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Full Length Research Paper

The role of methanolic extract of *Quercus infectoria* bark in lipemia, glycemia, gastric ulcer and bacterial growth

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Nowadays, the surge of consumption of herbal supplements is encouraged by several factors, including the common belief that all herbal products are relatively safe and effective. The present investigation explores the effects of methanolic extract of *Quercus infectoria* bark upon rat blood lipid profile, glycemia, inflammation, gastric ulcer and bacterial growth. After one month of chronic extract (0.5% w/v) intake via drinking water, there was a significant increase in serum HDL-cholesterol level. This was accompanied with an increase in both serum glucose and insulin levels. No significant changes were observed in other lipid parameters studied. Liver enzyme activities as well as urea and creatinine levels were not negatively affected. Extract at 250, 500 and 1000 mg/kg body weight exhibited substantial anti-inflammatory effects in cases of acute and chronic inflammation induced by carrageenan and formalin respectively. Pre-treatment of fasted rats with the extract (100 and 500 mg/kg body weight) also demonstrated significant protection against ethanol-induced gastric ulcer. Anti-bacterial activity against *Proteus mirabilis*, *Citrobacter braaki*, and *Staphylococcus aureus* methicillin resistant and sensitive was also noticed. In conclusion, these findings suggest that the methanolic extract of *Q. infectoria* bark provides an inexpensive and powerful source of herbal supplement used to treat various conditions.

Key words: Glycemia, Inflammation, lipids, *Quercus infectoria*, Ulcer

INTRODUCTION

Long before the development of modern medicine and the widespread use of pharmaceutical drugs, traditional healing methods had been in use, and are still being used today all over the globe. The healing powers in plant extracts, is having great recognition especially for people in developing countries. Side effects or toxic reactions associated with herbal medicine are relatively rare. This may be attributed to the fact that adverse reactions following their use are not properly reported or because the side effects are of such a nature that reporting them is not done, such as the case with minor allergic reactions (Farnsworth, 1993). Nowadays, plant extracts are considered as an attractive source of new drugs and are expected to produce promising results for the treatment of health problems due to some effective compounds they contain.

About 600 species of oak trees make up the genus Quercus of the Family Fagaceae. Oak trees, varying from small bushes to great trees, are found mainly in the North Temperate Zone, growing in a variety of habitats includeing seacoast, mountain slopes and wet lowlands. Pharmacologically, a great importance was accorded to *Quercus infectoria* galls, which exhibit astringent, anti-inflammatory (Kaur et al., 2004), antiviral (Dar et al., 1976), antidiabetic (Hwang et al., 2000), larvicidal (Redwane et al., 2002), antibacterial (Voravuthikunchai et al., 2005; Basri and Fan, 2005; Pithayanukul et al., 2005; Voravuthikunchai et al., 2004; Hwang et al., 2004; Hussein et al., 2000), antiulcerogenic and gastroprotective activities (Sawangjaroen et al., 2004). Gastroprotective effect against ethanol-induced gastric damage was also attributed to aqueous extract from *Quercus ilex* root bark (Gharzouli et al., 1999). Ethanolic extracts of *Quercus coccifera* and *Quercus aegilops* fruit showed a very

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high curative rate after ethanol-induced gastric damage in rats suggesting their use in treatment of stomach pain (Alkofahi and Atta, 1999). Similarly, Khennouf et al. (2003) showed that purified tannins, acetone extracts of *Quercus suber* and *Q. coccifera* leaves prevented the formation of ethanol-induced gastric lesions in the stomach.

Up to our knowledge, no studies have previously dealt with *Q. infectoria* methanolic extract of the stem bark. Based on the fact that *Q. infectoria* is widely available, the current study evaluates some potential medicinal role of its stem bark methanolic extract in lipemia, glycemia and hepatoxicity after one month of administration of the extract via drinking water to rats. In addition, the present investigation monitors the anti-inflammatory activity of the extract under acute and chronic inflammation conditions, and assesses its gastroprotective function against ethanol-induced gastric ulcer using *in vivo* models. The potential antibacterial effect of the extract on certain hospital isolates was also conducted.

