

## A review on *Lantana rhodesiensis* Moldenke: traditional uses, phytochemical constituents and pharmacological activities

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### Abstract

*Lantana rhodesiensis* Moldenkean herbaceous, belonging to the Verbenaceae family is widely used in Africa folk medicine for the treatment of cancer, measles, malaria, smallpox, strength, coughs, fever, rheumatism, body pains, diabetes mellitus arrhythmia, parasitic diseases, arterial hypertension, old diarrhoeas. Many studies have been conducted on the chemical composition of the whole plant of *L. rhodesiensis* as well as biological activities. The aim of the present review was to give a detailed literature survey on its traditional uses, phytochemistry and therapeutical properties of *L. rhodesiensis*.

**Keywords:** Verbenaceae, *L. rhodesiensis*, *L. ukambensis*, traditional uses, phytochemistry,

### Introduction

The genus *Lantana* belongs to the Verbenaceae family, which consists of 3000 species in 75 genera are found in the tropics and sub-tropics. The common species are *L. camara*, *L. trifolia*, *L. rhodesiensis* and *L. viburnoide* [1-3]. *L. rhodesiensis* is a synonym of *Lantanaukambensis* (Vatke) Verdc. or *Lippia ukambensis* [4], found in grassland (often with thatching grasses, *Hyparrhenia*) and wooded grassland (with *Combretum* spp.) open woodland (including *Brachystegia*), old cultivation, sometimes amongst granite rocks, bushland, secondary bushland. This plant generally is a woody herb or small shrub under 2 m tall often multi-stemmed. [4-6]. In Africa, it is found in Burkina Faso, Tanzania, Kenya, Uganda, west of Cameroon, the Congo basin, Burundi, Rwanda, Sudan, Ethiopia, south of Malawi, Zambia, Zimbabwe and Mozambique. This plant grows naturally in the wild but it can be propagated by seed and cuttings.

### Taxonomical profile

Kingdom: Plantae  
Division: Magnoliophyta  
Class: Magnoliopsida

Subclass: Asteridae  
Order: Lamiales  
Family: Verbenaceae  
Genus: *Lantana*  
Species: *Lantana rhodesiensis* Moldenke  
Synonyms: *Lantanaukambensis* (Vatke) Verdc. or *Lippia ukambensis*  
Vernacular name: Liuli-sibi (Mooré), O'kaotonjemoadigu jaaga (Gourmache)

### Botanical description

These species are differentiated by the colour of their flowers, whereby *L. camara* flowers have flat top that is pink, yellow or white showy with mono-seeded greenish blue or black fruits. *L. trifolia* has leaves in threes and pink or mauve flowers, *L. rhodesiensis* has crimson or purple flowers (Figure 1), while *L. viburnoide* has leaves which are opposite with white flowers [2].

*L. rhodesiensis* Moldenke species was very rare in and around the Eldoret area, especially as compared to the non-native introduced *Lantana*. At one point this plant was classified as a species of *Lippia* [4]. The inflorescence of *L. rhodesiensis* is elongate in contrast to the head-like form of the exotic *Lantana*. Also there are conspicuous bracts below each flower which become enlarged

DOI:10.5138/09750185.1941



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after anthesis as the fruit develops. The fruit are bright purple berries. The leaves are opposite on the stems and aromatic when

crushed [3].



**Figure 1:** *Lantana rhodesiensis* Moldenke (Photo catch in the forest of Gonsè, 25 km of Ouagadougou by Bangou M. Jean; 15h45 mn/29 August 2011)

