PHARMACOLOGICAL POTENTIAL OF *QUERCUS INFECTORIA*

Jalil Ur Rehman[1], Muhammad Shahid Sagheer[2], Muhammad Amjid Chishti[1]*

Abstract: After being infected by the Cynipsgallaetinctoriae wasp, popularly known as the Gall Oak and belonging to the Fagaceae family, Galls emerge on *Quercus infectoria* Olivier. Commonly, this plant is located in Syria, Asia Minor, Greece and Iran. Galls from *Quercus infectoria* have a variety of medicinal characteristics and are commonly employed as an astringent and anti-inflammatory drug in traditional medicine. The major constituents of *Quercus Infectoria* Galls are tannins (50 to 70 percent) and small quantities of free Gallic acid and starch *Quercus* Infectoria Galls has traditionally been used to treat diarrhea, bleeding, skin illness as well as used in postpartum care. *Quercus* Infectoria Galls has been shown to have antibacterial, antiviral, antifungal, larvicidal, antioxidant and anti-inflammatory activities in current pharmacology. In present review we will discussed about its all aspect including pharmacological actions and new researches on this plant.

1. College of Conventional Medicine,Faculty of Medicine and Allied Health Sciences, The Islamia University of Bahawalpur.
2. Department of Eatern Medicine, Hamdard University Karachi

* **Corresponding Author Email:** muhammadamjadchishti@gmail.com

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INTRODUCTION

Oak galls also called mazu or Turkish are rounded out growths shaped on young branches of *Quercus infectoria* belonging to Fagaceae family. The eggs are laid inside *Quercus infectoria* branches by the fly insect. The egg develops into a larva, which is surrounded by 4,5 growing gall tissues. The insects secrete secretions, containing enzymes. Abnormal tissues develop around the larva by enzyme present in secretion. The starch is converted in to sugar which stimulates cell multiplication. Insect passed into next larval and pupal stages. The gall grows until larva lives and passes into a cocoon. Finally, mature insect come out the gall and run away. Throughoutthis process the color of gall passes from bluish grey to olive green and to nearly white (2).

BOTANICAL DESCRIPTION

Q. infectoria is a tiny tree with numerous branches that grows to be approximately 2 meters tall. Its bark has a light grey color. The leaves are 4 to 6 cm long and have spiny teeth. It has short petiole, 6 elongate. Flowers are unisexual having 6-8 sepalsand 6-10 stamens. Fruits are 4 cm long, shiny brown and cylindrical and cover with narrow scales. Galls have a spherical form with a diameter of 10-25 mm, a tiny stalk plus rounded projections on their surface. These very astringent in taste.

CULTIVATION

Quercus Infectoria is cultivated in Persia, Turkey, Cyprus, Syria and Greece. Some Quercus species found in Turkey, Iran as well as Iraq. However, it is present all over the world now as well as more familiar in Europe, Asia and North Africa.

COMMON NAMES

Arabic: Ifas, Uffes, Ayurvedic: Maayaaphala English: Gall Nut, Oak Galls Gujrati: Mai phala Hindi: Majuphal, Mazu, Persian: Mazuand Urdu: Mazu

ACTIONS

Analgesic, anti-inflammatory, antidote antipyretic, anti-stomatitis, anti-septicdeodorant, desiccant, derivative, expectorant, germicidal, hypoglycemic, sleep inducing, powerful astringent, Sedative, styptic, tonic to teeth and gum, plus wound healing. Traditionally, *Q. Infectoria* used in different types of diseases for example, alopecia, hemoptysis, anal fissure, diabetes mellitus, nose bleeding, bronchitis, diseases of eye, Gonorrhea, hematuria, hemorrhoids, internal hemorrhage, herpes, nasal catarrh,

recurrent pyrexia, Scurvy, wound, ulcer and toothache. It is also used in the infections of teeth and gums like gingivitis and pyorrhea. It is used to treat the infections of oral cavitylike sore throat, tonsillitis and stomatitis. *Quercus Infectoria* also used to treat the skin diseases like eczema and impetigo. It is used to cure different GIT ailments such as chapped nipple diarrhea, dyspepsia, dysentery, and intestinal hemorrhage. *Quercus infectoria* has a great potential against different female disorders such as leucorrhoea, menorrhagia, prolapse of uterus, vaginal looseness as well as vaginal discharge.

