Quercus infectoria

Scientific Name

***Quercus infectoria* G. Olivier.**

Synonyms

Quercus infectoria ssp. *euinfectoria* A.Camus, *Quercus lusitanica* ssp. *infectoria* (G.Olivier) Mouillef., *Quercus lusitanica* var. *infectoria* (G. Olivier) A DC.

Family

Fagaceae

Common/English Names

Aleppo Oak**,** Asian Holly-Oak, Cyprus Oak, Downy Oak, Dyer's Oak, Gall Oak, Nut-Galls

Vernacular Names

Arabic: Afas, Afss, Ballut Afssi, Mazu, Uffes;
Czech: Dub Hálkovec;
Dutch: Eik Soort;
Eastonian: Tinditamm;
French: Chêne À Galles, Chêne d'Alep, Chêne d'Israel;
German: Gall-Eiche, Gallapfel-Eiche;
Hungarian: Kurdisztáni Tölgy;
India: Majuphal, Majuphul, Mazu, Muphal (Hindu), Machikai, Macike, Machi Kaayi (Kannada), Masikka, Mayakku (Malayalam), Majuphala, Maayaphal (Marathi), Ambastha, Majjaphala, Majuphal, Majuphul, Manjuphal, Mayakku, Mayaphala, Mayuka (Sanskrit), Cakkirakacikakkay, Cakkirakacikam, Civatakitakkay, Maasikkai, Macakkai, Macakkay, Macikkai, Macikkay, Machakai, Machikai, Machikkai, Maci, Masikkai, Mayakkay, Mayakkay (Tamil), Mashi Kaaya, Mashikaya, Masikaya (Telugu), Baloot., Mazu, Mazu Sabz, Mazu Subz (Urdu);
Indonesia: Manjakani;
Malaysia: Manjakani;
Persian: Mazu, Mazu-E-Sabz;
Spanish: Encina De La Agalla;
Swedish: Aleppoek;
Thai: Ben Ka Nee;
Turkish: Mazı Meşesi.

Origin/Distribution

Q. infectoria is indigenous to Turkey, Iran, Iraq, Kurdistan, Cyprus, East Aegean Islands, Greece, Lebanon and Syria. The tree is occasionally cultivated for production of tanning bark and for dye production of the wood.

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Agroecology

In its native range, it is usually found in semi-humid to semi-arid forests in areas with mean annual rainfall of 400–1,100 mm from 900 to 2,000 m altitude. It is intolerant of frost. It grows on a wide range of soil types from acidic to alkaline, in full to partial sun.

Edible Plant Parts and Uses

The seed can be thoroughly washed in running water to remove the bitter tannins and cooked. The seeds can be dried, ground into a powder and used as a thickening in stews etc. or mixed with cereals for making bread. When roasted the seeds can be used as a coffee substitute. The nut gall (Plate 1) extract or powder is used as a herbal drink or tea for health purposes.

Botany

A semi-evergreen, small tree or shrub, 1–4 (–10) m with grey, scaly, ridged bark. Juvenile shoots are pubescent, reddish or yellowish-brown; buds reddish-brown, about 3 mm and pubescent. Leaves are alternate, very variable in size and colour, 40–70(–100) by 10–45 mm, leathery, glabrescent, ovate to narrowly oblong, rounded or wedge-shaped at base, margins often wavy with 4–8 crenate to saw-toothed lobes, or entire (at base of twigs); primary veins 6–11; petiole 1–15(–25) mm. Inflorescences unisexual, in axils of leaves or bud scales, usually clustered at base of new growth; staminate inflorescences lax, spicate; pistillate inflorescences usually stiff, with terminal cupule and sometimes 1-several sessile, lateral cupules. Fruit is a smooth nut, called an acorn, mucronate, ovoid elongated, 2–3.5 cm long, 1.8 cm in diameter; glabrous and is more or less enclosed in a scaly involucre called the cup or cupule. Cupules solitary or in pairs, approximately hemispherical or cyathiform, 10–18 mm in diameter with lanceolate strongly adpressed, greyish pubescent scales.

