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REVIEW ARTICLE

Phytochemical and Biological Effects of *Newbouldia laevis* : A Review

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ABSTRACT

Newbouldia laevis (L) plant is a medium sized angiosperm and it is from Bignoniaceae family. In Nigeria vernacular, it is called Aduruku. It is popularly known as the tree of life or fertility tree in Nigeria. The plant has been found to be effective in the treatment of elephantiasis, dysentery, rheumatic swellings, syphilis, constipation, pile and as a vermifuge to round worms. It has also been found useful for earache, sore feet, chest pain, epilepsy and children's convulsion. Previous chemical studies proved that it has flavonoids, tannins, terpenes, phenolics, saponins, cardiac glycosides and alkaloids.

Keywords : *Newbouldia laevis*:, Chemical compounds, Plants, Bioactivities.

INTRODUCTION

The use of plants as medicine is an ancient practice common to all societies especially the African society. This practice continues to exist in the developing nations. It is on this basis that researchers keep on working on medicinal plants in order to produce/develop the best medicines for physiological uses. *Newbouldia laevis* is a tree called as 'Aduruku' and it is a medium sized angiosperm which belongs to the Bignoniaceae family. It grows to a height of about 7 – 8 (up to 15) metres, more usually a shrub of 2 – 3 metres, many–stemmed forming clumps of gnarled branches (Arbonnier, 2004). It is native to tropical Africa and grows from Guinea Savannahs to dense forests, on moist and well-drained soils. It inhabits the secondary forest extending from Senegal to Cameroon, Gabon, Democratic Republic of Congo, Angola (Arbonnier, 2004). In Nigeria, the bark is chewed and swallowed for stomach pains, diarrhea and toothache (Lewis, & Manony, 1977). The plant has been found to be effective in the treatment of elephantiasis, dysentery, rheumatic swellings, syphilis, constipation, pile and as a vermifuge to round worms. It has also been found useful for earache, sore feet, chest pain, epilepsy and children's convulsion (Lewis, & Manony, 1977).

The leaf, stem and fruits have been used for febrifuge; wound dressing and stomach ache (Iwu, 2000). Earlier studies on the leaves and bark of Congolese *Newbouldia leavis* revealed the absence of flavonoids; saponins, quinones, terpenes or steroids (Oliver-Bever,1986). Recent phytochemical studies on the root, root bark and stem of this plant revealed the presence of alkaloids, quinoid and phenylpropanoid amongst others (Gafner, *et al.* 1997, & Germann, *et al.* 2006). *Newbouldia laevis* has been reported to have medicinal value ranging from anti-inflammatory, antioxidant, antimicrobial, anti-fungi, analgestic and wound healing properties (Stefan, et al 1998, Aladesanmi, *et al.* 1998, Chukwujeku, *et al.* 2005, Kuete, *et al.* 2007, Akerele, *et al.* 2001 & Usman, *et al* 2007). Specifically, the stem bark mixed with clay and red pepper has been reported to be effective against pneumonia, fever, cold, cough and for treating different illness like bone lesions (Idu, et al 2009). This review gave the major chemical compounds and bioactivities of *Newbouldia laevis* plant.

CHEMICAL COMPOUNDS

Pyrazole alkaloids

N. laevis extracts contain a large amount of pyrazole alkaloids. Withasomnine and newbouldine derivatives were the main molecules (Schymanski, *et al.* 2014).

Lapachol derivatives

lapachol derivatives from *N. laevis* solvent extracts were more present in root bark extracts. 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 of sleeping sickness) are reported. More, lapachol was reported to inhibit Onchocerca ochengi parasites (Eyong, *et al* 2015). In addition, more recent investigations have shown that lapachol is an effective reagent for preparing new bioactive substances (Kumar, et al 2013). It is believed that the antitumor activity of lapachol may be related to its interaction with nucleic acids (Hussain, *et al.* 2017). The naphthoparaquinone β-lapachone potential as an anti-trypanosomal agent was also reported. Studies demonstrated that β-lapachone can directly target DNA topoisomerases and inhibit their activity, which results in cytotoxicity (Rao, *et al.* 1968).

