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ISONIAZID-INDUCED ANTI-CONVULSION ACTIVITY OF QUERCUS INFECTORIA EXTRACT

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Abstract
For the purpose of discovering and create novel antiepileptic drugs, scientists and researchers are still concentrating on medicinal plants as a potential source of lead compounds. Thus this study deals with effect of *Quercus infectoria* extract on Isoniazid-induced convulsion. The phytochemical studies revealed the presence of volatile oil, Cumarins, anthraquinones, triterpenes, flavonoids, phenol, saponin & tannin. The total flavonoid & phenol conbtent was found to be 13.9±0.21 mgQE/g and 7.30±0.15 mgGAE/g respectively. In case of *Q. infectoria* the onset of seizure was at 240 seconds while seizure duration lasted for 30 seconds only. *Q. infectoria* does not showed dose dependent manner but delayed onset of seizure and decreases duration of seizure. This study was the first to study and revealed anticonvulsant activity of *Q. infectoria* and this could be the better supplement or medication for prevention and treatment of epileptic seizure arising from down regulation of GABAergic transmission oxidative stress. This finding suggests that *Q. infectoria* supplementation may be used as a potential neuroprotective drug.

Keywords: Convulsions, Epilepsy, *Quercus infectoria*, Medicinal plants, Phytochemicals, Isoniazid

Introduction

Epilepsy is a frequent disorder of the central nervous system (CNS) and the fourth-leading source of illness burden globally. Recurrent, unprovoked seizures are its primary feature. These seizures can cause anxiety, sadness, cognitive decline, schizophrenia, and autism, all of which can worsen a patient's quality of life and raise the risk of death. The pathogenesis of epileptic seizures (ES) is frequently attributed to an imbalance caused by the inhibition of excitatory -aminobutyric acid (GABA)-mediated neurotransmission and the activation of inhibitory glutamatergic neurotransmission within the brain, including the hippocampal, neocortical, cortico-thalamic, and basal ganglia network. Epilepsy can originate from the brain's inherited propensity to produce seizures or it can be brought on by brain damage brought on by a tumor, accident, stroke, infection, etc. that can create a wide range of anomalies leading to seizure generation. A person may have a variety of symptoms when they have a spasm. These could include momentary breaks in stuttering, bewilderment, drooling, losing control of the bowels or bladder, abrupt shaking of the entire body, uncontrollable muscular spasms, and brief pauses in breathing (Thijs *et al*., 2019; Beghi, 2020; Shin *et al*., 1994).

Antiepileptic medications are unable to manage the seizures of about 25% of patients who have been diagnosed with epilepsy. But there are numerous treatment strategies that work to stop epileptogenesis following a SE or an IPI. Antiepileptic medications (AEDs) have been used effectively to control seizures in order to provide neuroprotection (Perucca, 2005).

Natural medicine has been discovered to be more effective at treating epilepsy with fewer adverse effects. The regulation of synapses, receptors, and ion channels, the prevention of inflammation, and the control of the immune system are just a few of the documented mechanisms of natural medicine. Additionally, natural medicine can repair mitochondrial dysfunction, reduce oxidative stress, and control apoptosis. A well-liked complementary and alternative therapy is herbal medicine. Patients' concern of the adverse effects of Western medicine or surgery is what has driven a trend toward turning to traditional medicine for therapy. Traditional herbal medicine may be more readily available to patients and less expensive than conventional therapies (Mohsin and Choudhary, 2000; Chauhan *et al*., 1988).

