine and the production of phytomedicines, it develops research guided by the health priorities identified by the supervisory ministry. The work from the laboratories of this department has revealed the biological properties of plant extracts which validate traditional therapeutic indications. This is the case with LAMIC, a galenic formulation of a phyto-medicine resulting from preclinical work on extracts from the trunk bark of Lannea microcarpa.

However, recent interest in medicinal plants due to increased and advanced research, safety, availability and lower costs has led to the need to produce more safer formulations to meet demand (Vasisht and Kumar, 2002). Thus this present study seeks to synthesize the previous studies already carried out on the different parts of the plant.

Objective of Review

This review focuses on the ethnobotanical and ethnopharmacological studies of *Lannea microcarpa* with its beneficial health effects. Some information on phytochemical makeup and its effects on human health are already documented. However, information concerning its ethnopharmaceutical and phytopharmaceutical potential is scarce and poorly documented. Therefore, this review has been written to emphasise the raw material to be used in the galenic formulation of a phytomedicine.

MATERIALS AND METHODS

A literature search was conducted on different scientific search engines, including Google Scholar, Science Direct, Scopus, ResearchGate, PubMed, and

SCIENCEDOMAIN, from theses, dissertations and scientific articles (Figure 1). Additional information was obtained from classic books about herbal medicine and others scientific databases.

RESULTS

Description of Lannea microcrapa

Taxonomical profile

The genus *Lannea* belongs to the Anacardiaceae family with more than 40 species Ouattara *et al.* (2010). Among these species, 06 are found in Burkina Faso. These are *Lannea acida, Lannea vélutina, Lannea barteri, Lannea edulis, Lannea kerstingii* and *Lannea microcarpa* (Ouattara *et al.*, 2010; Semde *et al.*, 2015). They are characterised by compound leaves, imparipinnate, with 4 to 9 pairs of leaflets (Arbonnier, 2009). In this study, we were interested in *Lannea microcrapa*.

The classification of this plant is that proposed by Cronquist and Takhtadzhian (Cronquist and Takhtadzhian, 1981).

Kingdom: Plantae; Phylum: Magnoliophyta; Division: Angiosperms; Class: Dicotyledons; Subclass: Magnolidae; Order: Sapindales; Family: Anacardiaceae; Genus: *Lannea*; Species: *Lannea microcarpa* Engl. & K. Krause

Lannea microcarpa Engl. & K. Krause is a plant that belongs to the Anacardiaceae family (Alexandre, 2002; Abubakar *et al.*, 2007); Scientific name : *Lannea microcarpa* Engl. & K. Krause.

Synonymies

Lannea djalonica A. Chev.; Lannea oleosa A. Chev.; Lannea egregia Engl. & K. Krause; Lannea grossularia A. Chev.; Odina acida (A. Rich.) Oliv.; Common name: French: Vrai raisinier; English; African grape

Vernacular names: Gourmantche: Tchissab'golugon; More: Sabga; Gourounsi (Nouni): Atjoun-thio; Bambara: Pegun yiri; Hausa / Fulani: Babban baraan

Botanical characteristics

It is a relatively dense hemispherical crown tree 6 to 8 m in height, sometimes reaching 15 m (Adjanohoun *et al.*, 1987; Arbonnier, 2002). The trunk can reach 70 cm in diameter with a smooth or thin-scaled bark of light grey colour and a striped reddish fibrous slice. The leaves are alternate, imparipinnate, up to 25 cm long and made up of 2 to 5 pairs of opposing leaflets. The inflorescence is a terminal raceme up to 15 cm long, dotted with glandular points. The yellowish-green flower is approximately 4 mm in diameter and has 4 petals.

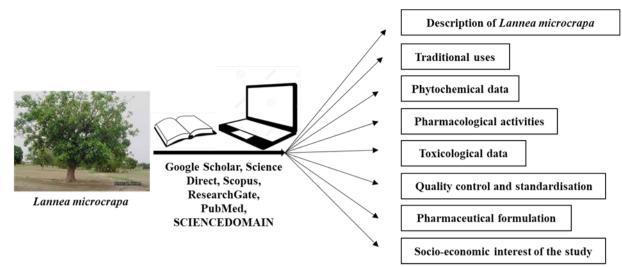


Figure 1: Graphical Methodology



Figure 2: Lannea microcarpa plant

Table 1: Anti-inflammatory activity of L. microcarpa extracts after 6h induction of croton oil
mouse ear oedema

Substance	Dose (μ cm $^{-2}$)	No. of mice	Oedema (mg)	Oedema reduction (%)
Controls	-	10	$7.2{\pm}0.5$	-
Extract A	100	10	6.2±0.3*	14
	300	10	5.0±0.3*	31
	900	10	3.6±0.4*	51
Indometacin	100	10	2.9±0.2*	60

Oedema values are expressed as mean \pm s.d. *P < 0.05 at the analysis of variance, as compared with controls

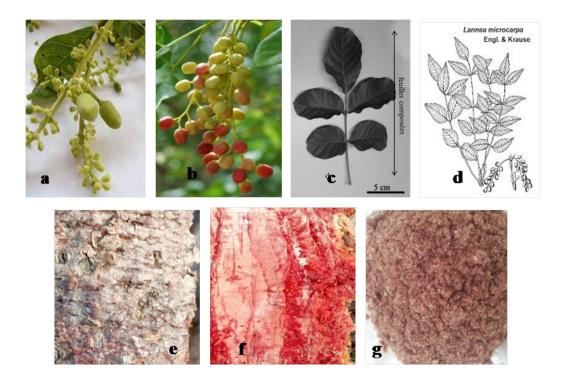


Figure 3: Flowers (a), fruits (b) and leaves (c and d), trunk bark (e and f) and freeze-dried powder (g) of *Lannea microcarpa*

The flowers are in small clusters, dioecious and inconspicuous. Flowering takes place before the new leaves sprout. The fruit is an ellipsoid clustered drupe and turns pale black purple or black-purple when ripe. The fruit ripens at the start of the rainy season. Harvest time varies between localities. For example, in Burkina Faso, the optimal time to harvest the fruits is between May and June (Daws *et al.*, 2005; Semde *et al.*, 2016). The seed does the multiplication. Figures 2 and 3 show the whole plant as well as its different parts.

