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Research paper

Medicinal Potential of Flavonoids Extracted from The Leaves of Lippia Multifora Moldenke: Review

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Abstract

Flavonoids are natural pigments found throughout the plant kingdom. They are present in certain fruits, vegetables, drinks, plant-based foods, and medicinal plants. They form a large family of several natural compounds. They include flavanols, flavanones, isoflavones, flavonols, flavones, and anthocyanins. The organoleptic properties and therapeutic effects of flavonoids extracted from the leaves of Lippia multifora Moldenke have been the subject of numerous studies. Flavonoids extracted from Lippia multifora Moldenke leaves are claimed to be antioxidant, anti-allergic, anti-inflammatory, antimicrobial, and anti-carcinogenic. They are used in a wide range of sectors, including food processing, cosmetology, and the pharmaceutical industry.

Keywords: *Lippia multiflora, Flavonoids, Leaves, Medicinal potential.*

1. Introduction

Medicinal plants are used to prevent and treat various illnesses [1,2]. Medicines are mainly of natural origin. Pharmaceutical laboratories are looking for active compounds, turning to the identification and characterization of molecules from natural matrices [3,4]. They draw inspiration from their molecular structure to develop new drugs [5]. Many scientists are therefore interested in adding value to plants. The vital elements of phytodiversity for human well-being are being studied [2,6]. Plants contain a range of polyphenolic compounds [1,4,6]. These include flavonoids [3,4]. These are natural pigments found in vegetables and fruit. Flavonoids are essentially of plant origin. They form one of the most extensive families of antioxidants and free radical scavengers. They comprise several classes of compounds with similar structures and have a wide range of biological activities [3,4]. They have a protective role in carcinogenesis, inflammation, and atherosclerosis, as well as significant antioxidant activity [2,3,4]. The Lippia genus includes several species of herbs, shrubs, and small trees. The multiflora species is found in Central Africa and Central and South America. Moldenke's classification is the most widely used [7]. This species is traditionally used as a remedy for gastrointestinal and respiratory ailments. Various experimental studies have demonstrated antiviral, antioxidant, cytostatic, anti-inflammatory, and antiplasmodial activities [5,6,8]. *Lippia multiflora* Moldenke or Bulukutu in Kongo is often used as a conventional tea in the Congo [2,9]. Numerous studies have been reported on the essential oil, aqueous, hydro-ethanolic, and ethanolic extracts and leaf fractions of this species in Congo Brazzaville [10,11,12]. The leaves of *Lippia multiflora* Moldenke, containing flavonoids, are used in the treatment of malaria and arterial hypertension [13,14,15]. The aim of this study was therefore to summarize what is known about the medicinal potential of flavonoids extracted from the leaves of *Lippia multiflora* Moldenke, their applications, and therapeutic advances.

2. *Lippia* Multiflora Moldenke

2.1 Synonyms

Lippia multiflora Moldenke is a common plant, commonly used by local people and in traditional medicine. It has different vernacular names depending on the people [2].

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Table 1: Common names for *Lippia multiflora* Moldenke

Vernacular names	Languages	Country	Regions	References
Avudati, Ahamé, hamé, kidinkon, aganra,	Ewé Bassar Fé	Togo	West Africa	[16]
Agalala, kanhoun, nyèya, Kanhoun	Fon et Goun Yoruba	Benin	West Africa	[17]
Nbornbor, mbalat, duté Ganéla	Wolof Bambara	Senegal	West Africa	[18]
Nasu	Adangbe	Ghana	West Africa	[19]
Eforomoba, Efirin-oko,	Yoruba	Nigeria	West Africa	[20]
Bulukutu	Kongo	Congo	Central Africa	[2,21]
Angasani	Lonkundo	DRC	Central Africa	[7,22]
Ndembi	Umbundu	Angola	Central Africa	[1,23]

2.2 Taxonomy

Lippia multiflora Moldenke has a sequence of elements [2].
Kingdom: *Plantae*
Superdivision: *Spermatophyta*
Infradivision: *Angiosperma*
Class: *Dicotyledons*
Order: *Tubiflorales*
Suborder: *Verbenale*
Family: *Verbenaceae*
Subfamily: *Verbenoideae*
Genus: *Lippia*
Species: *multiflora*

2.3 Geographical Distribution

Lippia multiflora Moldenke is a fast-growing aromatic and medicinal plant with several virtues. This plant is found in sub-Saharan Africa [1]. This heliophilous plant can grow in a variety of ecosystems. Lippia thrives on average annual rainfall of 1,600 mm, average temperatures of 25°C and high humidity [2]. In the Republic of Congo, *Lippia multiflora* Moldenke is found in the departments of Brazzaville, Bouenza, Pool, Niari, Plateaux and Cuvette. It is widely consumed in the Congo [2,9].

