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PHYTOCHEMICAL PROFILE AND ANTIMALARIAL ACTIVITIES OF AFRICAN BAOBAB *ADANSONIA DIGITATA* L - A REVIEW

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ABSTRACT

Baobab (*Adansonia digitata*) is a multi-purpose tree with tender root, tubers, twigs, fruit, seeds, leaves and flowers which are edible. Owing to the nutritional and medicinal benefits of baobab tree parts, it has been used for various purposes for the past two centuries in Africa, and some parts of Asia. This has in recent times led to some statutory bodies approving its use in certain food products. *Adansonia digitata* has popular ethnomedicinal application in the treatment of malaria in sub-Saharan Africa. Medicinal plants have been found to contain phytoconstituents of relevance in phytomedicine. Plants have provided active ingredients of medicines for years and are still sources of lead compounds in the development of new therapeutics *A. digitata (*baobab tree in both English and French), are used in the treatment of malaria, fever, among other ailment. The mechanism of anti plasmodial action of this extract has not been elucidated, however, anti plasmodial effects of natural plant products have been attributed to some of their active phytochemical components. *A. digitata,* having reported to be a rich source of antioxidant phytochemiclas different mechanism might be involved.

KEYWORDS

Phytochemicals, Baobab, (*Adansonia digitata* L.), Ethnomedicinal, Pharmacology and Malaria.

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INTRODUCTION

Africa has an abundant novel plant species which are known to be rich in health-promoting compounds, many of which remain undiscovered or unused by the western society (Lamien-Meda A, Lamien CE *et al*, 2008)[1]. The Baobab *(Adansonia digitata L.)* is widely distributed throughout the sub-Saharan Africa and Western Madagascar areas and has many uses, such as medicine, food, and beverages (Diop AG, *et al*, 2006)[2]. The name *Adansonia digitata* was given by Linnaeus, the

generic name honouring Michel Adanson who had been to Senegal in the eighteenth century and described Baobab. The history of the African baobab is well documented in Baum. Darwin documented baobab trees on the St Jago in the Cape Verde Islands in 1832 and he commented on their size and longevity (Armstrong P. 1977)[3]. *Adansonia digitata L.* is the most widely spread of the Adansonia species on the African continent which belongs to the family of Bombacaceae a sub family of the Malvaceae. Adansonia species comprises of 8 different species with large, spectacular, nocturnal flowers (Baum DA. 1995)[4]. One of these species is the *A. digitata L.*, it occurs throughout the drier parts of Africa. A second species is restricted to North-Western Australia (A. gibbosa), and the remaining six species are endemic to Madagascar (Baum DA. 1995)[5]. The African baobab is known by a very large number of local names: English (Baobab, Monkey bread tree, Ethiopian sour gourd, Cream of tartar tree, Senegal calabash fruit, Upside-down tree), French (pain de singe, arbre aux calebasses), Portuguese (Cabaçevre), Arabic (Buhibab, hamao-hamaraya, Habhab, Hamar, Tebeldi,), Afrikaans (Kremetart), Hausa (Kuka), sotho (Seboi), tswana (Mowana), Tsonga (Shimuwu), venda (Muvhuyu) (Burkill, 1985)[6]. African baobab is a very long-lived tree with multipurpose uses. It is thought that some trees are over 1000 years old. Since it is not grown agronomical nor properly domesticated (Chevalier MA. 1995)[7]. It has been introduced to areas outside Africa and grown successfully. The tree provides food, shelter, clothing and medicine as well as material for hunting and fishing[3]. Every part of the baobab tree is reported to be useful (Aitzetmuller K 1996)[8]. The baobab has an extensive root system and high water holding capacity. Its mean annual temperature range is 20-30°C, but it can tolerate well high temperatures up to 40-42°C (in West Africa), it's resistant to fire, and survive low temperature as long as there is no frost. It is drought tolerant and frost sensitive. This adaptation allows it to grow in zones with 100-1000mm annual rainfall, but trees are often stunted in the lower rainfall areas. The tender root, tubers, twigs, fruit, seeds, leaves and flowers are all edible and they are common ingredients in traditional dishes in rural areas in Africa. The fruit is said to have high vitamin C content 10 times that of an orange, while leaves are high in mineral content and pro-vitamin A. the oils extracted from the seeds are said to be edible due to the fatty acid composition. Knowledge of all this properties is limited due to the consumers and researchers (FAO, 1998)[9].

