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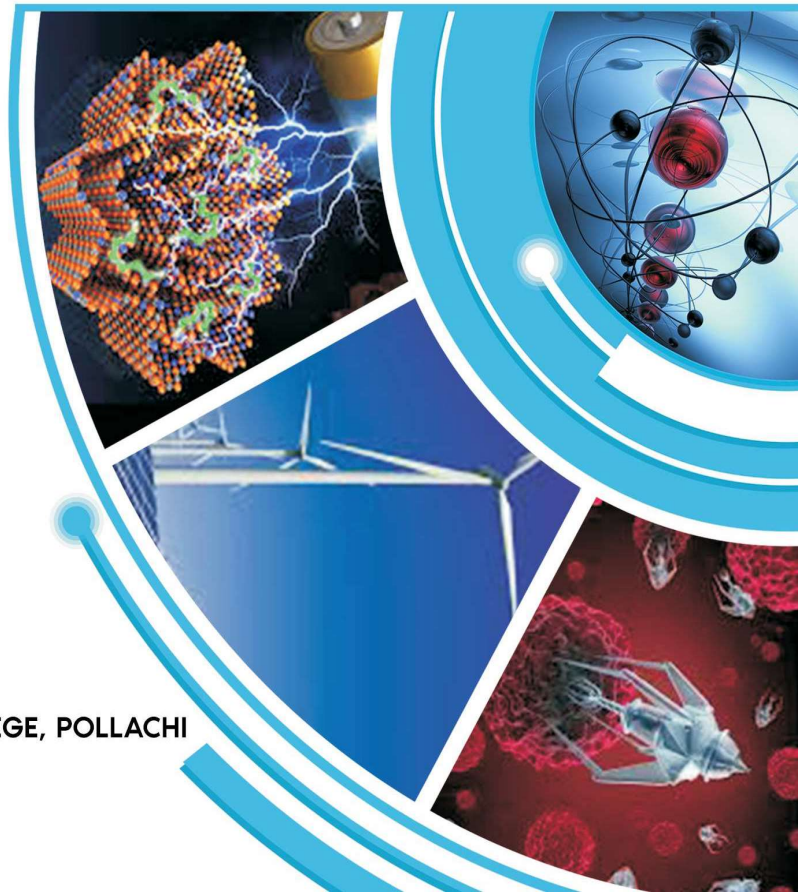

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PHYTOCHEMICAL AND PHARMACOLOGICAL STUDIES OF *ADANSONIA DIGITATA*- AN UPDATED REVIEW

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ABSTRACT

Adansonia digitata L. (Malvaceae) is a majestic tree revered in Africa also found in India for its medicinal and nutritional value. It is one of the tallest trees in the world, commonly known as baobab. It is regarded as the "Queen of all carbon storage trees" and is commonly referred to as the 'upside down tree' or the 'tree of life'. It is reported that it is an excellent anti-oxidant due to the vitamin C content which is seven to ten times higher than the vitamin C content of oranges. The tree has mythological significance and is known as 'Kalpa Vriksha' in India. The tree is rarely found and the only countable number of trees are available in India. The tree is thus named as "The small pharmacy or chemist tree".

