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Review

Ethnomedicinal and Pharmacological properties of *Morinda lucida*

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ABSTRACT

In this review, different research works related to phytochemistry, pharmacological and toxicological activities as well as tradomedicinal use of *Morinda lucida* Benth plant by different researchers have been compiled. The objective of it is to reveal the potential effect of this plant in the development of the chemotherapeutically active herbal drugs which also gives opportunity to pharmaceutical companies interested in the formulation and production of herbal drugs targeted towards specific ailments. Synergy of *Morinda lucida* with other medicinal plants having related properties and activities is also discussed in this paper. This review work therefore focuses good Formulations, Development and Production of Safe and Standardized High Quality Herbal Products from *Morinda lucida* with bias in Good Collection and Manufacturing Practices (GCMP.)

Keywords: *Morinda lucida*; Pharmacological activity; Phytochemistry.

INTRODUCTION

The use of medicinal plants has always been part of human culture and is wide spread in Africa. In some countries, like Ghana, government encourages the use of indigenous forms of medicine rather than expensive imported drugs. Also in Nigeria, a large percentage of the populace depends on herbal medicines because the commercially available orthodox medicines are becoming increasingly expensive and out of reach (Fasola, et al., 2005). Amongst the medicinal plants commonly use in Nigeria for management/treatment of various types of ailments is *Morinda lucida* Benth. *Morinda lucida* (L.) (*Rubiaceae*) is a tropical West Africa rainforest commonly known as Brimstone tree (Adeneye, et al., 2008). *Morinda lucida* is a medium size tree about 15m tall with scaly grey bark, short crooked branches and shining foliage. The leaves are used as “oral teas”, which are usually taken orally for the traditional treatment of malaria, and as a general febrifuge, analgesic, laxative and anti-infections (Makinde, et al., 1985). The leaves have also been reported to possess strong trypanocidal and aortic vasorelaxant activities (Asuzu, et al., 1990). Further studies have shown that leaf and stem bark of *M. lucida* posses anticancer (Sowemimo, et al., 2007), hepatoprotective (Oduola, et al., 2010), cytotoxic and genotoxic (Akinboro, et al., 2005), antispermatogenic (Raji, et al., 2005), hypoglycemia and antidiabetic (Daziel, 1973) activity.

The major constituents of *M. lucida* extract are the various types of alkaloids, anthraquinones and anthraquinols (Adesogan, 1973). Two compounds (oruwalol and oruwal) and 10 anthraquinones have been isolated and characterized from the stem of the plant (Adewunmi, et al., 1984). Despite the profound therapeutic advantages possessed by various parts of this plant, no work has been done to bring together all the researches carried out by different researchers from different parts of the world in order to identify research gaps for further research works and also to enable the development of potent herbal drugs from this plant and or its synergy with other plant to treat common ailments plaguing human lives. This paper review is, therefore, designed to compile most of the research works to be able to identify research gaps and also to enable pharmaceutical companies interested in herbal medicine to tap from the results of various researches carried out on different parts of the plant and formulate, develop and produce effective, non-toxic herbal medicines.

