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Antipyretic and Phytochemical screening of Aqueous extract of evergreen Medicinal plant *Glycyrrhiza glabra* L.

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Several of the indigenous medicinal plants are also utilized as food and spice plants. The immense chemical diversity observed among the millions of plant species makes nature a fascinating reservoir of new therapeutic candidate substances. *Glycyrrhiza glabra* L. is indeed an ancient remedy. Antipyretic efficacy was assessed using a brewer's yeast-induced pyrexia assay. Five mouse groups were employed to test the mice's antipyretic effect. Prior to the yeast injection, the rectal temperatures for each of the mice were observed. Phytochemical analysis of the plant suggests that the aqueous extract comprised glycosides, alkaloids, sugars, tannin, volatile oils, and phenol. Results indicate that the aqueous extracts of *G. glabra* can greatly decrease the rectal temperature that brewer's yeast developed at doses of 50 mg/kg, 100 mg/kg, and 150 mg/kg. In conclusion, the aqueous extract of *Glycyrrhiza glabra* has significant dose dependent antipyretic properties. This exploratory screening provides a baseline data for future studies.

Keywords: ***Fever; Phytochemicals; Antipyretic activity; Glycyrrhiza glabra L.; Medicinal plants***

INTRODUCTION

Since the earliest days of human agriculture, plants have remained one of the most significant medicinal sources. Interest for food supplements, plant-based drugs, health products, and other products is rising. Individuals' and communities' health largely depend on medicinal plants. These plants' medicinal potential originates from a few chemical constituents that have a clear physiological impact on our bodies. Saponin, triterpenoid, flavonoids, phenolic compounds, tannins, and alkaloids are the most essential of these phytochemical constituents. Several of the indigenous medicinal plants are also utilized as food and spice plants. They are often included within diets prepared for pregnant and nursing women for medicinal reasons (Haq et al., 2023; Ali et al., 2018; Sharma et al., 2017). If a person's body temperature rises just above standard limits (36.5-37.5°C) as a response of an infection, inflammation, tissue injury, graft rejection, or other inflammatory disease circumstances, a fever is a common medical indication. (Sullivan and Farrar, 2011). Because a number of the microbes that trigger infection proliferate most successfully at body temperatures which are lower than fever, the body's natural defense is to establish a condition where an infectious agent or diseased tissue cannot persist (Dalal and Zhukovsky, 2006). Hence, a decrease of fever may cause a reduction in infection response, a slower rate of healing, and less than ideal results. The poor prognosis and mortality rate of any human illnesses are both linked to decreased febrile responses to infections (Ogoina, 2011). Conventional medicine has already used traditional medicinal plants for ages to cure human illnesses all around the globe. Because of their advantageous biological and therapeutic features, availability, and affordability, herbal medicines largely contribute to the enhancement of basic healthcare in both developing and developed nations (Ali et al., 2018; Li and Tian, 2016).

Glycyrrhiza glabra is among the plants that is capable of serving as medicine. The word glycyrrhiza is taken from the Greek words glykos, which means sweet, and rhiza, which means root. In northern India, *Glycyrrhiza glabra* is termed to as “mulaithi”. The licorice and sweet wood plant, *Glycyrrhiza glabra*, is indigenous to some part of Asia and Mediterranean. Being a diuretic, insecticide, choleretic, and prescribed in traditional medicine for colds, coughs, and severe swellings, several conventional physicians have proclaimed the efficiency of Glycyrrhiza species for a range of disease states (Sherma et al., 2018).

G. glabra rhizomes and roots have expectorant, demulcent, and memory-boosting characteristics. The plant showed anti-hepatotoxic, anti-inflammatory, anti-viral, anti-allergic, antipyretic, antibacterial, antiulcer, and

antidepressant properties. Furthermore, it is employed to cure congestion in the throat, boils, skin inflammation, cough, and respiratory issues. Root is utilized in medications that strengthen bones and muscles. moreover, it heals stomach discomfort and wounds. Moreover, Addison's illness, malignancies, tumors, epilepsy, hypertension, and dermatitis, are all cured with licorice. (Sherif *et al.,* 2013). Licorice contains licochalcone, which has antimalarial activity (Hassan et, al., 2021). The efficiency of the plant's aqueous extract was currently determined based on its antipyretic properties.

