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(REVIEW ARTICLE)

Newbouldia's Laevis biological effects against metabolic syndrome components: A review

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Abstract

This study focused on a review of existing data on *Newbouldia laevis* and its potential effects on metabolic syndrome. Progressive changes in lifestyle that promote sedentary lifestyle, nutritional imbalances associated with excessive levels of refined sugars and fat that promote excess calories, and genetic factors have contributed significantly to the increase in cardiovascular disease, diabetes and the emergence of the concept of metabolic syndrome. Metabolic syndrome refers to an aggregation of factors that intervene, most often together, it is defined as a set of biological and clinical disorders whose metabolic aberrations are mainly: Insulin resistance and dysglycemia, obesity (general and abdominal), atherogenic dyslipidaemia, high blood pressure pro-inflammatory and prothrombotic states. The management of metabolic syndrome is very complex, because the components are associated differently in each patient due to the genetic susceptibility of each to develop one component over another, and the many environmental factors influencing the development of the pathology. The African continent is full of a great diversity of plant species, most of which are used by people as medicines to solve their health problems, because they are readily available. The African hyssop or *Newbouldia laevis* is a plant in the family Bignoniaceae. The qualitative phytochemical screening revealed the presence of alkaloids, tannins, saponins, terpenes, flavonoids, and cardiac glycosides anthraquinones in *Newbouldia laevis* leaf extract. Several therapeutic properties have been attributed to the plant *Newbouldia laevis* including anti-hyperglycemic, cardio-protective and hypotensive activity, body weight reduction, anti-inflammatory, antithrombotic, hepato-protective, antiparasitic, antibiotic. Herbal medicine is an alternative way to treat metabolic syndrome, and its importance is growing.

Keywords: *Newbouldia laevis*: Plant; Biological effects; Metabolic syndrome

1. Introduction

Metabolic syndrome (Smet) refers to an aggregation of factors that intervene; most often together; it is defined as a set of biological and clinical disorders whose metabolic aberrations are mainly: Insulin resistance and dysglycemia; obesity (general and abdominal); atherogenic dyslipidemia; high blood pressure; pro-inflammatory and pro-thrombotic states[1–3]. Progressive changes in lifestyle that promote sedentary lifestyle; nutritional imbalances associated with excessive levels of refined sugars and fat that promote excess calories; and genetic factors have contributed significantly

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to the increase in cardiovascular disease; diabetes and the emergence of the concept of metabolic syndrome (Smet)[4–7]**.** Substances of plant origin have recently acquired a great deal of interest due to their versatile applications. Medicinal plants are the richest bio-resource of drugs in traditional systems of medicine; modern medicine; nutraceuticals; dietary supplements; folk medicine; pharmaceutical intermediaries and chemical entities for synthetic drugs[8]. The management of metabolic syndrome is very complex; because the components are associated differently in each patient due to the genetic susceptibility of each to develop one component over another; and the many environmental factors influencing the development of the pathology[9]. The African continent is rich in a wide variety of plant species; most of which are used as medicines[10]. Indeed; of the 300;000 plant species recorded worldwide; more than 200;000 species live in tropical African countries and have medicinal properties[11]. Plant species are very important to human populations in sub-Saharan Africa because of their contribution to meeting the needs of food; health; energy; income and other aspects of human well-being[12–14]. The African hyssop or *Newbouldia laevis (N. Laevis*) is according to the taxonomic classification a perennial plant of the

- Domain : Eukaryote ;
- Kingdom: Plantae;
- Branch: Spermatophytes;
- Subbranch: Angiosperms;
- Class: Dicotyledons;
- Order: Lamiales;
- Family: Bignoniaceae;
- Genus: *Newbouldia*;
- Species: *Newbouldia laevis*[9;14;15].

N. Laevis is native to tropical Africa; it is found in the Guinean savannahs; and also grows on the humid and well-drained soils of dense forests. It is a very popular plant on the African continent; with diverse claims of effectiveness; widely utilized in traditional medicine by various cultures throughout the tropical Africa; including but not limited to Nigeria; Togo; Senegal; Ghana; Congo; ivory coast; and Cameroun[17]. It is found in secondary forests stretching from Burkina to Senegal; Benin; Côte d'Ivoire; Nigeria; Cameroon; Gabon; Democratic Republic of Congo; Angola[18–20]. Africa is currently undergoing one of the fastest demographic and epidemiological transitions in the history of the world. The future impact of this situation on the prevalence of Smet remains unknown and worrisome with the increase in cardiovascular disease[2;4]**.** Reasons for studying herbal medicines especially *N. Laevis* include the widespread use of herbs in the manufacture of drugs and their immediate availability[12]. Numerous studies have shown the beneficial therapeutic effects both curative and preventive of the leaves of *N. Laevis*: hypoglycemic; anti-hypercholesterolemic; hypotensive; nutritional…[8;20–22]. Plant resources are a real source of pharmaceuticals and therapeutics; but some have not been sufficiently documented[12].

2. Ethno pharmacological use of *Newbouldia laevis*

The World Health Organization (WHO) has recognized the role of herbal medicines or traditional medicine in the administration of primary health care; particularly in developing countries; and has encouraged members of nations to develop national policies for the adequate; sustainable identification; proper exploitation; scientific development and appropriate use of herbal medicines adapted to the prevailing situation[8;23]. In Benin; some studies have been carried out on the traditional use and socio-cultural values of *N. Laevis*. Through the research of Dassekpo et al. in 2017 and 2020; the specific uses of *N. Laevis* have been documented; so in the African culture; *N. Laevis* is very sought after plant and is sometimes associated with other plants during ceremonies (marriage; coronation; for peace; fertility. . .)[12]. Four traditional methods of preparation of *N. Laevis* (boiled in infusion or decoction; macerated and pressed; cold powder often produced by manual grinding; hot powder or inflammation) and several routes of administration (oral; dermal and inhalation) were identified. Plant and all parts of *N. Laevis* were used as drugs[19]. Medicinal plants are the backbone of traditional medical practice; and indigenous knowledge needed for effective herbal medicine practice differs between cultures in different communities (Dassekpo et al.;2017). The African hyssop is thus used in the treatment of several ailments such as: ear infections; bronchopneumonia; malaria; abscesses; dysentery; arthritis; conjunctivitis; in the treatment of wounds; painful pathologies: dental pain; chest pain; otalgia; neuralgia; migraine abdominal pain; in the treatment of hypertension; type 2 diabetes; diarrhea; constipation; epilepsy; convulsions; elephantiasis; joint rheumatism; gastrointestinal ulcer and buruli ulcer; sickle cell anemia dysmenorrhea; hemorrhoid disease; typhoid fever cough; snake bites; the plant is used as an oxytocic during childbirth and as a deworming agent[11;18;24–31].

