

Review Article

MEDICINAL PROPERTIES OF DIFFERENT PARTS OF *ACACIA NILOTICA* LINN (*BABUL*), ITS PHYTOCONSTITUENTS AND DIVERSE PHARMACOLOGICAL ACTIVITIES

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ABSTRACT

Acacia nilotica Linn commonly known as *Babul* is a multipurpose tree. As the world is turning back towards the herbal drug, it is the need of the hour to re-evaluate the knowledge of traditional medicine through vast review. In the Unani traditional system of medicine, all parts of the plant have been used as a remedy for various diseases and are imputed for their medicinal properties. Hence, this review presents an overview of the medicinal properties of different parts of *A. nilotica* L. used in Unani medicine, its phytochemical constituents, and diverse pharmacological activities. The information related to this drug was retrieved using the classical Unani sources viz., Al-Qanun fi'l Tibb (Canon of Medicine), Iksir-i-A'zam, Al Hawi fi'l Tibb (Continens Liber), Tarjuma Kamil al-Sana'a al-Tibbiyya, Dhakhira Khawarizm Shahi, Biyaz-i-Kabir and Tibb-i-Akbar for medicinal properties used in Unani Medicine. Further for other traditional uses, phytoconstituents and pharmacological activities, different search engines like PubMed, Medline, Google Scholar, Ovid, Science Direct and Scopus were also browsed.

A. nilotica possesses various medicinal properties as per classical Unani texts such as astringent, tonic, wound healing, aphrodisiac, expectorant, resolvent, and antispasmodic. *In vivo*, *in vitro*, and clinical studies from the published articles validate the fact that *A. nilotica* is a potential source of various bioactive compounds having various pharmacological properties and therapeutic uses. The various pharmacological activities are anti-inflammatory, analgesic, antibacterial, anticancerous, antidiabetic and antihypertensive properties. This review concludes that the Unani medicinal effects of *A. nilotica* are proven by scientific studies.

Keywords: *Acacia nilotica* Linn, Analgesic, Antibacterial, Anti-inflammatory, Antioxidant

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INTRODUCTION

Medicinal plants have a long history of use for the benefit of mankind. According to the report of the World Health Organization (W. H. O), about 80% of the world's population relies chiefly on traditional therapies [1]. *Acacia nilotica* Linn commonly known as *Babul* and *Kikar* has been used in Unani and other Indian System of Medicine for hundreds of years for the prevention and treatment of various health ailments. It was first described by Linnaeus in 1773 [2]. *A. nilotica* L belongs to the kingdom Plantae and family Fabaceae [3]. It is the second-largest genus of the family Fabaceae, with about 1350 species. It is distributed throughout tropical and warm temperate areas of the world like Asia, Australia, Africa and America [4, 5]. *A. nilotica* has various complex phytoconstituents including alkaloids, volatile essential oils, phenols, phenolic glycosides, and terpenes. These types of phytoconstituents play a role in the therapeutic actions of *A. nilotica*. Earlier traditional description confirmed that *A. nilotica* has a rich amount of nutrients and contains a high therapeutic value which is capable of prevention, mitigation, and treatment of various infectious diseases and deleterious conditions [6]. The studies based on the animal model established that *A. nilotica* and its chief phytoconstituents play a pivotal role in anti-bacterial, anti-inflammatory, anti-diabetic, anti-cancer, and anti-hypertensive management. It is considered a safe medicinal plant and modulates the numerous therapeutic actions without any adverse effect.

The main objective of this review article is to describe a comprehensive therapeutic Unani traditional uses and novel scientific studies of *A. nilotica*, which will be noteworthy for the design and synthesis of new promising leading compounds with all plant parts.

Literature sources were from the Unani classical texts viz., Al-Qanun fi'l Tibb (Canon of Medicine), Iksir-i-A'zam, Al Hawi fi'l Tibb (Continens Liber), Tarjuma Kamil al-Sana'a al-Tibbiyya, Dhakhira Khawarizm Shahi, Biyaz-i-Kab'ir and Tibb-i-Akbar for medicinal properties used in Unani Medicine. For recent scientific studies

articles published in Pub Med, Ovid, Medline, Science Direct, Springer, Scopus, Google scholars, and Google electronic databases were retrieved.

