Review Article

Review of some evidenced medicinal activities of *Acacia Nilotica*

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Abstract

Introduction: The natural medicinal plants can boost self-cure, perfect health, and longevity. *Acacia nilotica* Lam (*Acacia*) is an imperative plant that possesses many medicinal uses. *Acacia* trees are vastly spread in Saudi Arabia. In folk medicine, various parts of *Acacia* tree, including the leaves, bark, seeds, roots, gum, flowers, fruits, and young pods are utilized as nutrients and therapeutic remedies to hinder, alleviate, or manage many illnesses. *Acacia* is wealthy in antioxidant phenolics, mainly condensed tannin and phlobatannins. **Objective:** This review aimed to collect the early and recently published research articles that confirmed various medicinal activities of *Acacia*. **Results:** The results obtained from the previously published studies showed that *Acacia* extract possesses many therapeutic effects including antimicrobial, antiparasitic, antidiabetic, antihyperlipidemic, anticancer, antimutagenic, antipyretic, anti-inflammatory, antinociceptive, antiulcer, antihypertensive, antispasmodic, antidiarrheal, and antioxidant activities. **Conclusion:** *Acacia* may become a natural, inexpensive alternative to pharmaceuticals and prescription drugs.

Keywords: *Acacia nilotica*, medicinal activities, active constituents

Introduction

Talh tree is mentioned in Surah Al-Waqi'ah (56: 29) in the Holy Quran, where Allah said, "Watalhinmandood". All sources identified Talh as either banana or *Acacia*. Although banana is not native to Arabia, Talh trees spread in the Arabian Peninsula. In many references, Talh is known as *Acacia* [1, 2]. In Kingdome of Saudi Arabia, genus *Acacia* has been believed as one of the extremely valuable trees and shrubs. *Acacia* is a great genus in family Fabaceae that contains nearly 1350 species. Almost all species are located in the Western area, and they are few in Eastern and Northern areas of Kingdom Saudi Arabia [3–5].

The trend of using plants both in a traditional and modern way is still popular and practiced worldwide [6, 7] for the prevention and treatment of certain illnesses [8, 9]. The natural therapeutic herbs can boost self-cure, perfect health, and longevity. *Acacia nilotica* Lam *(Acacia)* is an imperative plant that possesses many medicinal uses [10, 11]. *Acacia* trees are vastly spread in Saudi Arabia, India, Sudan, and Egypt, and Sri Lanka [12]. In folk medicine, *Acacia* is utilized as nutrients and therapeutic remedy to hinder, alleviate, or manage many illnesses. The acacia tree is five to twenty meters high, and the tree has a thick round crown with branches and stems black, greyish pink slash, cracked bark, and red gum [13]. *Acacia* is rich in antioxidant phenolics, mainly condensed tannin and phlobatannins, gallic acid, protocatechuic acid, pyrocatechol (+) catechin (-) epigallocatechin-7-gallate, and (-) epigallocatechin-5, 7-digallate [14-16]. Feeding this antioxidant-rich medicinal herb can block the exaggeration of oxidative stress states, ultimately causing the prohibition of many diseases [17]. Various parts of this *Acacia* tree including the leaves, bark, seeds, roots, gum, flowers, fruits, and young pods have anticancer, antimutagenic, antispasmodic, antipyretic, antidiabetic, antifungal, antiviral, antibacterial, antihypertensive, and antioxidant activities [14].

This review aimed to collect the early and recently published research articles that confirmed various medicinal activities of *Acacia*.

Medicinal Activities of *Acacia*

Antimicrobial Activity of *Acacia*

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How to cite this article: A. Abduljawad, E. Review of some evidenced medicinal activities of *Acacia Nilotica*. Arch Pharma Pract 2020;11(4):20-5.

Acacia is one of the plants rich in antimicrobial compounds, where many studies have demonstrated the ability of *Acacia* extracts and some of the compounds separated from them to kill bacteria, viruses, as well as parasites [17].

The experiments confirmed the effectiveness of *Acacia* bark extract against *Streptococcus viridans*, *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis,* and *Shigella sonnei* using the agar diffusion method [18]. Scientists also demonstrated in a subsequent study the effectiveness of the *Acacia* plant against three types of bacteria (*Salmonella typhi, Staphylococcus aureus,* and *Escherichia coli)*, and two types of fungi (*Aspergillus niger* and *Candida albicans)*[19].