3. Chemical composition of *Newbouldia laevis*

Several studies have been conducted on the preliminary and quantitative phytochemical constituents of leaves and stems of *N. Laevis;* as well as their toxicological potentials. Thus; after preliminary phytochemical screening; these studies show that leaf and stem extracts and roots contain metabolites which undoubtedly constitute a potential indication of the medicinal utility of *N. Laevis* plant extracts[8;15;30–33;33–47].

Table 1 below represents the chemical composition of *N. Laevis* according to different studies carried out.

Table 1 The chemical composition of *Newbouldia laevis*: Review

Reference	Data from studies
Houghton et al.; 1994 [42]	Small amounts of the three known naphtaquinones (lapachol; dehydro-α-lapachone; and 3-hydroxy-dehydroiso-α-lapachone; and a new alkaloid pyrrolo (1; 2b) pyrazole); newbouldin; were isolated from the root bark of *N. Laevis*.
Eyong et al.;2005[40]	Isolated from *N. Laevis* Newbouldia quinone; a new coupled pigment naphthoquinone-anthraquinone and a new ceramide Newbouldiamide; in addition to the known compounds; lapachol; canthic acid; oleanolic acid; 2-Methyl-9;10-anthracenedione; 2-acetylfuro-1;4naphthoquinone; 2;3-dimethoxy-1;4benzoquinone; 2- (4hydroxyphenyl) ethyl triacontanoate; b-sitosterol and b-sitosterol glucopyrane
Eyong et al.;2006 [39]	In a study of root chemical constituents of *N. Laevis* (Bignoniaceae) isolated and characterized a coupled pigment naphthoquinone-anthraquinone called newbouldiaquinone A; and 14 known compounds: apigenin; chrysoeriol; newbouldiaquinone; lapachol; 2-methylanthraquinone one; 2-acetylfuro-1;4-naphthoquinone; 2;3-dimethoxy-1;4-benzoquinone; oleanolic acid; canthic acid; 2- (4-hydroxyphenyl) ethyl triacontanoate; newbouldiamide; 5;7-dihydroxidehydroiso-alpha -lapachone; beta-sitosterol and beta-sitosterol glucopyranoside.
Usman and Osuji; 2007[47]	Preliminary phytochemical screening of the methanolic extract from leaves of *N. Laevis* revealed the presence of flavonoids; tannins; terpenes; steroids; and cardiac glycosides.
Yemoa et al.; 2008[32]	The results of the phytochemical analysis revealed the presence of flavonoids and the absence of saponin tannins; quinonic derivatives; terpenes and steroids; and alkaloids.
Owolabi et al 2011 ; Okonkwo et al 2009 ; Yusuf et al.; 2013[20;47;48]	Phytochemical screening revealed the presence of saponins; tannins; alkaloids and flavonoids
Akerele et al.; 2011[33]	Phytochemical screening of the pulverized stem bark sample of *N. Laevis* revealed saponins; tannins; flavonoids; steroid glycosides; and alkaloids; while cyanogenic glycosides and anthracenic derivatives were absent.
Olounladé et al;.2012 [50]	In a program aiming at the evaluation of plant as sources of new active molecules; the anthelmintic activities of the essential oils (EOs) obtained from either 2 plants were evaluated against *Strongyloides ratti* by analyzing the results of two in vitro bioassays. the essential oil of the leaves of *N. Laevis* consisted of the following compounds: β-caryophyllene (36%) and eugenol (5. 8%)
Emeka et al.; 2013[37]	The quantitative phytochemical analysis showed that the leaf and stem extracts contained: alkaloids; flavonoids; cardiac; tannins; saponins; steroids and terpenoids. Vitamin A; vitamin C and vitamin E; minerals: Mg; Fe and Se
Bothon et al.; 2014[35]	Qualitatively; the phytochemical screening of *N. Laevis* revealed the presence of mucilage; tannins (gallic and catechin); coumarins; flavonoids. They noted a total absence of anthocyanins and alkaloids in samples studied

Udeozo et al.; 2014[51]	The freshly prepared extracts of *N. Laevis* revealed the presence of Alkaloids; Tannins; Saponins; flavonoids and steroids.
Tuo; 2015[16]	Phytochemical screening of raw extracts and active partitions revealed the presence of a group of secondary metabolites such as sterols and polyterpenes; Polyphenols; Flavonoids Anthocyanins; Lucoanthocyanins; Gallic Tannins Catechic Tannins; Quinones; Alkaloids Coumarines; Cardiotonic glycosides Saponosins and Absence Steroids
Ayoola et al.; 2016[34]	The *N. Laevis* leaves used in this study contained flavonoid; terpenoid; tannin; alkaloid; phytic acid; trypsin inhibitor; phenol; antioxidants; carotenoid; oxalate and cyanide containing
Fatunla et al.; 2017[41]	the qualitative analysis of the methanolic extract of *N. Laevis* revealed the presence of flavonoids; tannins; terpenes; steroidal and cardiac glycosides; alkaloids and saponins were found to be present.
Osigwe et al.; 2017[31]	The preliminary phytochemical tests on the extract gave positive results to alkaloids; flavonoids; glycosides; steroids; saponins; tanins; terpenoids; carbohydrates; proteins; oils; acidic compounds; reducing sugars and resins.
Eneh et al.; 2019[38]	The qualitative phytochemical screening revealed the presence of alkaloids; tannins; saponins; terpenes; flavonoids; cardiac glycosides and anthraquinones in *N Laevis* leaf extract.
Dermane et al.; 2020 [36]	The use of high-performance liquid chromatography method showed to be suitable for the determination of withasomnine; newbouldine; and lapachol derivatives together with other known bioactive compounds like phytosterols and triterpenoids.
Ndidi et al.; 2020 [43]	The phytochemical analysis shows the presence of Phenols; flavonoids; glycosides; tanins; oxalate; terpenoids; anthraquinolones; alkaloids and tanins in both methanolic and aqueous extracts of *N. Laevis.*
Ogbe et al.; 2020 Akande ET AL 2020 [43;51]	The phytochemical constituents of *N. Laevis* include saponins; anthraquinones; tannins; reducing sugars and phenols.
Rashed.; 2021 [45]	Previous chemical studies prouved that *N Laevis* has flavonoids; tannins; terpenes; phenolics; saponins; cardiac glycosides and alkaloids.
Ushie; O. A.; et al.; 2021 [8]	The ethyl acetate; acetone; hexane; and methanol extracts of the *N. Laevis* revealed the presence of such as alkaloid; anthraquinones; saponins; steroids; terpenes; flavonoid; tannins; phenol; and glycosides. The results showed the absence of phlobatannins and tannins in all the extract; steroid is present only in acetone.