Ethnobotanical description

The vernacular names of *A. nilotica* are Ammughilam, Ummughilam, Akakia [7] in Arabic. Babbuula, Babbuuri, Baavari, Aabhaa, Shuulika, Shitaka, Kinkiraata, Yugmakantaka, Sukshmaptra, Pitapushpaka [8] in Ayurvedic medicine. It is known as Babul, Black babul, Indian gum Arabic tree [7-10] and Karemugila [7, 11] in Persian. The other synonyms of *A. nilotica* are *Acacia arabica* Willd [8, 10], *Acacia scorpioides*, *Mimosa Arabica* and *Mimosa nilotica* [12].

A. nilotica L. is described as a perennial tree, 2.5-10 m tall. Branches spread, forming a dense flat or rounded crown with dark to black coloured stems. Bark thin, rough, fissured, deep red-brown. Spines (thorns) thin, straight, light grey in axillary pairs, usually in 3-12 pairs, 5-5.7 cm long in young trees. Leaves bipinnate 30-40 mm long, often with 1-2 petiolar glands; pinnae 2-11 pairs, with 7-25 pairs of leaflets per pinnae. Peduncles clustered at nodes of leafy and leafless branchlets. Flowers prolific, golden yellow, in globules heads 1.2-1.5 cm in diameter. Pods straight or slightly curved 5-15 cm long on a pedicel, 0.5-1.2 cm wide, with constrictions between the seeds giving the appearance of a string of pearls, fleshy when young indehiscent, becoming black and hard at maturity. Seeds are deep blackish-brown, smooth, sub-circular, compresses, areole 6-7 mm long, 4.5-5 mm wide. Branches are scattered and the bark is thick and fissured. The orange-brown coloured sticky resinous substance is present inside the plant [11, 13-16].

As per Unani classical texts, the parts used are flower [15-17], leaves [7, 10, 15-18], roots [19], stem/bark [7, 8, 10, 11, 15, 16], gum [7, 8, 10, 12, 15-17, 20], pods [7, 10, 16, 17, 20, 22], seeds [8, 7] and branches [15, 19]. The temperament as per Unani classical texts is Hot and Dry 2 ° [14, 15], Cold and Dry 2 ° [11, 13, 16, 17, 23, 24], and gum-moderate [25]. The dosage mentioned in classical texts for

roots decoction is 84 g to 112g[15] and 5 to 7 g [17] for powder. The compound formulations of *Babul* are *Habbe tappe balghami*, *Habbe sil*, *Laoq sapistan* [11, 14] and *Sanoone mughilan* [14].

Medicinal properties of *A. nilotica* in unani traditional medicine

Qabiz (Astringent), *Habis-i-dam* (Haemostatic), *Mujaffif* (Desiccant), *Mubarrid* (Cooling), *Muqawwi* (Tonic), *Mufattih* (Deobstruent), *Muqi* (Emetic), *Mudammil-i-juruh* (Wound healing), *Mumsik* (Aphrodisiac), *Muzeeqi-i-farj* (Constricts vagina), *Munaffith-i-balgham* (Expectorant), *Muqawwi-i-mida wa jigat* (Liver and stomach tonic), *Rada* (Divergent), *Muhallil* (Anti-inflammatory), *Muqawwi basr* (Eye tonic) and *Dafi-i-tashannuj* (Antispasmodic) [8, 11, 13-, 15, 20, 24].

Phytoconstituents of *a. nilotica* l. (*babul*) with the possible mechanism of action

A. nilotica has a therapeutic implication in disease prevention and treatment as it is a source of various types of phytoconstituents like tannins, alkaloids, polyphenolic compounds, and flavonoids. The most characteristic types of secondary metabolites of this genus are flavonoids [26]. The compounds such as kaempferol-3-glucoside, isoquercetin, catechin, kaempferol, galactose, l-arabinose, l-rhamnose, etc are also present in this plant. The isolated bioactive constituents of *A. nilotica* are summarized in table 1. [8, 9, 18, 27-38].