Triterpenoids

Triterpenoids are the most abundant compounds in *N. laevis* plant extracts. Triterpenoids are widely distributed in the vegetable kingdom. 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. They are highly multifunctional and the antitumor activity of these compounds is measured by their ability to block nuclear factor-κ Bactivation, induce apoptosis, inhibit signal transducer, and activate transcription and angiogenesis (Petronelli, *et al.* 2009). According to the available evidence, triterpenoids provide an excellent base from which to develop new agents that are markedly more potent. The fact that humans have safely been ingesting significant amounts of structurally related triterpenoids compounds as long as they have been consuming for instance olives (rich sources of triterpenoids) suggests that triterpenoid platform might be a relatively safe one for the design of new drugs (Rodriguez, *et al.* 2010). Ursolic acid present here in N. laevis proved antitumor and anti-inflammatory properties and has been investigated for its hepatoprotective effects. The mechanism of effect includes suppression of enzymes that play a role in liver damage such as cytochrome P450, cytochrome b5, CYP1A and CYP2A, and an increase in antioxidant substances such as glutathione, metalothionein, zinc, glutathione-S-transferase and glucuronosyltransferase, with simultaneous protective effects on liver mitochondria (Dzubak, *et al.* 2006). Stigmasterol decreased Ehrlich Ascites Carcinoma tumor volume in mice and increased life span of tumor bearing mice (Ghosh, *et al.* 2011). Canthic acid was first isolated from *Canthium dicoccum* (Chatterjee, *et al.* 1979) at a very poor yield. Our work determinate this acid in *N. laevis* with a relatively high concentration inmethanol leaves extract. This will aid to isolate canthic acid from *N. laevis* leaves and evaluate its biological activity including anticancer activities.

Sphingolipids

Sphingolipids (SLs) were the main compounds and potentially contribute to N. laevis bioactivity. In recent years, there is more and more evidence that SLs function as key components inmodulating cell responses and act as signaling and regulatory molecules. Sphingolipids represent a major class of lipids that are ubiquitous constituents of membranes in eukaryotes. Intensive research on SL metabolism and function has revealed members of the SL family as bioactive molecules playing roles from regulation of signal transduction pathways, through direction of protein sorting to the mediation of cell-to-cell interactions and recognition. SLs have also been reported to dynamically cluster with sterols to form lipid microdomains or rafts, which function as hubs for effective signal transduction and protein sorting (Bartke & Hannun, 2009) ion induced by K+ and that induced by external Ca2+ in the depolarized muscle (Yamahara, *et al.* 1988). Apigenin, a naturally occurring plant flavone, abundantly present *N. laevis*, is recognized as a bioactive flavonoid shown to possess anti-inflammatory, antioxidant and anticancer properties. Epidemiologic studies suggest that a diet rich in flavones is related to a decreased risk of certain cancers, particularly cancers of the breast, digestive tract, skin, prostate and certain hematological malignancies. It has been suggested that apigenin may be protective in other diseases that are affected by oxidative process, such as cardiovascular and neurological disorders (Shukla, *et al.* 2010). Harmalol was reported to decrease heart rate and increased pulse pressure, peak aortic flow, and myocardial contractile force in dogs and could be useful to relieve cardiovascular pains.

Proximate composition of *Newbouldia laevis* leaf

Newbouldia laevis leaves in this study contained 55% moisture, 5.68% crude protein, 5.61% crude fat, 10.54% crude fiber, 2.15% total ash, 21.02% NFE, 626.80 kcal/kg ME and 20.22% NDF. The results on the proximate composition of Newbouldia laevis contradicts the findings of who reported higher contents for crude protein (28.11%) and nitrogen detergent fiber (46.34%) but lower ash (4.81%) relative to that obtained in this study (Gidado. *et al.* 2003).