***Ethnomedicine*:** Ethnomedicine from native's point of view is the study of the indigenous way of treating and managing certain diseases affecting people living in a particular environment. This approach is particularly useful for the study of indigenous therapeutic agents since it allows the researcher to understand treatment patterns according to native explanatory models instead of only through the lens of biomedicine. *Morinda lucida* is a medicinal plant growing in many African countries and widely used as a medicine in West Africa. It is generally used as ingredients of fever teas, which are usually taken, for the traditional treatment of malaria. In West Africa *Morinda lucida* is an important plant in traditional medicine. In Nigeria *Morinda lucida* is one of the four most used plants in the preparation of traditional medicines against fever. Decoctions and infusions or plasters of root, bark and leaves are recognized remedies against different types of fever, including yellow fever, malaria, trypanosomiasis and feverish condition during childbirth. In some cases, the plant is employed in the treatment of diabetes, hypertension, cerebral congestion, dysentery, stomach-ache, ulcers, leprosy and gonorrhea (Adesida, et al., 1972).In Côte d'Ivoir a bark or leaf decoction is applied against jaundice and in DR Congo, the decoction of the stem bark or leaf is combined with a dressing of powdered root bark against itch and ringworm (Abbiw, 1990). Adewunmi, et al. (1984) reported in their work that the bark, root and leaf are bitter. They stated that the infusion or decoction of these parts is used for the treatment of yellow fever and other forms of fever. They also reported that the decoction of the leaf is applied to the breast of women at weaning of their infants to prevent infections. However, *Morinda lucida* is used generally for febrifuge, analgesic and laxative (Bever, 1996) while the decoction of the stem bark is used for the treatment of severe jaundice. As reported by Adjanohoun, et al. (1991) *Morinda lucida* is used locally in the treatment of irregular menstruation, insomnia and jaundice though did not stated the parts that are useful in this purpose. Burkill, (1991) also stated that locally, *Morinda lucida* is used in the treatment of wound infections, abscesses and chancre (The primary syphilitic ulcer associated with swelling of local lymph glands and is painless, indurated, solitary and highly infectious)

Also amongst the Igede People in Benue State, Nigeria, it was reported by Igoli, et al. (2005) and Ogaji, et al. (2006) that the decoction of the *Morinda lucida* is used twice or thrice daily as anti – diarrhea, while the leaves are used for treatment of infertility in women.

***Phytochemistry*:** The major constituents of *M. lucida* extracts are various types of alkaloids - anthraquinones and anthraquinols (Adewunmi, et al., 1984). From the wood and bark of *Morinda lucida*, 18 anthraquinones have been isolated, including the red colorants 1-methylether-alizarin, rubiadin and derivatives, lucidin, soranjidiol, damnacanthal, nordamnacanthal, morindin, munjistin and purpuroxanthin. Two compounds (Oruwalol and Oruwal as well as ten anthraquinones) were isolated and characterized from the stem (Adesogan, et al., 1984).In addition to anthraquinones, tannins, flavonoids and saponosides have been isolated. Adesogan, et al. (1983), Rath, et al. (1995) and Koumagho, et al. (1992) isolated anthraquinones and oruwacin from the roots of *M. lucida*. Trease and Evans, (2002) also confirmed the presence of the above constituents in their publication. Two known triterpenic acids (Ursolic and oleanolic acids) were isolated from the leaves (Richard, et al.,

2006). Three compounds (digitolutein, rubiadin 1-methyl ether and damnacanthal) were extracted from the stem bark (Koumaglo, et al., 1992).

***Pharmacological activity*:** Test with animals confirms the attributed activity of several Traditional Medicinal Applications of *Morinda lucida*. Extracts showed anti-inflammatory, antifever and pain-reducing activity in tests with rats and promoted gastric emptying and intestinal motility. Leaf extracts showed in vitro antimalarial activity against *Plasmodium falciparum* while in several other tests antidiabetic properties were confirmed. Inhibiting effects on cancer tumours in mice have also been reported. A leaf extract gave 100% mortality in the freshwater snail *Bulinus globulus* at a concentration of 100 ppm.