2.4 Botany

Lippia multiflora Moldenke is found in sub-Saharan Africa [1,2]. This plant has a woody stump that grows upright in clumps, reaching 2 to 4 m in height [1,2,24]. The stems are sharply angled and branched at the ends. They have oblong, whorled, bluish-green leaves with a long cuneate base, a finely toothed margin, and an acuminate apex, as well as whitish pubescence. *Lippia multiflora* has white flowers in short, cylindrical glomerules. Arranged in terminal colymbiform panicles, they are 5 to 7 mm wide and 5 mm to 2 cm long. This plant produces a sweet, edible fruit with dark yellow flesh. The fruit contains seeds.

2.5 Phytochemical Composition

Lippia multiflora has been the subject of several studies [25,26,27]. Kanko et al. highlighted three molecules, n-tritriacontane (I), ursolic acid (II), and salvigenic acid (III) [28]. Their studies showed that the Verbenaceae family is home to several chemical constituents. Polyphenolic compounds, including flavonoids and lignins, appear to be the dominant constituents, followed by sterols, iroids, and tritepenes.

2.6 Traditional Medicinal Use

Lippia multiflora Moldenke is a plant with a variety of uses [1,2]. The plant is used for food, medicinal, cosmetic, and pharmacological purposes. Local people use it as a tea drink for its aroma [9,29,30]. In traditional African pharmacopoeia, it is used to treat jaundice, colds, coughs, fevers, and nasopharyngitis, and as an insecticide by fumigating the leaves. This plant is a constituent of several improved medicinal recipes, such as Malaria in Mali and Tetra in Congo [2,5].

3. Flavonoids

3.1 Situation about the Plant

Flavonoids are found in the leaves of *Lippia multiflora* Moldenke [2,6,8,11,31].

3.2 Extraction of Flavonoids

Lippia multiflora Moldenke is a source of flavonoids. These flavonoids have a range of positive effects in the food, health, and other sectors, hence their growing importance. The plant material processing stage aims to extract and isolate the target compounds [11,12,31]. The quality of the extract and the effectiveness of the method are influenced by the extraction equipment, the plant material and preparations, as well as the extraction techniques and physicochemical conditions [31]. This summary presents extraction methods and different mechanisms for the selective extraction of flavonoids from plant material [3,4,31]. There is no single extraction procedure for flavonoids,

and each method is unique. For an extraction procedure to be selective, it must combine an optimal solvent or mixture of solvents with an appropriate technique. The method used must be levelled and must achieve an acceptable level of reproducibility and repeatability [6,11,12,31]. The extraction process can raise several questions. Firstly, the type of plant material and secondly, the potential application of the flavonoid extract. The standard extraction algorithm must be methodical to mimic a traditional herbal remedy [31]. The aim of the process is the selective separation of the flavonoid fraction. Selection of the flavonoid extraction process is important and considers the research objectives [31]. Selection of the extraction technique involves several options, divided into two categories. There are modern techniques (extraction by ultrasound, microwave, pressurized liquid, supercritical fluid, enzymatic assistance, and solid phase matrix dispersion) and conventional techniques (maceration, Soxhlet extraction, and reflux). Figure (1) shows the extraction scheme for flavonoids from *Lippia multiflora* Moldenke [11,31].

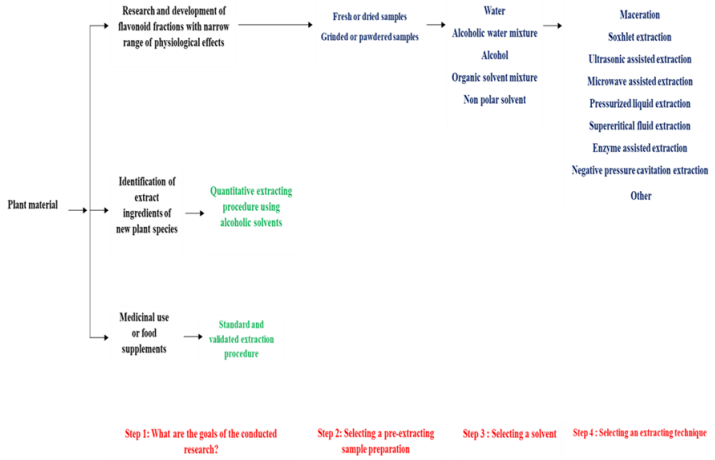


Fig 1.: Flavonoid extraction [31].