The Possible mechanism of action of *A. nilotica* is presented as follows

Flavonoids present in the flower, fruit, and leaves are the key constituents responsible for an anti-microbial property. The plant parts exhibit anti-microbial role through inhibition of microbial growth, inhibition of cytoplasmic membrane function, inhibition of the attachment and biofilm formation, and alteration of the membrane permeability [39].

A. nilotica plays an important role as free radical scavenging properties due to a rich source of antioxidants like flavonoids, phenolics, tannins, curcumin, and terpenoids. They can reduce the contact of oxidants and other toxic molecules due to their ability to scavenge oxygen-nitrogen-derived free radicals by donating hydrogen atom or an electron, chelating metal catalysts, activating antioxidant enzymes, and inhibiting oxidases. *A. nilotica* ingredient shows an effective role in the management of cancer through the regulation of cell signalling pathways. It modulates the activity of various tumour suppressor genes, angiogenesis, and apoptosis [38]. *A. nilotica* also plays a role as an anti-inflammatory via regulation of pro-inflammatory enzyme activities including cyclooxygenase and lipoxygenase enzyme. Among the phytoconstituents found in plants like flavonoids, polysaccharides and organic acids may be mainly responsible for its pharmacological action [40]. Tannin is an active chemical responsible for its anti-diabetic activity [41].

Table 1: Phytoconstituents of *Acacia nilotica* Linn

Composition	Bioactive constituents	References
Alkaloids	Dimethyltryptamine, N-methyltryptamine, tryptamines	[27]
Tannins	Methyl gallate	[28]
	Ethyl gallate	[18]
	Gallic acid-Egallic acid	[29]
	Galocatechin-5-O-gallate, Dicatechin, Polygalloytannin	[30]
Proteins	Cysteine, Methionine, Threonine, Lysine, Tryptophan	[31]
Polysaccharides	D-pinitol	[32]
	T-Sitosterol	[33]
	Acanilol	[34]
Terpenes	Lupenone, Lupeol, Niloticane	[35]
Gums/Fatty acids	D-Galactose, L-Arabinose, L-Rhamnose	[36]
	6-O-(β-D-glucopyranosyluronicacid)-D-galactose	[32]
	4-O-(α-D-glucopyranosyluronicacid)-D-galactose	[32]
	Gallic acid, Tannic acid, Cresol	[37]
Flavonoids	Kaempferol kaempferol-3-glucoside, iso-quercetin, leucocyanidi, Catechin, Catechin-7-O-gallate, Quercetin, Quercetin-3-O-β-glucopyranoside, Naringenin, Naringenin-7-O-β-glucopyranoside, Chalconaringenin-4'-O-β-glucopyranoside	[38] [8-9]

Therapeutic implications and pharmacological studies of *A. nilotica*

Anti-microbial potential

A. nilotica fruit is used for the treatment of sore throat, cold, bronchitis, pneumonia, ophthalmia, diarrhoea, dysentery, leprosy and venereal diseases as per Unani traditional medicine. The decoction of the bark is largely used as an astringent douche in *sozak* (gonorrhoea), *waram al-mathana* (cystitis), *waram-al-mahbil* (vaginitis), *sayalan al-rahim* (leucorrhoea) [17].

A study was conducted to investigate the *in vitro* antibacterial activity of *Acacia nilotica* methanolic fruits extract against clinical isolates performed by cup-plate agar diffusion method against five gram-negative bacteria (*E. coli*, *S. flexneri*, *Salmonella typhi*, *Pseudomonas aeruginosa*, and *Klebsiella pneumonia*) and 2 gram-positive bacteria i.e., *Listeria monocytogenes* and *Bacillus cereus*. Out of 7 cultures tested, it showed good activity against *Salmonella typhi* and *Bacillus cereus*. The authors concluded that the methanolic fruit extract of *A. nilotica* showed significant inhibition against gram-positive and gram-negative species [42]. One of the studies found that the methanolic extracts of *A. nilotica* pods were most active against different bacterial and fungal strains. The methanolic extract of pods showed the highest activity against *E. coli*, *S. aureus* and *A. niger* [43]. The antimicrobial property of 50 percent aqueous ethanolic leaf extract of *A. nilotica* (L.) exhibited antifungal property against *Rhizoctonia solani*. [44]. *A. nilotica* demonstrated the highest activity against three bacterial strains (*E. coli*, *S. aureus* and

Salmonella typhi) and two fungal strains (*Candida albicans* and *Aspergillus niger*) [18]. Pods and leaf extracts exhibited the anti-viral effect [45]. Pods of *A. nilotica* were reported to inhibit HIV-1 induced cytopathogenicity [46].