Ethnomedicinal Uses

This majestic tree is revered in Africa for its medicinal and nutritional value. Many parts of the plant are used to treat various ailments, such as diarrhea, malaria, and microbial infections. Other activities include use for urinary tract disorders; as adiaphoretic for fevers; as an anti-inflammatory for mild asthma, fatigue, dysentery, kidney and bladder diseases; and as an expectorant, astringent, and tonic. It is reported that it is an excellent antioxidant due to the vitamin C content. It has a widely held reputation as an antiviral and anti-inflammatory medicine. The leaves are most valuable for medicinal uses, but the fruits and stem bark are also used in the preparation of remedies.

Constituents

Baobab fruit pulp has 10 times the Vitamin C content of orange (w/w). It also contains the following, per 100g: water 8.7g, energy 1290kJ (308kcal), protein 2.7g, fat 0.2g, carbohydrate 73.7g, fiber 8.9g, Ca 335mg, Mg 167mg, P 76.2mg, Fe 2.7mg, Zn 1.0mg, thiamin 0.62mg, riboflavin 0.14mg, niacin 2.7mg, ascorbic acid 209mg. The seed, which is about 55% seed coat and 45% kernel, contains the following, per 100g of kernel: water 8.1g, energy 1805 kJ (431kcal), protein 33.7g, fat 30.6g, carbohydrate 4.8g, fiber 16.9g, Ca 273mg, Mg 640mg, P 5.1mg, Fe 6.6mg, Zn 6.7mg, thiamin 0.25mg, riboflavin 0.14mg, niacin 1.0mg. The fatty acid composition is linoleic acid 34.9%, oleic acid 32.3%, palmitic acid 26.5%, and stearic acid 4.4%. Phytochemical investigation has also revealed the presence of flavonoids, amino acids, fatty acids, vitamins, and minerals. Phytosterols such as campesterol, stigmasterol, isoflucasterol, and

avenasterol are present in the seeds. An alkaloid, adansonin, has been identified from the bark of the baobab tree, and it is believed to be the active agent that is responsible for the antimalarial properties of baobab tree bark. The seed protein contains a large amount of lysine, but its use as a protein source is limited by the presence of antinutritional factors such as trypsin, tannins, oxalic acid, protease inhibitors, phytate, and amylase inhibitors (African Herbal Pharmacopoeia Brendler, T 2010)[10].