Quercus infectoria is a little tree with a height of one to two meters (four to six feet), native to Greece and Asia Minor. Almost every single part of the plant, including the fruit, bark, and leaves, has been proven to have therapeutic properties. With the help of indigenous peoples in many parts of the world, they are used as antiseptics and to treat gastrointestinal tract (GIT) disorders like diarrhea and hemorrhoids. In addition to gonorrhea, gastritis, asthma, pyrexia, Parkinson's disease, and hepatoprotective illnesses, it is frequently used to treat superficial wounds, hemorrhoids, varicose veins, diarrhoea, and stomach ulcers. The oak tree's bark is highly prized and regularly used in therapy as an energizing agent and antibacterial. Infectoria galls are utilized to treat a number of inflammatory diseases as well as to restore the suppleness of the uterine wall. Additionally, they are frequently utilized in Malay recommended remedies to treat wound infections during childbirth. They have a long history of use in India for dental purposes, including the treatment of gingivitis and toothaches. Infections, skin problems, and inflammatory conditions are among the conditions for which it is frequently used in Asia (Ikram and Nowshad, 1977; Elham *et al*., 2021). This study will further study the effect of *Quercus infectoria* extract on Isoniazid-induced convulsion.

Materials & methods

Collection of plant material

The galls of *Q. infectoria* were purchased from the local market of Sagar (M.P.) in the month of December 2022.

Chemical reagents

All the chemicals used in this study were obtained from HiMedia Laboratories Pvt. Ltd. (Mumbai, India), Sigma Aldrich Chemical Co. (Milwaukee, WI, USA), SD Fine- Chem. Ltd. (Mumbai, India) and SRL Pvt. Ltd. (Mumbai, India). All the chemicals used in this study were of analytical grade.

Defatting and extraction

Q. infectoria gall powder was shade dried at room temperature. The shade dried material was coarsely powdered and subjected to extraction with petroleum ether (60- 80°C) in a soxhlet apparatus. 200gm of dried plant material were exhaustively extracted by refluxing in ethanol at room temperature. The extract was evaporated above their boiling points. Finally the percentage yields were calculated of the dried extracts and preserved in a refrigerated at 4^{o}C for the experiments.

Phytochemical screening

Phytochemical screening to detect the presence of bioactive agents was performed by standard procedures. After the addition of specific reagents to the solution, the tests were detected by visual observation of color change or by precipitate formation (Kokate *et al*., 2005).

Animals

Mice of either sex (18 to 22 g) were group housed (n= 6) under a standard 12 h light/dark cycle and controlled conditions of temperature and humidity (25±2 °C, 55- 65%). Mices received standard rodent chow and water *ad libitum*. Animals were acclimatized to laboratory conditions for 7 days before carrying out the experiments. All the experiments were carried in a noise-free room between 08.00 to 15.00 h. Separate group (n=6) of mice was used for each set of experiments. The animal studies were approved by the Institutional Animal Ethics Committee (IAEC), constituted for the purpose of control and supervision of experimental animals by Ministry of Environment and Forests, Government of India, New Delhi, India.

Experimental group

Ten mice of either sex with a weight of 18 to 22 g are treated with the test compound or the standard (e.g. Diazepam 10 mg/kg i.p.) by oral or intraperitoneal administration. Controls receive the vehicle only. 30 min after i.p. or 60 min after p.o. treatment the animals are injected with a subcutaneous dose of 300 mg/kg isoniazid (isonicotinic acid hydrazide). During the next 120 min the occurrence of clonic seizures, tonic seizures and death is recorded. The percentage of seizures or death occurring in the control group is taken as 100%. The suppression of these effects in the treated groups is calculated as percentage of controls. ED50-values are calculated. The method has been proven to be of value amongst a battery of tests for CNS-activity.

Results & Discussion

The phytochemical studies revealed the presence of volatile oil, Cumarins, anthraquinones, triterpenes, flavonoids, phenol, saponin & tannin. The total flavonoid & phenol conbtent was found to be 13.9±0.21 mgQE/g and 7.30±0.15 mgGAE/g respectively. Anticonvulsant activity of *Q. infectoria* were carried out using INH as a chemoconvulsant where diazepam and normal saline were used as positive and negative control respectively. Diazepam is standard anticonvulsant drugs which inhibit seizure induce by INH by potentiating GABArgic transmission.

