

# Biochemistry, Medicinal Properties & Toxicity of Acacia Nilotica Fruits

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## Abstract

Acacia nilotica tree is native to Africa, the Middle East and the Indian subcontinent. Due to its wide medicinal properties & uses this plant attracted the attention of many scientists. Its fruits are rich in more than 16 classes of different bioactive molecules & elements very beneficial for human health. These molecules & elements include tannins, saponins, phytosterols, cyclitols, alkaloids, anticoagulant agents, regulatory molecules, amines, mucilage, fibers, gums, proteins, various classes of amino acids, carbohydrates, terpenes, crude fats, oils, fatty acids & minerals. The fruits are used to treat various human disorders including cancers, heart & liver diseases, diabetes mellitus, malaria, asthma, arrhythmias, acquired immune-deficiency syndrome, coronavirus disease 2019, spleen disorders, for weight loss, colds, congestion, coughs, diarrhea, dysentery, fever, gallbladder, hemorrhage, hemorrhoids, leucorrhea, ophthalmia, sclerosis, tonsillitis, pharyngitis, skin eruptions smallpox and tuberculosis. Acacia nilotica fruits are very beneficial for human health, safe & effective to treat various human diseases if it is used in appropriate dose & period. It has been in use in Sudan & in other parts of Africa widely & safely for generations to treat various diseases without any reports of toxicity or adverse effects. Moreover, human body has efficient detoxification mechanisms to process and detoxify toxic substances and toxicity in human occurs only from known high toxic substances, overdose, regular and long period of using of herbs or medicines with known side effects. It is apparent that toxicity of acacia nilotica fruits comes from over dosage & longer than required duration of uses or regular consumption and the solvent/s as well. However, further works are needed by pharmaceutical industries to authentically formulate various components of the of acacia nilotica fruits to be used as medicines & supplements to enhance the therapy of several human diseases.

**Key words:** acacia nilotica; medicinal properties; toxicity; covid-19; chemistry

## Introduction

In most countries of Africa including Sudan, health facilities & services are weak in big cities & not available in most of the rural areas. The situation is more worsening by poverty, high prices of drugs, the lack of paved roads and appropriate transportation facilities; all these together make the movement of patients from the rural areas to city hospitals in Sudan & Africa to seek medical help a painful journey. In such situations, it is better for urban & rural residents in Africa & Sudan to have at home local natural medicines to be used in the times of emergency. African in general & Sudan in particular is a reservoir of potent potential natural medicines that are not yet fully studied & utilized. Therefore, there is an urgent need for better knowledge & uses of these natural medicines in Sudan & Africa for the use of human wellbeing.

The invention of new techniques of isolation, structure identification & functional characterizations of plant compounds has assisted tremendously in the development of the field of phytochemistry. Plant compounds have interest as a source of safer or more valuable substitutes than synthetically created antimicrobial agents. In all parts of the world and more precisely in Africa and other least developed countries of Asia,

plants are used in traditional medicine to treat different communicable and non-communicable diseases. It is estimated that more than 80% of people living in developing countries frequently use traditional practices for their primary health care needs [1, 2, 3].

*Acacia nilotica* is a tree belongs to the family of Fabaceae native to Africa, the Middle East and the Indian subcontinent & it is naturalized widely outside its native lands [4, 5]. Its name was derived from a Greek word meaning “thorn” while nilotica means along the Nile river [6]. Due to its wide medicinal properties & uses this plant attracted the attention of many scientists. Biochemistry, medicinal properties & toxicity endorsed to the fruits of the *Acacia nilotica* are discussed in details in this manuscript.

## Biochemical & Medicinal Properties of Acacia Nilotica Fruits

Acacia nilotica fruits are rich in more than 16 classes of different bioactive molecules & elements very beneficial for human health. These molecules & elements include tannins, saponins, phytosterols, cyclitols, alkaloids, anticoagulant agents, regulatory molecules, amines, mucilage, fibers,

gums, proteins, various classes of amino acids, carbohydrates, terpenes, crude fats, oils, fatty acids & minerals [7, 8, 9, 10, 11, 12].