The methanolic extract (10%) of the pods of the *Acacia* plant showed a bactericidal effect around 100% versus the antibiotics-resistant microbes, *Escherichia coli*, *Klebsiella* spp, and methicillin-resistant *Staphylococcus aureus*[20].

An *in vitro* laboratory study demonstrated the efficacy of both aqueous and methanolic extracts of *Acacia* pods as inhibitors of the human immunodeficiency virus (HIV)-1 reverse transcriptase enzyme compared to the standard anti-HIV drug, azidothymidine. The $ED_{50\%}$ for both aqueous and methanolic extract was 200 mg/ml, while the tannin portion of the aqueous extract was more effective ($ED_{50\%}$ = 10 mg/ml) compared to the non-tannin portion ($ED_{50\%}$ = 50 mg/ml) [21].

Another study reported that the active compounds extracted from *Acacia* leaves, especially alkaloids and flavonoids, showed a wide-ranging antibiotic effect against many types of Gram-positive (*Bacillus subtilis* and *Staphylococcus aureus*) and Gram-negative bacteria (*Salmonella typhi*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa*) using disc diffusion method. The order of sensitivity of the microbe to *Acacia* leaves active substances was in descending order, as follows *Staphylococcus aureus*, *Escherichia coli*, and *Salmonella typhi* [22].

In a study aimed at investigating the antimicrobial effect of the combination of the *Acacia* leaves extract with the following plant extracts: *Psidiumguajava*, *Murrayakoenigii* L. Sprengel, and *Eucalyptus hybrid* on different types of primary plaque colonies, the combination of the *Acacia* extract and guajava extract showed the highest average inhibition zone diameter against *Streptococcus mutans*. The combination also showed the highest antimicrobial effect against both *Streptococcus salivarius* and *Streptococcus sanguis*. The study concluded that the double combination of *Acacia* leaves extract with the previous herbal extracts can prevent the occurrence of tooth decay as well as plaques, and this is due to the synergistic effect and delay of antibiotic resistance occurrence [23].

Sharma et al. [24] reported that the hot aqueous extract of *Acacia* leaves possessed an antibacterial (*Streptococcus uberis, Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli, Bacillus cereus, and Klebsiella pneumoniae*) and antifungal (*Aspergillus fumigates* and *Aspergillus niger*) impacts. In contrast, the extract did not show any antiviral effect versus Bovine Herpesvirus-1 (BHV-1).

Gupta and Gupta [25] conducted their study on 90 human volunteers most exposed to tooth decay. They studied the use of ten ml of 50% *Acacia* mouthwash twice a day compared with the effect of ten ml standard mouth wash chlorhexidine 0.2% on the growth of oral *streptococcus mutans* (anaerobic, gram-positive coccus). The study concluded that the use of *Acacia* mouthwash caused a sharp decline in the growth of the buccal *streptococcus mutans* after one and two months of use. The effect of the mouthwash containing *Acacia* was similar to that of chlorhexidine.

Another study compared the antibacterial effect of ethanolic, methanolic, and acetone extracts to *Acacia* leaves. The ethanol extract was the most effective among the rest of the extracts, especially against *Escherichia coli* and *Bacillus subtilis*. The study also reported the antifungal effect of the ethanolic extract against *Aspergillus niger*, while the acetone extract of the *Acacia* leaves was the least effective [26].

In a study conducted to determine the antibacterial effect of *Acacia* fruit extract versus the clinical isolates of many types of Gram-negative (*Klebsiella pneumonia*, *Escherichia coli, Salmonella typhi, Shigellaflexneri,* and *Pseudomonas aeruginosa*) and Gram-positive (*Bacillus cereus* and *Listeria monocytogenes*) bacteria, the results evealed an antibacterial effect against the majority of the bacteria under test. The largest diameter of the inhibition zone was towards *Salmonella typhi* and *Bacillus cereus* compared to the known antibiotic gentamicin [27].

In another *in vitro* study, the effect of hot ethanolic extract of *Acacia* fruits and seeds was tested on the ongoing growth of various types of bacteria using agar well diffusion method. The results found that the concentration of 100 mg/ml eliminated the growth of *Proteus mirabilis, Staphylococcus aureus,* and *Streptococcus pneumonia*. In comparison, the concentration of 75 mg/ml was sufficient to eliminate both *Pseudomonas aeruginosa* and *Escherichia coli* [28].