BIOLOGICAL ACTIVITIES

Antidiabetic and Hypolipidemic Effects

The antidiabetic, hypolipidemic, liver and kidney function effects of the methanol leaf extract of Newbouldia laevis (NLE) was carried out in wistar albino rats. Diabetes was induced by single intraperitoneal administration of 150 mg/kg alloxan monohydrate in overnight fasted albino rats. Newbouldia laevis extract (NLE) caused a significant ($P < 0.05$) time-and dose-dependent reduction in FBS especially at the dose of 250 mg/kg which caused 60.2% reduction of FBS at 24th h compared to the negative control. All doses of NLE used in the study caused significant ($P < 0.05$) doses-dependent decrease in all serum lipids except high density lipid level of treated rats compared to the negative control. It significantly ($p < 0.05$) reduced the cardiovascular risk index as represented by coronary risk and atherogenic indices, just like glibenclamide. The extract caused significant ($p < 0.05$) dose-dependent decrease in Alanine Aminotransferase (ALT) in the liver. Kidney function test showed significant ($P < 0.05$) dose-dependent decrease in serum urea and creatinine levels. The extract (NLE) has demonstrated good antidiabetic and hypolipidemic activities comparable to glibenclamide a standard antidiabetic drug (Bosha, *et al.* 2019).

Antinociceptive Effect

This study showed the effect of a hydro-alcoholic extract of N. leavis 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 behaviour. Nocifensive response for morphine was four fold higher in the first phase (ED50;1.79 ± 0.63 mg kg-1) compared to the second (ED50 ;7.59± 2.26); however the response for the extract was similar in both phases (ED50; first phase 28.28±7.02; ED50; second phase 25.07 ± 5.83). Diclofenac (10-100 mg kg-1) was effective only in the second phase (ED50 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).

Antibacterial Effect

The methanol, chloroform and aqueous leaf extracts of *Newbouldia laevis* were tested for antibacterial effect. The bacterial isolates including Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Proteus mirabilis, Streptococcus pnuemoniae and Salmonella sp. Antibacterial activity revealed that methanol extract had the highest potency with 23.03±0.33e mm, followed by aqueous extract with 21.75±0.22d mm zones of inhibition against S. aureus, and the chloroform extract had the highest activity of 16.0±0.59d mm zone of inhibition against Salmonella sp. while aqueous extract had the least zone of inhibition against P. mirabilis with 10.07±0.67a mm on isolates. All the extracts, irrespective of the extracting solvents had a minimum inhibitory concentrations {MIC} range of 6.25 – 50 mg/ml and minimum bactericidal concentrations {MBC} range of 12.5 – 100 mg/ml. Findings from this research shows that N. laevis has high antibacterial potency against pathogens in blood even in comparison with some conventional antibiotics used (**Akande, *et al.* 2020**).

Anti-inflammatory activity

The ethanol extract of *Newbouldia laevis* flower was investigated for possible anti-nociceptive and anti-inflammatory effect in rats. Acetic acid induced writhing in mice and formalin test in rats were used in the study. The extract caused a significant decrease (P<0.05) which was not a dose dependent inhibition on acetic acid induced writhing and the neurogenic pains induced by formalin. 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 intraperitoneal LD50 value of the extract was found to be 1264.9 mg/kg body weight in mice. The results from this research corroborated the claim that Newbouldia laevis could be used as health remedies for diarrhoea, typhoid fever and abdominal discomforts. Newbouldia laevis could be used in making antibiotics but that should be after its toxicological and active ingredient elucidation (**Udeozo, *et al.* 2014**).

Anti-plasmodial Potential

The Anti-plasmodial activities of both extracts were investigated individually and combined in mice infected with the chloroquine sensitive ANKA-65 Plasmodium berghei strain. Five groups of four mice each were used in our experiments. The LD50 was determined, using the line equation of the mortality against dose levels plot. The extracts of N. laevis and C. adansonii had a safety level of 200 mg/kg (LD50= 471.43 mg/kg) and 600 mg/kg (LD50=3,500 mg/kg), respectively. Each experimental group was infected with P. berghei strain. The percent inhibition of parasitemia induced by the extracts of N. laevis and C. adansonii were 30.14±2.88% and 61.35±1.41%, respectively, compared to the 78.89% achieved for the standard drug (chloroquine). Mice treated with the combined extracts had a parasite inhibition of 24.23±0.86%. Upon the analysis of the extracts, there were tannins, steroids, flavonoids, saponins and alkaloids in both. The quantitative analyses revealed that tannins were the most abundant (261.85±4.76 mg/100 g & 92.71±6.58 mg/100 g) while saponins were the least abundant (15.09±1.13 mg/100 g & 14.08±1.28 mg/100 g) phytochemicals in both extracts. The findings support the notion that the traditional use of either plant in the management of malaria in Nigeria appears to be logical (Ndarubu, *et al.* 2020).