3.3 Benefits of Flavonoids

Flavonoids play a role in plant pigmentation. These pigments give different plant organs their red, yellow, orange, and violet colors [3,4]. The pigments responsible for flower coloring are visual signals that attract pollinating animals. Most of these pigments are anthocyanins, aurones, and chalcones [3,32,33]. By complexing specific enzymes, they can metabolize oxygen and nitric oxide or stop the action of radicals. However, they can also exhibit pro-oxidant activity, responsible for lipid peroxidation and damage to DNA and certain proteins. The variety of structures and biological activities makes flavonoids a particular object of study [3,6,11,34]. Flavonoids are involved in plant reproduction, legume-rhizobium interactions during nodulation, auxin transport, seed growth, and protection against microbial invasion, as well as tissue protection against the harmful effects of ultraviolet radiation [3,4]. Flavonoids are present in red wine, tea, coffee, and beer [29,32]. These drinks contain large quantities of flavonoids. They are also found in several medicinal plants. Herbal remedies containing flavonoids are used in traditional medicine throughout the world [1,2,5,28]. Figure 2 shows a summary of some of the roles of flavonoids extracted from the leaves of *Lippia multiflora* Moldenke [3,4].

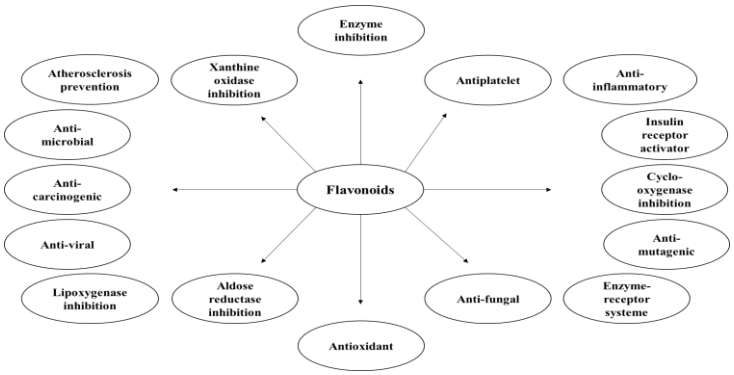


Fig 2.: Role of flavonoids [3,4].

3.4 Description of Flavonoids

Flavonoids are an important family of polyphenols, comprising over 4,000 molecules. They constitute a group of natural compounds that are universal in plants. They are classified into different categories [3,33,35,36]. Among these, flavanones are the most important and are present in citrus fruits (grapefruit, lime, lemon, and oranges). Flavanols are also present in onions, cabbage, apples, tea, and wine, among others. Flavones are found in hot peppers, thyme, parsley, celery, and oregano. And flavanols are found in apples, cherries, tea, wine, and cocoa. Isoflavones are found in soy, beans, and peanuts. Finally, anthocyanins are found in blueberries, raspberries, blackberries, cherries, grapes, and red cabbage. They are responsible for red, purple, and blue hues [4,35,37,38].

Flavanols and flavones are widespread flavonoid compounds, notably quercetin, kaempferol, apigenin, and myricetin. Flavanols (catechin) and flavanones (naringenin), as well as dihydroflavonols (dihydrokaempferol, dihydroquercetin) and dihydroflavan-3,4-diols (leucopelargonidol, leucocyanidol) are considered minority flavonoids due to their restricted natural distribution [3,33,35,38]. Lippia multiflora leaves contain compounds such as 5-hydroxy-6,7,4′-trimethoxyflavone, n-tritriacontane, and urolic acid [12]. Nevertheless, flavonoids found in Lippia multiflora include Kaempferol, quercetin, luteolin, and their derivatives [12,28,29,33]. Flavonoids are present in

leaf cuticles and epidermal cells [3,36,38,39]. These pigments are aurones, anthocyanins, and chalcones [4,33,36,40]. In addition, other colorless flavonoids such as flavonones and flavonols interact with anthocyanins to alter the color of flowers and fruit through copigmentation [32,36,38].