### Traditional uses

*Lantana rhodesiensis* Moldenke is widely used traditionally in the management of several diseases including diabetes mellitus arrhythmia, cancer, parasitic diseases, congestive heart failure and cardiac arrhythmia [1-9]. *Lantana rhodesiensis* or *Lippia ukambensis* used in traditional medicine in several treatment like measles, malaria, smallpox, strength [10]. The stem leaves are traditionally used in the treatment of arterial hypertension, stimulant, oliguria, lithiasis, old diarrhoeas and antilithiasic [1-11]. The stems are used for starting fire and as torches. The plant is suitable as an ornamental and hedge and provides forage for bees. Leaves are used as insect repellent. The ripe sweet berries collected during the rainy season are eaten by children fresh [1]. The leaves are chewed, or pounded and soaked in warm water and

the resulting liquid is drunk to treat coughs, fever and sores in the throat and on the tongue. Roots are boiled in water and drunk for rheumatism and generalized body pains [4-14]. Especially in Burkina Faso, *L. rhodesiensis* is used in folk medicine to treat chronic wounds and skin diseases [15]. According to Teketay *et al.* [13], leaf of *L. rhodesiensis* is used like wild edible plants of Ethiopia [12-16]. The literature enabled us to know that the plant is variously used in traditional medicine.

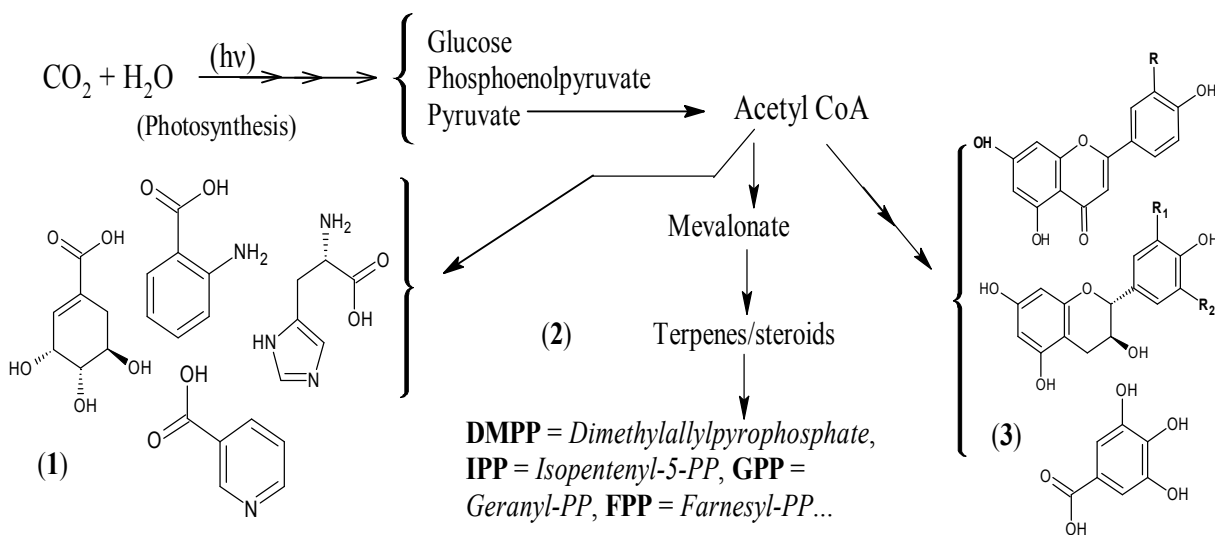
### Phytochemistry investigation

A study were interested to the evaluation of the total phenolic, total flavonoid and tannin content capacities to inhibit different enzymes [11]. The extracts of 36 species of plants were concerned belonging to 6 families. The results were expressed in mg



equivalents of reference compound per 100 mg extract. The results of the polyphenolic quantification of *L. rhodesiensis* are respectively  $21.55 \pm 0.75$  mg GAE/100 mg extract for total phenolic content,  $5.09 \pm 0.19$  mg QE/100 mg extract for total flavonoid content and  $14.52 \pm 0.25$  mg TAE/100 mg extract for tannin content. We note that flavonoids represent the low value in term of content. Among these 36 species of plants, the tannins content comes in third position respectively after those from *Cassia mimosoides* L. ( $33.60 \pm 0.57$  mg TAE/100 mg), *Cassia nigricans* Vahl. ( $20.73 \pm 0.53$  mg TAE/100 mg). The same tendency was found by Piero *et al.* [4]. They quantified in aqueous extracts of *L. rhodesiensis* (leaves) the polyphenolic compounds content and find that the levels of phenols and tannins were  $685.25 \pm 30.77$  and  $323.61 \pm 61.54$  mg/g gallic acid equivalent, respectively while flavonoids and alkaloids were  $187.33 \pm 54.97$  and  $32.67 \pm 10.07$  mg/g, respectively [4]. In term of strong content of totals phenolic and tannins, these results are