MATERIALS AND METHODS

Plant material collection and extraction procedure

Q. infectoria bark was collected from diverse oak trees widely distributed throughout Lebanon, from young branches ranging in age from 3 to 4 years. Collected branches were peeled and chopped into small pieces, dried in shade, and then soaked in methanol for 72 h. The suspension was filtered and the pooled filtrate was subjected to rotary evaporation (45° - 50°C) and then lyophilization. The lyophilized extract was stored in a well-sealed dry box in the fridge until use (Jose et al., 2004).

Animal treatment

Male Sprague-Dawely rats (n = 30) (Lebanese American University stock) were randomly divided into two groups comprising 15 animals each with an average weight of 200 g. The first group served as a control and received 6.5 g of food per 100 g body weight. Food consisted of standard rat chow (19% protein, 9.6% fat, 4.3% fiber and 61% carbohydrate) to which 5% coconut oil was added. Coconut was used to make the diet more atherogenic (Daher et al., 2003). The second group referred to as treatment group received the same food as the control in addition to 0.5% w/v of methanol extract of Q. *infectoria* in drinking water. Animals were maintained at an ambient temperature of 20 - 22°C and 12 h photoperiod during the whole study period. All experimental protocols complied with the Guide for the Care and Use of Laboratory Animals (National Research Council of the United States 1985).

After one month of extract intake, fasted animals (18 h) were rapidly anesthetized using diethyl ether and a midline abdominal incision was made for about two-thirds of the length of the abdomen. About 8 ml of blood were withdrawn from the inferior vena cava and then divided into two tubes with and without Na_2EDTA (1 mg/ml) to collect plasma and serum samples respectively after centrifugation (2000 g; 20 min; 4°C). Plasma samples, kept on ice, were immediately used for lipoprotein (d<1.063 g/ml) isolation by ultracentrifugation and determination of apo B concentration, while serum samples were used for analyses of serum lipid (TAG, total cholesterol, HDL-cholesterol and LDL-cholesterol), glycemia (glucose and insulin), liver enzyme (sGOT, sGPT and LDH), urea and creatinine.

Determination of total plasma apo B

To minimize proteolytic degradation of apoB48 and apoB100 the following were added: 5 µl/ml plasma of aprotonin (Fluka, Switzerland), 2 mg/liter, and 5 µl/ml plasma of phenylmethylsulfonyl fluoride (PMSF), 5 mM in 2-propanol. Total apoB (apoB48 and apoB100) content in the plasma of fasted animal was estimated in the lipoprotein fraction (d < 1.063 g/ml) that includes CM, VLDL, intermediate density lipoprotein (IDL) and low density lipoprotein (LDL). Briefly, 2 ml of plasma were put in a 10 ml polycarbonate ultracentrifuge tube (Sorvall, Kendro Laboratory Products) and 140 mg/ml of solid NaCl added to increase the density to 1.1 g/ml. The plasma sample was over layered with 5 ml of NaCl solution (d = 1.063 g/ml) containing 0.01% w/v Na_2EDTA and 0.02% w/v NaN_3 (pH = 7.4). The top 0.5 ml lipoprotein layer was collected after 48 h of centrifugation at 28,000 rpm at 15°C (Sorvall RC 28S centrifuge; Supraspeed F-28/13 fixed angle rotor). Samples containing the lipoprotein fractions (d = 1.063 g/ml) were delipidated in a methanol-diethyl ether solvent system (Karpe et al., 1996). Protein material was dissolved in 0.15 M sodium phosphate, 12.5% v/v glycerol, 2% w/v sodium dodecyl sulfate (SDS), 5% v/v mercaptoethanol, 0.001% w/v bromomophenol blue, pH = 6.8, at room temperature for 30 min, denatured at 90°C for 4 min and centrifuged for 4 min at 15680 g. Samples, frozen at -20°C, were subjected to 4-20% SDS-PAGE within 3 days, and then analyzed for apoB concentration (Daher et al. 2003). All samples were run in duplicates.