Geographical distribution

Lannea microcarpa (Anacardiaceae) is found in intertropical Africa (Sahel), in the Sahelo-Sudanese and Sudanese savannas and soils with a sandy texture (Nacoulma, 1996). This plant is found in several countries such as Sudan, Burkina Faso, Ethiopia and Uganda. It is also seen from Senegal to Cameroon (Adjanohoun *et al.*, 1986).

Traditional uses

The fruits are edible and sold commercially. They are used for cooking, wine and dyeing. *Lannea microcarpa* has a great therapeutic use, and all the parts of the plant used in traditional medicine (Belemnaba *et al.*, 2014; Hilou *et al.*, 2017). According to the same authors, the leaves are used to treat bloody diarrhoea, febrile muscle aches, symptoms of hypertension, gastroenteritis, malaria, colic,

burns (powder from charred leaves) and generalised oedema. They are also used as an astringent, antibacterial, stimulant and diuretic.

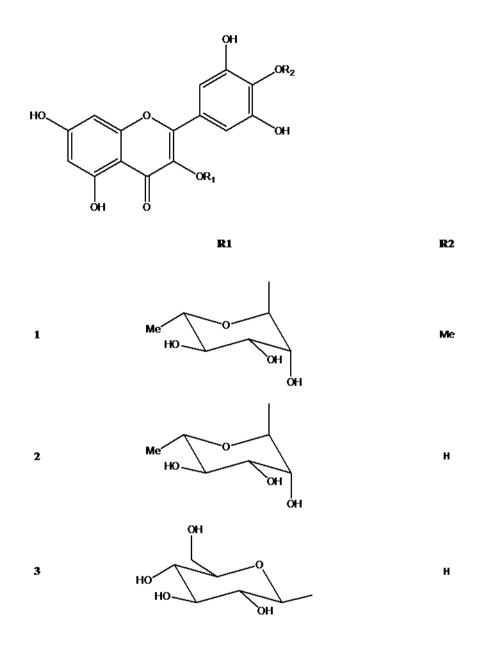
The trunk barks are recommended to treat dysentery form diarrhoea, female infertility, dysmenorrhea, hemorrhoids, gonorrhea, dermatoses, wounds, epilepsy, vomiting, dizziness, fainting, they are also used as an astringent, diuretic and antibacterial.

The roots are used to treat coughs, abdominal bloating, poisoning, gingivitis, diseases of the oral mucous membranes, etc.

Besides medicinal use, *Lannea microcarpa* has other uses. In fact, the bark of the plant is used for dyeing fabrics (Arbonnier, 2004; Goudégnon *et al.*, 2018). The wood is used in carpentry, and the leaves are used as hay for cattle.

Ethnobotanical survey

An evaluation of traditional health practitioners' knowledge and the use of products from the traditional pharmacopoeia in the treatment of arterial hypertension in two health districts of Burkina Faso was carried out through open and semi-structured interviews. The plants used were collected during the stay in the field with the herbal healer. Reference samples were collected and identified by the authors with the help of botanical specialists. In this study, seventy-one (71) healers were enrolled in the



* (1) 4'-methoxy-myricetin 3-O-α-L-rhamnopyranoside, (2) methoxy-myricetin 3-O-α-Lrhamnopyranoside, (3) myricetin 3-O-α-L-glucopyranoside

Figure 4: The 03 major molecules in the n-butanolic fraction of Lannea microcarpa leaves

health district of Ioba and thirty-four (34) in Passoré. A total of fifty-two (52) plant species belonging to twenty-seven (27) plant families were recessed. Among them, Sclerocarya birrea A. Rich. Hochst, Parkia biglobosa R. Br. Ex G, Anogeissus leiocarpus, Guiera senegalensis J. F. Gmel and Lannea microcarpa Engl. And K. Krause were the most cited. Thus, these five (5) species have been the subject of bibliographical research and biological studies to seek their potentially antihypertensive biological properties. Bibliographic research indicates that these plants are endowed with vasorelaxant, hypotensive and antihypertensive properties (Belemnaba *et al.*, 2014).

The investigations of the biological activities *in vitro* and *in vivo* carried out oriented the choice on the bark of the trunk of *Lannea microcarpa* as a right candidate for future investigations for their antihypertensive properties (Nitiéma *et al.*, 2018a; Belemnaba *et al.*, 2014).

Previous experimental studies

Phytochemical data

Work carried out on extracts of Lannea microcarpa

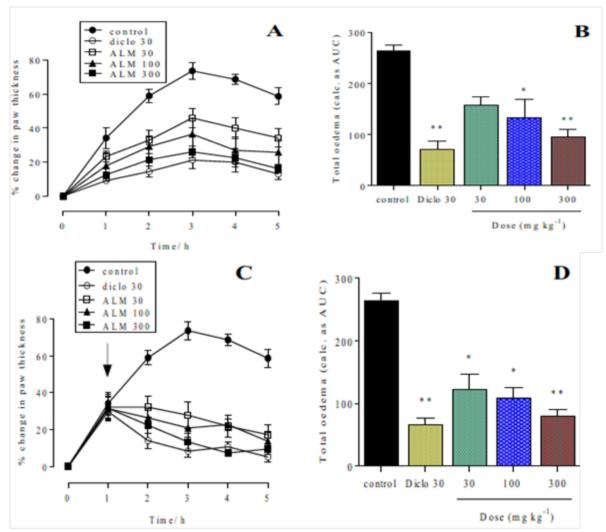


Figure 5: Effects of *Lannea microcarpa* extracts in the prophylactic and therapeutic studies of dextran sulphate-induced paw oedema in rats

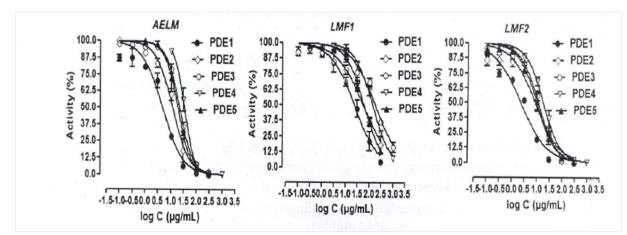


Figure 6: Concentration-response curves of AELM, LMF1 and LMF2 on PDEs isoforms activities. Each point represents the means \pm S.E.M of 5 assays