SIDE EFFECTS

Side effects are noticed on throat and chest.

PHYTOCHEMISTRY

Gallotannic acid 50-70% gallic acid (2 to 4 percent) Elagic acid, methyloleanolate, sitosterol, calcium oxalate, Starch, methyl betulate, Roburic acid, syringic acids as well as Nyctanthic.

PHARMACOLOGICAL STUDIES

Pharmacological studies conducted on *Q. infectoria* are:

ANALGESIC POTENTIAL

Pain is a condition of "an unpleasant sensory and emotional experience connected with real or potential tissue damage," according to the International Association for the Study of Pain (IASP) (2). Aspirin and morphine, two common pain relievers, are frequently utilized. Analgesic medications, particularly opioids plus non-steroidal anti-inflammatory drugs, can only alleviate 50 percent of pain in about 30 percent of people in most cases [3]. Furthermore, several of these medications have substantial negative effects**.** Researchers tested the analgesicefficacy of *Quercus Infectoria* Galls methanol extract in rats using the hot plate and tail-flick techniques. The extract was introduced i/p (intraperitoneal) with a dosage of twenty milli gram per kilo gram, while as a control drug sodium salicylate and morphine were given at a dose of ten milli gram per kilo gram. The *Quercus Infectoria* Galls methanolic extract exhibited significant analgesic efficacy in the tail-flick method, prolonging the rats' response latency to 8.0 seconds after thirty minutes of treatment, compared to 4.4 seconds in the control group. In the same test, morphine sulphate formed a reaction time of 11.9 seconds. The extract produced 34.2 percent maximum potential analgesia (MPA) at the top of activity (30 minutes), whereas morphine sulphate produced 70.9 percent MPA. The tail-flick model revealed no analgesic effects when sodium salicylate was used. The *Quercus Infectoria* Galls extract and sodium salicylate had similar response times in the same model. Tail-flick was a superior technique for assessing analgesic activity than the hot platetechnique, excluding of morphine sulphate that exhibited important effect 45 as well as 60 minutes at the end of treatment. Finally, the methanolic extract of *Quercus Infectoria* Galls had a modest analgesic effect (4).

ANTIBACTERIAL POTENTIAL

Quercus Infectoria Galls was tested for antibacterial efficacy against oral pathogensthat causes dental carries and periodontitis.
2 Gram +ve bacteria (*Streptococcus salivarius* ATCC 13419; *Streptococcus mutans* ATCC 25175S) as well as 2 Gram - ve bacteria (*Streptococcus mutans* ATCC 25175; *Streptococcus salivarius* ATCC 13419) were examined with methanol and acetone extracts (*Streptococcus mutans* ATCC 25175; *Streptococcus salivarius* ATCC 13419) (*Fusobacterium nucleatum* ATCC 25586; *Porphyromonasgingivalis* ATCC 33277). The minimum inhibitory concentration (MIC) was then measured using two-fold serial microdilution at values ranging from 0.01 to 5 milli gram per milli liter. MCB (The minimum bacterial concentration) was determined through subculturing microtiter wells that exhibited

no variations in the indicator color following incubation. Each of the examined bacteria was inhibited by both extracts. *S. salivarius* was the most sensitive of all the microorganisms tested. The MIC range for methanol and acetone extracts is the same (0.16- 0.63 mg/ml). The MBC values of the methanol and acetone extracts are 0.31 to
1.25 mg per ml as well as 0.31 to 2.50 mg per ml, respectively. Antibacterial efficacy against oral pathogens was similar in both QIG extracts. As a result, *Quercus Infectoria* Galls is a promising medicinal plant to cure oral cavity infections [5]. Antibacterial potential plus mechanism of action of *Quercus infectoria* contrary to Shiga toxin creating *E. coli* O157:H7has been described (6, 7, 8). The antibacterial effects of *Quercus Infectoria* Galls against STECO157:H7 were explored in one study (9) by looking at cell viability as well as ultrastructural and morphological alterations. The capability of *Quercus Infectoria* Galls to deteriorate cell membranes owing to high tannic plus Gallic acid concentration is considered to be mechanism of action against STEC O157:H7 (10).