Measurement of serum lipid, glucose, insulin, SGPT, LDH, SGOT, urea and creatinine

The serum concentration of total serum cholesterol, TAG, glucose, urea and creatinine and the enzyme activities of serum SGOT-AST, SGPT and LDH were measured using appropriate kits purchased from Dialab, Austria. HDL cholesterol levels were measured directly using an enzymatic colorimetric method that incorporated polyethylene glycol-modified cholesterol ester oxidase (Sugiuchi et al., 1995). LDL cholesterol was measured using a direct LDL cholesterol kit (Roche, USA). Serum insulin concentrations were measured using an enzyme-linked immunosorbant assay kit (Linco, Research, Inc., USA).

Anti-Inflammatory effect

(a) Carrageenan induced paw edema in rats: Animals were divided into five groups of six animals each. In all groups acute inflammation was produced by a single subplantar injection of 0.02 ml of feshly prepared 1% carrageenan in normal saline in the right hind paw of rats (Ajith and Janardhanan, 2001). One group served as a positive control (no treatment), three groups received the methanolic extract of *Q. infectoria* at a concentration of 250, 500, or 1000 mg/Kg body weight (BW) intraperitoneally (i.p.) 30 min prior to carrageenan injection, and the last group received diclofenac (10 mg/Kg BW, i.p), as a standard reference drug, 30 min prior to carrageenan injection. The paw thickness was measured using vernier calipers before and 3 hours after carrageenan injection (Ajith and Janardhanan, 2001).

(b) Formalin induced paw edema in rats: Animals were divided into five groups of six animals each. In all groups, chronic inflammation was produced by a single subplantar injection of 0.02 ml of 2% formalin in the right hind paw (Ajith and Janardhanan, 2001). Thirty min prior to formalin injection, 3 groups received the methanolic extract of *Q. infectoria* (i.p.) at a concentration of 250, 500 or 1000mg/Kg BW, one group the standard reference drug diclofenac (10 mg/Kg BW, ip), and one group served as a positive control (no treatment). The administration of the extracts and diclo-

fenac was continued once daily for 6 consecutive days. The paw thickness was measured using vernier calipers before and 6 days after formalin injection (Jose et al., 2004).
The increase in paw thickness in both models was calculated using the formula:

$P_t - P_0$

Where P_t is the thickness of paw at time t (that is, 3 h after carrageenan injection and 6 days after formalin injection) and P_0 is the paw thickness at 0 time. The percent inhibition was calculated using the formula:

(C – T)/C x 100

Where *C* is the increase in paw thickness of the positive control and *T* is that of treatments.

Effect of methanol extract of *Quercus infectoria* bark on ethanol induced gastric damage in rats