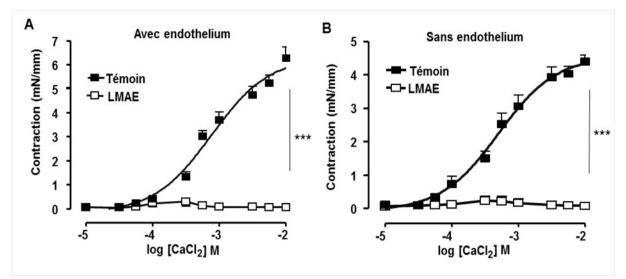


Figure 7: Inhibitory effect of LMAE on contractions induced by $CaCl_2$ on mouse aortic rings in the presence of endothelium (A) and in the absence of endothelium (B), (n = 5) ***p < 0,001

has revealed certain phytochemical groups and molecules. The presence of triterpene sterols, anthracenosides, steroid and triterpene glycosides, coumarin derivatives, saponosides, reducing compounds, anthocyanins and phenolic compounds (tannins) have been demonstrated in the bark of the trunk of Lannea microcarpa (Nacoulma, 1996; Ouédraogo *et al.*, 2010). The fruits of the plant contain total polyphenols but also flavonoids (Lamien-Meda et al., 2008). Also, 4'-methoxy-myricetin 3-0- α -L-rhamnopyranoside, vitexin, isovitexin. myricetin 3-0- α -L-rhamnopyranoside, myricetin 3-0- α -L-glucopyranoside, gallic acid and epicatechin have been identified in the leaves of Lannea microcarpa. Figure 4 shows the 03 significant molecules in the n-butanolic fraction of the leaves of Lannea macrocarpa (Hilou et al., 2017; Picerno *et al.*, 2010). Cyanidin 3-0- (2-0-β-Dxylopyranosyl) β -D-galactopyranoside, cyanidin 3-0- β -D-galactopyranoside and anthocyanin have also been identified in the dried fruit epicarp (Pale, Compounds such as γ -tocopherol, α -1998). tocopherol and δ -tocopherol have also been found in seed oils (Bazongo et al., 2014).

Pharmacological activities

The different extracts of the fruits and bark of the trunks of *Lannea microcarpa* have several pharmacological properties (Lamien-Meda *et al.*, 2008; Bationo *et al.*, 2012).

Antioxidant properties (In vitro studies)

Three methods (DPPH, ABTS and FRAP) were used to assess the antioxidant activity of lyophilised aqueous extracts of the trunk bark of *Lannea microcarpa*. These methods are distinct, each evaluating antioxidant activity differently, but remain complementary. The extract exhibited anti-free radicals with the DPPH method comparable to that of Trolox (reference product) (Belemnaba et al., 2019). The ABTS method makes it possible to evaluate the anti-free radical activity of the hydrophilic and lipophilic compounds present in an extract (Prior et al., 2005), these results had an IC₅₀ (μ g / mL) 0.05 \pm 0.04 (APR = 20). The results obtained with the FRAP method were (255.06 \pm 34.39 mmol EAA / g) (Bationo *et al.*, 2015). This is because the ethyl acetate fraction of fruits and leaves has the ability to reduce Fe^{3+} to Fe^{2+} . The strong activity of the trunk bark extract is believed to be due to its high content of polyphenolic compounds. In 2008, Lamien Meda et al. showed that the antioxidant activity of Lannea microcarpa fruits was correlated with the content of phenolics and flavonoids (Lamien-Meda et al., 2008). The antioxidant activity attributed to polyphenols is partly explained by their ability to capture free radicals and complex metals (Bahorun et al., 2004).

Epidemiological, clinical and animal studies confirm the role of polyphenols in preventing various chronic diseases, including cardiovascular diseases, inflammatory and metabolic diseases, neurodegenerative diseases and certain cancers (Middleton *et al.*, 2000; Mitjavila and Moreno, 2012).

Anti-inflammatory properties (*In vitro* and *in vivo* studies)

Extracts from the leaves and trunk bark of *Lannea microcarpa* have anti-inflammatory properties (Antwi-Adjei *et al.*, 2017; Bationo *et al.*, 2015). No increase in the release of interleukin IL-1 α was observed on reconstituted human skin cells (RHE; Skinethic, Nice, France) in culture treated

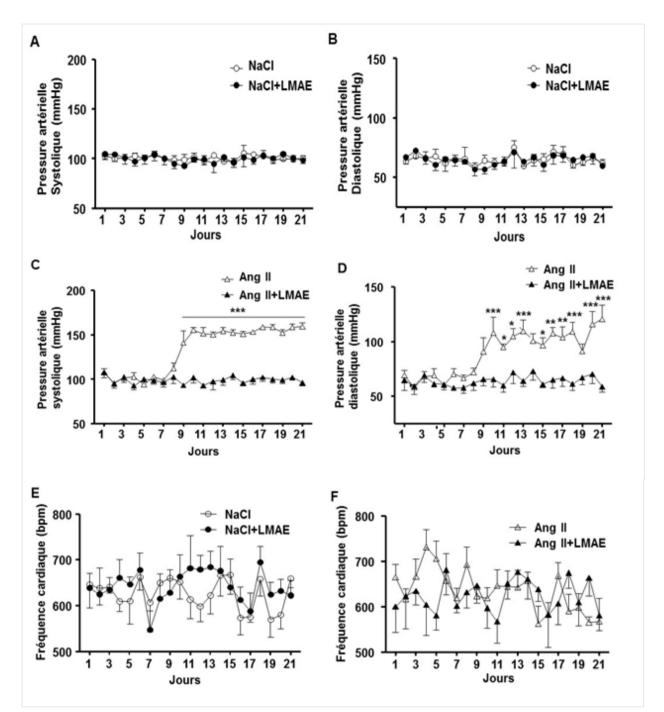


Figure 8: Evolution over time of changes in systolic and diastolic blood pressure after 21 days in the presence/absence of LMAE and Ang II, ***p <0.001

with the lyophilised n-butanol fraction (extract A). leaves of *Lannea microcarpa* or its major compound myricetin 3-OL-rhamnopyranoside, both at 24 and 72 h, compared to the control. Under the same test conditions, the irritant reference compound SDS (0.25%) caused an increase in the release of the proinflammatory mediator to approximately 250 pg / mL at 24 h and to 110 pg / mL at 72 h (Picerno *et al.*, 2010). The anti-edematous effect with croton oil on mice of the lyophilised n-butanol fraction (extract A), at inhibitory doses (ID) of 100, 300 and 900 μ g / cm², is shown in Table 1. The dose-activity relationship of the extract has been studied compared to that of indomethacin, the reference drug for NSAIDs (DI₅₀ = 93 μ g/cm²). The extract caused a significant and dose-dependent inhibition of oedema with a potency ten times lower (DI₅₀ = 900 μ g/cm²) than that of indomethacin h (Picerno *et al.*, 2010).