4. Chemical effects of *Newbouldia laevis* compounds and their biological activities: A review

In general; preliminary and secondary phytochemical screening has shown that extracts from leaves; stems and roots of *N. Laevis* contain metabolites which are undoubtedly an indication of the medicinal potential of plant extracts[32;36;40].

4.1. Flavonoids

Phenolic compounds; such as flavonoids; are partly responsible for the sensory and nutritional qualities of plant foods. Astringency and bitterness of food and beverages depend on polyphenol content[53–55]. These natural products are well known for their beneficial effects on health and efforts are being made to isolate the ingredients so-called flavonoids. Flavonoids are now considered as an indispensable component in a variety of nutraceutical; pharmaceutical; medicinal and cosmetic applications. This is attributed to their anti-oxidative; anti-inflammatory; anti-mutagenic and anti-carcinogenic properties coupled with their capacity to modulate key cellular enzyme function. Research on flavonoids received an added impulse with the discovery of the low cardiovascular mortality rate and also prevention of coronary heart disease[56–58]. Flavonoids have many activities: antioxidants; anti-inflammatories; enzyme inhibitors; and prevention of cardiovascular disease. Some have hepato-protective; diuretic; vasodilator; antibacterial; chemo protective; anti-inflammatory; antidiabetic; aldolase reductase inhibitor and anti-allergic activities[55;58;59].

4.2. The tannins

Tannins are water-soluble plant polyphenols that precipitate proteins. Overall; tannins have various physiological effects such as anti-irritant; anti-secretolytic; anti-inflammatory; antimicrobial and anti-parasitic effects. Tannins have also been reported to exert other physiological effects; such as to accelerate blood clotting; reduce blood pressure; decrease the serum lipid level; produce liver necrosis; and modulate immune-response[61]. They have been reported to be responsible for decreases in feed intake; growth rate; feed efficiency; net metabolizable energy; and protein digestibility in experimental animals. Therefore; foods rich in tannins are considered to be of low nutritional value[52;60–62].

4.3. Saponins

Saponins are steroid or triterpenoid glycosides; several biological effects have been ascribed to saponins. Extensive research has been carried out into the membrane-permeabilising; immunostimulant; hypocholesterolemic and anticarcinogenic properties of saponins; and they have also been found to significantly affect growth; feed intake and reproduction in animals. These structurally diverse compounds have also been observed to kill protozoans and molluscs; to be antioxidants; to impair the digestion of protein and the uptake of vitamins and minerals in the gut; to cause hypoglycemia; and to act as antifungal and antiviral agents[21;30;36;44].

4.4. Anthraquinones

Anthraquinones; also called anthracenediones or dioxoanthracenes; are important members of the quinone family; and constitute a large structural variety of compounds among the polyketide group. Anthraquinones possess antiviral; antifungal; antibacterial; laxative; Emetic; insecticidal and antioxidant properties; which makes it suitable to be used in the treatment of various ailments[40].

4.5. Pyrazole alkaloids

N. Laevis extracts contain a large amount of pyrazole alkaloids. Alkaloids have diverse physiological effects they are medicinally known as local anesthetic and stimulants; psychedelics; stimulants; analgesics; antibacterials; anticancer drugs; antihypertensive agents; cholinomimetics; spasmolysis agents; vasodilators; antiarrhythmic; antiasthma therapeutics; antimalarials; etc[32;48;63]

4.6. Withasomnine and newbouldine

They are the new main molecules found in *N Laevis* and have been used in traditional Ayurvedic medicine for the treatment of enlarged spleen; migraines; and many infections and as an aphrodisiac. Withasomnine displays both Central nervous system and circulatory system depressant properties as well as being a mild analgesic[35;41;63]

4.7. Naphtoquinones: Lapachol

Lapachol derivatives are naturally occurring naphthoquinones compounds having cytotoxic properties that can be advantageous for treating some types of cancer. These compounds induce oxidative stress and nucleophilic alkylation. Lapachol antiviral; antimicrobial; anti-inflammatory; and antimalarial effects; as well as its significant effect on *Trypanosoma cruzi* (responsible for sleeping sickness) are reported[35;41;64;65].

4.8. Triterpenoids and phytostérols

Multiple triterpenoids and phytosterols have been identified in some *N. Laevis* extracts. Because of their ability to modulate the activity of several signaling networks; triterpenoids and phytosterols seem to be particularly promising for the prevention or treatment of various pathological states in terms of cardiovascular complications; tumor and cell proliferation; inflammation or hepatotoxicity. Ursolic acid (phytosterols) present here in *N. Laevis* demonstrated antitumor and anti-inflammatory properties and has been investigated for its hepato-protective effects[21;35;66].

4.9. Cardiac glycosides

Cardiac glycosides are medicines for treating heart failure and certain irregular heartbeats. They are one of several classes of drugs used to treat the heart and related conditions[45,68,69].

Cardiac glycosides are used to treat patients with atrial fibrillation and atrial flutter. In addition; they can be prescribed for congestive heart failure when the use of other medications fails. The mechanism of action of cardiac glycosides involves inhibiting the Na^+ K^+ ATPase enzyme; also known as the sodium-potassium pump. This causes sodium to build up inside the heart cells; decreasing the ability of the sodium-calcium exchanger to push calcium out of

the cells; consequently, causing calcium to build up in the sarcoplasmic reticulum. Increased intracellular calcium results in a positive inotropic effect; which in turn has the effect of increasing the force of the heart's contractions[44;62;67–70].