Some of these diseases such as venereal diseases, diarrhoea, vaginitis, cystitis, pneumonia, and sore throat are microbial diseases mentioned in Unani medicine [15, 17]. *A. nilotica* is effective in aforementioned conditions because of its anti-microbial activity.

Anti-inflammatory activity

Traditionally, *A. nilotica* is used in various inflammatory conditions like bronchitis, pharyngitis, vaginitis, and conjunctivitis as it possesses *Muhallil al waram* (anti-inflammatory) property. The decoction of the bark is locally useful in cystitis, and vaginitis [7]. The juice of bark mixed with breast milk is dropped into the eye in conjunctivitis [7, 15]. The ointment of the young leaf around the eyes is beneficial in *Ashob-i-chashm harr* (Acute conjunctivitis) [17]. It is used in ophthalmia, tender leaf fried in ghee and wrapped around the eyes in chronic ophthalmia and subconjunctival haemorrhage [15]. The bruised leaves are applied to sore eyes in children [47]. The tender leaves growing tops rubbed into a paste with sugar and water and given two times a day are useful in cough [7]. The bark is also used in asthma and bronchitis [47].

Plants or their isolated derivatives are in practice to treat/act as anti-inflammatory agents. Study results had confirmed that ethyl extract of *A. nilotica* bark showed significant anti-inflammatory activity in 12-O-tetradecanoylphorbol-13-acetate (TPA) induced mouse ear oedema

[48]. Other study results revealed that its pod aqueous extract at a dose of 50 and 100 mg/kg b.w. showed significant anti-inflammatory activity in cotton pellet granuloma assay in rats [40]. Another study investigated the anti-inflammatory effect of *A. nilotica* on albino rats using carrageenan-induced paw oedema and yeast induced pyrexia at a dose of 100 mg/Kg b.w. The results exhibited an increased inhibition of paw oedema and pyrexia (20%) [49].

Anticancerous activity

Cancer is a multifactorial disease and a major health problem worldwide. Earlier studies reported that plants and their constituents show inhibitory effects on the growth of malignant cells through modulation of cellular proliferation, tumour suppressor gene, apoptosis, etc. It contains flavonoids and various other constituents that play an important function in the inhibition of cancer development. The experiment was made to evaluate the anticancer activity of aqueous extracts of gum, flower and leaves of *A. nilotica* in 7, 12-dimethylbenz(a) anthracene (DMBA) induced skin papillomagenesis in Swiss albino mice. The results showed a significant reduction in the values of tumour burden, tumour incidence and cumulative papillomas [50]. A study finding revealed that methanolic pods extract showing anti-uvéal melanoma activity [38].

Antioxidant activity

Free radical or reactive oxygen species are one of the main causes in the genesis of various diseases. Antioxidants deactivate free radicals, often before the attack targets in cells. Medicinal plants have been reported to have antioxidant activity. A valuable study was carried out to evaluate *in vitro* antioxidant activity in 8 different crude extracts of the pods of *A. nilotica*. The results obtained strongly indicated that green pods of *A. nilotica* are an important source of natural antioxidants [29]. Other results revealed that umbelliferone a coumarin derivative studied *in vitro*, and exhibited a higher antioxidant activity [51]. Another study revealed that *A. nilotica* was an easily accessible source of natural antioxidants, which can be used as a supplement to aid the therapy of free radical-mediated diseases such as cancer, diabetes inflammation, etc [52]. Furthermore, the high scavenging property of *A. nilotica* may be due to hydroxyl groups existing in the phenolic compounds that can scavenge the free radicals [The antioxidant activity of fruit extract of *A. nilotica* and leaves extract of the date palm revealed that the methanol extract of each plant powder was obtained by dissolving 5g of each plant powder in 50 ml methanol-water had rich sources of total phenol content and Trolox Equivalent Antioxidant Capacity (TEAC) radical scavenging activity [53].