A recent study reported a bactericidal effect of the ethanolic extract of *Acacia* leaves alone or in combination with extracts of some other plants (*Psidium guajava, Eucalyptus hybrid,* and *Murraya koenigii* L. Sprengel*)* versus *Porphyromonas gingivalis* and *Fusobacterium nucleatum* using the method of agar well diffusion. The combination of the *Acacia* extract with the other extracts was more effective than *Acacia* extract alone, but the inhibition zones remained more with chlorhexidine. The superiority of the combination is due to synergism and reduced antibiotic resistance to bacteria [29].

Another recent bioassay-guided fractionation study showed an antibacterial effect of a specific fraction of *Acacia* leaves extract versus multidrug-resistant pathogens (*Pseudomonas*

aeruginosa and *Staphylococcus aureus*). The study recommended exploring, isolating, and characterizing the active substances of this fraction to develop a new antimicrobial drug [30].

Antiparasitic Activity of *Acacia*

The ethyl acetate extract of *Acacia* possessed a powerful *in vitro* antimalarial impact versus both chloroquine-sensitive and resistant *Plasmodium falciparum* [31]. Besides, Jigam et al. [32] showed that, in mice, *Acacia* root extract showed antimalarial activity versus *Plasmodium falciparum* and *Plasmodium berghei*.

In a study aimed to investigate the therapeutic effect of raw methanolic extract (70% v/v methanol/water) and the partially purified extract of *Acacia* stem bark against laboratory-induced trypanosomiasis (*Trypanosoma brucei*) in mice. The raw extract (400 mg/kg) completely eliminated the disease in eight days. Interestingly, the researchers confirmed that the effect of the partially purified extract (50 mg/kg) completely abolished the parasite in just two days. The study also showed that injecting healthy mice with the blood of the treated mice did not cause trypanosomiasis infection during the observation period (28 days) [33].

The aqueous extract of *Acacia* root exerted a dose-dependent (100, 200, and 400 mg/kg) antimalarial effects against *Plasmodium berghei* in mice and the result was comparable to chloroquine (5 mg/kg) [34].

The results of a recent study that investigated the antimalarial effect of *Acacia* root extract (eluted fractions, 50 and 100 g/kg) showed a marked decrease in the *Plasmodium berghei* count in the diseased mice. The extract also prolonged the survival age of the infected mice and improved the haemoglobin deficiency in the cured mice [35].

Sadiq et al. [36] reported the antimalarial effect of *Acacia* leaves, pods, and stem bark extracts in 48 hours schizont maturation inhibition test. Furthermore, all extracts also hindered the development of mature schizont after 96 hours, confirming schizonticide activity against *Plasmodium falciparum*.

Antidiabetic and Antihyperlipidemic Activity of *Acacia*

Previous studies have confirmed the antidiabetic effect of *Acacia*. Research also informed about the role of this herb in stimulating pancreatic beta cells to release insulin [37].

In an early study, the researchers found that administering an oral dose (400 mg/kg) of the aqueous methanolic extract of *Acacia* pods reduced the level of glucose, cholesterol, triglycerides, and low-density lipoprotein (LDL) in serum compared to the group of alloxan-induced diabetic rabbits. The extract also reduced liver function (alanine aminotransferase (ALT) and aspartate aminotransferase (AST)) while not affecting kidney function (creatinine clearance) in diabetic rabbits. The level of high-density lipoprotein (HDL) increased significantly in the treated rabbits compared to untreated diabetic rabbits [38].

In a study conducted on 120 mice that had their diabetes model developed by injecting 50 mg/kg streptozotocin (STZ), the researchers found that oral administration of a single dose in the morning for three weeks from the methanolic aqueous extract of *Acacia* leaves (300 mg/kg) had caused a significant decrease in the serum level of glucose and triglycerides. While administering the extract increased the concentration of insulin in the serum compared to the diabetes group. The effect of *Acacia* extract did not reach the antidiabetic effect of glyburide (900 µg/kg). The extract also showed no effect on serum total cholesterol, HDL, or LDL [39].

An experimental study conducted in the Kingdom of Saudi Arabia advised the use of the methanolic extract of *Acacia* in the treatment of complications of diabetes and hyperlipidemia associated with diabetes. The study found that feeding 200 mg/kg of the extract in rats with diabetes induced by alloxan (150 mg/kg) reduced the level of triglycerides and LDL while the level of glucose did not change compared to the diabetic rats [40].

The administration of the ethanolic extract of *Acacia* leaves (300 mg/kg) to the hyperglycaemic rats (alloxan model) for 6 weeks caused blood sugar control, as well as the return to the normal lipid profile. Besides, the study confirmed the superiority of the therapeutic effect of the *Acacia* extract on the impact of glibenclamide [41].