Table 2: Some flavonoids

Polyphenols	Groups						References
	Flavanones	Flavonols	Flavones	Flavanols	Isoflavones	Anthocyanins	
Flavonoids	Naringenine Naringine	Quercetine Kaempferol Myricetine Quercitroside	Apigenine, Luteoline, Apigenine-7-neohesperidoside	Catechine	Daidzeine, Genisteine	Cyanidine, Malvidine Petunidine	[3,4,33,34,36]
Flavonoids from *Lippia multiflora*		Quercetine Kaempferol	Luteoline				[12,28,39,40]

3.5 Medicinal Properties of Flavonoids

Flavonoids are antioxidants offering a whole range of biochemical functions of health interest [4,6,11,12]. They are involved in immune function, blood circulation in capillaries, and the brain [3,11,13,34]. They are also involved in liver function, enzyme activity, and platelet aggregation, as well as the metabolism of collagen, phospholipids, cholesterol, and histamine [3,5,33,38]. Flavonoids have been the subject of several studies [3,6,36,37,39].

Table 3: Some medicinal properties of *Lippia multiflora* Moldenke concerning flavonoids

Polyphenols	Medicinal properties	References
Flavonoids	Antioxidant	[3,4,35]
	Anti-inflammatory	[3,36,37]
	Antiplatelet agent	[3,34]
	Pigments and bioconservatives	[4,31,32]
	Bioactive agent	[3,4,26,38]
Flavonoids from *Lippia multiflora*	Antioxidant	[6,11,12]
	Antifalcemic	[9]
	Anticoagulant	[11]
	Anti-inflammatory	[8]
	Antimalarial	[8,13]
	Antihypertensive	[14,15,24]
	Cardiovascular goodness	[15,25]

3.6 Dietary Use

Frequent consumption of flavonoid-rich foods enables the human body to naturally fight certain diseases and maintain good health [3,4,9,39]. The European Food Safety Authority and the European Commission have issued statements on certain health claims for foods and dietary supplements containing flavonoids for all substances combined. The nutritional distribution of certain flavonoids is well documented [2,3,36,38]. Molecules such as naringin, hesperetin, eriodictyol, naringenin, and epigallocatechin gallate are flavanones. They are found in cabbage, garlic, olives, onions, bananas, kiwi fruit, sprouted seeds, and lemons. And molecules such as epigallocatechin, luteolin, epicatechin, and catechin are flavanols. These flavanols are found in green tea, red wine, berries and grapes, as well as apples. And apigenin, wogonin, nobiletin, and diosmin are flavones found in kiwifruit, lettuce, broccoli, green tea, oregano, peas, chamomile flowers, oranges, grapes, pumpkin, spinach, watermelon, brown rice, and rosemary. Flavonols such as kaempferol, malvidin, morin, and galangin are found in peas, grape seeds, apples, citrus fruits, soybeans, onions, cucumbers, strawberries, and tomatoes. In addition, pelargonidin, genistein, cyanidin, and hirsutidin are anthocyanins, found in blue, purple, and red berries. Anthocyanins are found in apricots, black beans, red cabbage, red grapes, pomegranates, red apples, and purple carrots, as well as in red onions, red or purple radishes, eggplant, and colored cereals. Isoflavones (glycitein, equol, and daidzein) are found in soy preparations, parsley, tofu, legumes, beans, and red clover. Flavonoids from *Lippia multiflora* can be safely and beneficially used in everyday foods, offering both interesting flavours and health benefits.

3.7 Traditional Use

The use of *Lippia multiflora* Moldenke, in connection with flavonoids, is widely accepted by populations according to its implications for human health and daily life [1,2,9,39].