The galls or nut-galls are hard, corky, resinous, greyish-brown, nearly round excrescences formed on the young branches. The excrescences vary from the size of a large pea to that of a small hickory-nut. They are the result of a puncture made in the bark by an insect (*Diplolepis gallae tinctoriae*, or *Cynips quercufolii*) for the purpose of depositing its egg. A small tumour soon follows the puncture, and forms a very dense mass about the egg. The egg hatches into the fly while in these tumours, eating its way by a small opening. The nut gall has an integument with rugae-like surface interspersed by protruding blunt horn-like lumps (Soon et al. 2007) imparting to it a tuberculate appearance (Plate 1). Cross section of the gall revealed a whitish core and concentric circles of resinous materials constituting the middle layer.

Plate 1 Nut galls of *Quercus infectoria*

Nutritive/Medicinal Properties

Nut-galls abound in tannins (36–60%). The constituents of galls was found to comprise a large amount of tannins: gallic acid, syringic acid, ellagic acid, β-sitosterol, amentoflavone, hexamethyl ether, isocryptomerin, methyl betulate, methyl oleanate, hexagalloyl glucose (Aroonrerk and Kamkaen 2009) and ellagic acid-4- O -[β-D-glucopyranosyl]-10- O -[β-D-glucopyranosyl]-(4→1)-β-D-rhamnopyranoside, and 2-methyl-3-hydroxymethylene-4,5,6,7,

8-pentahydroxynaphthalene (Hamid et al. 2005). The nut-galls also contained useful minerals of carbon, oxygen, silica, magnesium, aluminium, potassium and calcium (Soon et al. 2007).

Studies had shown that the nutgall extract had antioxidant, antiinflammatory, antiviral, analgesic, antitremorine, skin whitening, antidiabetic, antibacterial, larvicidal, molluscicidal, anti protozoal, antivenom, and anti-amoebic activities.

Antioxidant Activity

Two compounds isolated from the ethanol extract of the galls of *Quercus infectoria* exhibited nitric oxide (NO) and superoxide inhibiting activity (Hamid et al. 2005). Their structures were established as ellagic acid-4- O -[β-D-glucopyranosyl]-10- O -[β-D-glucopyranosyl]-(4→1)-β-D-rhamnopyranoside and 2-methyl-3-hydroxymethylene-4,5,6,7,8-pentahydroxynaphthalene. Umachigi et al. (2008) reported *Quercus infectoria* nutgalls to have potent antioxidant activity. Its extract strongly scavenged DPPH radical with the IC_{50} being 0.25 mg/ml in a dose dependent manner. The total antioxidant capacity of the extract was found to be 152.91 nmol/g ascorbic acid. *Quercus infectoria* extract also moderately inhibited nitric oxide in dose dependent fashion with the IC_{50} being 0.258 mg/ml. It was also determined that the 50% aqueous alcoholic extract of *Quercus infectoria* inhibited $FeSO_4$ induced lipid peroxidation in a dose dependent manner. IC_{50} value was found to be 0.124 mg/ml. The decrease in the MDA (malondialdehyde) level with increases in the concentration of the extracts indicated the role of the extract as an antioxidant. The extract also moderately scavenged superoxide radical with the IC_{50} value of 1.024 mg/ml. Gallic acid was found to be 0.68% w/w in the methanolic extract. The high percentage of the gallic acid in the extract underpinned the potent antioxidant activity exhibited. The results obtained indicated that *Quercus infectoria* extract had potent antioxidant activity, achieved by scavenging abilities observed against DPPH, and lipid peroxidation.