Pharmacology

The plethora of biological activities attributed to baobab are traceable tothe constituents found in the plant. The analgesic effect of the hot aqueous fruit of *A. digitata in vivo* (mice) has been established. It was noted that the extract exhibited analgesic activity 2 h after administration. At 800mg/kg, the reaction time was 15.4 min in comparison to the negative control (10.2 min). The petroleum ether extract containing seed oil of baobab also showed analgesic activity. The extract exhibited analgesic activity with the tail flick response in 6.1s, which was not statistically different from aspirin used as a positive control. The antipyretic activity of baobab extract has been established by laboratory studies in rats. The hot water extract of the fruits showed *in vivo* anti-inflammatory activity in the rat paw formalin-induced edema test. The extract tested at a dose of 400 and 800mg/kg inhibited formalin induced edema. After 24-h administration of the aqueous extract, the mean swelling of the foot was1.81 and 1.75mm for 400mg/kg and 800mg/kg, respectively, in comparison to the negative control (6.35mm) (Ramadan, A *et al*, 1994)[11]. The DMSO (dimethylsulfoxide) of fruit pulp extract and aqueous leaf extract showed significant inhibition against cytokine interleukin 8 (IL-8). (Vimalanathan, S and Hudson, J.B. 2009)[12]. The capacity of baobab extracts to reduce the mobility of *Trypanosoma brucei*, which causes sleeping sickness, was evaluated using four different extracts (petroleum ether, chloroform, water, and methanol) obtained from the leaves and the bark. The time at which mobility stopped ranged between 10 and 45 min for the root bark, while with the leaves, the mobility ceased between 25 and 45 min when various extracts were tested at 2mg/ml. The extracts also possess only modest activity against the malaria-causing parasite *Plasmodium falciparum.* Because of the widespread use of baobab extract in the treatment of viral infections in West African traditional medicine, several *in vitro* and *in vivo* studies have been carried out to determine the antiviral activity of various baobab plant parts. In comparative studies by (Ananil *et al*, 2000)[13]. Baobab extract was found more active than several herbal extracts tested against the herpes simplex virus (HSV) and sindbis and polio viruses. A later investigation was made by Vimalanathan and Hudson 1132 on the antiviral activity of the leaves, fruit pulp, and seed extracted with water, DMSO, and methanol. The study was conducted using the minimum inhibitory concentration (MIC) method against influenza virus, HSV and the respiratory syncytial virus. It was shown that the influenza virus was very susceptible, while the respiratory syncytial virus was resistant. The leaf extract exhibited the most promising activity against the influenza virus, with the MIC value ranging from 0.12µg/ml (DMSO) to 2.8µg/ml (water). The activity of the leaf extract was promising against the HSV (MIC value 1.0 to 11.7µg/ml), while the pulp and the seed exhibited much lower activity (MIC value 72.5µg/ml). The study clearly demonstrated variation in biological activity when different plant parts are investigated. Furthermore, the anti-HSV activity was considerably enhanced by light, especially long-wavelength ultraviolet (UV) light, although they all showed "dark" antiviral activity as well. Thus, all the extracts contained antiviral photosensitizers (Hudson *et al*, 2000)[14]. Baobab extracts have also been proved effective in laboratory studies to possess insecticidal and insect repellant activity; antioxidant, drug permeation enhancement; and hepatoprotective, hypoglycemic, and hypolidemic activities (Kamatou *et al*, 2011)[15].

Formulation and Dosage Forms

All parts of the plant are used for either food or medicine. Several proprietary products are available with baobab as a major ingredient. In most parts of

Africa, the leaves of baobab are used either fresh as a cooked vegetable or dried and powdered as an ingredient of soups and sauces. The shoots and roots of seedlings are eaten as well. The roots are boiled and eaten in West Africa in times of famine. The flowers are eaten raw. The fruit contains soft, white, edible, and nutritious flesh ("monkey bread"). It northern Nigeria, it is used to curdle milk; it is eaten as a sweet and is used in making gruel and refreshing drinks and ice cream. In Sudan, it is made into a milk-like drink called "gubdi". The powdered fruit flesh is added to cold liquid, thus preserving vitamins. An emulsion of the fruit pulp may be used to adulterate milk. The dried pulp is used as a substitute for cream of tartar in baking (PROTA 2013)[16]. The seeds are eaten raw or roasted and are used to thicken and flavor soup. Fermentation of the seed kernels improves the nutritional value. In coastal Kenya and Tanzania, the pulp-coated seeds are colored and sugar coated and sold as sweets. The seeds are used to adulterate groundnuts and sometimes as a coffee substitute. The oil extracted from the seed kernels by boiling and distillation is semifluid, golden yellow, gently scented, and nondrying and has a long shelf life. It is used for cooking and in the cosmetics industry. The most prominent commercial product is the sun-dried fruit pulp. Roasting and fermentation of both the fruit pulp and the seeds improve their chemical composition, and it is believed that the fermented product with decreased tannin content provides a better ingredient in traditional medicine.