Antimalarial potential

A study was performed to investigate the anti-plasmodium activity of aqueous and methanolic root extract of *Babul* in *Plasmodium Berghei* infected mice. The results revealed significant activity against chloroquine-sensitive strains [54]. Ethyl acetate extract of its root showed the highest activity against *P. falciparum*. Another *in vitro* study was made to evaluate the antimalarial activities of leaves, pods and bark extracts of *A. nilotica*. The results revealed that it had an antimalarial effect as all extracts inhibited the development of mature schizont indicating schizonticide activity against *P. falciparum* [55].

Analgesic and antipyretic activity

Traditionally, *A. nilotica* has been shown to be a potent analgesic as it is used in ophthalmic pain. The young leaves fried in ghee and wrapped around the eyes in chronic ophthalmia and subconjunctival haemorrhage [15, 20].

Modern researches also have revealed that it has analgesic and antipyretic activity. One of the studies examined antipyretic as well as the analgesic activity of an aqueous root extract of *A. nilotica* in Wistar Albino rat models. The antipyretic and analgesic activity of the extract was compared with acetaminophen. The results showed that extract produces a significant dose-dependent reduction in rectal temperature of rats at 200 and 400 mg/kg body weight. Significant analgesic activity was also observed which was comparable to the acetaminophen [56].

Degenerative diseases

Acetylcholinesterase (AChE) inhibitor has been used as a drug for the symptomatic treatment of Alzheimer's disease [57]. The root

aqueous, ethyl acetate leaf, ethanol leaf, and ethyl acetate bark extract of *A. nilotica* had AChE inhibitory activity [58]. Another study showed inhibition of acetylcholinesterase by diterpene niloticane isolated from stem bark ethyl acetate extract of *A. nilotica* [47]. TheeExperimentation showed potent that the AChE-inhibiting effect of *A. nilotica* was much more potent than Portuguese and Danish medicinal plants such as *Brassica nigra* and *B. alba*, *Myristica fragrans*, *Juniperus Sabina* and other plants [59].

Gastrointestinal tract

Traditionally, the decoction of leaves is used as astringent for the bowels [11, 14, 17]. Pods and bark are useful in piles [20]. Dry thorn of *Acacia*, boiled in 400 ml of water, filtered and add honey in it, is useful in hiccups [15, 20]. The gum mucilage in useful in diarrhoea and dysentery [7]. The paste of leaves with *Zeera siyah* (*Bunium bulbocastanum*) and *Zeera safaid* (*Cuminum cyminum*) is useful in phlegmatic diarrhoea. Powdered pods and leaf extracts are also useful in diarrhoea. Flowers are used as a tonic in diarrhoea and dysentery. Fresh leaves along with sugar and *Kali mirch* (*Piper nigrum*) are useful in intestinal abrasions and hemorrhagic diarrhoea. The decoction of bark causes constipation when used orally or as an enema [15].

The significant protective effect of 50% hydroethanolic and 70% hydroethanolic pods extract was revealed in gastric ulcers [22]. The methanol fruit (pods with seeds) extract of *A. nilotica* showed a dose and time-dependent antihelminthic effects in worms by inhibiting egg hatching and larval development [60]. The methanol bark extract was used to treat barium chloride-induced peristaltic movements and castor oil, magnesium sulfate-induced diarrhoea and *in vitro* antimicrobial activity against common micro-organisms causing diarrhoea in Swiss albino mouse model [61].

Metabolic disorders

Metabolic disorders consist of hyperglycemia, hypertension, hyperlipidemia, and central obesity. Each metabolic disorder is associated with other risk factors that promote cardiovascular disease [62]. Herbal medicines have therapeutic effects on regulating these disorders. *A. nilotica* is a useful drug for *Zyabetus* (diabetes) as stated in the traditional Unani medicine [20], which is scientifically proven in various *in vivo*, *in vitro* and clinical studies. An *in vitro* study was undertaken to evaluate the hypoglycemic activity of roasted *A. nilotica* powder in diabetic rats, statistically significant lowering of blood glucose levels from 132.23±26.68 to 106.1±10.92 was observed [63]. Another important study suggested that aqueous and methanol leaves extracts of *A. nilotica* exhibited hypoglycemic and anti-platelet aggregation activity in the streptozotocin-induced diabetic rats [64]. The hot water extract of pods showed hypoglycemic effects in adult male albino rat models [65]. However, pods and tender leaves are considered very beneficial in folk medicine to treat DM.