Studies showed that *Q. infectoria* galls possessed potent antioxidant activity, when tested both in chemical as well as biological models (Kaur et al. 2008) Ethanolic gall extract was found to contain a large amount of polyphenols and to possess potent reducing power. HPTLC analysis of the extract found it to contain 19.925% tannic acid (TA) and 8.75% gallic acid (GA). The extract strongly scavenged free radicals including DPPH (IC_{50} approximately 0.5 μg/ml), ABTS (IC_{50} approximately 1 μg/ml), hydrogen peroxide (H_2O_2) (IC_{50} approximately 2.6 μg/ml) and hydroxyl (OH) radicals (IC_{50} approximately 6 μg/ml). Gall extract also chelated metal ions and inhibited Fe^{3+}-ascorbate-induced oxidation of protein and lipid peroxidation. Exposure of rat peritoneal macrophages to tertiary butyl hydroperoxide (tBOOH) induced oxidative stress and modified their phagocytic functions. These macrophages exhibited increased secretion of lysosomal hydrolases, and mitigated phagocytosis and respiratory burst. Activity of macrophage mannose receptor (MR) also declined following oxidant exposure. Pretreatment of macrophages with gall extract maintained antioxidant protection close to control values and significantly protected against all the investigated functional mutilations. MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay revealed the gall extract to enhance percent survival of tBOOH exposed macrophages.

Antiinflammatory Activity

Galls of *Quercus infectoria* were found to possess manifold therapeutic activities, with particular efficacy against inflammatory diseases (Kaur et al. 2004). Oral administration of gall alcoholic extract significantly inhibited carrageenan, histamine, serotonin and prostaglandin E2 (PGE2) induced paw oedemas, while topical application of gall extract inhibited phorbol-12-myristate-13-acetate (PMA) induced ear inflammation. The extract also suppressed various functions of macrophages and neutrophils relevant to the inflammatory response. In-vitro exposure of rat peritoneal macrophages to gall extract dose

dependently ameliorated lipopolysaccharide (LPS) stimulated PGE2 and nitric oxide (NO) production and PMA triggered superoxide (O2*–) production. Gall extract also scavenged NO and O2*–. Probing into mechanism of NO inhibition in macrophages revealed gall extract to ameliorate the stimulation of inducible NO synthase (iNOS), respectively without any inhibitory effect on its catalytic activities even at higher concentrations. Gall extract also significantly inhibited formyl-Met-Leu-Phe (fMLP) triggered degranulation in neutrophils. These results suggested that alcoholic extract of galls of *Q. infectoria* exerted in-vivo antiinflammatory activity after oral or topical administration and also had the ability to curb the production of some inflammatory mediators. In separate studies, *Quercus infectoria* (QI) nutgall extract was found to exhibit potent antioxidant and antiinflammatory activities (Pithayanukul et al. 2009). Treatment of rats with nutgall extract reversed oxidative damage in hepatic tissues induced by carbon tetrachloride. It was suggested that the *Quercus infectoria* extract which was rich in hydrolysable tannins and known for their potent antioxidant and antiinflammatory activities, may potentially confer hepatoprotective effect against oxidative stress-induced liver injury.

Recent studies reported that the Thai herbal recipe for aphthous ulcer comprising *Quercus infectoria, Glycyrrhiza uralensis, Kaempferia galanga* and *Coptis chinensis* and the individual plant powder components exhibited potent anti-inflammatory activity (Aroonrerk and Kamkaen 2009). The four plant powders, *K. galanga, C. chinensis, G. uralensis* and *Q. infectoria* inhibited interleukin IL-6 production with IC_{50} value of 0.04, 0.07, 0.08 and 0.31 μg/ml respectively. They also displayed anti-PGE2 activities but lower than the aphthous powder and aphthous gel. The antiinflammatory activities were significantly higher than prednisolone and the COX-2 inhibitor. The plant powders and the herbal recipe had no growth inhibitory effect on the human gingival fibroblast cells even at the highest dose. No sign of irritation was noted during the dermal irritation test. It was postulated that the antiinflammatory activity of *Q. infectoria* was due to the presence of high tannin compounds and was mediated by either inhibiting the synthesis, release or action of mediators such as interleukin, serotonin, histamine and PGE2.

Antimicrobial Activity

The methanol extract of *Quercus infectoria*, exhibited potent antibacterial activity against the cariogenic bacterium *Streptococcus mutans* (Hwang et al. 2004). Recent studies also showed that methanolic extract had maximum anti-bacterial activity against the following dental pathogens – *Streptococcus mutans, Streptococcus salivarius, Staphylococcus aureus, Lactobacillus acidophilus* and *Streptococcus sanguis* (Vermani and Navneet 2009). The most susceptible bacteria were *S. sanguis* followed by *S. aureus, S. mutans, S. salivarius* and *L. acidophilus*. The MIC values showed that methanolic extract was more effective than the water extract.