Scientists have reported that the effect of the aqueous extract of the stem bark of *Acacia* given by intraperitoneal injection is most effective in reducing blood sugar in the diabetes model induced by alloxan (186.9 mg/kg) in mice. The effect was compared to both insulin and glibenclamide [42].

Recently, a scientific study found that daily feeding of a dose of the ethanolic extract of *Acacia* leaves for 20 days helps relieve symptoms of diabetes developed in mice with alloxan (150 mg/kg). In both doses (50 and 200 mg/kg), the extract reduced the levels of glucose, glycated hemoglobin (HbA1c), and insulin resistance compared to diabetic mice. The extract also managed to minimize complications of diabetes on the liver (ALT and AST) and the kidney (creatinine and blood urea nitrogen (BUN)). The effect of *Acacia* extract was comparable to glibenclamide [43].

Another recent study confirmed that feeding 800 mg/kg/day of ethanol extract of *Acacia* leaves for 6 weeks in mice of type 2 diabetes developed in the laboratory by injecting alloxan 150 mg/kg caused a significant decrease in the fasting blood sugar level, total cholesterol, and LDL compared to the diabetic mice group. The effect of the *Acacia* leaves extract was comparable to that of 100 mg/kg metformin [44].

In a recent study, depending on the model of hyperlipidemia induced in rats with oral feeding 10% fructose for 21 days, a lowering impact of *Acacia* pods (ethanol and ethyl acetate) on blood lipids was reported. The ethanolic extract of *Acacia* pods at a dose of 200 mg/kg was able to lower triglycerides, cholesterol, LDL, and very-low-density lipoprotein (VLDL). No extract was able to change the HDL reduction associated with this model. Results were compared to atorvastatin [45].

Anticancer and Antimutagenic Activity of *Acacia*

Meena et al. [46] reported the anticancer effect of the aqueous extract of gum, flowers, and leaves of *Acacia* against 7,12-Dimethylbenz[a]anthracene produced skin papillomagenesis in mice. Medication with the aqueous extract (800 mg/kg orally) for 15 days was the most effective. Treatment with various extracts resulted in decreased tumor load, tumor incidence, and a cumulative number of skins papilloma. The latency of the tumor in the groups treated with leaf and flower extracts was prolonged.

In another study, it was found that the ethanolic extract of *Acacia* leaves had cytotoxic activity against two cell lines, Hela (IC50 = 53.6 µg/ml) and Vero (IC50 = 28.9 µg/ml). In contrast, the extract did not show any toxicity towards the erythrocytes in humans or rats [47].

A subsequent study also concluded that the *Acacia* extract could be used to treat cancers in humans. As the methanolic extract of the aerial parts of the *Acacia* (10 mg/kg) showed a significant reducing effect on the development of the solid tumor induced in BALB/c mice by Dalton's ascitic lymphoma (DAL). Besides, the extract increased the number of white blood cells (WBCs) and hemoglobin compared to the ascitic tumor group [48].

In addition, the crude (chloroform, n-hexane, and ethyl acetate) extracts of *Acacia* root showed cytotoxic effect against the brine shrimp lethality bioassay, and it was dose-dependent [49].

Antipyretic, Antiinflammatory and Antinociceptive Activities of *Acacia*

Dafallah and Al-Mustafa [50] showed that *Acacia* calyces aqueous extract exerted an antiinflammatory (carrageenan-induced paw edema), analgesic (hot plate method), and antipyretic (Brewer's yeast caused pyrexia) activities.

The aqueous extract of *Acacia* root (200 and 400 mg/kg) provided antipyretic (Brewer's yeast caused pyrexia) and analgesic effect (acetic acid-induced writhing, hot plate, and tail immersion) compared to paracetamol (150 mg/kg) [51].

The aqueous extract of *Acacia* bark (150 mg/kg) reduced fever (Brewer's yeast caused pyrexia), inflammation (formalin caused inflammation), and pain (formalin-induced writhing) in experimental mice [52].

Antiulcer (Gastric and Oral) Activity of *Acacia*

A previous study conducted on 28 patients with recurrent mouth ulcers demonstrated that using adhesive paste from the extract of *Acacia* roots and barks three times daily reduced the inflammatory aura of the ulcer after 48 and 72 hours of treatments. The study also found that the combination of *Acacia* and licorice extract prevented the rapid recurrence of mouth ulcers and had a synergistic effect compared to the *Acacia* extract alone [53].