MATERIALS AND METHODS

Collection of plants

Specimen of the fresh and healthy plants were obtained. The samples were further authenticated and identified utilizing flora of Pakistan. The plant pieces were cleaned properly in distilled water and tap water, dried in the shade, and crushed into a fine powder. They were placed into sealed bottles after screening. 10 g of powdered plant was obtained and placed in a separate conical flask. 90 ml of distil water was then poured to the powdered plant, which was stirred for 72 hours. The extracts were filtered utilizing Whatman filter paper after 72 hours, and the filtrate was allowed to dry at a room temperature (Selvamohan *et al.*, 2012).

Phytochemical analysis

With respect to the procedure described, the qualitative phytochemical analyses for the determination of tannins, hydrolysable tannins, alkaloids, saponins, volatile oils, glycosides, and phenols were performed on Antioxidant Response Element (ARE). The crud extract of *Glycyrrhiza glabra* was investigated to determine the presence or absence of phytochemical components such as tannins, alkaloids, hydrolysable, carbohydrates, flavonoids, phenols, saponins, volatile oils, glycosides, proteins, resins, and cardiac glycosides utilizing Ethanol, Methanol and aqueous as the solvents (Soni *et al.,* 2011).

Pharmacological activity

Experimental animals

The animal house of Peshawar Agriculture Research Center (PARC) in Peshawar has offered both sexes with Albino mice weighing approximately 25 g and 30 g, respectively, and weighing among 150 g and 200 g. The animals received a regular pellet meal and had water readily available throughout the entire experiment time.

Antipyretic activities by (brewer's yeast induced pyrexia)

Antipyretic efficacy was assessed using a brewer's yeast-induced pyrexia assay. Five groups of mice were used to assess the antipyretic effects. Prior to the yeast injection, the rectal temperatures for each of the mice were observed. The brewer's yeast solution was developed by combining 7% brewer's yeast with 93 ml of water for antipyretic effect. The very first set of mice (the control group) were left untreated. Afterwards, the groups 2, 3, 4, and 5 each got an injection of 1 cc of brewer's yeast. One Paracetamol pill (10 mg) was dissolved in 50 ml of water to generate the standard Paracetamol solution. The mice of the 2nd group received an injection of one cc of Paracetamol solution. Aqueous extracts of *Glycyrrhiza glabra* were given into the remaining groups, 3, 4, and 5, at dosage of 50, 100, and 150 mg/kg each. All of the mice had their temperatures examined at frequencies of one hour to four hours after receiving doses of the conventional medication (Paracetamol) and aqueous extracts, which was accomplished after 18 hours of the pyrexia-inducing procedure. The formula below is employed to compute percent reductions in antipyretic activity (Yimer, *et al*., 2021).

% reduction = B – Cn/B – A × 100

Where, B = temperature after pyrexia induction, Cn = temperature after 1, 2, 3, and 4 hours, and A = normal t body temperature.

RESULTS

Phytochemical analysis

The pharmacological, phytochemical, and antioxidant properties of *Glycyrrhiza glabra* were explored in the current study utilizing an aqueous extract.

Qualitative phytochemical investigation of *Glycyrrhiza glabra*

The existence of phytochemicals in aqueous extracts of *Glycyrrhiza glabra* were explored qualitatively. As per the observations, aqueous extracts comprised sugars, alkaloids, glycosides, tannin, volatile oils, and phenol. (Table 1).

Table 1: Qualitative Phytochemical analysis of *Glycyrrhiza glabra* aqueous

Phytochemical	Result
Alkaloids	+
volatile oils	+
hydrolysable tannins	+
Tannins	+
Phenol	+
Glycosides	+

the test subject for *Glycyrrhiza glabra's* antipyretic properties

.

Antipyretic activity

Brewer yeast-induced pyrexia in mice functioned as

Table 2: Antipyretic activity of *Glycyrrhiza glabra*

Groups	Normal Temp	Temp after 18hours	Temp 1 Hour	Temp 2 hour	Temp 3 Hour	Temp 4 Hour
control	37.46±.08	37.86±.08	37.84±.08	37.86±.08	37.63±.08	37.43±.21
standard	37.56±.14	39.1±.47	38.1±.28	38.3±.11	37.2±.60	37.00±.08
50mg/kg	37.46±.14	39.73±.06	38.88±.40	38.63±.12	39.28±.00	37.63±.12
100mg/kg	37.33±.17	39.11±.20	38.87±.23	38.40±.10	39.51±.00	37.43±.08
150mg/kg	37.33±.18	39.01±.20	38.63±.28	38.13±.15	39.8±.00	37.23±.13

Aqueous extract dosages of 50 mg/kg, 100 mg/kg, and 150 mg/kg considerably decreased the rectal temperature that brewer's yeast developed, according to the current study's findings.