Numerous research studies conducted by Voravuthikunchai and co-workers in Thailand showed that the nut gall extracts of *Q. infectoria* had potent antibacterial activity against a broad spectrum of bacterial pathogens. Among the 38 Thai medicinal plants tested, only eight species (21.05%) exhibited antimicrobial activity against enterohaemorrhagic *Escherichia coli* (Voravuthikunchai et al. 2004). *Acacia catechu, Holarrhena antidysenterica, Peltophorum pterocarpum, Psidium guajava, Punica granatum, Quercus infectoria, Uncaria gambir,* and *Walsura robusta* demonstrated antibacterial activity with inhibition zones ranging from 7 to 17 mm. The greatest inhibition zone against *Escherichia coli* was produced from the ethanolic extract of *Quercus infectoria*. Both aqueous and ethanolic extracts of *Quercus infectoria* and aqueous extract of *Punica granatum* were highly effective against *Escherichia coli* with the best MIC and MBC values of 0.09, 0.78, and 0.19, 0.39 mg/ml, respectively. These plant species may provide alternative but bioactive medicines for the treatment of enterohaemorrhagic *Escherichia coli* infection. Of nine Thai traditional medicinal plants that

displayed activity against all 35 hospital isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) tested, the ethanolic extracts of *Garcinia mangostana, Punica granatum* and *Quercus infectoria* were most effective, with MICs for MRSA isolates of 0.05–0.4, 0.2–0.4 and 0.2–0.4 mg/ml, respectively, and for *Staphylococcus aureus* of 0.1, 0.2 and 0.1 mg/ml, respectively (Voravuthikunchai and Kitpipit 2005). MBCs for MRSA isolates were 0.1–0.4, 1.6–3.2 and 0.4–1.6 mg/ml, and for *Staphylococcus aureus* were 0.4, 3.2 and 1.6 mg/ml, respectively. In another study, of four medicinal plants used for traditional remedies for diarrhea, *Acacia catechu, Peltophorum pterocarpum, Punica granatum*, and *Quercus infectoria*, the ethanolic extract of *Q. infectoria* was the most effective against all strains of *E. coli*, with MICs of 0.12–0.98 mg/ml and MBCs of 0.98–3.91 mg/ml (Voravuthikunchai and Limsuwan 2006). Ethanolic extracts of *Q. infectoria, P. pterocarpum*, and *P. granatum* were among the most effective extracts against the two strains of *E. coli* O157:H7.

Acetone, ethyl acetate, 95% ethanol and aqueous extracts of *Quercus infectoria* nut-galls demonstrated significant antibacterial activities against all strains of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *Staphylococcus aureus* (MSSA) (Chusri and Voravuthikunchai 2008). Inhibition zones were in the range 11.75–16.82 mm. Both MRSA and MSSA strains exhibited minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values at 0.13 and 0.13–1.00 mg/mL, respectively. In another paper they reported the use of *Q. infectoria* nut galls, containing up to 70% tannin content, was effective in the treatment of methicillin-resistant *Staphylococcus aureus* infections (Chusri and Voravuthikunchai 2009). The appearance of pseudomulticellular bacteria in the treated cells and the synergistic effect of the *Q. infectoria* extract with β-lactamase-susceptible penicillins suggested that the extract may interfere with staphylococcal enzymes including autolysins and β-lactamase. Subsequent studies by Voravuthikunchaia et al. (2008) indicated *Quercus infectoria* galls to be potentially a good source of antibacterial substances with broad spectrum of activities against antibiotic-resistant bacteria. Ethanol extracts of *Quercus infectoria* galls demonstrated a broad spectrum of activity against *Acinetobacter baumannii, Bacillus cereus, Enterobacter faecalis, Escherichia coli, Helicobacter pylori, Klebsiella pneumoniae, Listeria monocytogenes, Pseudomonas aeruginosa, Salmonella spp., Shigella flexneri, Staphylococcus aureus, Streptococcus mutans* and *Streptococcus pyogenes.* The extracts of *Quercus infectoria* displayed remarkable activity against methicillin-resistant *Staphylococcus aureus* (MRSA) with MICs ranging from 0.02 to 0.4 mg/ml, and MBCs ranging from 0.4 to 1.6 mg/ml. More importantly, *Quercus infectoria* could exhibit strong antibacterial activity against all Gram-negative organisms. Its significant activity was shown with enterohemorrhagic *Escherichia coli* (EHEC), with MICs of 0.05–0.1 mg/ml and MBCs of 0.8–1.6 mg/ml.