INTRODUCTION

A .digitata, a tree plant belonging to the malvaceae family, is widespread throughout the hot drier regions of tropical Africa. *(*De Caluwe *et al.,* 2010*;* Bremer *et al.,* 2003*;* FAO*,* 1988*)*. It is deciduous, massive and majestic tree up to 25m high, which may live for hundreds of years *(*Gebauer *et al.,* 2002*)*. It has been introduced to areas outside Africa and grown successfully *(*Sidibe and Williams, 2002). Baobab is a very long lived tree with multipurpose uses. The different plant parts are widely used as foods, medicines, and the bark fibers are also used (Sidibe and Williams 2002*)*. Every part of the baobab tree is reported to be useful *(*Igboeli et al., 1997 and Gebauer *et al*., 2002*)*. The barks are used for the treatment of fever in Nigeria. Drinking of the aqueous extract of bark of *A.digitata* is used in Nigeria traditional medicine as treatment of sickle cell anemia. The leaves are used medicinally as a diaphoretic and as astringent. The leaves have hypo-sensitive and anti-histamine properties, which are used to treat kidney and bladder diseases, asthma, general fatigue, diarrhea, guinea worm *(*Burkill 1985 and Prajapati 2003). More than three hundred medicinal uses have collectively been documented in Benin, Mali, Zimbabwe, Cameroon, the central Africa Republic, Kenya, Malawi, South Africa and Senegal *(*Buchmann et al., 2010*)* various plant parts (eg. Leaves, bark, fruit pulp) have traditionally been used for immune-stimulant, anti-inflammatory, analgesic, insect repellant and pesticide properties, in the treatment of diarrhea and dysentery in many African countries, and have been evaluated as a substitute for imported western drugs *(*Rawy *et al,*. 1997; Ramadan *et al*., 1994).

Phytochemistry

Pulp and leaves of *A .digitata* exhibit anti-oxidant activity *(Chadare et al., 2009)*. Several compounds isolated from fruit pulp, seed oil root isolates terpenoids, flavonoids, steroids, vitamins, amino acids, carbohydrates and lipids. 10 aromatic compounds including isopropyl myristate and nonanal were identified in fruit pulp *(*Cisse *et al., 2009)*. Several compounds have been isolated from the pericarp using column chromatography and include: (-)-epicatechin, epicatechin-(4β→8)-epicatechin (B2),

epicatechin-(4β→6)- epicatechin (B5), epicatechin- (2β→0→7, 4β→8)-epicatechin (A2), and epicatechin-(4β→8)- epicatechin- (4β→8)-epicatechin (C1) *(shahat,2006)*. Other compounds such as 3,7- dihydroxy-flavan-4-one-5-O-β-D-galactopyranosyl (1→4)-β-D-glucapyroside and a flavonone 3,3′,4′-trihydroxy flavan-4-one-7-O-α-L-rhamnopyranoside and quercetin-7-O-β-D-xylopyranoside were isolated from the roots of A.digitata *(*Chauhan *et al., 1984;* Chauhan *et al., 1987;* Shukla *et al., 2001)*.

Traditional medicinal uses of *A.digitata*

S:No	Ailments	Parts uses	References
1.	Malaria, fever	Leaves	Watt J.M & Breyer (1962)
2.	Diarrhoea, fever, inflammation, kidney and bladder diseases, blood clearing, asthma.	Leaves	Brendler et al.,(2003)
3.	Tooth ache, gingivitis	Leaves	Tapsobatt & Deschamps JP (2006)
4.	Diaphoretic, kkidney nd bladder diseases, asthma, insect bites, expectorant, prophylactic against fever, excessive perspiration, stringent, guinea worm, hypo sensitive, anti histamine properties, sources with poultices.	Leaves	Wickens GE (1982)
5.	Diaphoretic, fever remedy.	Leaves	Abbiw DK (1990)
6.	Diarrhoea, fever, inflammation, kidney and bladder diseases, blood clearing asthma.	Leaves	Van Wyk and Gericke (2000)
7.	Fever, dysentery.	Leaves	Gebauer et al., (2002)
8.	Diarrhoea, worms.	Leaves,seeds,fruit pulp	*Ake Assi (1992)*
9.	Respiratory disorders.	Leaves, flowers	*Addy et al., (1995,* cited in *shukla et al., 2001*)
10.	Anti pyretic, febrifuge.	Leaves, pulp	*Sidibe & Williams (2002)*
11.	Emollient, maturant, diuretic, diaphoretic, febrifuge.	Leaves	*Kritikar (1993,* cited in *Shukla et al., 2001*)
12.	Anti inflammatory, insect bites, Guinea worm, sores, astringent, sudorific, tonic, ear ache, opthalmia, prevent guinea pigs from asthmatic crisis induced by histamine aerosols.	Leaves	*Shukla et al (2001)*
13.	Anti- asthmatic, anti histaminic, anti tension properties, treatment of fatigue, insect bites, guinea worm, internal pains, treatment of dysentery, diseases of the urinary tract, opthalmia, otisis, excessive perspiration painful swellings.	Leaves	*Sidibe* and *Williams (2002)*
14.	Fever, dysentery, eye drops in cases of measles.	Pulp	*Burkill Cined.*, cited in *Wickens, 1979*); FAO (*1988*, cited in *Gebauer et al., 2002)*
15.	Excipient in tablet formulation, lubricant, glidant and diluent properties.	Pulp	*Arama et al.,(1989*, cited in *Shukla et al., 2001*)