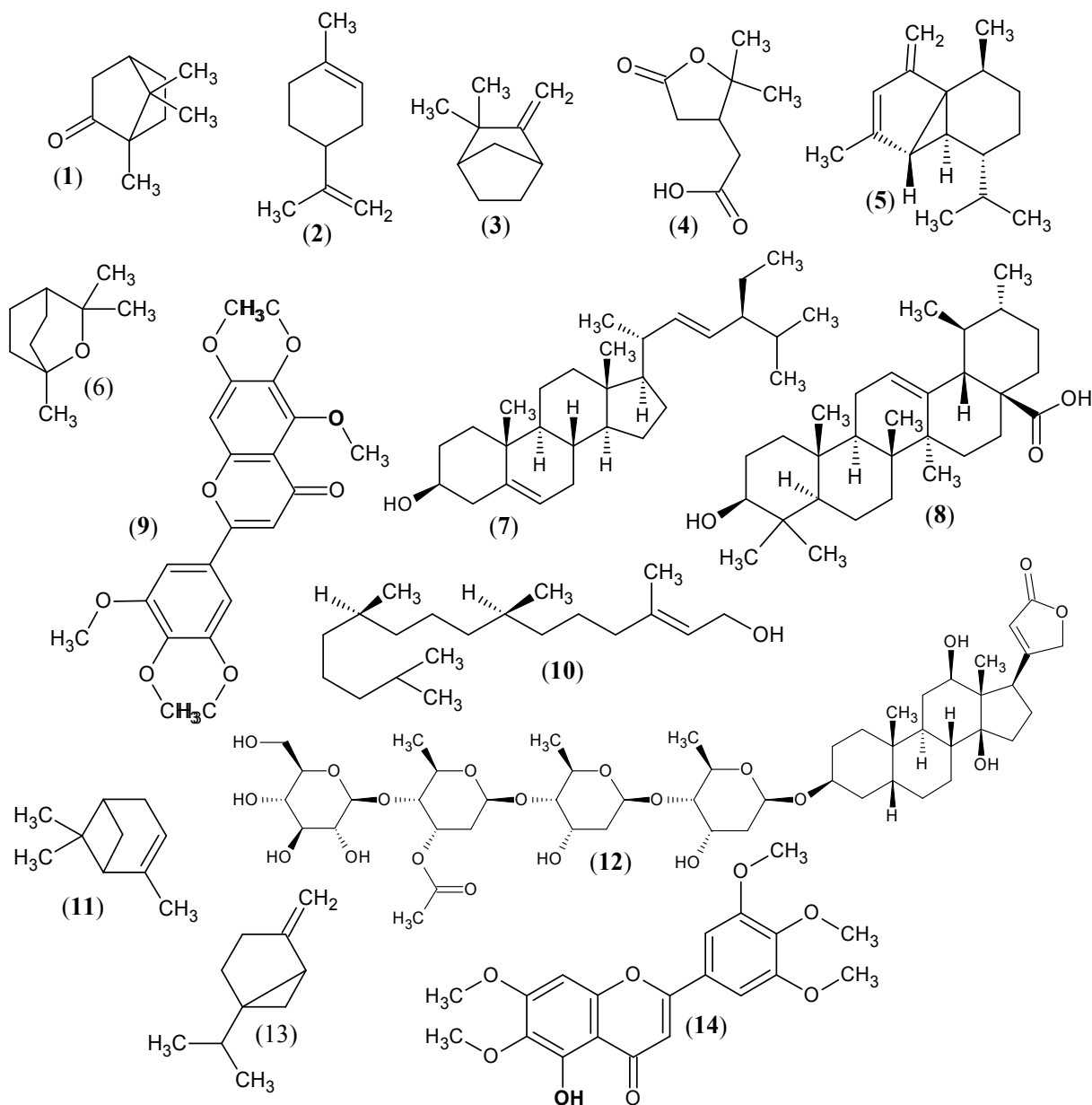
comparable with those of Bangouet *et al.* [11]. Started from two different extracts (methanolic and aqueous), these two groups of researchers of Burkina Faso [11] and Kenya [4] showed that the prevalent compounds in the plant are the totals phenolic and the tannins content. Piero and its collaborators [4] also highlighted in these extracts (aqueous) the presence of flavonoids, alkaloids, sterols, terpenoids, cardiac glycosides, phylobatannins, resins, and bound anthraquinones. Potassium, calcium, manganese, iron, lead and zinc levels in the extracts were below the recommended daily allowance. We propose possible ways of biosynthesis (Figure 2). In conclusion, the observed hypoglycemic activity and slight toxicity which could be associated with the phytonutrients present in this plant [1-11]. Other investigations demonstrated that *L. rhodesiensis* extracts contain anthraquinones which have previously been reported to lower blood glucose [17,18].