The anti-inflammatory effect with carrageenan of aqueous extracts of fruits and leaves with mouse paw has been evaluated. At the doses of 100 mg/kg,

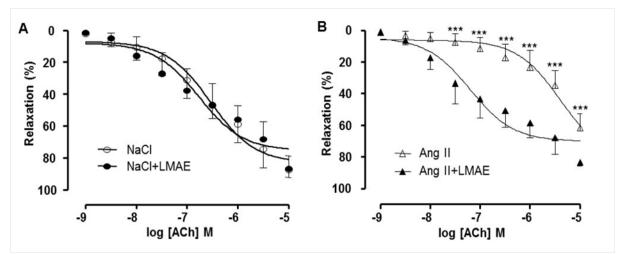


Figure 9: Protective effect of vascular endothelium by LMAE. ACh release curves (A, B) on intact endothelial aortic rings pre-contracted with U46619, n = 7-8 / group; *p <0.05

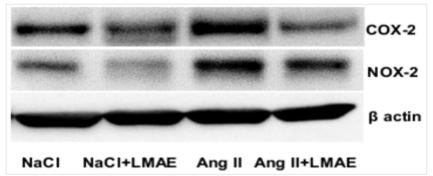


Figure 10: Representative images of the activation of the COX-2 and NOX-2 pathway by Ang II, LMAE downregulates them in the thoracic aorta of hypertensive mice

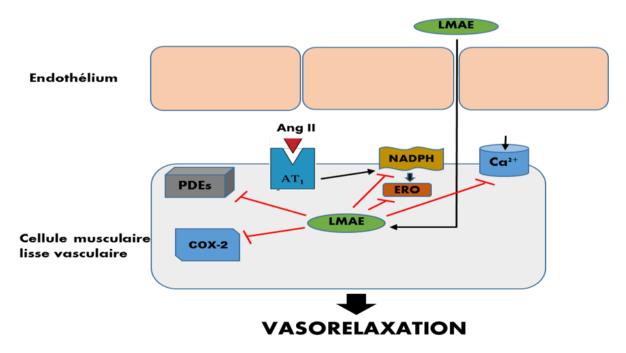


Figure 11: Diagram showing the vascular signalling pathways of LMAE

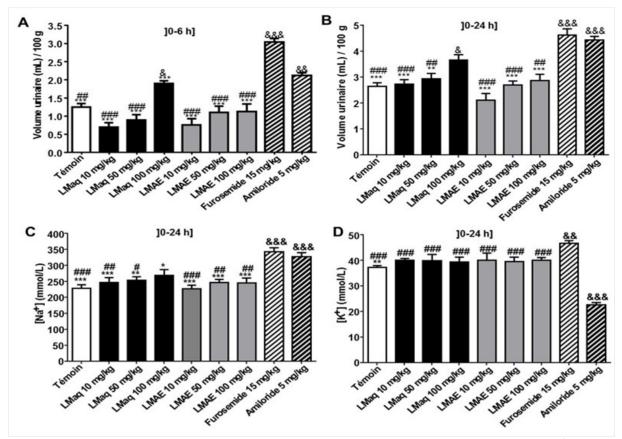


Figure 12: Diagrams of volume of urinary excretion and electrolytes concentrations (Na ⁺ and K ⁺). n = 6;&&& p <0.001 vs Control; *** p <0.001 vs Furosemide; ### p<0.001 vs Amiloride

200 mg/kg and 400 mg/kg, the extracts showed a significant reduction in oedema induced by carrageenan compared to the control.

measured after 2 h.

Results

The 200 mg/kg dose gave the best inhibitory effect at the 5th hour for fruit extract (78.44%) and leaf extract (58.02%). Besides, statistically significant, the ethyl acetate fraction of the fruit and the leaves respectively inhibited lipoxygenase, xanthine oxidase, and lipid peroxidation by 32.85% and 78.07% (Bationo *et al.*, 2015).

Oedema was induced in the right hind paws of Sprague Dawley rats (200-250 g, 12 weeks old, n=5) using dextran sulphate solution, while ear oedema was induced in ICR mice (25-30 g, 6 weeks old, n=5) using xylene solutions. Aqueous extracts of ALM (30, 100 and 300 mg kg-1) were administered in a set of rats and mice for both prophylactic and therapeutic studies. In the dextran sulphate-induced paw oedema, rats (200-250 g) were treated orally with ALM (30, 100 and 300 mg kg-1) for prophylactic and therapeutic studies. The rats' paw thickness was measured before and after dextran sulphate injection at an hourly interval for 5 h. For xylene-induced ear oedema, ICR mice (25-30 g) were given the same doses of the ALM, and the ear weight of mice were In the dextran sulphate-induced paw oedema, the ALM reduced the mean maximal paw oedema significantly (P \leq 0.05) to 36.392 \pm 9.207% and 26.050±3.396% at 100 and 300 mg kg-1 (prophylaxis) and 32.192 \pm 5.670%, 31.398 \pm 6.921% and $31.593 \pm 5.841\%$ at 30, 100 and 300 mg kg-1 (therapeutic) in dose-dependent manner when compared to the control respectively. Similarly, the ALM dose dependently showed a significant (P \leq 0.05) reduction of percentage mean oedema in xylene-induced ear oedema by 43.56%, 59.63% and 68.07% at 30, 100 and 300 mg kg-1 when compared to the control respectively (Antwi-Adjei et al., 2017). Figure 5 shows effects of Lannea microcarpa extracts on the maximal (A and C) and the total oedema responses (B and D) in the prophylactic and therapeutic studies of dextran sulphate-induced paw oedema in rats, respectively (n=5) denotes time of drug administration.