Effects of Newbouldia laevis on Hepatic and Renal Systems in Albino Rats

This study investigated possible toxicity of leaf and root extracts of the plant to liver and kidney in albino rats. Extractions were performed with deionized water and ethylacetate to produce deionized water leaf (DWL), deionized water root (DWR), ethylacetate leaf (EAL) and ethylacetate root (EAR) extracts. A total of 85 adult male albino rats, used in the study, were placed in 16 test and one control groups of five rats in each group. The test groups were given oral administration of 200, 400, 600 and 800mg/kg body weight of the extracts, the control received normal saline for 21 consecutive days. The activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and gamma glutamyltransferase (GGT) in the serum were used to assess hepatobilliary toxicity, while serum creatinine, urea and uric acid were used as renal toxicity indicators. The activities of ALT, AST, ALP and GGT decreased insignificantly (P>0.05) in the groups given 200 and 400mg/kg of DWL extract, while the enzymes activity groups given 200 and 400mg/kg of other extracts increased insignificantly (P>0.05). The increases obtained at 600 and 800mg/kg of deionized leaf extracts were not significant (P>0.05), while those of ethylacetate extracts were significant (P<0.05). The concentration of creatinine, urea and uric acid obtained from serum of the animals treated with DWL extract was insignificantly higher (P>0.05), while the values recorded with other extracts were significantly higher (P<0.05) than in control. These results suggest that deionized water extracts of Newbouldia laevis, as used, may not be toxic to the liver and kidney, while those of ethylacetate may be. Doses of 200 and 400mg/kg DWL extract may be hepatoprotective (Agbafor, *el al.* 2015).

Antioxidants effect of *Newbouldia laevis*

Bioactivity of the extract was determined at 10 µg/ml, 50 µg/ml, 100 µg/ml, 200 µg/ml and 400 µg/ml concentrations expressed in % inhibition. The yield of the ethanolic leaf extract of *N.laevis* was 30.3 g (9.93%). Evaluation of bioactive metabolic constituents gave high levels of ascorbic acid (515.53 ± 12 IU/100 g (25.7 mg/100 g)), vitamin E (26.46 ± 1.08 IU/100 g), saponins (6.2 ± 0.10), alkaloids (2.20 ± 0.03), cardiac glycosides(1.48 ± 0.22), amino acids and steroids (8.01 ± 0.04) measured in mg/100 g dry weight; moderate levels of vitamin A (188.28 ± 6.19 IU/100 g), tannins (0.09 ± 0.30), terpenoids (3.42 ± 0.67); low level of flavonoids (1.01 ± 0.34 mg/100 g) and absence of cyanogenic glycosides, carboxylic acids and aldehydes/ketones. The extracts percentage inhibition of DPPH, hydroxyl radical (OH.), superoxide anion (O2.-), iron chelating, nitric oxide radical (NO), peroxynitrite (ONOO-), singlet oxygen (O2), hypochlorous acid (HOCl), lipid peroxidation (LPO) and FRAP showed a concentration-dependent antioxidant activity with no significant difference with the controls. Though, IC50 of the extract showed significant difference only in singlet oxygen (O2) and iron chelating activity when compared with the controls. The extract is a potential source of antioxidants/free radical scavengers having important metabolites which may be linked to its ethno-medicinal use (Josiah & Bartholomew, 2015).

CONCLUSION

This review showed the literature of *N. laevis* and this plant has many chemical compounds and also many of biological activities.

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