5. Toxicity Studies of *Newbouldia laevis*: A review

One of the basic goals of researchers in their effort to discover new drugs is to develop new products with high therapeutic efficacy and low toxicity profile. To accomplish this; more attention has been given to medicinal plants in recent years. This is because medicinal plants present a rich source of compounds that possess different therapeutic effects[72]. Esom-Ibe et *al*. in 2018 evaluated the acute and sub-acute toxicological potentials effect of ethanol extract of *N. Laevis* leaf on serum levels of some liver enzymes and proteins; of urea; creatinine and some electrolytes in rats. Their results showed that ethanol extracts of *N. Laevis* have high safety margins from the oral acute toxicity. Median lethal dose (LD50) was measured; an LD50 of >5000 mg/kg is considered to be very safe[73]. Toxicity studies in animals are usually necessary for any drug intended for human consumption. Kolawole et *al*. in 2013 evaluated; the acute and sub-chronic toxicity profiles of the ethanolic extract of the leaves of *N. Laevis*. In the acute toxicity study; adverse reactions such as sedation; reduced motor activity; unresponsiveness to light touch and auditory stimuli were observed only when the dose of the extract was increased above 1000 mg/kg body weight. The toxic effects observed at very high doses were likely caused by the chemical constituents of the leaves of *N. Laevis* such as tannins; saponins; terpenes and flavonoids. The LD50 (dose of the extract that caused 50 % mortality in the animals) was calculated from the dose-response curve as 5400 mg/kg. This suggests that the extract was non-toxic according to a toxicity classification[74]. In the sub-chronic toxicity study; all the biochemical and hematological parameters assessed in the treated albino rats were not significantly different from the control except the platelet count that was significantly high at high doses. Likewise; examination of liver and kidney sections did not show any morphological changes and inflammatory cells infiltrations. The results of their study suggest that the ethanolic leaf extract of *N. Laevis* has low toxicity profile regarding hematological; blood biochemical and histological parameters in albino rats. When large quantities are used and for a prolonged period; plant extracts may be injurious to health[73;74]. Tsado et al.; 2020 in their study; investigated the acute toxicity and anti-plasmodial effects of the leaf extracts of 2 plants in mice. The safe intraperitoneal dose of the methanol extract of *N. Laevis* in the mice was 200 mg/kg. The doses between 100-200 mg/kg were safe and caused no adverse effects. The LD50 dose of the *N. Laevis* extract was 471.43 mg/kg. The percent inhibition of parasitemia induced by the extracts of *N. Laevis* was 30.14±2.88% compared to the 78.89% achieved for the standard drug (chloroquine). The methanol extract of *N. Laevis* showed a high suppression of the parasite[23]. Itez et *al*. in 2020 examined ameliorative potencies of *N. Laevis* on monosodium glutamate induced toxicity in female albino rats (divided in 6group) for 14 days. Histopathological results showed evident toxicity by disruption of hepatic cords; varying sizes of nuclei; loss of sinusoidal spaces; portal inflammation and dilated central vein. The results from the animal studies confirmed toxicity on monosodium glutamate -exposed rats; while the co-administration of methanol extract of *N. Laevis* indicate its ameliorating efficacy on monosodium glutamate -induced toxicities in rats via anti-oxidation mechanisms. This finding suggest that *N. Laevis* extracts possess medicinal properties that may be effective in management of monosodium glutamate toxicity[76]. Emeka et *al*.; 2013 and Owolabi et *al*.; 2011 have indicates that the leaves and stem extracts are safe for human and animal consumption and (LD50) test of the ethanol extracts of *N. Laevis* leaf and stem have shown that the plant extracts were not toxic respectively up to 5000 mg/kg and 6 g/kg body weight; mortality was at 8 and 1 g/kg. The histopathological examination showed clear restoration of diabetes induced pathological changes in tissue sections. The plants studied here can be seen as a potential source of useful drugs. Udeozo et al.; conducted a study and have determined the acute toxicity by using in the initial phase. Mice were treated with the ethanol flower extract of the plant at doses of 10; 100 and 1000 mg extract per kg body weight and were then observed for 24h for signs of toxicity including death. Signs of toxicity were first noticed after 46 h of extract administration. There was decreased sensitivity to touch and jerking. Also; there was decreased feed intake; tachypnea and prostration after 10 h of extract administration. The median lethal dose (LD 50) in mice was calculated to be 1264.9 mg/kg body weight[51]. The same result was found by Usman et *al*. in 2008[77]. For Murtala et *al*. in 2020; there was no mortality recorded when the extract was given orally up to 5 g/kg; but the animals showed some behavioral manifestations such as dullness; calmness and reduced locomotion within the 2 h post-treatment period of observation. There were no signs of delayed toxicity and mortality in the mice when monitored for 2 weeks' post-treatment. Following intraperitoneal administration; 0; 0; 20; 60 and 100% mortality were recorded at doses of 50; 100; 200; 400 and 800 mg/kg of *N. Laevis*; respectively. The observed behavioral manifestations between 200 and 800 mg/kg were increased respiratory rate; writhing; reduced locomotion and loss of pupillary reflex. The estimated median lethal dose (LD50) was 390 mg/kg[78]. Linus Anderson et *al.* in 2015 tried to check if *N. Laevis* can inhibit cadmium induced testicular toxicity. The histological results revealed that *N. Laevis* treated rat has normal testicular morphology as compared with the control. Co-administered and later treated group still showed testicular damage. From the sections above; it is revealed that *N. Laevis* is unable to reverse the testicular damage caused by cadmium. Since animals given *N. Laevis* alone did not show testicular disruption; it then suggests that *N. Laevis* is non-toxic. The Co-administered; Pre-treated and Post-treated groups showed binuclated

hepatocytes; mild infiltration of inflammatory cells which further explain the *N. Laevis* ameliorated histopathological damage induced by cadmium. The *N. Laevis* reduces the toxicity and absorption of cadmium[79]. Olounladé et *al.;* 2012 in a program aiming at the evaluation of plant as sources of new active molecules; the anthelmintic activities of the essential oils (EOs) obtained from 2 plants leaves were evaluated against *Strongyloides ratti* by analyzing the results of two in vitro bioassays. The toxicity of *N. Laevis* essential oils on the Vero cell line was assessed. No cytotoxicity was found in Vero cells because both essential oils had IC 50 values greater than 50 µg/ml[50]. The results of Solomon et *al.* in 2019 showed that the methanol extract had an IC of 50 = 176. 28 µg/ml; while the standard vitamin C had an IC of 50 = 76. 9 µg/ml. The result of the brine shrimp lethality test of the extract was relatively safe (LC 50 = 2690. 3 µg/ml) compared to the reference potassium dichromate (LC 50=629. 93 µg/ml). This report indicates that the plant's leaf is relatively safe for the purposes used in this study; and is therefore a potential source of antioxidants that may provide protection against oxidative stress[80].