16.	Tooth ache, gingivitis, diaphoretic in fever, diarrhoea, dysentery, haemopytosis, relief from bronchial asthma.	Pulp	Shukla et al.,(2001)
17.	Mixed with butter milk in cases of diarrhea, dysentery.	Pulp	Sidibe and Williams (2002)
18.	Immunostimulant, anti-inflammatory, analgesic, pesticide, anti-pytetic, febrifuge, astringent in treatment of diarrhea and dysentery.	Pulp	Ramadan et al., (1993); El.Rawy et al., (1997); Tuani et al., (1994) (all cited in Al-Qarawi et al., 2003)
19.	Hepatoprotective activity	Pulp	Al.Qarawi et al., (2003)
20.	Dysentery, diaphoretic.	Pulp, seeds	Sidide and Williams (2002)
21.	Diarrhoea, hiccough inflamed gums, easing of sore teeth, skin complaints, cosmetics.	Seeds	Sidibe and Williams (2002)
22.	Emmenogogue	Inner fibrous part of fruit shell	Kritikar (1993, cited in Shukla et al., 2001)
23.	Stimulating and promoting granulation of foul sores.	Bark, fruit shell	Addy et al., (1995, cited in Shukla et al., 2001)
24.	Febrifuge	Bark	Wickens (1982 cited in Sidibe &Williams, 2002)
25.	Neutralizes the arrow wound in flesh of animal killed by poisoned arrow, before meat is eaten. Bathe rickety children mouth wash for tooth ache.	Bark	Wickens (1979 & 1982)
26.	Treatment of sores.	Bark	FAO (!988, cited in Gabauer et al., 2002)
27.	Substitute for quinine for curing fever.	Bark	Kritikar (1993, cited in shukla et al., 2001)
28.	Febrifuge (anti pyretics)	Bark	Shukla et al.,(2001)
29.	Substitute for quinine in cases of fever, prophylactic, anti pyretic, anti periodic.	Bark	Sidibe & Williams (2002)
30.	Increase weight gain of infants.	Bark	Lockett & Grivetti (2000)
31.	Anaemia	Bark	Adesanya et al., (1988)
32.	Malaria	Bark, Leaves	Ajaiyeoba et al., (2004)
33.	Wound healing	Stem bark	Innjerdinger et al., (2004)
34.	Fever, diarrhea.	Seeds	Watt and Breyer-Brandwijk (1962)
35.	Dysentery, fever	Seeds, fruits	Watt and Breyer-Brandwijk (1962)
36.	Coughs	Powdered seeds	Watt and Breyer-Brandwijk (1962)
37.	Dysentery, fever, haemoptysis, diarrhea.	Fruits, seeds	FAO (1993)
38.	Microbial diseases	Fruits	Hostettmann et al., (2000)

39.	Refreshing, tonic, diuretic, cystitis, dysentery, hepatic disorders, hypoglactia.	Flesh with peel	Kerhro and Adam (1974); Nacoulm (1999)
40.	Bathe babies to promote smooth skin	Roots	Wickens (1979 & 1982)
41.	Tonic for malaria patients	Roots	FAO (1988, cited in Gebauer et al., 2002)

Pharmacological uses of Adansonia Digitata.