Hyperlipidemia one of the risky metabolic disorders can progressively cause and/or exacerbated a wide spectrum of co-morbidities. Animal studies have shown that *A. nilotica* is protective against hyperlipidemia. In an animal study, *A. nilotica* extract was given in doses of 100 mg/kg and 200 mg/kg orally for 21 d to the streptozotocin-induced diabetic female albino rats to assess antidiabetic, antihyperlipidemic and antioxidant effects. Its treatment had decreased total cholesterol level (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), malondialdehyde (MDA) and a significant increase in high-density lipoprotein cholesterol (HDL-C) was observed [65].

Traditionally, flowers of *A. nilotica* are powerful tonic and enrich the blood [49]. The flower extract is useful in *Khafaqn harr* (palpitation) [13, 23].

A decrease in arterial blood pressure was reported with the use of a methanolic extract of *A. nilotica* pods and provided evidence of antihypertensive activity independent of muscarinic receptor stimulation. In the *in vitro* study, *A. nilotica* has an inhibitory effect on force and rate of spontaneous contractions in guinea-pig paired atria and rabbit jejunum. Another study showed that methanol extract of *A. nilotica* pods had antihypertensive and antispasmodic activity [32]. It also inhibited K⁺-induced contraction in rabbit jejunum and suggested the antispasmodic action of *A. nilotica*, which was mediated through the calcium channel blockade, hence also be responsible for the blood pressure-lowering effect of *A. nilotica* observed in the *in vivo* studies [66].