Table 4: Traditional use of *Lippia multiflora* Moldenke in connection with flavonoids

Polyphenols	Traditional applications	References
Flavonoids	Food source (tea and cocoa)	[3,4]
	Antioxidant properties	[3,4]
	Boost the immune system	[3,4]
	Hepatoprotective	[3,4]
	Antimalarial	[3,4]
	Food supplements	[3,4]
Flavonoids from *Lippia multiflora*	Herbal tea and/or tea	[1,2]
	Arterial blood pressure	[2]
	Cough	[1,2]
	Reduce fever	[1,2]
	Malaria	[1,2,8,13]
	Influenza	[1,2]

3.8 General Chemistry

Flavonoids belong to the large family of polyphenols. These are subdivided into ten classes, of which flavonoids are the most abundant [3,4]. Flavonoids are made up of the same basic structural element, formed by two benzene rings (rings A and B), linked by a three-carbon linear chain that forms an oxygenated heterocycle (ring C) [3,4,32,33].
Flavonoids are divided into six main subclasses. Variations in structure within the same class of compounds are based on their molecular structure. This is a function of the position of the bond between the B and C rings; the degree of saturation of the C ring; and the degree of oxidation and hydroxylation of the central heterocycle.

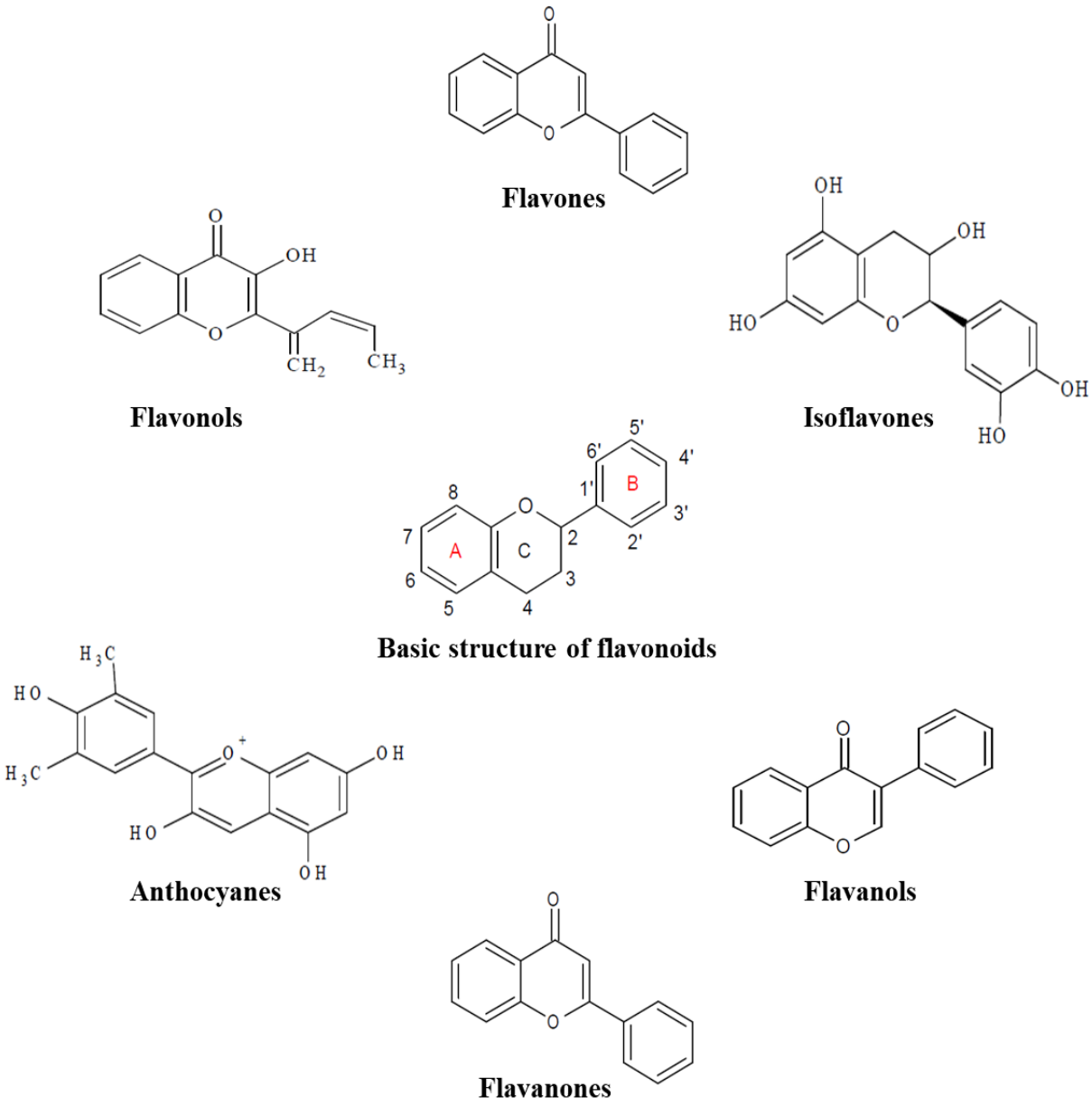


Fig 3 : Structure of flavonoids [4].