***Antimalarial activity*:** Obih, et al. (1985) investigated the various extracts (stem bark, root bark and leaves extracts) of *M. lucida* for antimalarial activity in a 4 – day schizontocidal test against a chloroquine sensitive strain of *Plasmodium berghei* in mice. The result showed that the stem bark extracts had the most promising result with 96.4% suppression of parasitaemia. They also investigated the antimalarial activity of the leaves extract collected in the month of August as compared to chloroquine and pyrimethiamine on the early and established infections caused by Plasmodium berghei in mice for 4 days. The result showed that 1.0mg/kg of the leaf extract equivalent of chloroquine produced positive effect on early infection. Awe, et al. (1997) evaluated the antimalarial effect of the leaf extracts sample of *M. lucida* against *Plasmodium berghei* in mice during various seasons (March, June, September and December) of the year for schizontocidal activity during early and established infections in 4 – day test and in addition to repository test. The result showed that both the March and June samples were found to be active, while September sample was less active than June sample, the December sample was devoid of activity in the entire test carried out on the early and established infections as well as repository test. Sittie, et al. (1999) studied the structural activities in vitro of anthraquinones extracted from the roots of *M. lucida.* The result showed that an aldehyde group at C-2 and a phenolic hydroxyl group at C-3 enhance the activity of anthraquinones against the growth of *Plasmodium falciparum*. Richard, et al. (2006) also discovered that the petroleum ether extracts from *M. lucida* leaves exhibited in vitro, antiplasmodial activity against *Plasmodium falciparum* with IC_{50} at 3.9±0.3µg/ml. This result was attributed to the presence of Ursolic acid found in the leaves.

Trypanocidal activity: Asuzu, et al. (1990) investigated the effect of the dried leaves methanol extract of *M. lucida* on *Trypanosoma brucei* infected mice. The result showed that the intraperitoneal injection of the extract significantly suppressed the level of parasiteamia after *Trypanosoma brucei* infection in mice which is dose dependent with 1000mg/kg i.p. producing the maximum effect. They however concluded that the best trypanocidal activity was obtained when treatment with *M. lucida* extract commenced simultaneously with Trypanosome inoculation.

***Antifungal activity*:** Rath, et al. (1995) investigated the anti-fungal activity of ten anthraquinones isolated from a dichloromethane extract of the roots of *M. lucida.* The result showed that four of these anthraquinones were active against *Cladosporium cucumerinum* and *Candida albicans*. The result concluded that the most potent anti – fungal anthraquinone was identified as alizarin -1- methyl ether, which exhibited activity against *Aspergillus fumigatus* and *Trichophyton mentagrophytes* at MIC dose of 100 and 50µg/ml, respectively.

***Antidiabetic activity*:** Kamanyi, et al. (1994) investigated the hypoglycemic effect of the aqueous extract of the root of *M. lucida* in alloxan – induced diabetic mice. The result showed that the extract at a dose of 148mg/kg and 280mg/kg produced a significant hypoglycemic effect by causing a fall in blood sugar by 51% and 60% respectively after 4hrs of administration. The result concluded that the aqueous root extract of *M. lucida* exhibited dose dependent potent hypoglycemic effects in both normal and alloxan – induced diabetic mice by oral administration and it is more potent than that observed with chlorpropamide(1 –(p – chlorobenzen-sulphanyl)-3-propylurea). Olajide, et al. (1999) also evaluated the hypoglycemic and anti – hyperglycemic activities of methanol extract of *M. lucida* leaves in normal and streptozotocin-diabetic rats. The result showed that the extract, at MIC dose of 400mg/kg demonstrated a significant($P < 0.05$) and dose dependent hypoglycemic activity

within 4hrs after oral administration while the plasma glucose level was brought down to 42.5±0.4mg/100ml as compared to control value of 67.4± 1.2mg/100ml. The extract also produced a significant (P<0.05) anti-diabetic effect in hyperglycemic rats having a plasma glucose level of 248.7 ± 5.3mg/100ml as compared with animals treated with 10mg/kg of glibenclamide with a plasma glucose level of 251.5± 5.8mg/100ml from day 3 after oral administration with 400mg/kg of the extract. The result suggested that the leaves of *M. lucida* have a strong glucose lowering property when administered to streptozotocin-treated rats. It was then concluded that, the plasma glucose in normal rats decreased from 67 to 42mg/100ml when given 400mg/kg of a methanol extract of *M. lucida* leaves while the extract also improved streptozotocin diabetic rats as much as glibenclamide did.

***Gastrointestinal activity*:** Olajide, et al. (1999) studied the effect of the methanol extract of the leaves on the gastric emptying in rats and intestinal motility in mice while they also investigated the effect of the extract on acetylsalicylic acid – induced ulcer in rats. The results showed that the extract promoted gastric emptying time in rats and intestinal motility in mice. Though, the extract did not induce gastric ulceration in rats, however, it failed to protect against acetylsalicylic acid –induced ulcer in rats.