ANTI-CARCINOGENIC POTENTIAL

Gallic acid has recently been discovered to suppress the development of skin cancer, prostate cancer, lungs cancer, pancreatic cancer as well as other malignancies by researchers (11). Gallic acid causes tumor cells to die, which is thought to be its principal anti-tumor action. According to Wang et al. through the mitochondrial signaling system, Gallic acid (22.2 to44.4 g per ml) can trigger apoptosis in mia-2 cells [12]. HeLa cells blocked by Gallic acid in a time and dose dependent manner, stopping the G2/M phase cell cycle, lowering centrosome accumulation, enhancing the existence of multinucleated cells, generating mitotic failure, as well as eventually killing the cells. Normal cells without a superfluous centrosome are unaffected by Gallic acid (13). Cell adhesion, migration, and invasion are common ways for tumors to spread. Gallic acid has been shown to decrease kyse150 cell proliferation, migration, and invasion in a concentration-dependent manner. By raising the fraction of cells in the G0/G1 phase, Gallic acid reduced the number of S-phase and G2/M-phase cells as well as the expression of cyclind1, a G1/S-phase regulatory protein. Gallic acid halting the cell cycle, inhibits cells from entering the S phase for DNA synthesis and preventing cancer cells from proliferating, migrating, or invading (14). Gallic acid also greatly slows the movement as well as attack of SCC-4. Gallic acid reduces NF-B as well as RhoA from the cytoplasm to the nucleus, inhibiting MMP-2 and MMP-9 activity, cell migration, and invasion (15). When

Gallic acid concentration was greater than 200 m, Liu *et al* (16) revealed that B16F10 melanoma cell apoptosis may brought by the mitochondrial pathway; the effect of Gallic acid on the protein expression profile was investigated by means of proteomics, plus 4 protein locations were noticeably dissimilar. Glucokinase, aldolase, enolase, pyruvate kinase, as well as other glycolysis related proteins were considerably increased as well as proteins related to apoptosis. However, no link has been established between Gallic acid's influence on glycolysis and anti-tumor properties.

Gallic acid can also defend as well as prevent tumor induction in the skin; however, the inhibitory impact of Gallic acid alters as the incubation period and tumor formation progresses. Gallic acid also prevents the development of initial and middle term skin tumors as well as lowers the possibility of chemically produced skin cancer in SENCAR mice (17). Gallic acid can kill tumor cells directly, according to Ruohola et al. (18); this cytotoxic impact differs from that of other organic acid. Furthermore, Zhong *et al* (19) demonstrated that Gallic acid killed human hepatoma cell BEL-7404, human gastric cancer cell SGC-7901, mouse hepatoma cell H22 plus mouse sarcoma cell S804. Perchellet et al (20) employed ellagic acid, tannic acid, plus Gallic acid as anticancer agents and discovered that these substances inhibited ornithine decarboxylase activity, H2O2 (hydrogen peroxide) production, plus DNA synthesis produced via TPA (12-o-tetradecyl-phorbol-13-acetic acid).

ANTI-INFLAMMATORY POTENTIAL

Quercus Infectoria Galls has pleiotropic

medicinal properties, including anti-inflammatory properties in particular. An earlier study looked at the effects of *Quercus Infectoria* Galls's ethanolic extract on several in vivo and in vitro experimental models of inflammation., Histamine, carrageenan, PGE2 as well as serotonin induced paw edema were greatly reduced by oral administration of the extract, whereas phorbol-12-myristate-13-acetate (PMA) brought ear inflammation was significantly reduced by topical application. The extract also inhibited a number of neutrophil and macrophage activities associated to the inflammatory response. Not only did *Quercus Infectoria* Galls extractsignificantly inhibit formyl-Met-Leu-Phe (FMLP)-stimulated degranulation in neutrophils, but it also looked into the mechanism of Nitric oxide suppression in macrophages plus discovered that extract improved inducible nitric oxide synthase without inhibiting its catalytic activities, even at greater doses. These findings imply that *Quercus Infectoria* Galls alcohol extract has anti-inflammatory effect in vivo and can also suppress the generation of several inflammatory mediators following oral or topical administration (21). Using an experimental swollen joint rat model, Liu *et al* (22) investigated the anti-inflammatory effects of Gallic acid. The acute inflammation caused by hydroxytryptamine and the chronic inflammation caused by formaldehyde were significantly reduced when different dosages of Gallic acid were given intraperitoneally, the medicinal index of Gallic acid higher as compared to the positive control sodium salicylate. Moreover, Gallic acid inhibits IL-6 (interleukin-6), TNF (tumor necrosis factor) plus histamine reducing mast cell produced inflammatory anaphylaxis and opening up advance pathways to prevent and treat the mast cell produced allergic disorders (23).