Commerce

Baobab is a major nontimber forest product (NTFP) that plays a significant role in the lives of communities in the savanna, and its many products (seeds, oil, leaves, and fruits) constitute a source of income for many rural people in Africa. Baobab products are used in pharmaceutical and cosmetic industries. According to a United Nations Conference on Trade and Development (UNCTAD). (Gruenwald, J and Galizia, M. 2005)[17]. Baobab is highly sought after in several market segments, such as for food and beverages (Germany, France, and the Netherlands); botanical remedies (Germany, France, and the Netherlands); and nutraceuticals as well as natural cosmetics (European Union, United States, and Japan). Baobab fruit is an ideal candidate in the functional food market as it is very high in Vitamin C and other vitamins and minerals; the powder may be used as a thickener due to its high pectin and fiber contents. The import value of the product class of rare edible dried fruit, which includes baobab fruit pulp, grew by 13% in 2003. The U.S. Food and Drug Administration (FDA) approved on 25 July 2009 the designation of baobab dried fruit pulp (BDFP) as GRAS, indicating it is a substance that is generally recognized as safe, which was based on a submission by Phytotrade in 2008 to that agency. According to the Federal Food, Drug, and Cosmetic Act, Sections 2012 and 409, any substance that is intentionally added to food as an additive is subject to premarket review and approval by the FDA. This makes baobab a major article of international commerce. The designation of BDFP as GRAS, through scientific procedures, allows for its use as an ingredient in blended fruit drinks and fruit cereal bars at levels of up to 10% and 15%, respectively. Similar classification of baobab as a safe food ingredient exists in the European Union.

PHYTOCHEMICAL SCREENING

Phytochemicals can have complementary and/or overlapping mechanisms of action in the body, including antioxidant effects, modulation of enzyme actions, and stimulation of the immune system, modulation of hormone metabolism, anti-bacterial and antiviral effect, bonding, covalent bonding, and nonspecific interactions. The main targets for complexing are cell wall and cell membrane adhesion proteins, hence inactivating microbial adhesion which is the first step in establishment of infections. They also cause cell wall/membrane disruption (Cowan, 1999)[18], (Okuda, 2005)[19], (Biradar *et al*, 2007)[20], (Ngoci *et al*, 2011)[21]. This also inactivates microbial enzymes and cell envelope transport proteins by processes that may involve reaction with sulfhydryl groups of proteins (Samy and Gopalakrishnakone, 2008)[22], (Kaur and

Arora, 2009)[23], Ngoci *et al*, (2011)[21]. They also accumulate/complexes metal ions (e.g. cobalt, manganese, iron, copper, etc.) necessary for microbial growth as co-factors and activators of enzymes. They also inhibit viral reverse transcriptase (Okuda, 2005)[19], (Biradar *et al*, 2007)[21], (Ogunwenmo *et al*, 2007)[24], (Ngoci, *et al*, 2011)[21]. Toxicity to microorganisms in phenolic compounds depends on the site and the number of hydroxyl groups, with evidence that increased hydroxylation results to increased toxicity (Przybylski *et al*, 1998), (Cowan, 1999)[18], (Biradar *et al*, 2007)[20], (Samy and Gopalakrishnakone, 2008)[22], (Ngoci, *et al*, 2011)[21]. They have endocrine role by interacting with estrogen receptors. They are also anti-inflammatory, molluscicidal and hence important in the control of schistosomiasis. They also have antidiarrhoeal, anti-septic anti-fungal properties, anti-parasitic, anti-irritant properties and also used in curbing hemorrhage, in wound healing, and improving vascular health by suppressing peptides that harden arteries (Awoyinka *et al*, 2007)[25], (Ogunwenmo *et al*, 2007)[24], Ngoci, *et al*, (2011)[21]. Also, they have economic role of tanning leathers in leather industry. Nevertheless they affect intake and digestibility of feeds among livestock, and excess can be carcinogenic on normal tissues (Scalbert, *et al*, 2005)[26], (Ngoci, *et al*, 2011)[21].