***Antibacterial activity*:** Ndukwe, et al. (2005) investigated the antibacterial activity of the aqueous extracts from the seventeen selected chewing sticks used in oral hygiene in Nigeria amongst which was the aqueous extract of the root of *M. lucida*, against type cultures of *Staphylococcus aurens, Bacillus subtilis, Escherichia coli, and Pseudomonas aeruginosa* as compared to a standard reference compound – Chlorocresol. The result showed that *M. lucida* aqueous root extract showed appreciable activity against all classes of bacteria isolates, especially, the Gram positive strains (*S. aurens and B. subtilis*) at a minimum inhibitory concentration <2.5mg/ml. It was suggested that the chewing stick extracts of *M. lucida* is a potential source of agents that can be used in the treatment of oral infections and further studies are required to evaluate its value in this regard. Adomi, (2006) also investigated the effect of water and ethanol extracts of the stem bark of two Nigerian medicinal plants amongst which was *M. lucida* on clinical isolates of two Gram - positive and five Gram - negative (*S. aureus, S.typhi, K. pneumonia, P.aeruginosa, E. coli, B. subtilis and Flavobacterium sp.*) bacteria using two standard antibiotics (Chloramphenicol and Ampicilin) as reference drugs. The result showed that, the aqueous extract of the stem bark of *M. lucida* at a concentration of between 500-1000mg/ml inhibited the growth of *S. aureus* and *P. aeruginosa* only. The ethanol extract of the stem bark however, gave the best result at MIC dose of between 250-1000mg/ml by inhibiting the growth of *S. aureus, K. pneumonia, E. coli, B. subtilis* and *Flavobacterium sp*.

Purgative induction in mice by the methanolic leaf extract: Asuzu, et al. (1990) carried out acute toxicity tests of the methanol leaf extract in mice by injecting intraperitonealy the *M. lucida* leaf extract. The result showed that the extract induced purgation in mice from the first hour after oral administration and reached its peak between the third and fourth hour. The LD_{50} was found to be 2000mg/kg.

***Impact of the leaf and bark aqueous extracts on cell populations in various organs of mice*:** Agomo, et al. (1992) studied the impact of extracts of some anti - malaria medicinal plants amongst which was the leaves and barks aqueous extracts of *M. lucida,* on cell populations in various organs of mice and compared the effect with chloroquine treated mice. The result showed that all infected mice treated with the plant extract exhibited chemosuppression activity of early parasitaemia which did not lead to their survival. The result further showed that the total number of nucleated cells in the liver, spleen and peripheral blood of malaria – infected mice increased enormously before the animals died. However, all infected mice treated with chloroquine survived and the number of nucleated cells in both the malaria infected and uninfected mice were decreased.

***Anti-spermatogenic activity of the methanol extract of the leaf*:** Raji, et al. (2005) investigated the effect of *M. lucida* methanol leaf extract on male albino rat reproductive functions by treating two groups of rats with 400mg/kg of the extract for 4 and 13 weeks. The result showed that the methanol leaf extract of *M. lucida* did not cause any changes in body

and somatic organ weights, but significantly increased the testis weight ($P < 0.05$). The result further showed that the sperm motility and viability, as well as the epididymal sperm counts of rats treated for 13 weeks were significantly reduced ($P < 0.05$), which could be due to the acetyl cholinesterase inhibition and glucose lowering properties of this plant since it has been shown to possess hypoglycemic and anti – hyperglycemic activities and fructose utilization as well as glucose oxidation are important means by which spermatozoa derive energy for motility. Also, sperm morphological abnormalities and serum testosterone levels were significantly increased($P < 0.05$), which was supported by the various degree of degeneration in the histologic sections of the testes and this suggested that *M. lucida* methanol extract administration for a long period was capable of permeating the blood testis barriers. There were also various degrees of damage to the seminiferous tubules. The result suggested that, since several studies have reported anti-fertility effects of anti- malarial agents including chloroquine, the anti-fertility activities exhibited by *M. lucida* in this study could be associated with anthraquinones presented in the extract. It was concluded that the chronic administration of *M. lucida* leaf extract could impair reproductive activities in male albino rats, the reversal of which however occurred after a period of time, hence, the extract of *M. lucida* has reversible anti-spermatogenic properties.