ANTIOXIDANT POTENTIAL

The development of various clinical illnesses, as well as the normal ageing process, depends on oxidative damage to cells (24, 25). Resveratrol and quercetin, forexample, are plant-based antioxidants that boost the body's antioxidant defenses while remaining comparatively harmless. Accordingly, Plants with antioxidant properties are the subject of a significantamount of scientific research. Kaur et al.
(26) revealed that *Quercus Infectoria* Galls has significant free radicals reducing plus antioxidant potential in a prior investigation. Several well-established in vitro model systems were used to examine QIG's antioxidant effectiveness. The protective effects of QIG on murine macrophage oxidative modulation were also investigated. Furthermore, Kerem et al (27) found that Gallic acid has antioxidant properties and prevents fat oxidation. According to Krishnaraju et al, Gallic acid has significant antioxidant potential on hydroxyl sequences, peroxide as well as DPPH(28). To avoid unfavorable effects, the right concentration of GA should also be used. Small concentrations of Gallic acid (25gml- 1) may enhance cell proliferation, increase mitochondrial antioxidant potential, restore radiation then chemical injury, motivating cell and tissue renewal by inhibiting appearance of MIR421, MIR-21, 17-9p and further antioxidant target genes of glioblastoma T98G (29). Furthermore, Liu et al. (30) demonstrated that together propyl gallate plus Gallic Acid may prevent the oxidation of oyster lipids through the drying procedure, with propyl gallate having a stronger inhibitory potential.

WOUND CURATIVE POTENTIAL

The goal of this study was to create a new topical medicinal agent based on *Quercus Infectoria* nutgalls for the cure of diabetic ulcer. In diabetic rats, QiF10, the best dynamic preparation designed on antibacterial action, displayed an outstanding capacity to improve wound healing (31). By increasing cell proliferation, re-epithelialization, and granulation tissue development, QiF10 was able to improve

the wound healing process of diabetic ulcers. As a result, it might be utilized as a unique wound therapy option for diabetics (32).

ANTI-ATHEROGENIC AND HYPOLIPIDEMIC EFFECT

Many health problems are caused by hyperlipidemia. The effects of Quercus Infectoria galls plus *Rosa damascenea* mill flower methanol extract on lipid profile plus atherosclerotic plaque development in hyperlipidemic rabbits were investigated. Consumption of QIG methanol extract reduces the levels of total cholesterol, low density lipoprotein and triglyceride in the plasma in addition preventing plaque development in the semilunar valve as well as thoracic aorta. *Rosa domestica* methanolextract significantly reduced the levels of total cholesterol, low density lipoprotein, triglyceride then plaque formation, but not significantly. As a result, the *Quercus Infectoria* galls methanolic extract is lipid lowering and anti-atherogenic (33).

ANTI-DIABETIC POTENTIAL

The inhibition rate of amylase activity was 95.52 percent when Gallic acid concentration was fifteen mg ml-l plus 99.24 percent when Gallic acid concentration was
3.2 mgml-1, according to Qin et al. (34). GA has been proposed to control glucose plus lipid metabolism via reducing the activity of these 2 enzymes. Gallic acid is an antioxidant that has been shown to neutralize free radicals because it is a natural polyphenol. The biochemical indices plus islet cell morphology of hyperglycemia produced by means of streptozotocin can be greatly improved by oral path of twenty milli gram per kg Gallic acid. Gallic acid controls insulin discharge as well as defends islet cells from streptozotocin's cytotoxicity (35,36). In vitro, GA improves glucose uptake and reduces hyperglycemia in FL83B hepatocytes; in vivo it inhibits the inflammatory reaction of liver tissue, inhibits glucose formation, increases glycogenformation plus improves glucosemetabolism in HFD rats through considerably lowering TG and total cholesterol levels. GA improves glucose metabolism by increasing GSH and SOD activity, motivating the IRS-1 and P13K Akt paths in liver tissues, Glucose transportor-2 appearance in liver tissue should be increased, the insulin signaling pathway should be improved as well as insulin resistance should be reduced (37).