The effect of methanolic extract of *Q. infectoria* bark on ethanol-induced gastric ulcer was conducted on male Sprague-Dawley rats according to the method described by Alkofahi and Atta (1999). Briefly, male Sprague-Dawley rats (250-300g) were randomly assigned to 5 groups of 6 rats each. Forty-eight hours before use, animals were starved to ensure an empty stomach. Furthermore, they were kept in cages with raised floors of wide wire mesh to prevent coprophagy. To prevent excessive dehydration during starvation, all groups were supplied with sucrose 8% (w/v) in NaCl 0.2% (w/v) which was removed 1 hour before experimentation (Alkofahi and Atta, 1999; Gharzouli, 1999). Group II, which served as a control group was given water (10 ml/kg body weight) while the treatment groups III, IV, V received respectively 100 and 500 mg/kg of methanol extract of *Quercus infectoria* bark and 11.5 mg/kg of the reference drug Cimetidine (Xu et al., 1998). Doses were administrated orally with water (10 ml/kg body weight) via a stainless steel intubation needle. Two doses were given on the first day at 9:00 h and 17:00 h; a third dose was given on the second day 1.5 h before induction of gastric ulceration. To induce gastric ulcer, the controls as well as the treatment groups received by gastric gavage 10 ml/kg body weight ethanol 50% (v/v) in water. Group I served as the reference group (no ulcer induction by ethanol) and received equivolumes of water instead. One hour after ethanol administration, all animals were sacrificed by an overdose of diethyl ether, stomachs rapidly removed, opened along their greater curvature and rinsed under running tap water. Using illuminated stereomicroscope long lesions were counted and measured along their greater length. Petechial lesions (very small lesions) were also counted and each five were considered as 1 mm of ulcer. The average total length of long ulcers and petechial lesions in each group of rats represented the ulcer index (mm). The curative ratio was determined by the formula:

$$\text{Curative ratio} = \frac{\text{(Control ulcer index)} - \text{(test ulcer index)} \times 100}{\text{(Control ulcer index)}}$$

Screenings of extract antibacterial activity

Methanolic extract of *Q. infectoria* bark was tested for its ability to inhibit the activity of 11 hospital isolates from different patients by disc diffusion method. The bacterial strains used were *Enterobacter agglomerans* (Gram-), *Proteus mirabilis* (Gram-), *Salmenella spp.* (Gram-), *Citrobacter braaki* (Gram-), *Escherichia coli* (Gram-), *Klebsiella pneumoniae* (Gram-), *Pseudomonas aeruginosa* (Gram-), *Heamophilus parainfluenza* (Gram-), *Streptococcus pyogens (S. pyogens)* (Gram+), *Staphylococcus aureus* methicillin-resistant (MRSA), and *S. aureus* methicillin-sensitive (MSSA) (Gram +). All the bacterial species tested were identified by API 20E except for *S. pyogens* (API Streptococcus) and MRSA and MSSA, which were identified by *Staphylococcus* coagulase test.

(a) Disc diffusion assay: Sterile 5 mm diameter filter paper disks containing 400 µg of extract were placed on the surface of Muller-Hinton agar inoculated with the appropriate bacteria tested except for *S. pyogens* and *H. parainfluenza* that were grown on blood agar and chocolate agar respectively. The inoculum size of each test strain was standardized by adjusting the optical density of the bacterial suspension to 0.08 (OD620 = 0.08) at 620 nm that corresponds to 10^8 bacteria / ml of suspension. All the plates were then incubated at 37°C for 24 h. The antibacterial activity was evaluated by measuring the diameter of the inhibition zone. A specific reference drug was used for each type of bacteria (Table 4).

(b) Minimal inhibitory concentration (MIC): The MIC values were studied for the microorganisms that were determined to be sensitive to the *Q. infectoria* extract in the disc diffusion assay. The MIC was determined using the two-fold serial microdilution method with normal saline. The final concentration ranged from 20 to 0.00976 mg/ml. The tested extracts were added to sterile NaCl into microtiter plates before the diluted bacterial suspension was added (OD620 = 0.08) and the background contributed by the extract color was determined. Maxipime (500 µg/ml) was used as a reference drug for the bacteria tested. The MIC values were taken as the lowest concentrations of the extracts that showed inhibition after 24 h at 37°C. The absorbance of the microtiter plates' wells was read at 620 nm (Basri and Fan, 2005) using an E-LizaMat 300 reader and the DGR ELISA regression program.

Statistical analyses

Values are presented as means ± SEM. Normal distributions of the data were confirmed using the kolmogorov-Smirnov one-sample goodness of fit test. Unacceptable heteroscedasity was eliminated, where possible, by the logarithmic transformation of the data. Where data were normally distributed comparisons between groups were made using oneway analysis of variance with localization of differences being achieved with Duncan's multiple range test. Where data were not normally distributed and could not be transformed to achieve normal distribution, the Kruskall-Wallis nonparametric analysis was used and differences located using the Mann-Whitney "U" test with appropriate adjustment to the critical value of p. Statistical significance was assumed at $p \leq 0.05$.