3.9 Precautions to be Taken with Flavonoids

The use of flavonoids should be avoided by pregnant and breastfeeding women, children, people taking anticoagulants, or suffering from hypotension (low blood pressure). Some flavonoid-rich products, such as coffee and cocoa [3,4], contain caffeine. Consuming too much of these foods can expose you to the undesirable effects of caffeine, such as palpitations, insomnia, and nervousness. Finally, the rich flavonoid content of red wine should not blind us to the toxicity of alcohol [4,32,36,38].

Table 1: Some research on *Lippia multiflora* Moldenke about flavonoids

Authors	Titles	Years of publication	References
Jigam AA. And *al.,*	In vivo antiplasmodial, analgesic, and anti-inflammatory activities of the leaf extract of *Lippia multiflora* Moldenke	2009	[8]
Constantin M. a*nd al.,*	Total phenolic content, flavonoid profiling, and antioxidant activity of *Lippia multiflora* leaves extracts from Burkina Faso	2015	[6]
Dossa Clément Gandonou a*nd al.,*	Ethnobotanical, phytochemical, and toxicity analysis of a Beninese antihypertensive plant: *Lippia multiflora*	2017	[40]
Clément D. Gandonou, a*nd al.,*	Antiradical activity and determination of phenolic compounds of extracts of *Lippia multiflora* (verbenaceae): a plant traditionally used against arterial hypertension in Benin	2018	[41]
Adrien T.uwisana Masunda a*nd al.,*	. Traditional uses, Physical properties, Phytochemistry and Bioactivity of *Lippia multiflora* Moldenke (Verbenaceae): A Mini-review3	2020	[39]
Lêniféré Chantal Soro a*nd al.,*	Nutritional valorization of Côte d'Ivoire Savannah tea plant leaves	2021	[29]
N'Dri Koffi Emmanuel a*nd al.,*	Optimization of the Extraction of Total Flavonoids and Antioxidant Activity from Lippia multiflora Moldenke (Verbenaceae) Leaves using Experimental Design	2021	[42]
Fako Kane a*nd al.,*	Biochemical composition and sensory characteristics of infusions of leaves from two morphotypes of *Lippia multiflora* (verbenaceae) grown in Côte d'Ivoire	2021	[43]
Joseph Ngaibi a*nd al.,*	Potential of an aqueous extract of *Lippia multiflora* Moldenke (Verbenaceae) in the treatment of anxiety disorders: Possible involvement of serotonergic transmission	2021	[44]
Landry, Martial Miguel, a*nd al.,*	Phytochemical analysis and in vitro evaluation of antioxidants and anticoagulant activities of *Lippia multiflora* Moldenke leaves	2022	[11]
C.A. Massengo a*nd al.,*	Phytochemical study and evaluation of the anti-radical, anti-inflammatory, anti-sickle cell, and cytotoxic activity of the leaves of Lippia multiflora Moldenke (Verbenaceae)	2023	[45]

4. Conclusion

Flavonoids extracted from the leaves of *Lippia multiflora* Moldenke display important medicinal properties in a variety of biological systems. The medicinal potential of flavonoids from *Lippia multiflora* has yet to be fully realized. Nevertheless, numerous studies support their potential for the development of new herbal medicines and phytotherapy. In addition, the use of plants containing flavonoids, such as those from *Lippia multiflora* Moldenke, is steadily increasing due to growing consumer demand for products of natural origin. Flavonoids extracted from the leaves of *Lippia multiflora* Moldenke have properties that justify their use in the prophylaxis of certain pathologies.

Conflict of Interest

The authors declare that they have no conflict of interest in this article.

Author Contributions

AMEMM, OJOM, LMM, and BSWL contributed to the processing, data analysis, and writing of the article. AMEMM and CL did the reading. LMM, DM, and AAA did the proofreading. OJOM was involved in all aspects of the work. AAA is the coordinator of this work.

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