Tannins in acacia nilotica fruits exist as condensed & hydrolysable tannins with relative proportion of 50% [11, 13]. Tannins in the fruits include gallic acid, ellagic acids, m-digallic acid, me-ester-n-digallic acid, m-digallic dimer 3,4,5,7-tetrahydroxy flavan-3-ol, oligomer 3,4,7-trihydroxy flavan 3,4-diol, flavonoids, protocatechuic acid & epicatechol [7,10,11]. Tannins are natural polyphenols that categorized into different classes as phenolic acids, flavonoids, lignans, and stilbenes. Hydrolysable tannins react & hydrolyze in water to give different water-soluble products, such as gallic acid, protocatechuic acid and sugars. Gallotannin (tannic acid) is the best condensed tannins (polyflavonoids). Flavonoids are antioxidants involved in plant immunity & regulation of plant growth [14, 15]. Antioxidants are protective against cancers, including colon, prostate, breast, endometrial, lung, and pancreatic tumors. It can protect cells and other structures in the body from harmful reactive oxygen species & thus helping the body develop resistance against infectious agents and scavenge harmful free radicals.

Tannins possess anti-infective, anti-inflammatory, anticarcinogenic, antimutagenic and anti-hemorrhagic properties & it has been used to treat tonsillitis, pharyngitis, hemorrhoids and skin eruptions & an antidote for metallic alkaloidal and glycosidic poisons, with which it forms insoluble precipitates [16].

Tannins inhibit the growth of many fungi, yeasts, bacteria, and viruses and it have also been reported to exert physiological effects that are dose-dependent, such as to accelerate blood clotting, reduce blood pressure, decrease the serum lipid level, produce liver necrosis and modulate immune-responses [17]. Gallic acid exists as free and as part of hydrolysable tannins. The acid groups are usually polymerized to form dimers such as ellagic acid [18]. Gallic acid possesses antioxidant properties, anticancer, cytotoxicity against cancer cells, without harming healthy cells, anti-parasitic, antimicrobial, anti-inflammatory, bacteriostatic and bactericidal effects, neuroprotective, cardioprotective, gastroprotective, anti HIV effects by inhibiting HIV-1 integrase [19,20]. Gallic acid is used a remote astringent in cases of internal hemorrhage & to treat albuminuria and diabetes [21]. It is also involved in various signaling pathways that regulate wide range of biological functions including pro- and inflammatory pathways, intrinsic and extrinsic pathways of apoptosis. Gallic acid and its derivatives are safe and stable that can to be used as dietary supplements [19]

Epicatechin (catechin) is a powerful antioxidant. Catechins have a flavon structure and are called flavonoids. Catechins possesses antiviral & antibacterial activities; useful for treating heart diseases, it may have an effect on endothelium-dependent vasodilation which could improve blood pressure, it reacts with toxins created by harmful bacteria and harmful metals such as lead, mercury, chrome, and cadmium [22,23,24,25,26].

Protocatechuic acid (PCA, dihydroxybenzoic acid) belongs to polyphenols. PCA is a major metabolite of antioxidant polyphenols. It has effects on normal and cancer cells [27]. PCA possesses antioxidant, antibacterial, anticancer, antiulcer, antidiabetic, antiageing, anti-brotic, antiviral, anti-inflammatory, analgesic, cardiac, neurological, nephroprotective, hepatoprotective & anti-atherosclerotic activities [28, 29]. PCA induces apoptosis of human leukemia cells, as well as malignant HSG1 cells taken from human oral cavities [30]. PCA effectively inhibits the replication of herpes simplex virus type 2 and the activity of urease [31].