RESULTS

Blood lipid profile

Animals maintained for a period of one month on methanolic extract of *Q. infectoria* bark in drinking water were subjected for analyses of blood lipid profile and glycemia in the fasted state (Table 1). The serum total cholesterol, LDL cholesterol, total apo B and TAG levels were similar in the treatment group and control. However, the treatment group exhibited a significant increase in HDL-cholesterol levels with respect to control. Determination of serum glucose and insulin revealed that both parameters were significantly higher in the treatment group than in

Table 1. Serum concentrations of total cholesterol, LDL cholesterol, HDL cholesterol, triacylglycerol, total apoB, glucose and insulin after one month of supplementation with methanolic extract of Quercus infectoria bark in drinking water. Values denote mean ± SEM (n=15).

Parameter in Serum	Control group	Treatment group
Total Cholesterol (mg/dl)	57 ± 1.68	62.7 ± 1.68
LDL Cholesterol (mg/dl)	17.5 ± 1.44	17.6 ± 1.6
HDL Cholesterol (mg/dl)	23.5 ± 0.6	26.4 ± 0.77*
Triacylglycerol (mg/dl)	81.4± 6.27	93.8 ± 8.59
Total Apo B (mg/dl)	32.6 ± 3.11	28.7 ± 2.52
Glucose (mg/dl)	106 ± 3.61	133 ± 5.43*
Insulin (ng/ml)	0.655 ± 0.04	1.07 ± 0.15*

* Significant difference ($p < 0.05$) with respect to control

Table 2. SGOT, SGPT and LDH activities, urea and creatinine concentrations in fasting serum after one month of supplementation with methanolic extract of *Quercus infectoria* bark in control and treatment groups. Values denote mean ± SEM (n=15).

Parameter in Serum	Control group	Treatment group
SGOT (U/L)	60.2 ± 2.6	66.4 ± 4.64
SGPT (U/L)	21.9 ± 1.27	20.2 ± 1.28
LDH (U/L)	286 ± 59.1	141 ± 20.6*
Urea (mg/dl)	35 ± 1.5	33.1 ± 1.9
Creatinine (mg/dl)	0.47 ± 0.02	0.48 ± 0.02

* Significant difference ($p < 0.05$) with respect to the control.

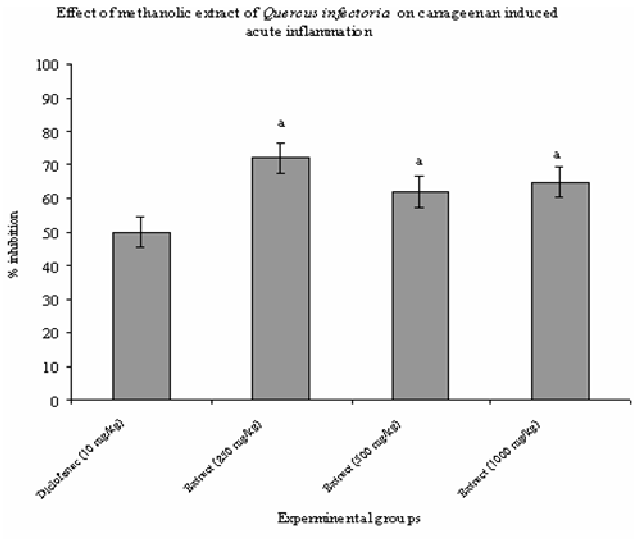

Figure 1. Diclofenac, *Q.infectoria* methanolic extracts (250mg, 500mg and 1000mg) and their percentage inhibitory rate on inflammation in carrageenan induced paw-edema.
Values denote mean ± SEM (n=6)
[a] Significant difference ($p< 0.05$) between extract and non-treated control group.