Chusri et al. (2011) reported the minimal inhibitory concentration (MIC)/minimal bactericidal concentration (MBC) values of ethyl acetate I, ethyl acetate II, 95% ethanol and 30% ethanol fractions of *Q. infectoria* nutgalls against MRSA (methicillin resistant *Staphylcoccus aureus*) to be 0·06/0·25, 0·13/0·25, 0·25/0·5 and 0·5/1·00 mg/ml, respectively. Among its purified major components: ellagic acid, gallic acid, syringic acid and tannic acid, good MIC/MBC values were obtained with gallic acid (0·06/0·06mg/ml) and tannin acid (0·13/0·25 mg/ml). Both MRSA and *Staphylcoccus aureus* ATCC 25923 treated with the ethanol extract, ethyl acetate fraction I, gallic acid and tannic acid displayed significant loss of tolerance to low osmotic pressure and high salt concentration.

Voravuthikunchai and Suwalak (2008) reported that the fractions Qi2, Qi3, and Qi4 of *Q. infectoria* galls demonstrated good antibacterial activity against enterohemorrhagic *E. coli* O157:H7, with MICs and MBCs ranging from 250 to 500 μg/ml. *Escherichia coli* O157:H7 is one of the most important food-borne pathogens, causing non-bloody and bloody diarrhea, hemorrhagic colitis, and hemolytic uremic syndrome. The results indicated that fraction Qi4 markedly

inhibited the release of verocytotoxin, VT1 and VT2 from VT-producing enterohemorrhagic *E. coli* (VTEC) cells at both inhibitory and sub-inhibitory concentrations. Use of antibiotics had been demonstrated to result in increased levels of verocytotoxin (VT) production as well as antibiotic resistance. Further, verotoxicity assay demonstrated that bacterial cultures treated with fraction Qi4 exerted less toxic effect on Vero cells. These in-vitro results distinctly indicated that the fraction Qi4 may constitute a promising natural food additive for the control of food poisoning by E. coli O157:H7 as well as other VTEC strains. Recent studies showed that ethanolic extract of *Q. infectoria* demonstrated inhibitory and bactericidal effects on all of the strains of Shiga toxigenic *Escherichia coli* tested with minimal inhibition concentrations (MICs) at 0.78–1.56 mg/ml and minimal bactericidal concentrations (MBCs) at 1.56–3.12 mg/ml (Suwalak and Voravuthikunchai 2009). *E. coli* cell numbers treated with 4×MIC of the extract decreased at least two log-fold within 4 hours and were completely killed within 12 hours Scanning electron microscopy revealed a complete loss of surface appendages and pronounced morphological changes of *E. coli* cells at MIC and 2×MIC. At 4×MIC, the damage to *E. coli* cells was extensive, and there was loss of their cellular integrity followed by cell collapse. The ethanolic extract of *Q. infectoria* modified the bacterial cell surface hydrophobicity enabling the extract to partition the lipids of the bacterial cell membrane, rendering the membrane more permeable and allowing leakage of ions and other cell contents, leading to cell mortality (Voravuthikunchai and Suwalak 2009).

Studies in Malaysia showed that the aqueous and acetone *Quercus infectoria* gall extracts displayed similarities in their antimicrobial activity on tested bacterial species indicating the galls to be potentially good source of antimicrobial agents (Basri and Fan 2005). Out of the six bacterial species tested, *Staphylococcus aureus* was the most susceptible to the gall extract of *Q. infectoria*. In contrast, the extracts showed weak inhibitory effect against *Staphylococcus epidermidis, Bacillus subtilis, Salmonella typhimurium* and *Pseudomonas aeruginosa* while there was no inhibition zone observed for *Escherichia coli* O157. The MIC values of the extracts ranged from 0.0781 to 1.25 mg/ml whereas the MBC values ranged from 0.3125 to 2.50 mg/ml. The MBC values of aqueous extract against *S. aureus* and *S. typhimurium* were higher than their MIC values. The MBC value of acetone extract against *S. aureus* was also higher than its MIC value. However, the MIC and MBC values of acetone extract against *S. typhimurium* were the same (1.25 mg/ml).