Anti oxidant activity:

The anti-oxidant capacity of baobab fruit pulp was investigated using the phytochemiluminescence (PLC) assay, comparing the anti-oxidant properties of the fruit pulp to the anti-oxidant properties of several other fruits including kiwi, orange, apple and strawberry (Vertuani et al., 2002). Anti-oxidants could help to prevent oxidative stress related diseases such as cancer, aging, inflammation and cardio vascular diseases as they may eliminate free radicals which contribute to these chronic diseases (Kaur and Kapoor, 2001; Bolmhoff *et al.,*2010).

Besco *et al*., (2007) evaluated the anti-oxidant activity of baobab red fibre. The results obtained clearly demonstrated the lipid soluble anti-oxidant capacity of baobab red fibre was high (508.0 ± 0.008 µmol/g). Similarly, the water soluble anti-oxidant capacity, corresponding to the activity expressed as µ mol/g equivalents of ascorbic acid for each gram showed the same pattern with ascorbic acid equivalents of baobab red fibre particularly high (386.0 µmol/g).

According to Ateya *et al.,* (2016), the free radical scavenging activity of extracts was measured by DPPH method (Ratty and Sunamoto (1988)) (Harborne *et al*., (1975). The most potent active extracts (gave 90%); were (100% methanol extract of leaves and 100% methanol extract of pulp) against standard vit C (IC_{50}= 4.8 µg/ml).

Samatha talari *et al*., (2017), concluded that all the methanolic extracts of different parts of the *A.digitata* showed the free radical scavenging activity and exhibited different radical scavenging activities due to the possession of different amounts of phytochemical constituents present in them.

Anti-diabetic activity

According to (Bhargav et al., 2009) the ethanolic extract of the bark was investigated for anti-hyperglycemic and antilipidaemic activities in alloxan induced diabetic female rats. Baobab bark extract was administrated orally for seven days in doses of 250 and 500 mg/kg bw to diabetic rats, while the anti-diabetic drug glipizide (500 µg/kg bw) was administrated to the control group. The bark extract exhibited hypoglycemic activity as they decreased plasma glucose levels by 26.7% and 35.9% and increased glycogenesis by 11.3% and 32% respectively.

Hypo glycemic activity of *A. digitata* stem bark, fruit pulp extract was studied against streptozotocin induced diabetic rats. Methanol used as a solvent. Fruit pulp 300 mg/kg ability to lower serum glucose comparable to chlorpropamide (Tanko *et al*., 2010).

Anti microbial activity

According to Yusha *et al.,* (2010), anti-bacterial activity of *A.digitata* stem bark extracted was studied against clinical bacterial isolates of *Escherichia coli, klebsiella, pneumonia, proteus mirabilis* and *staphylococcus* species using disc diffusion and micro

broth dilution techniques. In phytochemical screening confirmed the presence of alkaloids, flavonoids, reducing sugars, steroids, presence of flavonoids may reason for their anti-bacterial activity.

Yagoub (2008) who investigated the anti-bacterial activity of a solvent extract of A.digitata against E.coli isolated from urine and water. The results clearly indicated that the solvent extract inhibited bacterial growth with the inhibition zone ranging from 20 to 30 mm depending on the concentration at which the sample was tested.

Masola *et al*., (2009) investigated the anti-microbial activity of baobab plant parts (stem and root barks) against gram-positive bacteria, gram-negative bacteria nd yeast. The results indicated that the aqueous and ethanolic root and stem bark extracts inhibited the growth of various micro-organisms with the MIC values ranging from 1.5 to 6 mg/ml. The anti-bacterial activity of the plant could be attributed to the presence of tannins, phlobatannins, terpenoids and saponins in the stem bark.

Nizar *et al*., (2013) concluded that *A.digitata* showed a remarkable anti-bacterial activity against all tested bacterial strains. The preliminary phytochemical screening revealed the presence of terpenes, tannins and saponins in all tested plant extracts, whereas alkaloids and cardiac glycosides were found in appreciable amounts in *A.digitata* fruit extarct respectively.