**Figure 2:** Pathway of biosynthesis of: (1) = alkaloids and proteins; (2) = essential oils, sesquiterpenes, diterpenes ..., ; (3) = flavonoids and tannins.

Former investigations highlighted in essential oils the presence of compounds such as camphor, trans-hydrate of sabinene, piperitone, *p*-cymene and linalool in the plant [5-19]. Other essential oils of *L. rhodesiensis* were quantified such as camphor (36.5%), 4-thujanol (18.5%), and seven (-pinene, camphene,  $\beta$ -pinene, limonene, cineole, -terpenoid and  $\beta$ -cubebene) other identified terpenoid substances. Leaves extracts of *L. rhodesiensis* contained common fatty acid, stigmaterol, phytol, ursolic acid, and camphene glycol [2-20]. Figure 3 summarizes the essence of these compounds. Recently, two polymethoxyflavones such as

5,6,7,3',4',5'-hexamethoxyflavone and its analogue, 5-hydroxy-6,7,3',4',5'-pentamethoxyflavone were isolated from *L. rhodesiensis* in dichloromethane Fraction [15]. The same authors have quantified some metal ions and showed the implication of molecules in the  $\text{Na}^+\text{-K}^+$ -pump action. These studies make possible to know for example that cardiac glycosides inhibit the  $\text{Na}^+\text{-K}^+$ -pump and increase the level of sodium ions in the myocytes, leads to a rise in the level of calcium ions. This inhibition increases the amount of  $\text{Ca}^{2+}$  ions used in heart muscle contraction in the distention of the heart [1-22].



**Figure 3:** Compounds the most quoted in *Lantana rhodesiensis*.

(1) = Camphor, (2) = Limonene, (3) = Camphene, (4) = Terpenoid, (5) = Cubebene, (6) = Cineole, (7) = Stigmasterol, (8) = Ursolic acid, (9) = 5,6,7,3',4',5'-hexamethoxyflavone, (10) = Phytol, (11) = pinene, (12) = Lanatoside C, (13) = Sabinene, (14) = 5-hydroxy-6,7,3',4',5'-pentamethoxyflavone

### Pharmacological investigation

The antiproliferative activity of *L. rhodesiensis* was evaluated in order to justify the traditional use for the treatment of cancer [9]. The antiproliferative activity was evaluated by MTS method on normal cells (Vero and MCR5) and cancer cells (KB) in contact with the extracts for 72 h. The results showed that the plant isn't genotoxic. *L. rhodesiensis* induced a very significant

antiproliferative effect against cancer cells with 94%. Then it was reported the significant anti-proliferative effect of *L. rhodesiensis* extracts against KB (KERATIN-forming tumor) cell lines and its anti-leishmanial property [9].