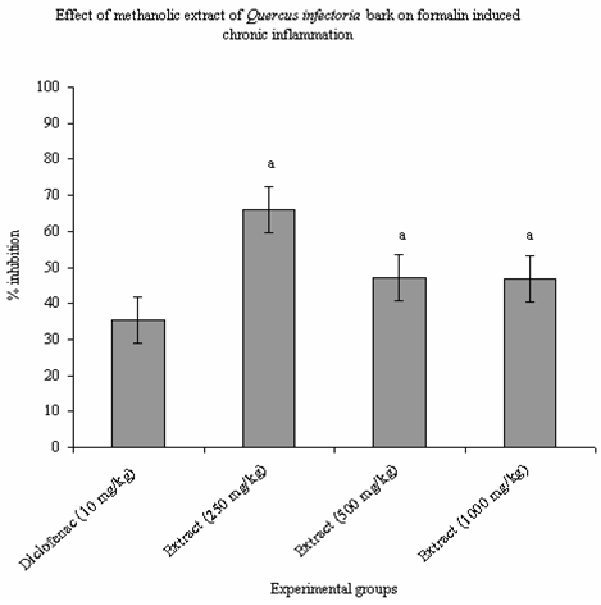

Figure 2. Diclofenac, *Q.infectoria* methanolic extracts (250mg, 500mg and 1000mg/kg body weight) and their percentage inhibitory rate on inflammation in formalin induced paw-edema.
Values denote mean ± SEM (n=6)
[a] Significant difference ($p< 0.05$) between extract and non-treated control group.

the control.

Liver enzymes, urea and creatinine

Serum activities of SGOT, SGPT, and LDH in both control and treatment groups as well as urea and creatinine levels in both groups were determined in the fasted state after one month period of extract intake (Table 2). Activities of SGOT and SGPT and the levels of both urea and creatinine in the serum were similar in both groups. However, a significant decrease in LDH activity was observed in the treatment group compared with the control.

Antiinflammatory activity

The methanol extract of *Q. infectoria* bark significantly inhibitted the acute inflammation induced by carrageenan (Figure 1), and the chronic inflammation induced by formalin (Figure 2) at concentrations of 250, 500 and 1000 mg/kg body weight in experimental animals. In both acute and chronic inflammation models, the 250 mg/kg body weight dose showed the highest inhibition.

Gastroprotective effect of *Quercus infectoria* against ethanol-induced gastric ulcer

Ethanol-induced gastric damage was characterized by the presence of elongated and petechial lesions confined

Table 3. Effect of methanolic extract of *Quercus infectoria* bark on ethanol-induced gastric damage in rats

Treatment groups	Ulcer index (mm)	Curative ratio (%)
Reference (Group I)	0	0
Control (Group II)	43.7	0
Extract (100 mg/kg) (Group III)	19.1	56
Extract (500 mg/kg) (Group IV)	14.2	67.5
Cimetidine (11.5 mg/kg) (Group V)	27.7	36.6

Each group included 6 animals.

Table 4. Antimicrobial activity of methanolic extract of *Quercus infecoria* bark against 11 bacterial strains based on disc diffusion method

Bacteria tested	Inhibition zone (mm)	Reference drug	Inhibition Zone (mm)
Citrobacter braaki	10	Gentamycin (10 µg/disc)	20
Enterobacter agglomerans	0	Ceftriaxon (30 µg/disc)	28
Escherichia coli	0	Ofloxacin (5µg/disc)	32
Heamophilus parainfluenza	0	Levofloxacin (5µg/disc)	24
Klebsiella pneumoniae	0	Bactrim (25 µg/disc)	21
Proteus mirabilis	10	Ciprofloxacin (5 µg/disc)	32
Pseudomonas aeruginosa	0	Astreonam (30 µg/disc)	24
Salmonella spp.	0	Bactrim (25 µg/disc)	29
MRSA	12	Vancomycin (30 µg/disc)	17
MSSA	12	Vancomycin (30 µg/disc)	17
Streptococcus pyogen	0	Ceftrtiaxon (30µg/disc)	31