***In vitro cytotoxicity of the stem bark methanol extract*:** Ajaiyeoba, et al. (2006) evaluated the in vitro cytotoxicity of 20 Nigerian medicinal plants collected from Southwest and Middle belt, amongst which was *M. lucida* plant sample by using the brine shrimp lethality assay. The result showed that, of the 20 plants studied, only two plants extracts were found to be cytotoxic and this included the methanol stem bark extract of *M. lucida* with LD50 of 2.6µg/ml.

***Hepatotoxicity and nephrotoxicity of the leaf extract in wistar albino rats*:** Oduola, et al. (2010) evaluated Hepatotoxicity and Nephrotoxicity of ethanolic leaf extract of *Morinda lucida* in albino rats. The result of acute oral toxicity (LD_{50}) of *M. lucida* leaf extract was found to be greater than 6400mg/kg body weight as no mortality was recorded in any group of experimental rats. Also, according to (Adeneye, et al., 2008) in an acute oral toxicity study of *Morinda lucida* leaf extract, it was documented that *M. lucida* leaf extract possesses no lethality in rats at 2000mg/kg body weight. However LD_{50} of greater than 6400mg/kg is an indication that the extract may be safe for human consumption, confirming the belief of the herbalists that *Morinda lucida* leaf extract is not harmful. It was also established that ingestion of *M. lucida* leaf extracts has no adverse effect on rat's liver and kidney function.

***Effect of ethanolic root extract of Morinda lucida in male wistar albino rats*:** Anofi, et al. (2011) evaluated the toxicological effect of ethanolic root extracts on rats at 50, 100, 200 and 300mg/kg body weight on hematology, kidney and liver function parameters in Wistar rats for 21days. They reported that the extract did not exhibit any significant ($P<0.05$) effect on red blood cells, hematotoxicity, heamoglobin, mean corpuscular volume, mean corpuscular heamoglobin, mean corpuscular heamoglobin concentration, red cell width coefficient of variation, platelet distribution width and level of total protein, albumen, globulin, sodium, potassium and calcium at all doses. The extract however, cause a significant reduction in the serum levels of white blood cells, platelets, alkaline phosphate, cholesterol, high density lipoprotein cholesterol and low density lipoprotein cholesterol. At lower dose, the extract increased the aspertate amino transferase, but at high doses the parameter was significantly reduced. Similarly, the extract at all doses led to significant increase in the body and absolute organ weights of the animals but no effect on the liver, kidney, heart and lungs body weight ratios. They concluded that though the extract produced some alterations in the parameters investigated, it is unlikely to be heamatotoxic, hematotoxicity and nephrotoxic if consumed repeatedly at the dose investigated in their study.

Synergy with other medicinal plants

Malaria: Aqueous extract of: Stem bark of *Alstonia boonei*, leaves of *Mangifera indica*, fallen dried leaves of *Carica papaya*, stem bark of *Parkia biglobosa* or *Parkia clappertoniana*, leaves of *Morinda lucida*, *Cymbopogon citratus* and leaves of *Cassia podocarpa* (Zac, et al., 1986). This is useful in the Management of malaria infections caused

by *Plasmodium falciparum* and *P. berghei* parasite. Aqueous extract of: Leaf of *Ocimum gratissimum,* leaf and bark of *Azadirachta indica,* leaf and bark of *Morinda lucida,* bark of *Enantia chloranta* (Agomo, et al., 1992). This is useful in the Management of malaria infections caused of *Plasmodium yoeli* caused malaria.