Leucocyanidin is a substrate for the enzyme leucocyanidin, 2-oxoglutarate: oxygen oxidoreductase (leucoanthocyanidin dioxygenase or anthocyanidin synthase), which participates in flavonoid biosynthesis [32]. Ellagic acid & epicatechin possess anti-SARS-CoV-2 effects, the

two molecules inhibit the activity of the SARS-CoV-2 main protease (Mpro), which has no similarity with the human enzymes [33, 34, 35, 36].

Saponins are glucosides that improve blood cholesterol, bone health and the immunity, they possess anticancer, antitumor and anti-mutagenic activities, they can lower the risk of human cancers, by preventing cancer cells from growing [37, 38].

Phytosterols are plant sterols. They competitively inhibit cholesterol absorption across the gut and thereby can reduce cholesterol levels and this might contribute in reduction the risk of heart diseases [37].

Cyclitols are alcohols multi-hydric cycloalkane, component of cell membrane. They involved in cell regulation, signal transduction, osmoregulation, and ion channel physiology. Cyclitols are efficiently used in the treatment of insulin resistant diabetes, obesity and polycystic ovarian syndrome; they possess anti-atherogenic, anti-oxidative, anti-inflammatory and anti-cancer properties [39].

Amines are vital biological compounds essential for human health.

Fibers assist in weight loss, elevate constipation, reduce absorption of fats and cholesterol, absorb many toxins and carcinogenic agents and prevent their absorption, delay the absorption of sugars, help in maintaining the health of the gastro-intestinal tract [40].

Mucilage are polysaccharides, which possess antidiabetes, antioxidant, anticancer, anti-inflammatory, antispasmodic, immuno-modulating & anti-allergic properties, they improves wound healing, immunity and angiotensin converting enzyme inhibition, they are used as cough suppressants and to treat respiratory disorders & they are the most proposed materials for modulating drug delivery, mucilage is perfect as natural laxative, and treats a lot of digestive problems, helps cartilage and joint building, maintains joint viscosity & lowers cholesterol.

[41].

Proteins, the end products of genes are the basis of life. Cystine, methionine, threonine, lysine and tryptophan in the form of proteins perform multiple of structural, hormonal, antibodies and catalytic functions that are essential for life. Amino acids serve in nerve transmission, regulation of cell growth and the biosynthesis of porphyrins, purines, pyrimidine and urea. Methionine & tryptophan are nutritionally essential amino acids and the human diet must contain them in quantities adequate to support infant growth to maintain health in adults. Cystine is the major amino acid in the proteins in the hair, skin and horns. Carbohydrates are the major and first sources for energy to the human body. They are precursors for many important cell molecules. They are metabolized to generate reduced nicotinamide adenine dinucleotide phosphate for reductive processes & other precursors for nucleic acid synthesis (eg. ribose and deoxyribose). They provide metabolites that are used in detoxification reactions & in the biosynthesis of certain polysaccharides important for normal formation of cartilage, tendons & bones. Amino-sugars are found in many cell and tissue important structures like blood groups [42].

Gums is used as astringent, emollient, liver tonic, antipyretic and anti-asthmatic & for stomach upset and pain [7].

Terpenes are essential plant oils. In human, they can induce biosynthesis of neurotransmitters such as serotonin a central nervous system neurotransmitter derived from the amino acid tryptophan involved in regulating mood, sleep, appetite, and sexuality & dopamine a neurotransmitter involved in motivation, reward, addiction, behavioral reinforcement, and coordination of bodily movement [43].