NB: each sterile disc contains 400 µg of *Quercus infectoria* bark methanolic extract.

in most cases to the glandular region. The number of long ulcers and the ulcer index were significant when compared with normal group (Table 3). Repeated oral administration of 100 and 500 mg/kg of methanol extract of *Q. infectoria* bark and cimetidine lowered the severity of gastric damage.

Antibacterial activity

The methanolic extract of *Q. infectoria* bark was tested against 11 bacterial hospital isolates as shown in table 4. The MIC values were determined for 3 strains (*P. mirabilis*, MRSA and MSSA) shown to be sensitive to the methanolic extract of *Q. infectoria* bark. Based on the results obtained, the MIC value for *P. mirabilis* was 5 mg/ml. MIC values for MSSR and MSSA were 1.25 mg/ml.

DISCUSSION

The intake of methanolic extract of *Q. infectoria* bark for a period of one month in drinking water appeared not to have a significant effect on blood lipid profile with the exception of HDL-cholesterol. The extract increased significantly serum HDL-cholesterol level, thereby conferring some cardioprotective effects. The increase in HDL-cholesterol concentration may be related to the presence of soluble fibers in the extract since Chai et al. (2003) showed that HDL-cholesterol levels were significantly higher in rats fed fiber from bark of *Quercus mongolica*. Extraction of soluble dietary fiber from bark or wood of *Q. infectoria* may provide an inexpensive source of natural dietary fiber that helps in increasing HDL- cholesterol.

On the other hand, the increase in HDL-cholesterol was accompanied with an increase in serum glucose and insulin concentrations, thereby raising the possibility of insulin resistance syndrome, especially that the mean serum triacylglycerol concentration was relatively higher than that of the control group. Previous studies by Hwang et al. (2000) showed that the methanol extract of galls of *Q. infectoria* significantly inhibited α-glycosidases such as sucrase, maltase and isomaltase, thus exhibiting a hypoglycemic activity. Such a finding on galls is not in contradiction with the present study conducted on stem bark since it represents the postprandial state. It may be possible that the extract inhibits sugar digestion, delays its absorption and consequently lowers postprandial glycemia. But, at the same time the extract may also have an inhibitory effect on insulin sensitivity when taken chronically leading to hyperglycemia and hypereinsulinemia. Previous *in vitro* studies showed that some polyphenols could increase insulin activity in epididymal fat cells

(Anderson and Polansky, 2002) and rat adipocytes (Hattori et al., 2003). This discrepancy in results may be attributed to the fact that the extract used in the present study is crude, chronically given to rats, and most importantly *in vivo* studies may completely give different results from *in vitro* studies because of complexity of the living organism.

The potential anti-inflammatory activity of methanol extract of *Q. infectoria* bark was investigated using in vivo models of acute and chronic inflammation. In both models, the three doses used showed potent anti-inflammatory activities if compared with the reference drug (diclofenac). Interestingly, the lowest dose used (250 mg/kg) was the most effective in reducing the inflammation. Further studies with doses smaller then 250 mg must be performed in order to locate the optimum dose that causes maximum anti-inflammatory activity. The reduced anti-inflammatory activity observed with higher doses of the extract may be due to the complex composition of the extracts where above a certain concentration some compounds present in the extract may antagonize the effect of some other compounds (e.g., tannins), as suggested by Khennouf et al. (2003). It is known that all Quercus species contain tannins in variable percentages according to the part of plant considered: leaves, bark and galls (Mammela et al., 2000; Ikram and Nowshad, 1977; Dar et al., 1976; Culberth et al., 1927). A recent study by Erdelyi et al. (2005) demonstrated that tannins have an anti-inflammatory activity manifested by the inhibition of transcription of nuclear factor kappa B. The nuclear factor kappa B is known to induce the transcriptional up-regulation of various inflammatory responses such as interleulkins and tumor necrosis factor alpha (TNFα) (Choi et al., 2003). In addition, the mechanism underlying the anti-inflammatory effect of tannins include the scavenging of radicals (antioxidant effect) and inhibition of expression of the mediators of the inflammatory response including cytokines, inducible nitric oxide synthase and cycloxygenase-2 (Erdelyi et al., 2005). Moreover, Oliveira et al. (2004), have shown that resin possess anti-inflammatory activity which did not modify the hind-paw edema induced by carrageenan but inhibited collagen formation. Consequently resin, present in the bark of *Q. infectoria* besides tannins (Culberth et al., 1927), may have partially contributed to the anti-inflammatory activity of the extract.