Alkaloids, anthraquinones, peptides, steroids, terpenes/terpenoids, tannins, with its extended groups are relevant pharmacophores in the anticancer properties [23]. They act are by cytotoxicity or phosphorylation on the cells [3-23]. Sometime their chemical structure (alkaloids, peptides, steroids, tannins, and

terpenes/terpenoids) of acetylpoaranotin contains disulfide bridges, which are able to generate reactive oxygen species and are responsible for their cytotoxicity properties. Other time, block their activation (alkaloids, anthraquinones) by reducing the amount of phosphorylation is an important attribute for cancer therapy [23-27]. Whole plant of *L. rhodesiensis* extract in Methanol and Methylene chloride was used in decoction to treat cancer [9]. According to these authors, the anticancer molecules isolated from West African plants are known. It's acetoxyljatropholone, balanitin-6/7, butyrospermol acetate, cinnamate, 15-Epi-4E-jatrogrossidentadion, 2-Hydroxy-isojatrogrossidion, 2-epi-hydroxyisojatrogrossidion, jatropholone, 4-Z, 4E-jatrogrossidentadion, kurubasch aldehyde, longistylin A, longistylin C, lupeol acetate, cinnamate, multidione, 2''-Oxovorucharin, pinostrobin, parkioside B, riproximin, 2-oxovorucharin, uscharin, voruscarin, curcusone A, B, C, D.

The presence of heterogeneous phytoconstituents such as alkaloids, saponins, tannins, terpenoids, flavonoids, anthraquinones and sterols have been associated with hypoglycemic activity [18-28]. The steroids and phylobatannins present in the plant make it a good source of steroidal compounds which are potent precursors for the synthesis of sex hormones [4-8]. Cardiac glycosides present in *L. rhodesiensis* have been shown to aid in treatment of congestive heart failure and cardiac arrhythmia [4-8].

However several authors meant toxicity related to the plant [4-29]. According to Piero *et al.* [4] which study (the antidiabetic and Safety of *Lantana rhodesiensis* in Alloxan Induced Diabetic Rats), the slight toxicity could be associated with the phytonutrients present in this plant. Other authors arrived to show that this toxicity was related to 5-hydroxy-6,7,3',4',5'-pentamethoxyflavone [15]. They speculated in the mechanism of toxicity of *Lantana rhodesiensis* extract bound to the loss of weight [4]. They initially noted that toxicity was related to a high dose and suggests that extract contained phytochemical constituents which promoted degradation of proteins from skeletal muscles and hence retarded growth. It's noted that among these former investigations, any indication on the cumulative aspect or not of toxicity is not found. According to the chemical structure comparison there are suspected the cytotoxic effect of 5-hydroxy-6,7,3',4',5'-pentamethoxyflavone is due to the hydroxyl and ketone moieties in carbons 5 and 6, respectively [15-29].

### Antimicrobial activity

The presence of phenolic compounds in the leaf extracts of *L. rhodesiensis* indicates its antimicrobial properties against pathogenic bacteria [4-31]. Thorough studies showed that the flavonoids and tannins were more effective on bacteria [32,34]. According to Vaquero and its collaborators [32], quercetin inhibits *P. mirabilis*, *K. pneumoniae* and *E. coli* with less than 25 µg/mL (concentration test range between 5 to 1000 mg/L). Thanks to their

property to precipitate proteins, the tannins inhibit the hydrolytic enzymes (protease and carbohydrate) or other interactions for inactivating the microbial adhesin of transport proteins [3]. It was already shown that Ca<sup>2+</sup> played a significant role in the elimination of the pathogenic agent through the improvement of the clearance [3-35]. The various studies went up that *Lantana rhodesiensis* was rich in tannins [4-11]. That could justify partly the various traditional uses. The glycosides highlighted in the plant also possess strong antibacterial properties. Antibiotics such as streptomycin, neomycin, kanamycin, paromomycin, gentimycin and tobramycin are glycosides [4-22]

Another searchers were previously showed that 5-hydroxy-6,7,3',4',5'-pentamethoxyflavone exhibited anti-microbial and anti-fungal activities against various pathogens, including *Staphylococcus aureus*, *Salmonella typhimurium*, *Candida tropicalis*, *Aspergillus niger*, *Aspergillus fumigatus*, *Trichopyton mentagrophytes*, and *Microsporium canis* [15].