Amrish Sharma and Vinod Rangari (2015) found that the anti-bacterial and anti-fungal activities of the extracts were tested against four gram-positive strains staphylococcus pneumonia and Bacillus subtilis. Four gram-negative strains Escherichia coli, Pseudomonas aeruginosa, salmponella typhi, vibrio cholera and three fungal strains-Aspergillus niger, aspergillus clavatus, candida albicans. The highest minimum inhibitory concentration (MIC) was showed by fruit pulp extract against *E.coli* and *C.albicans* at dose of 62 µg/ml and 250 µg/ml. zone of inhibition studies revealed that the maximum inhibition was showed by fruit pulp extract.

Based on the results Datsugwai & Yusuf concluded that baobab has effective and important ingredient in the treatment of wide variety of diseases. The anti-bacterial activity displayed by the isolates justified its ethno-botanical uses for the treatment of ophthalmic, coughs, colic and hemorrhoids. *A.digitata* could be taken alongside some synthetic drugs pending on the severity of the illness during the treatment of diseases caused by *Escherichia coli* & *Staphylococcus aureus.*

Abiona *et al*., (2015) investigated antibacterial activity against *Staphylococcus aureus, Escherichia coli, Bcillus subtilis, Pseudomonas aeruginosa, Salmonelle typhi, Candida albicans, Aspergillus niger, Rhizopus stolomifer* and Penicillum rotatumat.

Sanaa O.Yagoub (2008) the petroleum ether, ethanol and aqueous extracts of the A.digitata were screened for the presence of possible anti-microbial activity using the cup plate agar diffusion method. They were tested against *E.coli* that isolated from urine and water sources. The extract was used in concentration of 100, 75, 50 and 25% respectively.

Anti-viral activity

A.digitata leaves, fruit pulp and seeds have shown anti-viral activity against influenza virus, herpes simplex virus and respiratory syncytial virus (Vimalanathan and Hudson, 2009) and polio (Anani *et al.,* 2000). A.digitata root bark showed anti-viral activity. This study have evaluated the potentials of the methanolic root bark extract of *A.*

digitata as an anti-viral agent against ND virus using multiplication of the ND virus in embryonated egg as an indicator for anti-viral activity. The result of the viral propagation showed that250 and 200 mg/ml concentrations of the extract completely inhibited the growth of ND virus in embryonated chicken eggs, indicating that the methanolic root bark extract of *A.digitata* (Sulaimal *et al.*, 2011).

Vimlanathan and Hudson (2009) investigated the anti-viral activity of *A.digitata* leaves, fruit pulp and seed extracted with water, DMSO and methanol; the study was conducted using the minimum inhibitory concentration method against influenza virus, herpes simplex virus and the respiratory syncytial virus. 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 0.12 µg/ml (DMSO) to 2.8 µg/ml (water). The activity of the leaf extract was promising against the herpes simplex virus (MIC value: 1.10 to 11.7 µg/ml), while the pulp and the seed exhibited much lower activity (MIC value > 72.5 µg/ml).

Analgesic and Anti-pyretic activities

According to Ramandan *et al*., 1993 the analgesic effect of the fruit A.digitata extracted with hot water was tested in vivo (mice). It was noted that the extract exhibited analgesic activity 2h after administration. At 800 mg/kg. The reaction time was 15.4 min in comparison to the negative control (10.2 min).

According to Khal *et al*., 2006, the petroleum ether extracts containing seed oil of *A.digitata* was investigated for analgesic activity. The extract exhibited analgesic activity with tail flick response in 6.1 s which was not statistically different from aspirin used as positive control.

Ateya *et al*., (2016) said that significant analgesic activity (82.5%) was obtained in comparison with standard aspirin (79.6%) after 60 min according to previously reported method (Oktay et al., 2003).