Oral pre-treatment for 2 days with methanolic extract of *Q. infectoria* bark resulted in substantial protection (56 – 67%) against gastric lesions induced by ethanol. The inhibition observed exceeded that of the antisecretory agent cimetidine. In similar studies (Xu et al., 1998), cimetidine produced 33% protection, a value consistent with the present data (36.6%). Khennouf et al. (2003) showed that tannins from leaves of *Q. suber* and *Q. coccifera* given orally to mice prevented the formation of ethanol-induced gastric lesions. Gastroprotective effects against ethanol-induced ulcer in rats were also shown with intake of *Q. ilex* polyphenols (Khennouf et al., 1999) and Q. ilex root bark water extract (Gharzouli et al., 1999). Polyphenols such as tannic acid, quercetin and ellagic acid, present in *Q. infectoria* bark, are able to inhi-bit the proton pump present in paretial cells (Gharzouli et al., 1999; Khennouf et al., 1999; Khennouf et al., 2003), thereby leading to a reduced gastric acid secretion. Unlike the present and earlier studies (Xu et al., 1998), Toma et al. (2005) showed that ethanol-induced ulcers are not inhibited by antisecretory agents such as cimetidine, but by agents that enhance mucosal defensive factors such as endogenous prostaglandins and mucus synthesis. Tannins 'tan' the outermost layer of the mucosa and make it less permeable and more resistant to chemical and mechanical injury or irritation (Borrelli and Izzo, 2000). Bark of *Q. infectoria* is also known to contain resin, generally used in folk medicine to treat inflamematory conditions, hasten wound repair (Culberth, 1927), and have a protective effect in gastrointestinal disorders (Oliveira et al., 2004). Thus, the gastroprotective effect observed may be attributed chiefly to the presence of both tannins and resins present in the extract. The mechanism involved is most likely to be mediated through cytoprotective and antisecretory effects.

In the present study, methanolic extract of *Q. infectoria* bark showed potential antibacterial effect against 4 bacterial species including *P. mirabilis*, *C. braaki*, MRSA and MSSA. Studies conducted by Voravuthikunchai et al. (2005) also showed that ethanolic extract of *Q. infectoria* was active against hospital isolates of MRSA. In addition, Basri and Fan (2005) showed that water and acetone extracts from galls of *Q. infectoria* have a high potential antibacterial activity, which seemed to depend on the presence of tannins. The antimicrobial action of tannins may be related to their ability to inactivate microbial adhesions, enzymes, and cell envelope transport proteins (Cowan, 1999).

In conclusion, the crude methanolic extract of *Q. infectoria* bark displayed various important biological activities in the rat model. After one month of intake of the extract a significant increase in serum HDL-cholesterol level was observed with a concomitant increase in both serum glucose and insulin levels. The extract showed minor anti-bacterial activity, but substantial anti-inflammatory and anti-ulcerogenic activities, findings of particular therapeutic importance, as most of the anti-inflammatory drugs used in modern medicine are ulcero-genic.

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