Antihypertensive properties

Ex vivo studies - Vasorelaxant properties

The aqueous extract (LMaq) and its

dichloromethane (LMDCM) and ethyl acetate (LMAE) fractions of the trunk bark of *Lannea microcarpa* possess concentration-dependent and endothelium-independent vasorelaxant properties in Wistar rats. Of these three extracts, the most potent was the ethyl acetate fraction, followed by the aqueous extract and finally the dichloromethane fraction. This vasorelaxant property is partly due to an inhibition of phosphodiesterases. Figure 6 below gives the results of this study (Ouédraogo *et al.*, 2010).

To study the role of extracellular calcium influx in the vasorelaxation of *Lannea microcarpa* extracts, the aortic rings of mice with functional or non-functional endothelium were placed in a physiological saline solution deprived of Ca²⁺ containing 80 mM KCl to activate the voltage-dependent calcium channels (CCVD). Compared to the control rings (0.02% DMSO), LMAE (500 μ g / mL) incubated for 20 min completely inhibited the contraction induced by CaCl₂ (10⁻⁵-10⁻² M). Thus, Figure 7A and Figure 7B respectively show the results of the inhibitory effect of LMAE on the influx of extracellular calcium in the presence and absence of functional endothelium (p <0,001) (Nitiéma *et al.*, 2019).

In vivo studies

An evaluation of the antihypertensive properties by the invasive method of lyophilised aqueous extract (LMaq) and its dichloromethane (LMDCM) and ethyl acetate (LMAE) fractions was carried out in the Wistar rat. Hypertension was induced by intra-arterial administration through the carotid artery of 75 μ g / kg of adrenaline, and the extracts were administered at doses of 0.03-10 mg/kg through the jugular vein. This study showed that the LMAE fraction (Emax = $33.27 \pm 0.70\%$) is the most active, followed by LMaq (Emax = $26 \pm 0.90\%$) and finally the LMDCM fraction (Emax = $24.34 \pm 0.67\%$). These effects were associated with adrenergic receptor antagonism (Belemnaba et al., 2014). Also, an evaluation of the antihypertensive properties in vivo by the noninvasive method was made on Swiss mice implanted with osmotic mini-pumps delivering physiological solution NaCl (0.9%) or Ang II (0.5 mg/kg / day). Mice received LMAE (50 mg/kg/day) for 3 weeks by oral gavage and implantation of mini-pumps at the start of the last two weeks. LMAE completely prevented hypertension without a change in heart rate (Figure 8) with correction of Ang II-induced endothelial dysfunction (Figure 9). Echocardiographic and renal parameters were not affected. LMAE alone did not alter the production of NO in the femoral arteries of mice but significantly limited the production of O^{2-} induced by Ang II. The effects were associated with reduced expression of COX-2 and NOX-2 from NADPH oxidase in aortas by the western blot method (Figure 10) (Nitiéma *et al.*, 2019). Figure 8 shows effects of LMAE on systolic and diastolic blood pressure compared to control (A, B). Preventive effect of LMAE on hypertension induced by Ang II (0.5 mg/kg/day) by daily oral administration (C, D) and variation in heart rate for each group (E, F).

Vascular effects involve several signalling pathways (Figure 11). This is a simplified diagram of the vascular pharmacological targets of the ethyl acetate moiety (LMAE) of the trunk bark of *Lannea macrocarpa*.

Diuretic properties

Finally, the diuretic activity of LMaq and LMAE were evaluated in vivo in rats for 24 h according to the method described by Sundaresan *et al.* (2017). Thus, the results of Figure 12 showed that LMaq and LMAE have moderate diuretic activity. However, LMaq showed better activity compared to LMAE (Nitiéma *et al.*, 2018a). Figure 12 shows diagrams of urinary excretion volume from 0 to 6 h (A); from 0 to 24 h (B) and the electrolyte concentrations (Na ⁺ and K ⁺) from 0 to 6 h (C) and from 0 to 24 h (D) of control rats, treated with LMaq, LMAE, furosemide and amiloride in a function of time.

Toxicological data

The acute and subacute toxicity of LMaq and LMAE were investigated in vivo in NMRI mice and Wistar rats. Acute toxicity tests on the aqueous extract of the trunk bark of Lannea microcarpa showed an LD_{50} of 199.5 mg/kg body weight intraperitoneally in mice (Zagué, 2009). Other studies involving oral administration of the aqueous infused showed no mortality up to a dose of 3000 mg/kg and no signs of toxicity during 14 days of observation in Wistar rats (Owusu and Antwi-Adjei, 2017). Acute oral toxicity has shown that LMag has an estimated LD_{50} of 5000 mg/kg compared to 2500 mg/kg for LMAE (Nitiéma et al., 2018b). Subacute toxicity for 28 days has shown LMag to be non-toxic up to a dose of 1000 mg/kg (Nitiéma et al., 2018b). The subchronic toxicity of LAMIC, a prototype antihypertensive phytomedicine based on the aqueous decoct of the bark of the trunks of Lannea microcarpa in male and female Wistar rats is non-toxic up to a dose of 1500 mg/kg body weight given daily for 90 days (Belemnaba et al., 2019). Also, daily oral administration of the aqueous infused of the trunk bark of Lannea microcarpa did not show any toxidrome up to a dose of 3000 mg/kg for 14 days of treatment in Wistar rats (Owusu and AntwiAdjei, 2017). The crude extract of *Lannea micro-carpa* leaves shows no in vitro cytotoxic effect on cell viability [human kidney epithelial cells (HEK-293), murine fibrosarcoma cells (WEHI-164), and murine monocytes/macrophages (J774.A1)] up to a concentration of 1 mg / mL (Picerno *et al.*, 2010).