The ethanol extracts of *Quercus infectoria, Linusm usitatissium* and *Cinnamomum zeylanicium* were found to be more potent against *Escherichia coli* E45 and E62 isolates, than aqueous extracts (Khder and Muhammed 2010). The extracts exhibited most of the antibiotic activity against these two isolates irrespective of their antibiotic resistance behaviour. A comparative evaluation of plasmid elimination from *E. coli* E62 clinical isolate by sub-MIC of plant extracts showed that these extracts could cure plasmids effectively at their respective sub-MIC concentration. Sub-MIC of aqueous and ethanol of *Q. infectoria* cured 15 kb plasmid from E62 isolate.

Both aqueous and methanolic extracts of *Quercus infectoria* galls exhibited antibacterial activity against the Gram positive *Cellulosimicrobium cellulans* with MIC value of 0.5 mg/ml and MBC value of 2 mg/ml (Muskhazli et al. 2008). *C. cellulans* previously identified as *Oerskovia xanthineolytica* or *Brevibacterium fermentans* or *Arthrobacter luteus* is a virulent bacterium found in immunocomprised patients and has been reported to cause meningitis in infants and children.

Skin Whitening Activity

Rohana et al. (2004) reported that the *Q. infectoria* galls aqueous extract showed high potential in skin whitening and antioxidant properties as the extract inhibited the superoxide and DPPH radical scavenging activities, and tyrosinase activities. This was also confirmed by Vimala et al. (2007). They found that *Quercus infectoria* galls

had a high DPPH scavenging activity of 99.2% and 94.7% tyrosinase inhibition. The gall extract significantly reduced the activity of tyrosinase enzyme which catalyses the biosynthesis of melanin, the colour pigment. Thus, regular application of such plant extracts could reduce pigment formation in the skin which will lead to a lighter tone of skin color. The plant extracts could also be used to treat black spots, freckles and hyperpigmentation due to accident scars and pregnancy. The results indicated that aqueous extract of *Quercus* galls had potential to be used for modern medicinal products as well as cosmetics and skin care products.

Alpha-Glycosidase Inhibitory/ Antidiabetic Activity

Hexagalloylglucose (3-O-digalloyl-1,2,4,6-tetra-O-galloyl-β-D-glucose), which was isolated from the methanol extract of the galls of *Quercus infectoria*, significantly inhibited α-glycosidases such as sucrase, maltase and isomaltase (Hwang et al. 2000). Its inhibitory activity was comparable to acarbose, a hypoglycemic agent, while the inhibitory activity on α-amylase was approximately ten times lower than that of acarbose. The results indicated that, when compared to acarbose, hexagalloylglucose may reduce the side effects by reducing inhibition of α-amylase.

Antihyperlipidemic/ Antihypercholesterolemic Activity

Quercus infectoria, Rosa damascena and *Myrtus communis* methanol extracts showed more than 50% inhibitory effect on β-hydroxy-β-methylglutaryl coenzyme A reductase (HMG CoA reductase) activity (Gholamhoseinian et al. 2010a). HMG CoA reductase is the key enzyme in cholesterol biosynthesis and inhibition of this enzyme had been reported to reduce the synthesis of cholesterol and could be used in the management of coronary artery disease. Preliminary in-vitro studies showed that *Q. infectoria* extract showed more than 50% inhibition on pancreatic lipase activity (Gholamhoseinian et al. 2010b). Pancreatic lipase is the most important enzyme in digestion of triglycerides. One of the strategies in prevention or treatment of obesity is altering metabolism of lipids by inhibition of dietary fat absorption.