### Antioxidant activity

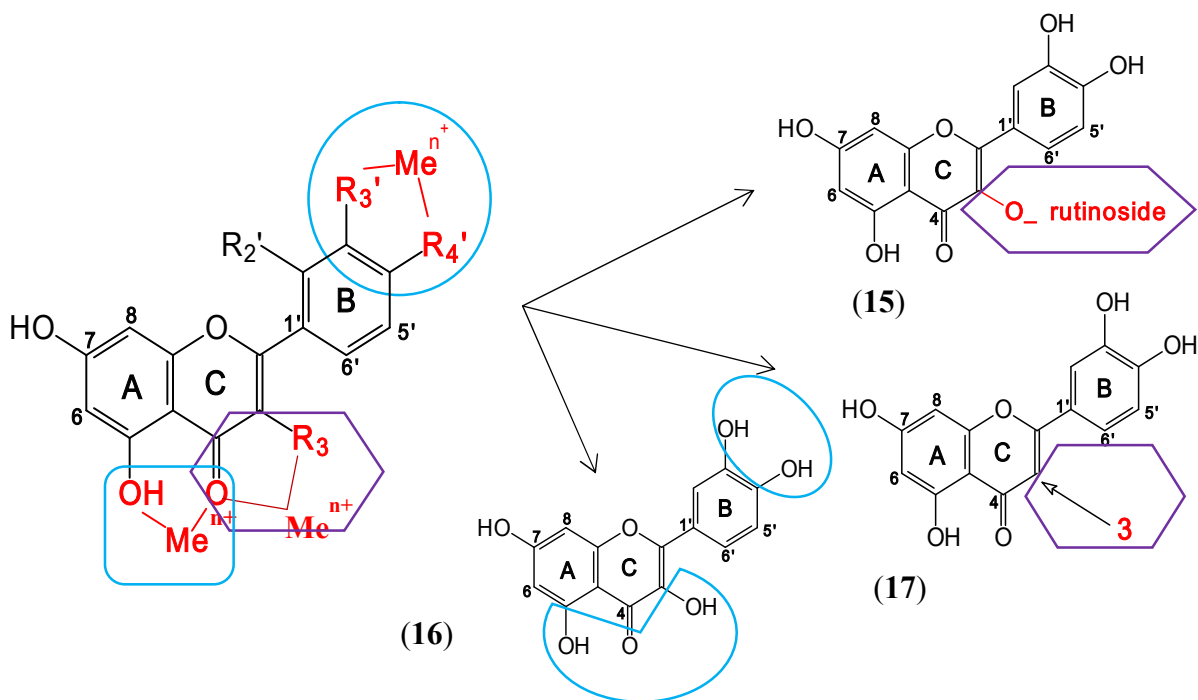
According to a study undertaken by Sawadogo and its collaborators in [9], *L. rhodesiensis* has a strong antioxidant activity. The IC<sub>50</sub> values were 5.96 ± 0.40 µg.mL<sup>-1</sup>. They used DPPH method to evaluate the antioxidant activity. The antioxidants of natural origins are present in all the parts of plants and are in general phenolic compounds. They act by the desactivation of the radicals, creation of covalent addition, the reduction of metals or peroxides, the complexation of ions and metals of transition and collecting from oxygen singulet [3-36].

The flavonoids are recognized for their biological activities. The flavonoids are likely to react with the majority of the oxygenated reactive species [37]. Because of their low potentials redox, the flavonoids are thermodynamically able to reduce the oxidizing of free radicals, like superoxide, peroxy, alkoxy and hydroxyl, by transfer of hydrogen and the radical flavonoxyl [38]. The consequences of this mechanism make it react with another radical to form a stable structure [3-38].