A study done by Bansal and Goel [54] showed that the aqueous ethanolic extract of *Acacia* pods (50% and 70%) had an antiulcer effect in rats induced by pylorus ligation. The aqueous ethanolic extract (70%) also showed a therapeutic effect against non-steroidal anti-inflammatory drug-induced ulcers and swimming stress-induced ulcers.

Antihypertensive Activity of *Acacia*

The aqueous methanolic extract of *Acacia* pods (80%) showed a dose-dependent (3-30 mg/kg) hypotensive effect in Sprague-Dawley rats. This effect was neither dependent on acetylcholine receptors noradrenaline receptors. The study attributed the hypotensive effect of *Acacia* extract to the blockade of calcium channel [55].

In addition, Reddy et al. [56] recently showed an antihypertensive impact of the ethanolic extract of *Acacia* pods in the model of chicks. This effect was consistent with increasing the dose (100 µg, 1, and 3 mg/kg) and comparable to that of isoprenaline.

Antispasmodic and Antidiarrheal Activity of *Acacia*

Gilaniet al. [55] reported that the aqueous methanolic extract of *Acacia* pods (80%) produced a dose-dependent (0.1-3.0 mg/ml) inhibitory impact on both the spontaneous and K^+-induced rabbit jejunum contraction *in vitro*.

The methanolic extract of *Acacia* bark produced antidiarrheal action against castor oil and magnesium sulfate-induced diarrhea in Swiss mice. The extract also relieved barium chloride-induced small intestinal spasm. The *in vitro* study showed a significant bactericidal impact versus the most common pathogens causing diarrhea [57].

In an experiment conducted on rats infected with diarrhea with castor oil, researchers found a dose-dependent antidiarrheal effect of the ethyl acetate extract of *Acacia* pods. The extract reduced the number of times of the unformed stools (200, 400, and 600 mg/kg) and reduced intestinal transit of charcoal (400 mg/kg) [58].

The methanolic extract of Acacia leaves showed an anti-colic effect against acetylcholine and amechol-induced contraction using isolated Guinea pig ileum. The extract also inhibited castor oil-induced diarrhea in albino rats [59].

Recently, Gilchrist et al. [60] showed that the aqueous extract of *Acacia* bark had an anti-colic effect, as the extract showed an ability to reduce spasms caused by 1µ Macetylcholine

(IC50 = 13.02 µg/ml) and 160 µg/ml barium chloride (IC50 = 117.2 µg/mL) on the isolated rat duodenum.

Antioxidant Activity of *Acacia*

The ethanolic extract of Acacia leaves showed significant antioxidant activity in carotene bleaching assay similar to butylated hydroxytoluene activity [47].

The methanolic and aqueous extracts of *Acacia* pods possess significant antioxidant capacity as appeared by reducing DPPH, nitric oxide, and lipid peroxide production [61].

The ethanolic extract of *Acacia* leaves showed a powerful antioxidant efficacy in 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay (IC50 = 75.2 µg/ml) plus a significant hydroxyl radical scavenging effect (IC50 = 159.6 µg/ml). The total antioxidant capacity of the extract equal to 152.8 µg/ml ascorbic acid. *Acacia* leaves extract markedly counteract the oxidative stress produced in the *Saccharomyces cerevisiae* system. These antioxidant effects could be attributed to the acacia active ingredients phytol and α-tocopherol [62].

The ethanolic extract of *Acacia* leaves, pods, and bark showed significant antioxidant action in favored the leaves extract using the reducing power capacity assay, the percent inhibition of lipid peroxidation, and ferric reducing assay [36]. It was also found that the methanolic extract of *Acacia* leaves exerted a powerful antioxidant capacity (94.3 %) in DPPH, hydrogen peroxide scavenging, metal chelating, and β-carotene-linoleic acid assays. A positive linkage was noticed among the total phenolic constituents, total flavonoid constituents, and the antioxidant efficacy [63].

Conclusion

In conclusion, this review of the early and recently published research articles confirmed many medicinal activities of *Acacia* of pods, stem bark, roots, and leaves extracts. Besides, this study mentioned many therapeutic effects for *Acacia,* including antimicrobial, antiparasitic, antidiabetic, antihyperlipidemic, anticancer, antimutagenic, antipyretic, anti-inflammatory, antinociceptive, antiulcer, antihypertensive, antispasmodic and antidiarrheal, and antioxidant activities. Therefore, *Acacia* extracts may become a natural, inexpensive alternative to pharmaceuticals and prescription drugs.

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