Wound Healing Activity

Ethanol extract of the shade-dried leaves of *Quercus infectoria* exhibited a positive effect on wound healing, with a significant increase in the levels of the antioxidant enzymes, superoxide dismutase and catalase, in the granuloma tissue when tested in rats, using incision, excision and dead-space wound models, at two different dose levels of 400 and 800 mg/kg (Umachigi et al. 2008). In studies using the excision wound model, animals treated with the ethanol extract of *Q. infectoria* showed a significant decrease in the epithelization period, as evidenced by the shorter period for the fall of eschar compared to control. The extract also facilitated the rate of wound contraction significantly at both dose levels.

Analgesic/Antitremorine Activities

Early studies reported that various solvent extracted fractions of *Q. infectoria* galls possessed neuropharmacological activities (Dar et al. 1976). Fraction A (dried acetone-treated methanol extract dissolved in water) was active as an analgesic in rats and significantly reduced blood sugar levels in rabbits. Fraction B (chloroform-methanol extraction) exhibited CNS depressant activity. It potentiated the barbiturate sleeping time significantly without changing the onset time or the loss of the righting reflex. Further, Fraction B showed a moderate antitremorine activity by causing a delay in the onset and a decrease in the severity of tremorine-induced tremors. The local anaesthetic action of Fraction B was evident due to the complete blockade of the isolated frog sciatic nerve conduction. Pure syringic acid was isolated from the methanolic fraction of the galls of *Quercus infectoria* and found to be a CNS active component with

significant local anaesthetic and sedative activity (Dar and Ikram 1979).

Larvicidal Activity

Ethyl-acetate extract of *Quercus infectoria* was found to be the most effective of all the five extracts tested for larvicidal activity against the fourth instar larvae of *Anopheles stephensi,* with LC_{50} of 116.92 ppm followed by gallotannin, n-butanol, acetone, and methanol with LC_{50} values of 124.62, 174.76, 299.26, and 364.61 ppm, respectively (Aivazi and Vijayan 2009). In separate studies, extracts and fractions of *Quercus lusitania* var. *infectoria* galls were found to have larvicidal activity against *Culex pipiens*, the urban nuisance mosquito (Redwane et al. 2002). Fraction F(2) had an interesting, low LC_{50} (24 h) of 60 ppm while the LC_{50} values of gallotannins were 335 and 373 ppm, respectively for the second and fourth instar period.

Molluscicidal Activity

The acetonic extract and gallotanin of *Quercus infectoria* galls exhibited high molluscicidal activity against *Bulinus truncates*, a vector of schistosomiasis (Redwane et al. 1998).

Antiprotozoal Activity

Dichloromethane and methanol extracts from the *Brucea javanica* seed and a methanol extract from *Quercus infectoria* nut-gall showed the highest inhibitory activity against the intestinal protozoan parasite, *Blastocystis hominis* (Sawangjaroen and Sawangjaroen 2005) At a concentration of 2,000 μg/ml, the three extracts killed 82%, 75% and 67% of the *Blastocystis hominis* samples tested and inhibited 94%, 100% and 76% of them, respectively. Metronidazole, used as a reference antiprotozoan drug, at a concentration of 40 μg/mL, killed 97% of the *Blastocystis hominis* isolates and inhibited all samples tested at levels that ranged from 1.25 to 20 μg/ml.

Antiamoebic Activity

Crude methanol extract of *Q. infectoria* displayed anti-amoebic effects against *Entamoeba histolytica* infecting the caecum of mice (Sawangjaroen et al. 2004). Extract of *Q. infectoria* nut gall at a concentration of 500 and of 250 mg/kg per day healed 26% and 13% of mice from amoebiasis, respectively. The severity of caecal wall ulceration was reduced in mice which received the extract.