6. Various therapeutic effects of *Newbouldia laevis*: A review

6.1. The cardio-protective effect of the extracts and anti-hypertension activity

Agbafor et *al.* in 2015 reported the cardio-protective potential of aqueous extract of leaf and root in ccl4 induced cardiotoxicity in Albino wistar rats. The extracts contained alkaloids; tannins; saponins; flavonoids; anthraquinones; terpenoids and cardiac glycosides in varied proportions which contribute to the various medicinal applications of leaves and roots of *N. Laevis*[81]. The phytochemical constituents of the extracts contribute to the various medicinal applications of leaves and roots of *N. Laevis*. The effect in the groups treated with leaf extract was significantly different (P< 0.05) from that in root extract treated groups. The cardio-protective potential of 800 mg/kg of leaf extract was significantly higher (P< 0.05) than that of 1.2 ml/kg of aspirin. However; pretreatment of animals with the extracts or aspirin resulted in a significant (P <0.05) and dose-dependent prevention of elevation in the levels of CK; LDH; AST; total cholesterol; triglycerides and HDL and reduction in HDL. The cardio-protective potential may be as a result of the antioxidant property of the phyto-constituents[81].

The results of the study by Fagninou et al.; 2010 showed that the brewing of *N. Laevis* had reduced significantly the arterial pressure after one week of treatment by passing from 174 mmHg after induction in the L-NAME to 160;5 mmHg. A significant difference was also observed with the aqueous extract (500 mg/kg) after two weeks of treatment; by passing from 162 mmHg to 146mmHg. These results show an effect antihypertensive of the leaves of *N. Laevis*[82].

6.2. Anti-oxidant: anticancer

It is probable that the various phytoconstituents of the extracts are involved in scavenging free radicals from tissues; thus; reducing oxidative stress. For example; flavonoids and tannins are phenolic compounds; and plant phenolics are a major group of compounds that act as primary antioxidants or free radical scavengers. Similarly; terpenoids; as vitamins; act as regulators of metabolism and play a protective role as antioxidants[80;82]. Results of the examination of the antioxidant activity of the extracts reported a significant (P< 0.05) increase in heart homogenate malondialdehyde levels and decrease in superoxide dismutase; catalase and glutathione reductase activities of group J; treated with carbon tetrachloride only relative to the untreated control group. The effects of the extracts were dose-dependent; and that of 800 mg/kg leaf extract was significantly higher (P<0.05) than 1.2 mg/kg aspirin. There was a significant difference (P<0.05) between the groups given leaf extract and those treated with root extract. These findings are indicative of possible cardio-protective potential of the extracts; and may be partly responsible for their efficacy against cardiovascular diseases[81]. Salemcity et *al.* in 2020 evaluated the antioxidant properties of *N. Laevis* leaf extracts. His research has provided useful information that shows that *N. Laevis* can inhibit lipid peroxidation; has high vitamin C content; significant antioxidant activity and high phenol content. The plant leaf also scavenged free radicals; as tested by DPPH scavenging assay and hydrogen peroxide assay. The extracts of *N. Laevis* leaf could thus find important application in producing excellent chemotherapeutic and phyto-therapeutic agents against diseases associated with oxidative stress[84]. Woode et al.; 2008 and Solomon et al.; 2019 reported that methanol extract of *N. Laevis* has significant amount of phenol which is a potential source of antioxidants and may be favorably used for the treatment of diseases caused by reactive oxygen species because antioxidants serve as radical scavengers *N. Laevis* possess antioxidant and immunosuppressive activities; which could be attributed to the presence of the secondary metabolites identified by dereplication[79;84]. Same findings were made by Habu and Ibeh; 2015; Ujam et *al*.; 2021 and dermane et *al.;*2020[35;85;86].

6.3. Anti-parasitic; Anthelmintic

In the studies conducted in 2017 and 2012; Olounladé et al*.* evaluated respectively in vivo of the effectiveness of pests leaves *N. Laevis* (Bignoniaceae) was tested on gastrointestinal strongyles of Djallonké infested lambs naturally or

artificially with larvae of *Haemonchus contortus* (*H. contortus*) and *Trichostrongylus colubriformis* in one hand; and in the second hand they realized an egg hatching inhibition test was developed and a larval migration inhibition test was used on *Strongyloides ratti* to examine the effects of essential oils and their inhibitory concentrations (IC 50 and IC 90) values on a *Strongyloides ratti* nematode[50,88]. The results in the first study showed that *N. Laevis* leaves significantly reduced (P <0.05) excretion of gastrointestinal strongyles eggs (80 -90%) in Djallonké lambs naturally infected; regardless of the dose. In the second study; *N. Laevis* gave an IC 50 value of 18. 2 µg/ml; which was approximately seven-fold higher than that of the control (thiabendazole; IC 50 = 2. 5 µg/ml). Therefore; we concluded that *N. Laevis* may contain compounds with antihelmintic activity and could be used as enhanced traditional drugs or; at least; as food additives in a combination therapy for the control of helminth infections[50,88]. Sidi et *al.* in 2015 conducted a study aimed at comparing the combination of powders and methanol extracts of two plants (*Zanthoxylum zanthoxyloides* and *N. Laevis*) on gastrointestinal parasites of Djallonke lambs. The powders were separately administered at the dose of 3.8 g/kg body weight for each plant; and then combined with 50% of this dose to each plant (Mixed 1) and up to 100% of the same dose (Mixed 2). For the methanol extract; a treatment on three consecutive days was tested at the dose of 0.6 g/kg body weight. Leaves powders of *Zanthoxylum zanthoxyloides* and *N. Laevis* administered separately or in combination on three consecutive days therefore disturb the prolificacy of *H. contortus* and *T. colubriformis* while the application of methanolic extracts of both plants alone or in combination; affect their viability[89].

6.4. Anti-hyperglycemic; fat loss

The aqueous leaf extract of *N. Laevis* have been reportedly evaluated by Igbokwe et al.; 2018 and Owolabi et al.; 2011 for its antihyperglycemic activity at 100; 200 and 400 mg/kg body weight as well as obinna et al.; 2016; Okonkwo and Okoye; 2009; Osigwe et al.; 2015; Owolabi et al.; 2011 and Osigwe et al.;2015 at 200 and 250; 500; 1000 mg/kg body weight respectively in alloxan-induced hyperglycemic rats; there is dearth of information in the open scientific literature on the possibility of antidiabetic activity of *N. Laevis* leaf on alloxan-induced hyperglycemia especially at the specific pharmacologic dose of 100 and 200 mg/kg body weight[20;48;89–91]. Those studies revealed a dose specific pharmacologic activity of the aqueous leaf extract of *N. Laevis* at 100; 200; 400; 500 and 1000 mg/kg body weight. The reduction in elevated blood glucose level by the extract of animals may be due to the anti-hyperglycemic effect of the extract; which could have acted by stimulating glucose utilization by peripheral tissues or increasing insulin production by the pancreas from regenerated β-cells[90]. Overall; available evidence from those studies suggests that the aqueous leaf extract of *N. Laevis* attenuated alloxan induced hyperglycemia in rats and facilitated pancreatic insulin secretion and glucose uptake. He observed activity of the extract does not appear at variance with known antidiabetic properties of flavonoids. Some authors observed that hypoglycemia could be a side effect when the extract is applied in folk medical treatment of non-diabetic ailments[20;91].