Quality control and standardisation

Ouality control studies were carried out on crude powders and lyophilised aqueous decocts of the trunk bark of Lannea microcarpa. Results from traits indicated that the trunk bark powders of Lan*nea microcarpa* were reddish in colour, practically odourless with a slightly bitter taste. These results can also be used to check the degree of purity according to the presence or absence of foreign elements and to detect possible adulterations or falsifications. The smell, the taste and the color can be used to differentiate from related drugs (Lehmann, 2013). The pH of the raw powders of the *Lannea microcarpa* bark was 7.16 \pm 0.08, the moisture levels were less than 10%. According to the European Pharmacopoeia, the powders had a content suitable for being stored over a long period without the development of molds or yeasts. The total ash content of the powders of the bark of the plant trunk was $6.27 \pm 1.42\%$ (Ouédraogo *et al.*, 2018, 2017).

The powders' microbial quality complied with the recommendations of the European Pharmacopoeia 6th Edition for raw materials of natural origin administered orally. The absence of specific pathogenic germs such as Salmonella and the low presence of total flora testify to the good microbial quality of the plant powders. Indeed, any contamination beyond the standards would lead to rejection or sterilisation of the raw material with the consequence of the risk of degradation of certain compounds and an increase in the raw material's cost price (WHO, 2011). The heavy metal contents sought were within limits authorised by the recommendations of the European Pharmacopoeia. This could be explained by the fact that the raw materials were harvested according to good cultivation and harvesting practices in sites far from roads, water drainage ditches, mine wastes, garbage dumps, and industries at risk of emitting toxic emissions (Chiffoleau et al., 2002). The residual levels of pesticides in the powders of the trunk's bark were lower than the limit values set by the European Pharmacopoeia 6.0 and the European Communities' directives (CE, 2006; WHO, 2011), including their annexes. Analysis of the leading chemical groups by thin-layer chromatography (TLC) showed five (05) main spots, observed in daylight after visualisation with sulfuric anisaldehyde with measured frontal references.

These CMMs have demonstrated a wide variety of chemical groups that will be used as chromatographic fingerprints in the quality control in terms of purities. According to the literature data, the results obtained by the TLC can be used for routine analyses of the powders in future harvests to check their quality (Katekhaye and Bhutani, 2011).

A standardisation study has made it possible to determine the optimal conditions for obtaining lvophilised aqueous extracts from the bark of Lan-Indeed, the results obtained nea microcarpa. showed that the optimum extraction yield is 33.46 \pm 0.36%, after a decoction of 40 minutes and then freeze-drying of 120 hours. The freeze-dried extracts of Lannea microcarpa were reddish in colour with a slightly bitter taste. Extracts were very hygroscopic, readily soluble in water, very little soluble in ethanol 96 ° and absolute, practically insoluble in chloroform, and readily soluble in buffers (pH 1.2 and pH 6.8). According to the European Pharmacopoeia, they have a mediocre flow and can be kept for six months without alterations of the physicochemical characteristics. These extracts can thus be used to formulate phytomedicines while ensuring reproducibility from one batch to another in the amount of the selected tracer.

Pharmaceutical formulation

A study of microencapsulation by atomisation of the extract of leaves of *Lannea microcarpa* was carried out using a matrix (Sansone *et al.*, 2014) based on sodium-carboxymethylcellulose (NaCMC). The concentration of myricetin 3-0- α -L-rhamnopyranoside, chosen as a marker (Haarmeyer *et al.*, 2013).

Socio-economic interest of the study

Medicinal plants have been playing an essential role in the development of human culture. As a medicine source, Medicinal plants have always been at the forefront of virtually all cultures of civilisations. Medicinal plants are regarded as rich resources of traditional medicines, and from these plants, many of the modern drugs are produced (Dar *et al.*, 2017). According to WHO African traditional medicine, traditional health practitioners could make significant contributions to the attainment of universal health coverage (Kasilo *et al.*, 2019).

CONCLUSION

The leaves and bark of the trunk and roots are used in traditional medicine to treat human pathologies. In recent years, research has focused on herbal remedies that have a long history of humans use. Extensive literature studies have revealed that *Lannea microcarpa* is a medicinal plant with beneficial effects on health. These results have been proven experimentally and have shown that the plant has antioxidant, anti-inflammatory, antihypertensive, etc. Further studies are needed to bring a stable form of use to the market that guarantees its quality and effectiveness.

ACKNOWLEDGEMENT

We acknowledge the support received from Centre d'Excellence Africaine de Formation, de Recherche et d'Expertises en Sciences du Médicament (CEA-CFOREM) of Université Joseph Ki-Zerbo in the finalisation of this article.

Declaration of Competing Interest

There is no conflict of interest or disclosure.

Funding Source

The authors have not declared a specific grant for this research from any funding agency in public, commercial or not-for-profit sectors.

REFERENCES

- Abubakar, M. S., Musa, A. M., Ahmed, A., Hussaini, I. M. 2007. The perception and practice of traditional medicine in the treatment of cancers and inflammations by the Hausa and Fulani tribes of Northern Nigeria. *Journal of Ethnopharmacology*, 111(3):625–629.
- Adjanohoun, E. J., Ahyi, M. R. A., *et al.* 1986. Traditional medicine and pharmacopoeia: Contribution to ethnobotanical and floristic studies in Togo. *Cultural and Technical Cooperation Agency*.
- Adjanohoun, E. J., Ahyi, M. R. A., *et al.* 1987. Contribution to the ethnobotanical and plant species studies of Togo. *Rapport ACCT*.
- Alexandre, D. Y. 2002. Introduction to agroforestry in the Sahelian zone: trees in the fields of the Central Plateau in Burkina Faso. *IRD Éditions/Karthala*, 224.
- Antwi-Adjei, M., Owusu, G., Ameade, E. P. K. 2017. Aqueous extract of Lannea microcarpa attenuates dextran sulphate-induced paw oedema and xylene-induced ear oedema in rodents. *International Journal of Basic and Clinical Pharmacology*, 6(5):1048.
- Arbonnier, M. 2002. Trees, shrubs and lianas of the drylands of West Africa. 2nd ed. CIRAD–MNHN, Paris, France.
- Arbonnier, M. 2004. Trees, shrubs and lianas of West African dry zones, Quae.
- Arbonnier, M. 2009. Trees, shrubs and lianas of the drylands of West Africa. Editions Quae.