Antiviral Activity

Of 71 plants used in Sundanese traditional medicine, *Q. infectoria* and *Syzygium aromaticum,* were the most active (>/=90% inhibition at 100 μg/mL) in inhibitory effects on hepatitis C virus (HCV) protease (Hussein et al. 2000). *Q. lusitanica (Q. infectoria)* extract was found to have good inhibitory effect on the replication of dengue virus type 2, both in conventional cell culture and proteomics technique (Muliawan et al. 2006). The extract exhibited dose-dependent in-vitro antiviral inhibition in C6/36 cells (cloned cells of *Aedes albopictus* larvae, vector of dengue fever). The extract at its maximum non-toxic concentration of 0.25 mg/ml completely inhibited 10–1,000 $TCID_{50}$ (median tissue culture infective dose) of virus, as reflected by the absence of cytopathic effect. The low dose of the extract (0.032 mg/ml) showed 100% inhibition with 10 $TCID_{50}$ of virus, but only 50% and 25% inhibition with 100 and 1,000 $TCID_{50}$, respectively. Using proteomics technique, the extract showed down-regulation of NS1 protein expression of infected C6/36 cells after treatment with this extract. The NS1 is a glycoprotein present in all flaviviruses and appears essential for virus viability.

Antivenom Activity

The aqueous extract of *Q. infectoria* galls was reported to have high hydrolysable tannin content which inhibited the lethality of the *Naja kaouthia*

(Thai cobra) venom (Pithayanukul et al. 2005). *Quercus infectoria* aqueous extract exhibited in-vitro inhibitory activity against *Naja kaouthia* but at much higher LD_{50} concentration of tannin than the aqueous extracts of *Pentace burmanica, Pithecellobium dulce,* and *Areca catechu*. The anti-venom activities of these plant polyphenols were attributed to the selective blocking of the nicotinic acetylcholine receptor and non-selectively by precipitation of the venom proteins. In another study, polyphenols from the extracts of *Areca catechu* and *Quercus infectoria* inhibited phospholipase A(2), proteases, hyaluronidase and L-amino acid oxidase of *Naja naja kaouthia* (NK) and *Calloselasma rhodostoma* (CR) venoms by in-vitro tests (Leanpolchareanchai et al. 2009). Both extracts also inhibited the hemorrhagic activity of *Calloselasma rhodostoma* venom and the dermonecrotic activity of *Naja naja kaouthia* venom by in-vivo tests. The inhibitory activity of plant polyphenols against local tissue necrosis induced by snake venoms may be caused by inhibition of inflammatory reactions, hemorrhage, and necrosis.

Antiparkinsonian Activity

Q. infectoria was found to have weak antiparkinsonian activity; the methanolic extract showed a weak activity in mice at a dose of 500 mg/kg i.p. (Dar et al. 1976).

Traditional Medicinal Uses

Nut-galls were reported to have a great medicinal value and had pharmacologically been reported to be astringent, antidiabetic, anti-tremor, local anesthetic, antipyretic and anti-Parkinson and used in the treatment of intertrigo, impetigo and eczema haemorrhages, chronic diarrhoea, dysentery, etc.

In Asian countries, the galls have been used for centuries for treating inflammatory diseases (Aroonrerk and Kamkaen 2009). Gargle of hot water extract of galls was claimed to be very effective against aphthous sores and putrid sore throat, while direct application of boiled and bruised galls on skin was claimed to effectively cure any swelling or inflammation. The application of powdered galls in the form of ointment and suppository was also utilised to cure hemorrhoids caused by inflammation of the skin. *Majuphal,* as it is widely known in Indian traditional medicine have been used as dental powder and in the treatment of toothache and gingivitis. *Quercus infectoria* (Manjakani) was claimed to be highly beneficial for the Malay Kelantanese postpartum women preparation and was thought to help in revitalization and full recovery of the reproductive functions; hazardous effects were not reported so far (Soon et al. 2007). Grieve (1971) reported that early studies showed that as part of postpartum care, the Arabs, Persians, Indians, Malays and Chinese had traditionally used *Quercus infectoria* gall nuts after childbirth to treat vaginal discharge and related postpartum infections. Its astringent property was held to play a role in the restoring of health, to tone and increase vigour of the vagina (Muhamad and Mustafa 1994).

Other Uses

An extract from the tannin-rich gallnut is mixed with ferrous sulphate together with a gum and colouring in order to make an ink. The gallnuts are also used to make a black dye besides providing a rich source of tannin and gallic acids.

Comments

Most of the gall nuts sold in Malaysia and Indonesia are imported from Turkey.

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