Emeka et al.; 2013 evaluated the effects of extracts from *N. Laevis* leaves and stem on liver marker enzymes and antioxidant enzymes in a rat model. Their results confirmed that the untreated diabetic rats were subjected to oxidative stress as indicated by significantly abnormal activities of their scavenging enzymes (low superoxide dismutase; catalase and glutathione activities) to the extent of liver enzyme's leakage from the hepatocytes when compared with apparently healthy rats. The ethanol extracts of *N. Laevis* leaves and stem possessed antioxidant activity as shown by increased activities of superoxide dismutase and catalase; and glutathione levels of the diabetic rats after treatment. High levels of alkaline phosphatase (ALP); and alanine amino-transaminase (ALT); which are typical of oxidative stress condition were differentially ameliorated after treatment with the ethanol extracts of *N. Laevis* leaves and stem in a dose dependent manner[37].

Mbagwu et al.; in 2020 obtained same results about the antidiabetic activity of the leaf extract of *N. Laevis* in a type-2 diabetic mice model *N. Laevis* exhibited wide actions in the regulation of glucose and fat homeostasis making it a potential novel agent for the management of diabetes; obesity and their likely associated complications[61].

6.5. Anti-nociceptive and anti-inflammatory

Kolawole et al.; 2013 showed neither morphological changes nor inflammatory cells were observed in the tissues during histopathological assessment of liver and kidney samples at all the test doses[74]. The ethanol extract of *N. Laevis* flower was investigated for possible anti-nociceptive and anti-inflammatory effect in rats by Udeozo et al. in 2014; they induced edema in rats at all the doses (25; 50 and 100 mg/kg body weight I.P) tested in rats when compared to the normal saline control. The activity resides more at the lowest dose of 25 mg/kg; with 42.5% inhibition after 5 h of extract administration. Also in regard to the other doses; 50 and 100 mg/kg; there was also significant decreased to 40.3% and 36.8% respectively after 5 h of extract administration[51]. Anti-nociceptive Effects of *N. Laevis* (P. Beauv.) Stem Bark Extract in a Rat Model were evaluated by Ainooson et al.; 2009. This study presents the effect of a hydro-alcoholic extract of *N. Laevis* stem bark in formalin-induced pain; a model of neuropathic pain; in rats. Morphine (1-10 mg kg^{-1} i.p) and stem bark extract of *N. Laevis* (10-300 mg kg^{-1} p.o.); Dose-dependently decreased both phases of the formalin-induced

nociceptive behavior. Diclofenac (10-100 mg kg^{-1}) was effective only in the second phase (ED_{50} 33.24± 5.20). The potency of the drugs was in the order; morphine > extract > diclofenac for the first phase and morphine > extract = diclofenac for the second phase. The results from this study show that *N. Laevis* extract has central and peripheral analgesic properties; and thus adds credence to its traditional uses (Ainooson et al.; 2009). Agbafor et al.; 2015 in their research investigated Anticonvulsant potential of the extracts against pentylenetetrazole-induced convulsion was tested in albino rats; by measuring time for convulsion onset; duration of convulsion and plasma glucose and Ca2+ levels before; during and after convulsion; using diazepam as standard[83]. All the extracts at all doses and 4 mg kg of morphine sulfate (an analgesic) showed a significant ($p<0.05$) percentage inhibition against hot plate induced pain. The difference between the analgesic potentials of 800 mg kg G1 of Deionized Water Leaf extract and 4 mg kg morphine sulfate was not significant ($p>0.05$)[83]. These findings indicate that the extracts may be effective in management/treatment of pains. They conclude that the leaves and roots of *Newbouldia laevis* contain pharmacologically active compounds; which are responsible for their medicinal applications. The extracts may be useful in management and treatment of nervous system related disorders such as convulsion; anxiety; pains; etc[83]. Hamidu Usman et *al*.; 2008 described similar findings in their studies. The results showed that the ethanol extract possessed significant ($p< 0.001$) anti-nociceptive activity between 50 and 200 mg kg-1 intraperitoneally (i.p.) in mice and also dose dependent anti-inflammatory activity between 50 and 200 mg kg-1 (i.p.) in rats. From the results obtained; although relatively toxic; the extract exhibited highest anti-nociceptive and anti-inflammatory activities at the dosage of 200 mg kg^{-1} (i.p.). These data corroborate with the traditional use of this plant in the treatment of rheumatic pain and other types of pain reported in traditional medicine[93].

6.6. Anti-microbial (antibiotic); healing effect on wounds

Several studies have reported the antimicrobial effect of the plant; a study conducted by Akande et al.; 2020 showed that the concentrations were varied from 100 mg/ml to 400 mg/ml and zones of inhibition at every concentration were recorded. The bacterial isolates including *Staphylococcus aureus (S. aureus); Escherichia coli (E. coli); Pseudomonas aeruginosa (P. aeruginosa); Klebsiella pneumonia (K. pneumonia); Proteus mirabilis (P. mirabilis); Streptococcus pneumonia (S. pneumonia)* and *Salmonella sp*. Findings from this research shows that *N. Laevis* has high antibacterial potency against pathogens in blood even in comparison with some conventional antibiotics used[52]. Other studies have reported similar results[40;65;93]. The bacterial isolated from the samples namely: *E. coli; K. pneumoniae; P. aeruginosa; S. aureus and P. mirabilis* were subjected to antibiotic sensitivity tests[52]. The isolates were resistant to vancomycin and methicilin. Antibacterial activity revealed that Methanol extract exhibited the highest potency against *K. pneumoniae* with 29.03 ± 0.01 and the least activity against *E. coli* with 22.90 ± 0.17. This study has shown that; isolated bacteria were resistant to vancomycin and methicillin[52]. The phytochemical investigation of *N. Laevis* leaf extracts revealed the presence of constituents which could be the basis for their medicinal potency against methicillin and vancomycin resistant organisms[41]. In a study carried out by Udeozo et al.; 2014; the extract at the doses of (25; 50 and 100 mg/kg) showed 59; 71 and 47% inhibitions of the abdominal construction in mice respectively. The highest activity was recorded at lower dose of 50 mg/kg of the acetic acid induced abdominal construction. The results from this research corroborated the claim that *N. Laevis* could be used as health remedies for diarrhoea; typhoid fever and abdominal discomforts. In another study; Akerele et al.; 2011 examined the phytochemical constituents and verifyed the ethno-medical claim of *N. Laevis* in treating septic wounds and eye problems. They have established that the stem bark of *N. Laevis* has antibacterial activities against bacterial isolates from infected wounds and eyes; as claimed in ethno-medicinal practice[33]. Some findings attributed antimicrobial activity to all naphthoquinones that showed antifungal activity against *Cladosporium cucumerinum* and *Candida albicans*; and activity against *Bacillus subtilis* and *Escherichia coli* bacteria[95].