- Bahorun, T., Luximon-Ramma, A., Crozier, A., Aruoma, O. I. 2004. Total phenol, flavonoid, proanthocyanidin and vitamin C levels and antioxidant activities of Mauritian vegetables. *Journal of the Science of Food and Agriculture*, 84(12):1553– 1561.
- Bationo, J. H., Hilou, A., Compaore, M., Coulibaly, Y. A., Kiendrebeogo, M., Nacoulma, O. G. 2015. Anti-inflammatory activities of fruit and leaves extract of lannea microcarpa england K. Kraus (anacardiaceae). *Int. J. Pharm. Pharm. Sci*, 7:177– 182.
- Bationo, J. H., Hilou, A., Savadogo, P. W., Nacoulma, O. G. 2012. Content of Polyphenolics Constituents and the Antioxidant and Antimicrobial Activities of Extracts from Leaves and Fruits of "Lannea microcarpa" Engl. & K. Kraus (Anacardiaceae). *Current Research Journal of Biological Sciences*, 4(3):290– 296.
- Bazongo, P., Bassolé, I., Nielsen, S., Hilou, A., Dicko, M., Shukla, V. 2014. Characteristics, Composition and Oxidative Stability of Lannea microcarpa Seed and Seed Oil. *Molecules*, 19(2):2684–2693.
- Belemnaba, L., Nitiema, M., Traoré, S., Somé, N., Traore, A., Ouédraogo, S., Guissou, I. 2014. Research of plants with antihypertensive potential in the biodiversity of Burkina Faso. *Pharmacopoeia and traditional African medicine*, 17.
- Belemnaba, L., Soubeiga, M., *et al.* 2019. Antioxidant properties and subchronic toxicity of the standardized extract of LAMIC, a phytomedicine prototype based on aqueous extracts from trunk bark of Lannea microcarpa Engl and K. Krause. *Journal of Drug Delivery and Therapeutics*, 9(5):1–8.
- Bell, K., Twiggs, J., Olin, B. R., Date, I. R. 2015. Hypertension: the silent killer: updated JNC-8 guideline recommendations. *Alabama Pharmacy Association*, 334.
- CE 2006. Commission Regulation of the European Communities (EC) No 1881/2006 of the Commission of 19 December 2006 fixing maximum levels for certain contaminants in foodstuffs (Text with interest for the EEA). *Official Journal of the European Community*, L 364:5–24.
- Chiffoleau, J. F., Auger, D., Chartier, E., *et al.* 2002. Determination of certain trace metals: (Cd, Co, Cu, Fe, Ni, Pb, Zn) dissolved in seawater by atomic absorption after liquid-liquid extraction. Editions Quae.
- Coulibaly, Y., Kone, M., Sacko, M., Diawara, A., Diarra, M. 2005. Morbidity and mortality related to high blood pressure and valve disease in the district of Bamako. *Médecine d'Afrique Noire*, 52:333–337.

- Cronquist, A., Takhtadzhian, A. L. 1981. An Integrated System of Classification of Flowering Plants. Columbia University Press. Columbia University Press.
- Dar, R. A., Shahnawaz, M., Qazi, P. H. 2017. General overview of medicinal plants: A review. *The Journal of Phytopharmacology*, 6(6):349–351.
- Daws, M. I., Gaméné, C. S., Sacandé, M., Pritchard, H. W., Groot, S. P., Hoekstra, F. 2005. Desiccation and storage of Lannea microcarpa seeds from Burkina Faso. *Comparative storage biology of tropical tree seeds*, pages 32–39.
- Goudégnon, E. O. A., Vodouhê, F. G., *et al.* 2018. Ethnic and generational differences in traditional knowledge and cultural importance of Lannea microcarpa Engl. & K. Krause in Benin's Sudanian savannah. *Bois and Forets Des Tropiques*, 334:49.
- Haarmeyer, D. H., Schumann, K., Bernhardt-Römermann, M., Wittig, R., Thiombiano, A., Hahn, K. 2013. Human impact on population structure and fruit production of the socio-economically important tree Lannea microcarpa in Burkina Faso. *Agroforestry Systems*, 87(6):1363–1375.
- Hilou, A., Bougma, A., Dicko, M. 2017. Phytochemistry and Agro-Industrial Potential of Native Oilseeds from West Africa: African Grape (Lannea microcarpa), Marula (Sclerocarya birrea), and Butter Tree (Pentadesma butyracea). *Agriculture*, 7(3):24.
- Kasilo, O. M. J., Wambebe, C., Nikiema, J.-B., Nabyonga-Orem, J. 2019. Towards universal health coverage: advancing the development and use of traditional medicines in Africa. *BMJ Global Health*, 4(Suppl 9):e001517.
- Katekhaye, S. D., Bhutani, K. K. 2011. Standardization of a polyherbal Ayurvedic formulation: Ayaskrti.
- Kearney, P. M., Whelton, M., Reynolds, K., Muntner, P., Whelton, P. K., He, J. 2005. Global burden of hypertension: analysis of worldwide data. *The Lancet*, 365(9455):217–223.
- Lamien-Meda, A., Lamien, C., Compaoré, M., Meda, R., Kiendrebeogo, M., Zeba, B., Millogo, J., Nacoulma, O. 2008. Polyphenol Content and Antioxidant Activity of Fourteen Wild Edible Fruits from Burkina Faso. *Molecules*, 13(3):581–594.
- Lehmann, H. 2013. The herbal medicine in Europe: status, registration, controls. Strasbourg University.
- Middleton, E., Kandaswami, C., Theoharides, T. C. 2000. The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. *Pharmacological Reviews*,

52(4):673-751.