Table 2: Clinical studies of *Acacia nilotica* linn

Title of the study, author with year	Study design	Sample size	Participants	Dosage with route of administration	Outcome	References
Short-term clinical effects of commercially available gel containing <i>Acacia arabica</i>	Prospective Randomized placebo control trial	90	Subjects having chronic generalized gingivitis.	Local application of gel on gums.	The gel contains <i>Acacia</i> showed significant clinical improvement in gingival and plaque index as compared to placebo gel.	[70]
Anti-gingivitis Effects of <i>Acacia arabica</i> -containing Toothpaste	Randomized , Double-blind crossover control trial	60	8-37 y of age with minimum of 15 teeth, good general health, a baseline plaque index (PI) mean>1.510 and the presence of established gingivitis along with mean gingivitis scores>1.0.	Subjects brush their teeth thrice daily with 50g Of non-fluoridated toothpaste containing <i>Acacia</i> .	PI and GI score change between baseline and 28 d was recorded in the test group before crossover is (0.69) and 0.94 whereas the lowest score differential was recorded in the control group after crossover i.e., 0.1 and 0	[71]
Evaluate the efficacy of <i>Aqaqia</i> (Gum of <i>Acacia</i>) in improving women quality of life in uterine prolapse with P-QOL Quetionnaire	Single-blind, Randomized study	30	Participants diagnosed with uterine prolapse.	<i>Acacia</i> powder orally as well in the form of pessary given	A group who is given <i>Acacia</i> powder shows a significant improvement in QOL in the uterine prolapse patient as compared to a CG.	[72]
<i>Babul</i> A potential source of tannin and its suitability in the management of type II diabetes mellitus	Pilot study	42	30 normal subjects (20 female and 10 males) for assessing the Glycemic index. 12 diabetic subjects (8 males and 4 females)	<i>Babul</i> pods powder incorporated in biscuits (3g per serve)-Blood sugar levels recorded at every 30 min interval for 2 hr	<i>Babul</i> powder is effective in management of blood glucose levels.	[41]
Efficacy of Herbal Formulation (containing <i>Acacia Arabica</i> and <i>Butea Frondosa</i>) In Treatment of Post-natal Backache	Open prospective clinical trial	12	21-45 age year women in the postnatal period complained backache, white discharge and fatigue without any other pathology.	6g of <i>Acacia</i> and <i>Butea</i> powder gave twice daily with a glass of milk for 30 d.	7 Out of 12 (75%) Patients respond well for pain relief. Relief in other symptoms is 77.7% patients for fatigue and 60% for white discharge	[73]
Efficacy of <i>Acacia arabica</i> gum as an adjunct to scaling and root planning in the treatment of chronic periodontitis	Randomized , triple-blind controlled trial	80	Age between 18-70 y with mild to moderate chronic periodontitis analyzed for clinical improvements in periodontal pocket depth and clinical attachment levels.	Application of <i>Acacia</i> gel twice daily after tooth brushing.	Statistically significant PPD and CAL gain was observed with the use of <i>Acacia</i> gel.	[74]
Efficacy of bark of <i>Acacia arabica</i> in management of bacterial vaginosis: a randomized controlled trial	Single-blind, randomized standard controlled study	45	Participants diagnosed with bacterial vaginosis	The decoction of <i>Chal babool</i> was given orally (30 gms twice daily) for one month and standard drug Tab. Metronidazole (400 mg twice daily) for 7 d was given	<i>A. nilotica</i> was found to have similar effects as the control drug in the management of Bacterial Vaginosis	[75]
Effect of <i>Abzan</i> of <i>Samar Babool</i> in <i>Sayalan al-Rahim</i> -A randomized controlled study	Single-blind, randomized placebo-controlled study	66	Married women within the age group of 18–50 y, presenting with <i>sayalan al-rahim</i> (abnormal vaginal discharge) and/or associated with any of these symptoms such as pain in the lower abdomen, low backache, dyspareunia, dysuria, burning micturition, vulvar itching and vulvar irritation	In the test group aqueous extract powder of <i>samar babool</i> (30g) followed by <i>hamul</i> (5 ml of the same solution) intravaginally and in the control group placebo palm sugar powder (30g) once daily for 10 d. In both groups, orally, one capsule of placebo was given daily for 10 d.	<i>Samar babool</i> is a safe and effective therapy for the treatment of <i>sayalan al-rahim</i> assessed by VAS scale and for the improvement in HRQoL of women assessed by EQ-5D-5L.	[76]
Gum arabic reduces C-reactive protein in chronic kidney disease patients without affecting urea or indoxyl sulfate levels	Open-label randomized clinical trial with parallel design	36	Eligible candidates were adult CKD patients in stage 3B/4	Each patient 28 labelled packages containing 10, 20, or 40 grams of gum <i>Arabica</i> in the form of instantly soluble granules	Supplementing the diet of CKD patients with 10–40 g/day of GA significantly reduced CRP level.	[77]

Oral cavity

Oral hygiene measures have been practiced by different populations around the world since antiquity. Dental caries is one of the most common human diseases that affect the vast majority of individuals. The bark of *Acacia* is used in toothpaste, which acts as a *Mujali-dandan* (tooth cleaner) [16]. Extract of leaves is used as hemoptysis, the paste of its bark makes the gum strong, strengthens the teeth and also checks bleeding gums. The bark decoction is used as a gargle in various throat problems. The bark of *Acacia* and the bark of mango in an equal quantity (6g) boiled in 750 ml of water for half an hour and gargled with the filtered solution is useful in mouth ulcers. Gargles with its leaves, bark and *Hardh* (*Terminalia chebula*) bark are also used in the treatment of sore throat [7, 15, 47].

An *in vitro* study was done to assess the effectiveness of 5%, 10%, and 50% extract of dried chewing sticks of *A. nilotica* on *Streptococcus mutans*. The results showed the effect of various concentrations of aqueous *A. nilotica* extracts on *Streptococcus mutans* [4].

Prolactin release and milk production

Stem bark aqueous extract in the dose of 280-560 mg/b. w was proven to have the stimulation of milk production and mammary gland development in the female rats [67].