6.7. Anti-malaria

Malaria is an acute febrile illness caused by *Plasmodium falciparum* parasites; which are spread to people through the bites of infected female *Anopheles* mosquitoes[96].

In order to give credence to the traditional practice of treating malaria; several studies have evaluated the effectiveness of the plant. Tsado et al.; 2020 in their study investigated; the acute toxicity and anti-plasmodial effects of the leaf extracts of 2 plants in mice. The parasitemia inhibition by the *N. Laevis* extract was less than half of that induced by chloroquine; the standard drug (30.14% vs. 78.89%)[23]. The methanolic extract of *N. Laevis* (200 mg/kg) showed a high inhibition of the parasite. The results of their study validate the efficacy of the extracts of *N. laevis* traditionally used in Nigeria for the treatment of the fever from malaria infection in human subjects[23]. in another study; Eyong et *al.* in 2006 investigated in vitro antimalarial activity of the plant against *plasmodium falciparum*; their results showed moderate chemo suppression of parasite growth[39]. Antimicrobial activity against a wide range of microorganisms was 13 and 24 times more active against *Candida gabrata* and *Enterobacter aerogens* than the reference names nystatin and gentamicin[39].

6.8. Oxytocic; dysmenorrhea; infertility

Several studies have reported effects of the plant on the uterus. Egba et *al*.; 2014 studied the uterine contractile effects of the aqueous and ethanol leaf extracts of *N. Laevis* in vitro[15]. This study revealed that *N. Laevis* leaves have modulated some of the fertility hormones assayed for. However; its consumption should be taken with caution because of it reduction in the level of testosterone; although not significant[15]. An effect on uterine contraction has been described by Bafor et *al*.; 2010 who reported the leaves of *N. Laevis* increase the frequency of spontaneously contracting tissues and directly stimulate uterine contractions which may account for the use of the leaf extract traditionally[97]. The physiological mechanism of stimulation suggested in one study was that the leaf extract of *N. Laevis* contracts the uterus by opening voltage-operated calcium channels and/or by activation of muscarinic receptors[97]. the oral administration of aqueous leaf extracts of *N. Laevis* can be used to manage hepatotoxicity but not testicular toxicity[79].

6.9. Antidiarrheal

Aderinola et al.; 2019 investigate the anti-diarrheal activity of ethanolic stem bark extract of *N. Laevis* in castor-oil induced diarrhea in rats[98]. The extract (250-1000 mg/kg) showed significant ($p = 0.0399$) anti-diarrheal activity by decreasing the distance of the gastrointestinal movement of charcoal meal in the treated rats and also inhibited the severity of diarrhea induced by castor-oil in a dose-dependent manner when compared with the control (distilled water)[98]. This activity could be attributed to phytochemicals like flavonoids and tannins present in *N. Laevis*. The results showed that stem bark extract of *N. Laevis* possesses a significant anti-diarrheal property; and this supports the traditional use of the plant in the treatment of diarrhea[98]. Same findings for Udeozo et *al*. in 2014[51]

6.10. Arthritis and rheumatism

Woode et al.; 2008 in their study validate the pharmacological use of *N. laevis* stem bark extracts in African traditional medicine for the management of inflammatory conditions such as arthritis. Overall; their results indicate that *N. leavis* has anti-arthritic and antioxidant properties[85].

6.11. Anticonvulsant; anxiolytic; antiepileptic

The anti-convulsivant effect of the ethanolic flower of N Laevis were studied by many authors; Agbafor et al.; 2015; Murtala and Akindele; (2021 and 2020) and Usman. H et al.; 2008[76;77;82;98]. In their investigation; the ethanolic flower extract of this plant was subjected to phytochemical and anticonvulsant study; with the view to evaluating its efficacy as a source of potential antiepileptic agents and the anxiolytic and antidepressant activities. The results showed that the extract under study possesses slight dose-dependent anticonvulsant activities between 40-60% (50-200 mg kg^{-1} body weight) protection against Pentylènetétrazole induced convulsion; they conclude that the anticonvulsant potency of ethanolic flower extract from this plant could favorably suggest the presence of bioactive phytochemicals effective in the therapy of absence seizures and thus help in the control of petit mal; more so; the extract could not be useful in the management of grand mal seizures[77]. The findings of Murtala et al.; 2021 in their study showed that hydro-ethanol leaf extract of *N. Laevis* possesses anticonvulsant; muscle relaxant and antioxidant activities[99]. This confirms the beneficial property of the extract in the treatment of seizures. The same authors in 2020 evaluated the anxiolytic and antidepressant activities of the hydro-ethanol leaf extract of *N. Laevis* in mice and discover the hydro-ethanol leaf extract of *N. Laevis* possesses anxiolytic- and antidepressant-like activities; the latter possibly mediated by dopaminergic enhancement(s)[78].

6.12. Hematopoietic regulators; antithrombotic; anti-sickling activity

Estimation of blood parameters is crucial in evaluating the toxicity of drugs; as changes in hematological system in animal studies have a high predictive value for human[73;99]. In the report of the study carried out by kolawole et *al.* in 2013; suggests that the ethanolic extract of *N*. *Laevis* has low toxicity profile regarding hematological; blood biochemical and histological parameters in albino rats[72]. All blood parameters estimated in the treated rats; except the platelets; did not show significant difference compared with the control group. However; it should be noted that the levels of erythrocytes; leukocytes; hemoglobin and packed cell slightly increased[72]. The slight increase in these parameters and the significant increase observed in platelets may be due to stimulatory effect of the extract on the production of hematopoietic regulatory elements such as thrombopoietin; erythropoietin and colony – stimulating factors by the stromal cells and macrophages in the bone marrow[73;100]. The slight increase in leukocytes may also be due to the normal immunological reaction of the animals to foreign substances[74]. Nwaehujor et al.; 2015 evaluated anticoagulant properties of the methanol extract of *N. Laevis* leaves using blood clotting time; bleeding time and thrombin-induced clotting assay as standard procedures[102]. The results showed that the prolonged in vitro time of blood clotting coupled with in vivo effects that culminated in increased bleeding times and the potentiated thrombin-induced clotting time with the extract demonstrated that the methanol leaf extract of *N. Laevis* possesses pharmacologically active