Lipids are important signaling molecules (such as Eicosanoids and steroid hormones). Fats are storage form of metabolic fuels and are the best heat producers in the body than carbohydrates & proteins, structural

components of cell membranes, insulators, thermal & electrical preventing body from cold, important dietary constituents, due to their high energy content, they are essential for absorption of fat- soluble vitamins. Fats are necessary for sex-maturation, pregnancy and lactation. The significance of dietary fats and oils is that they provide essential fatty acids. Deficiency of EFAs results in impaired brain growth, mental retardation and learning difficulties, dermatitis, hair loss, and poor wound healing. The four fat-soluble vitamins namely vitamin A, D, E and K are, in fact, require fats and oils in the food to be absorbed through the gut. Inadequate fats may results in the deficiency of these vitamins leading to serious metabolic derangements with subsequent manifestations like night blindness, osteoporosis, bleeding from skin and mucus membranes, phrenoderma, and susceptibility to infections [42]. The phospholipids of cell membranes and of the mitochondrial membranes contain essential fatty acids. Deficiency in essential fatty acids negatively affects the integrity of these membranes and many metabolic processes. Membranes of the red blood cells become fragile and may easily get haemolysed. The skin becomes abnormally permeable to sweat and loss of water from the body may occur. Essential fatty acids are important constituents of lipoproteins. Disposal and oxidation of cholesterol require essential fatty acids & it is believed that the efficacy of many vegetable oils in diminishing the plasma cholesterol is by virtue of the essential fatty acids content. Arachidonic acid is a direct precursor of prostaglandins in the body. Prostaglandins have several pharmacological effects [42].

Alkaloids are used in the treatment of malaria, asthma, cancer, hypertension, bacterial infections, arrhythmias, diabetes and pain [44,45,46].

Minerals in acacia nilotica fruits such as sodium, potassium, calcium, phosphorus, manganese, magnesium, iron & copper help promote good health and essential cellular functions.

[46] Conducted antibacterial study to evaluate the efficacy of different extracts of *Acacia nilotica* fruits against four bacteria species viz *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilus* and *Pseudomonas aeruginosa*. Their results showed the water and the methanolic extracts of the acacia nilotica fruits completely inhibited the growth of the 4 bacteria. *Escherichia coli* are the cause of 80–85% of the urinary tract infection in the world which is the second bacterial infections in human population after respiratory tract infections [47, 48]. Currently, antimicrobial resistance the major threat to public health in the World. These make acacia nilotica fruits a very good option to treat UTIs.

### Toxicity Studies on *Acacia nilotica* Fruits

There is a misconception about the safety & toxicity of acacia nilotica fruits. Here, I am giving a brief about the toxicity of acacia nilotica fruits for better understanding its uses.

[49] Investigated the toxicity of acacia nilotica fruit using its aqueous extract on rats in vivo through oral administration for 35 days. Their results revealed no significant disorders occurred in the hematological values, markers of renal and hepatic functions, body weight, absolute and relative organ weights as well as the structures of the kidney and the liver. These results demonstrated the safety of the acacia nilotica fruits in water. [50] Examined the methanol extract of acacia nilotica seeds in vitro to assess its toxicity on lymphocyte. The methanol extracts of seed and husk showed low toxicity effects to the tested lymphocyte at 100 ug/mL. Methanol is known for its toxicity to the brain and is prohibited for human consumption.

[51] Assessed the acute toxicity of acacia nilotica seed aqueous extract on mice in vivo intra-peritoneally & on cats intravenously, their results demonstrated occasional abdominal cramping.

[52] Investigated the toxicity of acacia nilotica fruit ethanol extract at lower doses on rats in vivo via oral administration for 21 days, their results showed passive behavioral changes of animals during early hours of

treatment. But on day 21 all the earlier noted behavioral changes disappeared. Then they used very high doses 50-500 mg/kg of acacia nilotica fruit ethanol extract intra-peritoneal for 7 and 14 days. The results showed 20-100% mortality in the tested rats. For safety uses of medicinal herbs, [53] mentioned that most herbal dosages for adults are calculated on the basis of a 150 lb (70 kg). According to this, if the latter dose of acacia nilotica fruits calculated to adult human it is 35-350 g/day which are very high doses & far from the reality. In this context, [54] conducted a research to assess the efficacy of acacia nilotica fruit powder to treat COVID-19, colds, UTIs, tonsillitis & idiopathic pain, he come to found that the appropriate & the effective dose for adults was 1.25g as a single dose per day after meal for three days and the dose for children was 0.5g. Also, he found *Acacia nilotica* fruit powder was very effective in treating teeth carious and pain when it was used topically. His results about the efficacy of the acacia nilotica fruits to treat the mentioned ailments support the existing knowledge and generate new findings.