Sexual and urogenital

Traditionally, *A. nilotica* has been used to treat sexual dysfunctions. Pods are *Muqawwi-i-bah* (strong aphrodisiac) and useful to treat *Salyan al-rahim* (leucorrhoea) [13, 15, 20, 47]. A douche of decoction of the bark is also useful in *Silsil al-bawl* (incontinence of urine) [16]. A douche of bark decoction with alum powder is useful in abnormal vaginal discharge. The oral intake of bark decoction is useful in *Istehaza* (Abnormal uterine bleeding) [15]. Powdered pods are used in impotency, spermatorrhoea and effective in urogenital disorders [47]. Recent scientific studies have also proven the same effect that the fresh pods extract are useful in the treatment of sexual disorders such as spermatorrhoea, loss of viscosity of semen, frequent night discharges and premature ejaculation [68].

In vitro study with ethanolic bark extract of *A. nilotica* 300 mg/kg b. w showed an increase in the volume of urine and concentrations of Na, K, and Cl ions proving its diuretic effect [69].

Smooth muscle relaxant property

An experiment was made to assess the smooth muscle relaxant activity of methanolic leaf extract against the acetylcholine and oxytocin-induced contractions in isolated Wistar rat uterus. The results showed excellent muscle relaxant activity of *A. nilotica* [35].

Clinical trials

Various clinical trials were conducted to study the effect of *A. nilotica* in gingivitis, uterine prolapse, leucorrhoea, diabetes mellitus, postnatal backache, chronic periodontitis, and bacterial vaginosis. The clinical trials are summarized in table 2 [41, 70-77].

Side effects as per unani classical texts

It affects stomach [11, 13, 14, 23], intestines [11, 13, 14]; rectum [23], brain [23], chest [15, 16]. To prevent these side effects *Kateera* (*Astragalus tragacanth*) [11, 13, 14, 16, 23], *Shehad* (Honey) [11, 13, 14, 16], *Mirch siyaah* (*Piper nigrum*) [13] and *Banafsha* (*Viola odorata*) [15]; *Bahi* (*Cydonia oblonga*) [23] is used.

Safety and toxicological studies

The measurement of toxicities of the natural compounds are crucial before their application in health management. Various studies based on animal models confirmed that *A. nilotica* is safe at a certain dose. One of the studies has proven that *A. nilotica* extract has hepatoprotective action and this effect relies on reducing the oxidative stress in acetaminophen-induced hepatic damage in the rat model [78]. Another study showed the protective effect of *A. nilotica* leaf extract and ethyl gallate on DNA and protein against oxidative stress in *in vitro* study [79].

A study showed that the bark extract of *Acacia* is very much toxic to Vero cells at concentrations ranging from 50 to 200 micro gm/ml

[45]. Another study revealed that LD50 was found to be 215.36 mg/kg for ethanolic extract of *Acacia* in rats. Further, the authors concluded that some toxicity was observed when administered subcutaneously and intraperitoneally in rats, especially at a higher dose of 60 mg/kg [80]. The possible toxicity of *A. nilotica* was examined in rats maintained at 2% and 8% acacia diet for 2 and 4 w. A significant reduction in body weight in all acacia fed rats and a significant decrease in the levels of hemoglobin, serum total protein, and total cholesterol in rats fed at 8% acacia diet for up to 4 w were noted [81]. One of the studies showed that goats who received oral doses of 1 g/kg/day of *Acacia* had an intermittent loss of voice, incoordination in movement and one goat died after 3 d of dosing, another died on day 15 and the last goat with this dose died on day 35. Goats who received oral doses of 5 g/kg/day of *Acacia nilotica* pods, the prominent signs observed from day one of dosing was the thick saliva, loss of voice, staggering movement, recumbence loss of appetite and all goats with this dose died between day 4 and day 8 of the experiment [82].

CONCLUSION

The popularity of Traditional medicinal plants or their derivatives role in disease prevention and management is increasing worldwide. The extensive survey of literature revealed that *A. nilotica* is an important traditional medicinal plant with diverse medicinal properties with an array of pharmacological activities. It has been traditionally used worldwide since ancient times. The clinical-based studies confirmed that it plays an important role in the prevention and management of various diseases. Further, evaluation needs to be carried out in order to explore the concealed areas and their practical clinical applications, which can be used for the welfare of mankind.

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CONFLICT OF INTERESTS

The authors declare that there are no conflicts of interest.

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