Table 3 : Percent antipyretic activity

Extract	Percent inhibition
Control	
Standard	100%
50mg/kg	92.51%
100mg/kg	94.38%
150mg/kg	99%

Anti-pyretic activity

Albino mice were utilized as research subjects for the antipyretic effects of *Glycyrrhiza glabra* aqueous extract in pyrexia generated by Brewer's yeast. Group 1 was control which shows the temperature of 37.86±, the rest of the groups were injected with brewer's yeast solution. Group 2 underwent a standard dosage of paracetamol (10 mg/kg) following 18 hours of the induced pyrexia, while groups 3, 4, and 5 underwent injections of an aqueous extract at doses of 50, 100, and 150 mg/kg in a volume of one cc. Before the brewer's yeast injection, all groups exhibited a normal body temperature of 37.46.08. After 18 hrs. of induced pyrexia the treatment groups 3rd, 4th and 5th were given the medicinal plant extract with concentration of 50, 100 and 150mg/kg. The aqueous extract of *Glycyrrhiza glabra* indicated antipyretic activity and decreasing temperature in mice. Following the initial hour of medication therapy, the temperature decreased dramatically, then following the second, third, and fourth hours of administration of drugs at dosages of 50, 100, and 150 mg/kg, it began to drop gradually (Table 2). It was discovered that the aqueous extract of *Glycyrrhiza glabra* had dose-dependent antipyretic properties. The decline in mice's rectal temperature after one hour of dosages with 50, 100, and 150mg/kg was determined to be 38.88.40, 38.87.23, and 38.63.28, respectively. *Glycyrrhiza glabra* had a better overall antipyretic performance profile than paracetamol. A significant drop in rectal temperature was noticed in mice following the second hour of doses with 50, 100, and 150mg/kg, with measurements of 38.63.12, 38.40.10, and 38.13.15, correspondingly. The antipyretic activity profile of *Glycyrrhiza glabra* L.'s aqueous extract is identical to the percentage of the positive control (paracetamol), which displayed the same pattern of temperature reduction (Table 3). The body temperature of the treated mice finally drops to average after 4 hours of the medicinal plant extract and routine medication administration. Our study revealed that the plant extract significantly decreased mouse fever.

DISCUSSION

Pyrexia is a definition of a variety of ailments that are usually driven on by infections or autoimmune diseases but which are not technically infections. More particularly, it is considered that some endogenous chemicals, such as prostaglandins, are what produce fever (Hasan et al., 2021; Alemu et al., 2018; Tesema and Makonnen, 2015) Substances that prevent prostaglandin formation typically demonstrate the antipyretic action (Yimer et, al., 2020). Hydro-alcoholic concentrates of *Tamarix dioica* and *Fagonia bruguieri* are supposed to have antipyretic capabilities since they prevent prostaglandin formation. The findings of the current investigation would agree with the earlier works by Mamedov and Egamberdieva (2019), Esmaeili, et al. (2020), and Pastorino et al. (2018) but are also in accord with the findings of Bao et al. (2021), El-Saber Batiha et al., (2020), and Jiang et al., (2020) and (2019).

Tannins may be beneficial for avoiding the production of ulcers because they have the capacity to precipitate proteins and tighten blood vessels (Veronica *et al*., 2021 and 2017). Tannins' astringent characteristics may have enabled microproteins to aggregate at the ulcer's area, building an impermeable protective pellicle that coats the lining and guards it from toxins and proteolytic enzyme damage (Hussain et al., 2018). Based on certain investigations, flavonoids' existence can hopefully minimize ulcers from emerging by strengthening capillary resistance and microcirculation, which enable the cells less susceptible to inflammatory factors (Estella, *et al*,