anticoagulant principles that could be isolated and evaluated for clinical and physiological applications. The methanol leaf extract of *N. laevis* significantly ($p<0.05$) prolonged blood clotting times from the baseline value of 11.0 ± 0.6 s for the blood sample to 18.0 ± 0.7 s and 32.0 ± 1.0 s at 5% and 10% concentrations respectively[102]. The crude extract also exhibited appreciable in vivo and in vitro anticoagulant potency[102]. The effects of the extract on the hematological and some biochemical parameters of alloxan-induced diabetic rats were investigated by Osigwe et al.; 2017; The results showed that Overall; administration of Dichloromethane-methanol has significant ameliorative effect on alloxan-induced anemia and other hematological alterations in diabetes and this may be of immense benefits in the management of diabetes and its associated hematological complications[31]. Improved liver and kidney functions as well as improved antioxidant status are beneficial in the management of chronic diseases such as diabetes[31]. Thus; *N. Laevis* leaf possesses the ability of managing hyperglycemia; improve hematological and biochemical derangements' in alloxan induced-diabetic rats. It can also control muscle wasting and induce adipogenesis[31]. Many studies evaluated the anti-sickling activity of the hydro-ethanolic extracts (leaves; roots and stem barks) of *N. Laevis* P. Beauv. Their outcomes proved that in vitro; roots and stem barks of *N. Laevis* extracts have an anti-sickling activity[35;102–105].

6.13. Hepatoprotective activity

Several studies investigate the effect of the ethanolic leaf extracts and reported The leaf and root extracts may not be as toxic as many medicinal plants; especially when used at doses not greater than 400 mg/kg. The deionized water leaf extract may be hepatoprotective at doses not greater than 400 mg/kg body weight; Histopathological examination of the liver and kidney in treated and untreated rats indicates that the extract is non-toxic at the doses and for the period of 28 days it was administered[73;78;106;107]. Administration of the extract did not cause any significant changes in the levels of these hepatic enzymes. This again indicates that the extract is not toxic to rats at the doses administered.

7. Metabolic syndrome: biological effects of *N. Laevis*

Metabolic syndrome (Smet) is the accumulation of several clinical or biological disorders that increase the risk of cardiovascular disease or type 2 diabetes. Pre-diabetes; Smet and diabetes are associated with an increased risk of cardiovascular disease[109]. In 2017; 15. 9 million people in Africa were living with diabetes and 42. 9 million between the ages of 18 and 99 were pre-diabetes. Pre-diabetes is characterized by abnormal glyco-regulation with fasting blood glucose levels greater than or equal to 6. 1 mmol/l (110 mg/dl); but less than 7. 0 mmol/l (126 mg/dl) according to the World Health Organization[109;110]. Smet refers to an aggregation of factors that most often occur together and for which the causes are often uncertain[3]. Smet is defined as a set of biological and anthropomorphic disturbances whose most readily observable clinical marker is overweight; particularly abdominal obesity[112]. We thus witness the coexistence of a set of metabolic aberrations; mainly:

- Insulin resistance and dysglycemia occur in the majority of people with metabolic syndrome;
- Obesity (general and abdominal): Abdominal obesity is the form of obesity most strongly associated with metabolic syndrome. It presents clinically as an increased waist circumference[7] ;
- Atherogenic dyslipidemia manifests itself in routine analysis of lipoproteins by increased triglycerides and low HDL cholesterol levels[113];
- High blood pressure is strongly associated with obesity and commonly occurs in insulin-resistant people. Hypertension is therefore commonly listed as a metabolic risk factor. However; some researchers believe that hypertension is less "metabolic" than other components of metabolic syndrome[114];
- A pro-inflammatory condition; clinically recognized by an elevation of C-reactive protein (PCR); is commonly present in people with metabolic syndrome[3];
- A prothrombotic state; characterized by increased plasma plasminogen activator (PAI)-1 inhibitor and fibrinogen inhibitor; is also associated with metabolic syndrome[115].

Current evidence suggests that diets high in fatty and/or sweet foods; referred to as "bad food"; associated with low energy expenditure; are one of the main etiologies of metabolic syndrome[112]. Given the variability of the thresholds used from one definition to another; the definitions most frequently cited in the literature are those of the World Health Organization (WHO); the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) and the consensus definition of harmonization formulated in 2009 by the International Diabetes Federation (IDF); the American Heart Association (AHA) / National Heart Lung and Blood Institute (NHBLI)[116]. In face with the variability of the thresholds used from one definition to another; the definitions most frequently cited in the literature are those of the World Health Organization (WHO); the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) and the consensus definition of harmonization formulated in 2009 by the International Diabetes Federation (IDF); the American Heart Association (AHA) / National Heart Lung and Blood Institute (NHBLI)[116].

More than 80% of people in developing countries use herbal medicines to solve their health problems[20;116]. Herbal medicine is an alternative way to treat metabolic syndrome; and its importance is growing despite the existence of some conventional drugs; which are sometimes expensive and unavailable[15;20]. Thus; many studies have demonstrated the beneficial therapeutic effects both curative and preventive of the leaves of *N. Laevis*: hypoglycemic; anti-hyper-cholesterolemic; hypotensive; nutritional[21–23]. The metabolites contained in *N. Laevis* could reduce the prevalence of the metabolic syndrome by acting on glycaemia through its hypoglycemic character; on blood pressure by reducing it and on obesity and cholesterol.

8. Conclusion

Newbouldia laevis is widely used in African traditional medicine and its biological properties have been investigated by researchers from different countries. Lifestyle changes such as lack of physical activity, a rich diet in large cities and genetic predispositions play a major role in the genesis of Smet. Several biological activities such as cardio-protective effect, anti-hypertension activity, antioxidant, antimalarial, antimicrobial, anthelmintic, analgesic, anti-inflammatory, antidiabetic, anti-thrombotic, gastro-hepato-reno-protective, antihypertensive, properties have been reported on the plant. These biological activities are attributed, in part, to the secondary metabolites isolated from the plant. Despite the numerous reports on the biological activities of the plant, there have not been clinical trials on it, partly due to poor study design in some studies. Additional studies in the human population will make it possible to establish the preventive and therapeutic character of the leaves of *Newbouldia laevis* on the metabolic syndrome which have been shown to possess good biological activities, and whose mechanisms of action and safety are already known, should be subjected to preclinical and clinical trials.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest.

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