The analgesic activity were also mentioned by Masola *et al*., (2009), probably due to the presence of sterols, saponins and triterpenes in the fruit pulp.

According to Samreen *et al.,* (2015) the isolated natural crude extract from *A.digitata* was evaluated for their Analgesic profile using Aspirin as a standard reference drug. Methanolic extract displayed maximum Analgesic profile. The extract collected using polar solvent DMSO also exhibited excellent profile; the extract collected using 1:1 methanol and water showed decreased in profile compare to methanol. Moreover the Analgesic activity profile of extract collected from hexane, dichloromethane and toluene was poor long with extraction % values.

According to Ramadan *et al., (*1993), the anti-pyretic activity of A.digitata extract was evaluated on twenty rats. Hyperthermia was induced by subcutaneous injection of a 12% yeast suspension and the temperature of the rats showed a slight decrease (37.3^0C) in comparison to the initial temperature of 38.6^0C, suggesting that baobab extract exhibited anti-pyretic activity.

Anti Inflammatory activity

According to Ramadan *et al*., 1994, the anti inflammatory activity of the fruit extracted with hard water was tested in vivo using the rat paw formalin-induced oedema test. The extract tested at a dose of 400 and 800 mg/kg inhibited formalin-induced

oedema. After 24h administration of the aqueous extract, the mean swelling of the foot was 1.81 and 1.75 mm for 400 mg/kg and 800 mg/kg respectively, in comparison to the negative control (6.35 nm).

Yihunie *et al*., (2013), this study based on high polyphone concentration inhibition of NO production. The methanol extract of *A.digitata* leaf showed anti-inflammatory activity, extract significantly inhibition of NF-KB activation, there by suppressing expression of the pro inflammatrory iNOS gene resulting decreased NO production.

According to Samreen *et al*., (2015), the evaluations of anti-inflammatory activity of naturally extracted crude were performed by the carrageenan induced rat paw edema method using ibuprofen as reference drug. Mean changes in paw oedema thickness after 30 min, 1 hr. 2 hrs and 4 hrs, from induction of inflammation and inhibition % of oedema by the tested compounds were recorded.

The extraction collected using non polar solvent hexane shown poor % extraction along with poor activity profiles in anti-inflammatory segments. Also the activity profiles for solvents toluene and dichloromethane was not good as MeOH, moreover the % extraction values for dichloromethane and toluene were also less than 0.5%

Hepato protective activity

According to Al-Qarawi *et al*., (2003), the hepato protective activity of a water extract of the fruit pulp was evaluated in vivo against chemical-induced toxicity with CCl_4 in rats. The results clearly showed that the water extract exhibited significant hepato protective activity. The liver protective ability of *A.Digitata* extract was 76, 77 and 87 % for alanine tranferance, aspartate transferase and alkaline phasphatase activity respectively.

Rafehivola *et al*., (1995) Carried out the effect of baobab seed oil on drug metabolizing enzymes(cyclopropenoid fatty acids) were evaluated in vivo in rats fed either with baobab seed oil (1.27 % cyclopropenoid fatty acids) or heated baobab seed oil (0.046 % cyclopropenoid fatty acids in the diet). The rats fed baobab oil showed retarded growth when compared to other groups of animals. Furthermore, the relative liver weights were markedly increased whereas cytochrome P-450 content and NADPH cytochrome C reductase and NADH cytochrome C reductase activities were decreased.

Anti-cancer activity

According to Dhana sree *et al*., (2018), on this study they have assessed cyto toxic activity of Adansonia digitata against human breast malignancy cell lines BT474. MTT examination showed that anti proliferative action of methanol and dichloromethane extracts of the plant. For both the concentrations, decreasing in cell expansion was dose dependant. At a dose of 30 mg/ml, there was a wonderful decrease in cell expansion by dichloromethane extract of leaves of *A.Digitata*. At this dose very nearly 42% of the aggregated cells survived and the rest 56% turned out to be dead.

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