In case of *Q. infectoria* the onset of seizure was at 240 seconds while seizure duration lasted for 30 seconds only. *Q. infectoria* does not showed dose dependent manner but delayed onset of seizure and decreases duration of seizure.

Flavonoids have been described as a family of benzodiazepine receptor ligands with CNS depressant activities. The presence of an essential oil, polyphenols, tannins, and flavonoids in the *Q. infectoria* may be responsible for anticonvulsant effects. Methanolic extracts of *Q. infectoria* at all doses delayed the latency and duration for clonic convulsions and death. The compound that can potentiate GABAergic transmission may show protection action in this INH model. It is also the mechanism for benzodiazepine and barbiturate class of anticonvulsants. - *Q. infectoria* showed protection against INH-induced convulsions Identified metabolites: hydrazine, ammonia, oxidizing free radicals, Ascorbic acid showed neuroprotective activity in rats' hippocampus while, Carotenoids reduced lipid peroxidation and increased antioxidants

Table 1: Qualitative analysis of phytochemicals present in the ethanolic extract of *Quercus infectoria*

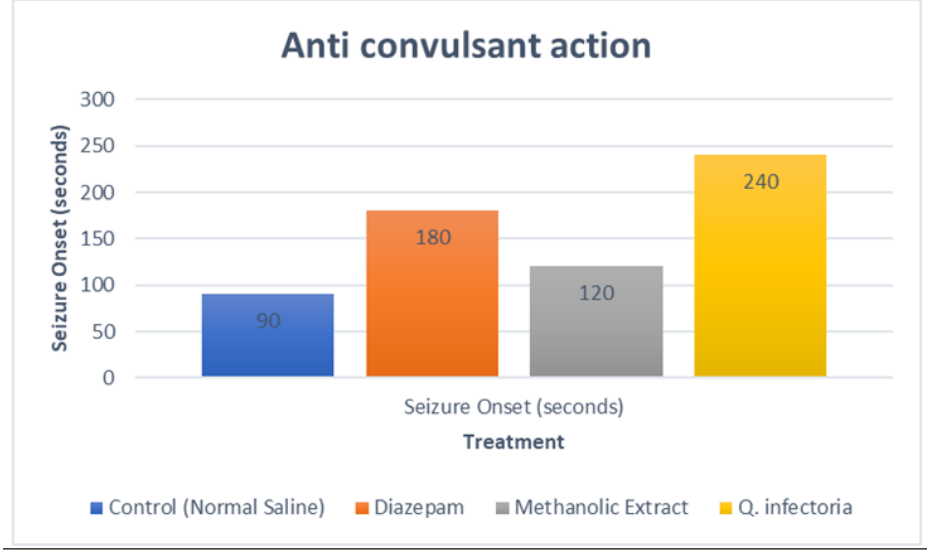
Phytochemicals	Result
Glucosides	-
Volatile oil	+
Cumarins	+
Anthraquinones	+ +
Alkaloids	-
Triterpenes	+ +
Flavonoids	+ + +
Phenols	+
Saponins	+ +
Sterols	-
Tannins	+++

Table 2: Total phenol & flavonoid content *in Quercus infectoria*.

Extract	Total flavonoids	Total phenol
Quercus infectoria.	13.9±0.21 mgQE/g	7.30±0.15 mgGAE/g

Table 3: Effect of extract of *Quercus infectoria.* on seizure induced by isoniazide rats by different timelines

Treatment	Seizure Onset (seconds)	Seizure Duration (seconds)
Control (Normal Saline)	90	180
Diazepam	180	60
Methanolic Extract	120	120
Q. infectoria	240	30



Conclusion

The finding of the present study revealed that the methanolic extract galls of *Q. infectoria* showed protective effect on Isoniazide induced convulsion. This finding suggests that the further chemical constituents and mode of action of plants should be elucidated. To completely understand the active ingredients, the mechanism of action, and the safety of the plant as a treatment, however, more thorough pharmacological, toxicological, and phytochemical investigations of this plant are required.

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