According to the literature, Hexagalloyl glucose extracted through methanolic extract of QIG inhibits alpha glucosidases like, maltase, isomaltase, plus sucrase. When employed as a hypoglycemic drug, the inhibitory action was equivalent to acarbose, whereas the inhibitory effect on alpha amylase was roughly lower ten times. The findings suggest that, when compared to acarbose, hexagalloyl glucose may minimise adverse effects by decreasing alpha-amylase inhibition (38).

CYTOGENETIC POTENTIAL

In albino male mice, the result of QIG methanolic extract on the MI (metaphaseindex) of spleen cells and bone marrow, as well as the development of MN (micronuclei) in bone marrow cells, was investigated. Treatment with *Q. infectoria* gall methanolic extract resulted in a considerable decrease in micronuclei development but a large fall in the metaphase index of bone marrow and spleen cells, according to genetic analyses. As a result, the extract can be considered an effective anti-mutagen, and these results are significant, especially given that most malignancies are preceded by mutations caused by various agents, particularly those with oxidant effects (39).

IMMUNOMODULATORY POTENTIAL

The gall extract of *Quercus Infectoria*is non-toxic and may play a role in macrophage proliferation and phagocytosis, as well as lowering NO generation in a dose-

dependent way and modulating macrophage cytokine levels. This extract can reduce iNOS and NO levels, as well as IL-4, IL-6, and IL-12 cytokines, while increasing the production of IL-13 and other cytokines, hence modulating macrophage inflammatory mode. Gall extract, according to our findings, has the potential to enhance immunomodulatory activity via a cellular- mediated mechanism and may play a role in modulating the innate immune response (40).

ANTI CLASTOGENIC EFFECT

The current study discovered that oral administration of QIG aqueous extract had inhibitory and protective effects on the cytotoxic and clastogenic damage caused by Dimethylbenz [a] anthracene (DMBA), suggesting that it could be a potential strategy for preventing genetic damage caused by chemical pollutants (41).

ANTI-PROTOZOAN PARASITE POTENTIAL

In vitro and in vivo studies have shown that QIG is effective against protozoan parasites such as Leishmania major (42), Blastocystishominis(43), and Entamoeba histolytica(44). A recent study observed at the toxicological and antimalarial characteristics of methanol, ethanol, acetone, plus water extracts of *Quercus Infectoria* Galls in vitro. The methanol and acetone extracts of *Quercus Infectoria* Galls displayed potential anti- malarial activity, according to the findings (45). The antimalarial activity of QIG extracts is linked to the high amount of phenolic chemicals (46, 47).

HEPATOPROTECTIVE POTENTIAL

The activation of hepatic stellate cells (HSCS) by liver damage is a key element in the progression of liver fibrosis. As a result, inhibiting HSCS activation or promoting HSCS death is an effective treatment for fibrosis liver (48). The suppression of HSCS, however, affects liver parenchymal cell and other normal cells because of deficiency of cell selectivity, limiting the dose plus efficiency of antifibrosis medications. By creating reactive oxygen species (ROS) such as O2, OH, and H2O2, Gallic acid may produce cytotoxicity and oxidative stress, which leads to cell death (49,50). However, studies show that Gallic acid defends the liver from harm by acting as an antioxidant (51). To put it another way, GA can both induce oxidation and protect the liver from harm by acting as an antioxidant. Catalase is an antioxidant that can prevent cells from destructive potential of ROS (reactive oxygen species). Glutathione peroxidase, SOD plus catalase activities in HSCS are lesser than in hepatocytes (52,53). Gallic acid may act specifically on HSCS, causing cells to produce and accumulate H2O2 and killing HSCS with limited antioxidant ability (54,55). GA can destroy HSCS cells selectively in a dose and time dependent method while causing no harm to hepatocytes. It's also been hypothesized that the amount of catalase in a cell determines its susceptibility to GA (56). An and et al.(57) also looked at how GA affected the biochemical and physiological alterations in the liver caused by carbon tetrachloride. The examination items included oxide, bilirubin, peroxide, transaminase, triglyceride, and glucose hex phosphate. GA has been discovered to protect the liver.

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Fig: 01 Dried Form

Fig: 02 Fresh Form