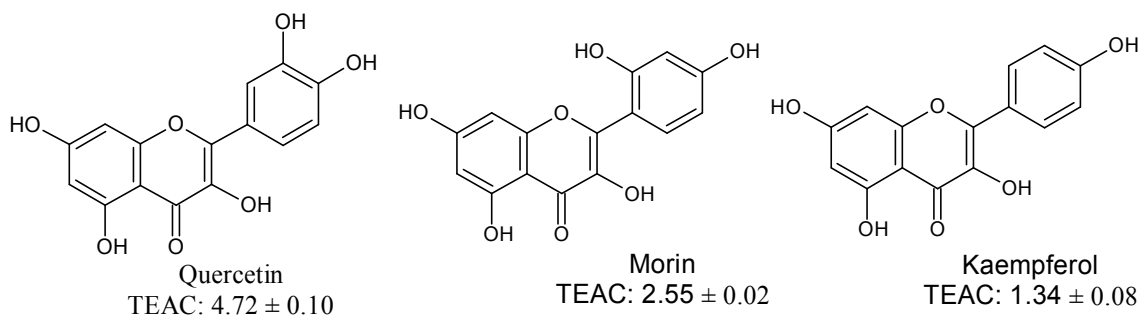
The flavonoids are also regarded as goods chelating of ions metal [39,40], like Fe<sup>2+</sup> and Cu<sup>+</sup> which are essential for certain physiological functions, but they are also responsible of the hydroxyl radical production by the reduction of hydrogen peroxide. Quercetin is most active of the flavonoids studied. Figure 4 summarizes the essential sites for the chelation of the metal ions: (a) a core catechol on the cycle B, (b) groups 3 hydroxyl and 4-oxo of the cycle C, and (c) the 4-oxo groups and 5-hydroxyl enters the cycles A and C [3-41].

Several works describes the relations structure-activities of the flavonoids [41-43]. This work makes it possible to know the antioxidant activities of these molecules according to their structural characteristics Figure 5. In fact, their antiradicalaire activity requires that:





**Figure 4:** Mechanism showing the sites of trapping of the free radicals by flavonoids. (15) = Rutin, (16) = Quercetin, (17) = Luteolin and saponarin.



**Figure 5:** Values of TEAC showing the importance of the catechol grouping on the cycle B level for the flavonols antioxidant activity.

The molecules having a double connection between carbons C2, C3 and carbonyl grouping in C4 [38-44],

The ortho-diphenolic structure of the cycle B (= hydroxyls groupings in position C3'-C4') as well as a significant number of residues hydroxyls would increase the antioxidant potential of the flavonoids having a heterocycle saturated [37-43].

The flavonoids inactive and stabilize the free radicals thanks to their hydroxyl grouping (C3-OH) strongly reactive. Rice-Evans and its collaborators [45] showed the importance of this last. Indeed, the glycosylation of the 3-OH quercetin group (case of rutin) or its suppression (case of the luteolin) decreases the antioxidant activity.

Rice-Evans and its collaborators [45] developed a test based on the antioxidant capacity to trap the radical chromophoric cation. The activity of the flavonoids is compared with that of Trolox (soluble form of -tocopherol), and expressed in TEAC (Trolox Equivalent Antioxidant Capacity). It should be noted that more the value of TEAC is high, more the compound is active. The results of this study showed that morin and kaempferol which have respectively two and one groupings hydroxyls in Meta are less active than quercetin (two groupings hydroxyl in Ortho). By analyzing all these results relating to the capacity of the flavonoids to trap the free radicals one can conclude that quercetin satisfied all

these criteria. It is the most active compound of the family of flavonoids [45].