2022). The findings of this study demonstrated that the plant had excellent antipyretic capability against mice brewer yeast produce pyrexia, and its inhibitory action was identical to that of the common medicine paracetamol. After the fourth hour of medication administration, the value risen dramatically, whereas the value of the common drug paracetamol operated as a baseline. Pyrexia is typically assumed to be triggered on by various endogenous chemicals. Aqueous extracts of *Glycyrrhiza glabra* may decrease the manufacturing of prostaglandins, which would describe their antipyretic properties. Acetylsalicylic acid, an antipyretic medication, decreases body temperature by preventing the hypothalamic formation of prostaglandin. In a similar fashion, paracetamol reduces the brain's cyclooxygenase (COX) isoenzyme to generate an antipyretic impact. Acetylsalicylic acid, a sort of NSAID, limits prostaglandin synthesis (E-type) in the hypothalamus, which is the reason they behave as antipyretics. As a result, fever-related plasma prostaglandin values that are high are lowered. The standard antipyretic medication utilized in this study, paracetamol, also has the same function by selectively acting on a certain cyclooxygenase (COX) iso-enzyme in the central nervous system (CNS). The manufacturing of prostaglandins may be prevented by *Glycyrrhiza glabra* extract, it may be assumed. Mice's rectal temperature was dramatically reduced by plant extract when contrasted with control groups. The aqueous extract of *Glycyrrhiza glabra* significantly decreased pyrexia, based on the data. These findings further indicate that the stated antipyretic impact of *Glycyrrhiza glabra* may be partially due to the occurrence of particular active principles, the dissociation of which could enable it to be simpler to perform better antipyretic medications with specific mechanisms of action. To figure out the precise pharmacological mechanism of the *Glycyrrhiza glabra* aqueous extract and to separate the active constituents from the plant, more investigations are needed. The chemical constituents in this plant that have a clear physiological influence on living organisms are what offer it its medicinal usefulness.

The findings of this investigation demonstrated that the plant has strong antipyretic capability against brewer's yeast-induced pyrexia in mice, and its inhibitory impact was identical to that of the common medicine paracetamol. All dosage percentages were noteworthy. With 150mg/kg in aqueous, the maximum percentage of inhibition was determined to be (99%), which is identical to the conventional medication utilized. Brewer yeast's cyclooxygenase and prostaglandin formation, together with additional temperature mediators like arachidonic acid, enable the elevation of rectal temperature (Cock, et al., 2022). Brewer's yeast enables the rectal temperature to elevate, whereas steroids terpenoids, and flavonoids present in plants perform an inhibitory action in prostaglandin generation that prevent this from proceeding (Saad et al., 2021). Conventional medicine utilizes licorice (*Glycyrrhiza glabra*) plant extracts to cure malarial fever. The saponin glycyrrhizin (GLR) and its active metabolite glycyrrhetinic acid (GA), both of which have antimalarial characteristics, are the major active ingredients (Soeiro, et al., 2021) have recognized three primary methods for how their anti-malarial or antipyretic effect first began: (i) Drug-induced membrane lipid raft disintegration, (ii) blockage of the alarmin protein HMGB1, and (iii) probable suppression of the detoxifying enzyme glyoxalase 1 (GLO-1), which is regarded to be a major treatment target for malaria fever, are just a few evidence of the medication's effects. Hence, it was postulated that either of these mechanisms is responsible for decreasing body fever. Fever can be driven on by an inflammation, infection, tissue injury, graft rejection, or another disease condition, among others. Antipyretic medicines can help to lower high body temp. The hypothalamus activates the set point at which body temperature is managed. Keeping an appropriate equilibrium between heat loss and heat production is crucial to preserving body temperature. When an individual has a fever, this set point climbs, and a medicine like paracetamol has no effects when the body temperature goes up because of circumstances like workout or an elevation in ambient temperature. (Oladeji, et al., 2021).

CONCLUSION

The globe's flora is getting less diverse, though several species still have tremendous quantities of medical uses. This study investigated the antipyretic properties of glycyrrhiza in mice. In these animal experimentations, utilizing the plant concentrates exhibited an incredibly effective antipyretic. The animals' mean body temperatures were substantially different (p 0.05) 4 hours following each treatment. Besides which, the plant extracts demonstrated potent dose-dependent antipyretic efficacy in the range of 50 to 150 mg/kg body weight. In light of these results, more exploration into the plant's potential uses is advised. The plant exhibits considerable medical properties.

CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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AUTHOR CONTRIBUTIONS

HAB conceptualized and supervised the study. SHY and KA contributed to manuscript writing. SMA, DR, RB, MA, N, and AM conducted experiments, collected and

analyzed data. HAB and KA reviewed and edited the manuscript. All authors have read and approved the final version.

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