Flavonoids

They are structural derivatives of flavones, containing conjugated aromatic systems, often bound to sugars as glycosides, and they are phenolic and water soluble in nature (Harborne, 1973)[27]. They exert their roles as anti-oxidants, and hence protecting against degenerative diseases. Flavonoids such as quercetin, act as chain breaking anti-oxidants, and by preventing oxidation of low-density lipoprotein by macrophages and metal ions like copper. This reduces the oxidative stress (Ngoci, *et al*, 2011)[21]. They also act as; 'nature's biological modifiers' as anti-allergens, anti-inflammatory, and induces phase two enzymes that eliminate mutagens and carcinogens (Ogunwenmo *et al*, 2007)[24], (Ngoci, *et al*, 2011)[21]. They also act as anti-microbial by complexing extracellular and soluble proteins, and by complexing bacteria cell wall. More lipophilic flavonoids may also disrupt microbial membranes (Navarro *et al,* 2003)[28], (Al-Bayati and Al-Mola, 2008)[29], (Samy and Gopalakrishnakone, 2008)[22], (Kaur and Arora, 2009)[23], (Ngoci *et al*, 2011)[21]. Probable targets on microbial cell are surface-exposed adhesins, cell wall polypeptides, and membrane bound enzymes. Still others like catechins found inoolong green tea inactivates bacterial toxins (e.g. cholera toxin) and inhibits bacterial glucosyltransferases. Flavonoids are also known to increase coronary flow, to reduce the myocardial oxygen consumption and to lower the arterial pressure (Dong, *et al*, 2005), (Ngoci *et al*, 2011)[21]. They are also known to reduce capillary fragility (Harborne, 1973)[27], to be antiallergic and also to be anti-spasmodic and hence applied to relief asthma and nose bleeding (Ngoci, *et al*, 2011)[21].

Tannins

Tannins are astringent, bitter plant polyphenols that either bind and precipitate or shrink proteins. They have physiological role by acting as antioxidants through free radical scavenging activity, chelation of transition metals, inhibition of prooxidative enzymes and lipid peroxidation Navarro *et al*, 2003)[28], (Vit *et al*, 2008)[30], (Ngoci *et al*, 2011)[21], hence modulating oxidative stress and preventing degenerative diseases. They also inhibit tumor growth by inducing apoptosis (Scalbert *et al*, (2005)[26] and inhibiting mutagenecity of carcinogens (Okuda, 2005)[19], (Ngoci, *et al,* 2011)[21]. They exhibit anti-microbial activity by complexing nucleophilic proteins by hydrogen bonding, covalent bonding, and nonspecific interactions. The main targets for complexing are cell wall and cell membrane adhesion proteins, hence inactivating microbial adhesion which is the first step in establishment of infections. They also cause cell wall/membrane disruption (Cowan, 1999)[18], (Okuda, 2005)[19], (Biradar *et al*, 2007)[20], (Ngoci *et al*, 2011)[21].

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Saponins

These are service active agents with soap-like properties and can be detected by their ability to cause foaming and to haemolyse blood cells (Harborne, 1973)[27]. They have a host of biological roles including boosting respiratory system as expectorant, and hence activity against cough. They also have anti-protozoa activity whereby they act by reacting with cholesterol in the protozoal cell membranes causing cell lysis, e.g. Yucca saponins are effective against protozoan *Giardia lamblia*. They serve as vaccine boosters by acting as adjuvant. They have anti- inflammatory, emetics, antiviral, antifungal, insecticidal, molluscicidal, piscidal and anti-bacterial activity (Ngoci, *et al*, 2011)[21]. The mode of action for the antibacterial effects involves membranolytic properties of the saponin as well as lowering of the surface tension of the extracellular medium (Al-Bayati and Al-Mola, 2008)[29]. They have antineoplastic activity without killing normal cells. This is by reacting with cholesterol rich membranes of cancer cells, and inducing mitotic arrest that causes apoptosis of cell (Ngoci, *et al*, 2011)[21].

Phytosteroids

Phytosteroids are plant steroids that may or may not act as weak hormones in the body. They share a common basic ring structure with animal steroids though they are not equivalent because of varying chemical groups attached to the main ring in different positions (Ngoci, *et al*, 2011)[21]. They are mainly used to treat reproductive complications such as treatment of venereal diseases, used during pregnancy to ensure an easy delivery, as well as to promote fertility in women and libido in men. They also act as sex hormones derivatives, (for example, they can be metabolized to either androgen or estrogen-like substances) and hence they are potential source of contraceptives (Edeoga *et al,* 2005)[31], (Ngoci *et al*, 2011)[21]. They are also anti-microbial, analgesic, anti-inflammatory, and of use in treating stomach ailments and in decreasing serum cholesterol levels Ngoci, *et al*, (2011)[21]. They have also been indicated as potent inhibitors of macrophage activation, blocking the production of pro-inflammatory cytokines and LPS-induced lethality and therefore they have potential use as immunosuppressive agents especially the physalins (Soares *et al*, 2005)[32], (Ngoci, *et al*, 2011)[21].