- Mitjavila, M. T., Moreno, J. J. 2012. The effects of polyphenols on oxidative stress and the arachidonic acid cascade. Implications for the prevention/treatment of high prevalence diseases. *Biochemical Pharmacology*, 84(9):1113–1122.
- MS 2017. Ministry of Health. Burkina Faso Comprehensive Health Profile 2015. Module 4: Key determinants of health., 31.
- Murray, C. J., Lopez, A. D. 2013. Measuring the Global Burden of Disease. *New England Journal of Medicine*, 369(5):448–457.
- Nacoulma, O. 1996. Medicinal plants and traditional medical practices in Burkina Faso: the case of the central plateau. *Faculty of Science and Technology, University of Ouagadougou*, 320.
- Nitiéma, M., Belemnaba, L., Ouédraogo, S., Ouédraogo, N., Ouédraogo, S., Guissou, I. P. 2018a. Diuretic activity of aqueous decoction extract and ethyl acetate fraction of Lannea microcarpa engl. And k. Krause (anacardiaceae) trunk barks in wistar rats. *World Journal of Pharmaceutical Research*, 7(19):39–51.
- Nitiéma, M., *et al.* 2018b. Acute and sub-acute toxicity studies of aqueous decoction of the trunk barks from Lannea microcarpa Engl. and K. Krause (anacardiaceae) in rodents. *World Journal of Pharmacy and Pharmaceutical Sciences*, 7(9):30–42.
- Nitiéma, M., Soleti, R., *et al.* 2019. Ethyl Acetate Fraction of Lannea microcarpa Engl. and K. Krause (Anacardiaceae) Trunk Barks Corrects Angiotensin II-Induced Hypertension and Endothelial Dysfunction in Mice. *Oxidative Medicine and Cellular Longevity*, 2019:1–13.
- Ouattara, L., Koudou, J., Zongo, C., Barro, N., Savadogo, A., Bassole, I. H. N., Ouattara, A. S., Traore, A. S. 2010. Antioxidant and Antibacterial Activities of Three Species of Lannea from Burkina Faso. *Journal of Applied Sciences*, 11(1):157–162.
- Ouédraogo, S., Belemnaba, L., Zague, H., Traore, A., Lompo, M., Guissou, I. P., Bucher, B. 2010. Endothelium-independent vasorelaxation by extract and fractions from Lannea microcarpa Engl. and K. Krause (Anacardiaceae): possible involvement of phosphodiesterase inhibition. *International Journal of Pharmacology and Biological Sciences*, 4(2).
- Ouédraogo, S., Sombié, B. C., Ouédraogo, J. C. W., Nitiéma, M., Belemnaba, L., Ouédraogo, S., Semdé, R. 2017. Quality control of trunk's barks of Lannea microcarpa Engl. and K. Krause and Anogeissus leiocarpus (DC) Guill. & Perr. for the manufacture of phytomedicines for the treatment of hyper-

tension. *International Journal of Phytopharmacy*, 7(4):36–41.

- Ouédraogo, S., Sombié, B. C., Ouédraogo, J. C. W., Traoré, T. K., Traoré, S., Nitiéma, M., Belemnaba, L., Ouédraogo, S., Semdé, R., Guissou, I. P. 2018. Standardization of Extracts from Trunks's Barks of Lannea microcarpa engl. and K. Krause (Anacardiaceae) and Anogeissus leiocarpus (DC) Guill. and Perr. (Combretaceae) for the Formulation of Antihypertensive Herbal Medicines. *International Journal of Pharmaceutical Sciences Review and Research*, 48(1):92–97.
- Owusu, G., Antwi-Adjei, M. 2017. Acute and Sub-Acute Oral Toxicity Studies of the Aqueous Extract of Lannea microcarpa Stem Bark on Rats. *International Journal of Pharmacy and Pharmaceutical Research Human*, 9(4):17–30.
- Pale, E. 1998. Contribution to the study of anthocyanin compounds in plants: The case of Hibicus sabdariffa, Lannea microcapa and Vigna sorghum caudatum from Burkina Faso. PhD, University of Ouagadougou.
- Picerno, P., Mencherini, T., Loggia, R. D., Meloni, M., Sanogo, R., Aquino, R. P. 2010. An extract of Lannea microcarpa : composition, activity and evaluation of cutaneous irritation in cell cultures and reconstituted human epidermis. *Journal of Pharmacy and Pharmacology*, 58(7):981–988.
- Prior, R. L., Wu, X., Schaich, K. 2005. Standardized Methods for the Determination of Antioxidant Capacity and Phenolics in Foods and Dietary Supplements. *Journal of Agricultural and Food Chemistry*, 53(10):4290–4302.
- Sansone, F., Mencherini, T., Picerno, P., Esposito, T., Gaudio, P. D., Russo, P., Aquino, R. P. 2014. Microencapsulation by spray drying of Lannea microcarpa extract: Technological characteristics and antioxidant activity. *Journal of pharmacy and pharmacognosy research*, 2(4):100–109.
- Semde, K., Dao, M. C. E., Diallo, B. O., Ganaba, S. 2015. In the stands of Lannea microcarpa, are there individuals with different botanical characteristics in the Zorgho zone (Burkina Faso)? *International Journal of Biological and Chemical Sciences*, 9(6):2623–2632.
- Semde, K., Ganaba, S., Dao, M. C. E., Thiombiano, A. 2016. Characterizations of the morphology and germination of seeds from morphotypes of Lannea microcarpa, in the Central Plateau region, Burkina Faso. *Afrique SCIENCE*, 12(6):168–177.
- Sundaresan, P. K., Prabhakaran, S. S., Palappallil, D. S., Chellappan, D. 2017. Diuretic activity of ethanolic extract of whole plant of Sphaeranthus indicus linn

in albino rats. *International Journal of Basic and Clinical Pharmacology*, 6(2):265–265.

- UA 2013. 6th African Union Conference of Ministers of Health: The Impact of Noncommunicable Diseases (NCDs) and Neglected Tropical Diseases (NTDs) on Development in Africa. Addis-Abeba (Ethiopie).
- Vasisht, K., Kumar, V. 2002. Trade and production of herbal medicines and natural health products. *ICS-UNIDO*.
- WHO 2011. Quality control methods for herbal materials. Accessed on: 25 Apr 2021.
- WHO 2013. A global brief on hypertension: Silent killer, global public health crisis. Accessed on: 25 Apr 2021.
- Zagué, W.-W. H. 2009. In vitro evaluation of the antihypertensive effect of the aqueous extract of the bark of the trunks of Lannea microcarpa (Anacardiacaea) on the musculature. Pharmacy thesis, University of Ouagadougou.