Ethanol extracts of**:** Root bark of *Cryptolepis sanguinolenta,* whole plant of *Euphorbia hirta,* leaves of *Morinda lucida* and whole plant of *phyllantus niruri* (Tona, et al., 1999).

This is useful in the Management of malaria infections caused of *P. falciparum* and *P. berghei* parasites.

Diabetes**:** Methanol, Ethanol and Aqueous extracts of *Mangifera indica* leaves, *Vernonia amygdalina* leaves, *Morinda lucida* leaves, *Momordica charantia* fruits and *Ocimum gratissimum* leaves useful as anti-diabetic (Lotlikar, et al., 1966; Akah, et al., 1992; Aguiyi, et al., 2000; Bamidele, et al, 2002).

Orofacial infections**:** Aqueous extract of: root of *Vitellaria paradoxa,* stem and twig of *Bridellia ferruginea,* stem of *Garcinia cola,* root of *Terminalia glaucescens,* root of *Morinda lucida* and fruit of *Cnestis ferruginea* (Ndukwe, et al., 2005). Treatment of oral infections caused by micro-organisms such as: *Staphylococcus aurens, Bacillus subtilis, Escherichia coli, and Pseudomonas aeruginosa*

Cancer**:** Methanol extract of: leaves of *Lippia multiflora* and bark of *Morinda lucida* are possible combination in the management of Cancer due to their in vitro cytotoxic effect.

This is a proposed activity profile of these two plants drawn from the publication of (Ajaiyeoba, et al., 2006).

Bacterial infections**:** Aqueous, ethanol and methanol extracts of: Stem bark of *Alstonia boonei,* Leaves *of Mangifera indica,* Leaves *of Psidium guajava* and Stem bark of *Morinda lucida* (Adoni, et al., 2005), (Akinpelu, et al., 2007). This combination is useful in the treatment of bacterial infections caused by the Gram +ve and Gram –ve organisms such as: *S. aureus, S.typhi, K. pneumonia, P.aeruginosa, E. coli, B. subtilis and Flavobacterium sp.*

Time and period of collecting *Morinda lucida* parts for effective herbal drug processing

Standardization and quality control of herbal medicine produced from medicinal plants are very essential steps to ensure that the drug used is of good standard and high quality. To achieve a good and effective herbal drug therefore, there is need to collect the plant samples at a time and period when the yield of the active components are at their appropriate levels when processing herbal drug from medicinal plants. Some research works establishing the appropriate period of collecting certain parts of *M. lucida* for crude drug processing to be used against specific ailment like malaria have been carried out. These include the work of (Obih, et al., 1985) the result of which showed that the extract of the leaf sample collected in the month of August has the same anti-malarial effect on both established and prophylactic malaria infections caused by *Plasmodium berghei* parasite, as compared with chloroquine and pyrimethamine respectively, while the work of (Awe, et al., 1992) showed that the antimalarial activity of the leaf extract of *M. lucida* was best with samples collected in March and weakest in December sample when tested against *Plasmodium berghei* caused malaria infections in mice. An unpublished review work by (Lawal, 2003) on the factors influencing the maximization of bio - active components of medicinal plants has also showed that, parts like stem, stem bark and roots are best collected in the evening while aerial parts are best collected in the day depending on the bioactive components of interest. For effective crude drug processing from *M. lucida* therefore, the plant samples are collected in March or August. The stem, stem barks and roots are collected in the evening, while the aerial parts like leaves and flowers are collected in the day time.

CONCLUSION

Morinda lucida benth is no doubt a potential medicinal plant considering its pharmacological activities and ethnomedical use though has some significant toxic effects which can be reduced by administering an appropriate amount of the extracts for a specific period, preferably short. Malaria is a common disease in Africa. The anti - malarial activity of this plant may be compared with that of *Artemisia annua* in that it has effect on both early and

established malaria infections. *M. lucida* in combination with other potential anti-malarial plants may therefore be a possible source for discovery of new chemotherapeutic agents in the treatment of *P. falciparum* and other related parasites causing malaria.

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