Terpenoids

These are derivatives of isoprene molecule having a carbon skeleton built from one or more of C15 units (Harborne, 1973)[27]. They exert their roles as anti-bacterial, anti-fungal, anti-viral, anti-protozoan, anti-allergens, as immune boosters and as antineoplastic (Roberts, 2007)[33], (Ngoci, *et al,* 2011)[21]. The mechanism of action is speculated to involve membrane disruption by these lipophilic compounds (Cowan, 1999)[18], (Ogunwenmo *et al*, 2007)[24], (Samy and Gopalakrishnakone, 2008)[22], Ngoci *et al,* (2011)[21]. From laboratory studies of terpenes from Ginseng, it has been suggested that the possible target of these compounds involves hypothalamus-pituitaryadrenal axis due to the observed effects on the levels of adrenocorticotropic hormone and corticosterone (Briskin, 2000)[34], (Ngoci *et al*, 2011)[21].

Cardiac Glycosides

Cardiac glycosides (also called cardenoloids) occurs as a complex mixture together in the same plant and most of them are toxic, however many have pharmacological activity especially to the heart (Harborne, 1973)[27]. They are used in treatment of congestive heart failure, whereby they inhibit Na+/K+-ATPase pump that causes positive

ionotropic effects and electrophysiological changes. This strengthens heart muscle and the power of systolic concentration against congestive heart failure (Ogunwenmo *et al*, 2007)[24], (Ngoci *et al*, 2011)[21]. They are also used in treatment of atrial fibrillation, flatter, and they acts as emetics and as diuretics (Harborne, 1973)[27], (Awoyinka *et al*, 2007)[25], (Ngoci *et al*, 2011)[21].

CONCLUSION

Medicinal plants have been found to contain Phytoconstituents of relevance in phytomedicine (Dahanukar *et al*, 2002)[35], (Somova *et al*, 2003)[36]. Plants have provided active ingredients of medicines for years and are still sources of lead compounds in the development of new therapeutics (Newman, 2008)[37]. *A. digitata* (baobab tree in both English and French), is used in the treatment of malaria, fever, among other ailment. Anti-plasmodial effect of medicinal plant substances have been shown to be caused by alkaloids, terpenes and flavonoids (Milliken, 1997, Christensen, 2001)[38]. The documented presence of secondary metabolites such as tannins, alkaloids and flavonoids, in *A. digitata*, may be responsible for anti-plasmodium activity of plant (Philipson, 1990[39], Milliken, 1997)[38]. *Plasmodium berghei* parasite is used in predicting treatment outcomes of any suspected antimalarial agent (Agbedahunsi, 2000[40], Adzu and Salawu 2009)[41], due to its high sensitivity to chloroquine making it the appropriate parasite for this study (Peter, 1998)[42], (David *et al*, 2004)[43]. *Plasmodium berghei* has been used in studying the activity of potential antimalarials in mice (Pedronic *et al*, 2006)[44]. It produces diseases similar to those of human plasmodium infection. (Kumar *et al*, 2006)[45], (Peter, 1998)[42]. Substances that reduces parasite multiplication (anti-plasmodial effect) in the host were considered to possess antimalarial activity (Ryley and Peters, 1970)[46]. The mechanism of anti plasmodial action of this extract has not been elucidated, however, anti plasmodial effects of natural plant products have been attributed to some of their active phytochemical components (Ayoola *et al*, 2008)[47], (Sofowora, 1980)[48]. Earlier studies revealed the roles of reactive oxidant specie in curing malaria by creating an unfavourable environment for plasmodial growth (Borris and Schaeffer 1992[49], Levander and Ager, 1993)[50] but with *A. digitata,* having reported to be a rich source of antioxidant phytochemicals (Blomhoff *et al*, 2010)[51], (Brady, 2011), different mechanism might be involved.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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