### Enzymes activities

The enzymatic activity consisted with the evaluation of the inhibition of four enzymes against the methanolic extracts of *L. rhodesiensis*. These investigations were reported by [11]. Among these enzymes, one counts the acetylcholinesterase, glutathione-S-transferase, carboxylesterase and xanthine oxidase activities. 100 µg/mL were used as concentration test of the extract. The author didn't determine a result on the Xanthine oxidase inhibition. On the other hand the allopurinol which is used like a reference (against Xanthine oxidase) compound gave a percentage of inhibition of  $96.38 \pm 0.59\%$ . However, the best percentage of inhibition was obtained on glutathione-S-transferase ( $39.76\% \pm 2.41$ ), which is enzymes when it's over-expressed is implied in the tumoral diseases [3-46]. With regard to the glutathione-S-transferase, the reference (ethacrynic acid) didn't displayed any inhibition. This result is followed of that of carboxylesterase inhibition. The ascorbic acid, used as reference for the carboxylesterase inhibition showed 56.72 % inhibition, while the extract of *L. rhodesiensis* showed 32.37 %. Comparatively, more than 55% of inhibition value of reference compound. Enzyme which is however implied in the chemoresistance of the cardiovascular diseases treatment in general [11-48]. The galantamine, used as reference for the inhibition of the acetylcholinesterase, displayed 50.76% inhibition, against the 17.65 % showed by the extract of *L. rhodesiensis*.

### Others activities

The repellency of *L. rhodesiensis* against *Anopheles gambiae* sensu lato and *Anopheles funestus* in Lwanda, western Kenya where shown by [49]. Malaria remains an important public health problem, and is endemic in more than 100 countries in the world [49]. These authors showed that malaria has large impacts on the sub-Saharan population (90% of the deaths are due to this disease).

Sawadogo [9], evaluated In vitro antileishmanial and antitrypanosomal activities of five medicinal plants from Burkina Faso. They used methanol extract to test and to reveal probable antileishmanial and antitrypanosomal activities. Colorimetric and spectrophotometric methods to detection of antileishmanial and antitrypanosomal activities. *Leishmania donovani* (LV9 WT) and *Trypanosoma brucei brucei* GVR 35 were used to test the antileishmanial and antitrypanosomal activities, respectively. All extracts of tested plants showed a significant antitrypanosomal activity with minimum lethal concentrations between 1.5 and 25 µg/ml, the *L. rhodesiensis* extract being the most active. In the antileishmanial test, only the extract from *L. rhodesiensis* showed significant activity with an inhibitory concentration (IC<sub>50</sub>) of 6.9 µg/ml.

### Conclusion

Moreover, preliminary phytochemical screening showed the presence of saponins, flavonoids, tannins, triterpenoids, and steroids. All of these compounds are well known for their anticancer properties and could be responsible for the beneficial effect of that plant.

We will retain that the plant with fact object of several studies especially in Africa. On the phytochemical level, several compounds were highlighted and/or isolated. The pharmacological properties of the isolated molecules especially were the subject of study on the carcinogenic level. *Lantana rhodesiensis* gave interesting activities on the studies of parasitologic, antioxidant, antimicrobial and carcinogenic. The various authors showed the interest of this plant in the food and the implication of these extracts in various activities. With the threshold of this investigation, we plan to evaluate the polyphenolic compound through the decoctions, acetone and the ethanol-water extracts. In a more specific way we count:

To quantify the phenolic compounds and the flavonoids in the total extracts and fractions,

To evaluate the antioxidants activities through three methods in the total extracts and the fractions,

To evaluate their content of metals in the total extracts,

To evaluate the anti-bacterial activities in the extract ethanol-water,

To evaluate the composition of essential oils through the mass spectrometry,

To study chromatographic profiles of phenols acids and flavonoids through HPLC-DAD method in the extracts and the fractions,

To consider the drafting of a monograph of the plant.

### Author's contribution

### Acknowledgement

We are grateful to the Interuniversity Council of the French Community of Belgium/University Committee for the Development (CIUF/CUD) for the financial support through the training and excellence research fellowship (2009-2012). The authors thank the World Academic Sciences (TWAS) and the Consejo Nacional de Ciencia y Tecnologia (CONACYT) for the financial support through the training and excellence research fellowship. Award of 2012 CONACYT-TWAS Postdoctoral Fellowship. FR number: 3240267272. Authors also gratefully acknowledge the financial support by the International Fondation of Sciences through the grand F3979-1 allowed to Dr. Martin Kindrebeogo.

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