[55] Studies toxicity of acacia nilotica pods methanol extract on rats for 35 days in vivo via oral route, their results showed no mortality and no toxic reactions.

[56] Studied the toxicity of acacia nilotica pods on goats for 90 days in vivo via oral administration, their result showed the metabolic status of the animal not affected. And when they studied the toxicity of acacia nilotica pods on Caco-2 in vitro, their results showed absence of significant cytotoxicity.

[57] Studied the toxicity of acacia nilotica fruits aqueous extract (100 or 150 µg/mL) in vivo on rats for 14 days, their results showed no abnormal behavior and no mortality during the treatment.

[58] studied the toxicity of acacia nilotica pods aqueous extract on rats in vivo via oral administration for 21 days, their results demonstrated no death in the treated groups; no significant alteration of the levels of red blood cells, hemoglobin concentration and packed cell volume; while an increase in body weight was observed in day 21.

[59] studied the toxicity of acacia nilotica pods in Nubian goats fed with whole acacia nilotica pods for 35 days at dose 5g/kg/d, their results showed clinical signs such as salivation, staggered gait, intermittent loss of voice and low appetite; presence of hepatic centrolobular necrosis lesions and fatty changes associated with the significant changes in  $\gamma$ -glutamyl transferase & alkaline phosphatase that indicate hepatic dysfunction; renal malfunction is indicated by hemorrhages in addition to the change in urea concentration. Obviously, these adverse effects of acacia nilotica pods were due the extremely high dose and the long period of use. 5g/kg/day of acacia nilotica pods for adult human of 70kg weigh are equivalent to 350g/day. Our experience demonstrated the effective dose of acacia nilotica fruits for adult human within the range of 1g for 3days, maximum for 5 days.

[60] studied the toxicity of acacia nilotica seeds methanol extract on mice in vivo via oral route at doses of 50, 100, 200, 500 & 1000 mg/kg body weight, their results showed no mortality in mice during the treatment; little behavioral changes, locomotor ataxia, diarrhea and weight loss were observed. From my experience, the dose 1g/kg of acacia nilotica seeds is extremely high dose; it is equivalent to 70g of adult dose of acacia nilotica seeds, although the adverse effects were mild & might due to methanol, which is known for its toxicity to the brain.

[61] Studied the toxicity of acacia nilotica pods aqueous extract on Rats for 14 days in vivo via oral route; their results showed no mortality at a limit dose of 3000 mg/kg body weight. Although, the dose is extremely high no mortality occurred. This demonstrates acacia nilotica pods are safe for human use.

[62] Studied the toxicity of acacia nilotica pods aqueous extract in rats maintained on 2% and 8% acacia diet for 2 and 4 weeks. Their results showed significant reduction in body weight; no significant changes in serum parameters of hepatic and renal functions, fasting glucose and triglycerides; no mortality and no significant histopathological changes in liver sections were noted.

## Conclusion

In conclusion, acacia nilotica fruits are very beneficial for human health, safe & effective to treat various human diseases if it is used in appropriate dose & period. It has been in use in Sudan & in other parts of Africa widely & safely for generations to treat various diseases without any reports of toxicity or adverse effects. Moreover, human body has efficient detoxification mechanisms to process and detoxify toxic substances and toxicity in human occurs only from known high toxic substances, overdose, regular and long period of using of herbs or medicines with known side effects. It is apparent that toxicity of acacia nilotica fruits comes from over dosage & longer than required duration of uses or regular consumption and the solvent/s as well. However, further works are needed by pharmaceutical industries to authentically formulate various components of the of acacia nilotica fruits to be used as medicines & supplements to enhance the therapy of several human diseases.

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## Conflict of interests

None.

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