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Assessment of Pharmacological Effects of Methanolic Extract of *Perovskia abrotanoides* as Anti-Asthmatic and Hepatoprotectant

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Perovskia abrotanoides, anti-asthmatic, hepatoprotective, antibacterial, CCl_4-induced hepatotoxicity, histamine-induced bronchospasm, natural remedies, phytochemical screening.
Disclaimers

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ABSTRACT

Background: Perovskia abrotanoides, a plant native to Pakistan, has traditionally been used to treat various ailments, but its pharmacological properties remain underexplored.

Objective: To evaluate the anti-asthmatic, hepatoprotective, antibacterial, and anticancer activities of the methanolic extract of Perovskia abrotanoides.

Methods: The methanolic extract was prepared via maceration and subjected to phytochemical screening. Anti-asthmatic activity was assessed using a histamine-induced bronchospasm model in guinea pigs. Hepatoprotective effects were evaluated in rabbits with CCl_4-induced hepatic damage, measuring liver function tests and conducting histopathological analysis. Antibacterial activity was tested against multiple bacterial strains using the Microplate Alamar Blue Assay, and anticancer activity was evaluated in Hela, 3T3, and MU7 cell lines.

Results: The extract significantly increased pre-convulsive time (58 ± 2.3 seconds) in guinea pigs ($P < 0.05$), improved liver function markers ($P < 0.01$), and reduced bilirubin and ALP levels. It showed 81% inhibition against Staphylococcus aureus but no significant anticancer activity.

Conclusion: The methanolic extract of Perovskia abrotanoides demonstrated significant anti-asthmatic, hepatoprotective, and antibacterial properties, with potential for therapeutic use in respiratory and liver conditions.

INTRODUCTION

Plants have historically been a vital source of therapeutic agents, serving as the primary source of medication for millennia. Even in contemporary medicine, a substantial proportion of therapeutic compounds are derived from plant sources, with nearly 70,000 plant species recognized for their medicinal potential. The World Health Organization (WHO) has identified approximately 21,000 medicinal plants used globally for a variety of medical applications. The continued use of natural products in medicine reflects their significant influence on modern healthcare and the pharmaceutical industry (1). Pakistan, with its rich biodiversity, contributes between 4,000 to 6,000 medicinal plant species, which are increasingly being employed in alternative therapies for a broad spectrum of diseases. These plants contain various bioactive constituents, including flavonoids, alkaloids, phenols, and glycosides, which have been reported to exhibit antimicrobial, anti-inflammatory, and analgesic effects (2). Consequently, they are widely used in the treatment of ailments such as asthma and neurological disorders (3).

Perovskia abrotanoides, a plant native to the northern regions of Pakistan and the Balochistan province, is the focus of this study due to its historical use in traditional medicine. The plant has been employed to treat conditions such as typhoid fever, vomiting, headaches, toothaches, gonorrhea, atherosclerosis, liver disease, and cardiac disorders (4). Previous studies have identified various therapeutic properties of P. abrotanoides, including cytotoxic, anti-inflammatory, and anti-plasmodial activities (5). Additionally, the essential oils derived from this plant have been investigated for their chemical composition and insecticidal effects, particularly against Sitophilus oryzae and Tribolium castaneum, as well as their efficacy in protecting against ringworms, cutaneous parasites, and fungal organisms (6). Despite its long history of use, many of the therapeutic properties of P. abrotanoides remain unexplored (7).

The present study aims to investigate the pharmacological properties of the methanolic extract of P. abrotanoides, focusing on its anti-asthmatic and hepatoprotective effects. Although previous research has highlighted the plant's cytotoxic and anti-inflammatory properties, the anti-asthmatic and hepatoprotective activities have not been thoroughly examined. In this study, we evaluated the anti-asthmatic activity using a histamine-induced bronchospasm model, a well-established method for assessing bronchoprotective effects (7). Additionally, we assessed the hepatoprotective potential by inducing hepatic damage with carbon tetrachloride (CCl4) and analyzing the biochemical and histological parameters to determine the extent of liver protection provided by the extract (8). Furthermore, the study extended its scope to examine the phytotoxic, antibacterial, and anticancer activities of the methanolic extract, contributing to a

comprehensive understanding of its pharmacological profile (8).

This research seeks to fill the gap in the existing literature by providing new insights into the pharmacological effects of P. abrotanoides, particularly in the areas of asthma management and liver protection. The findings of this study could potentially lead to the development of new therapeutic agents derived from this plant, offering alternative treatment options with fewer side effects compared to conventional medications. The investigation of P. abrotanoides is particularly relevant in the context of the increasing demand for herbal medicines, driven by the limitations and adverse effects associated with allopathic drugs. As the global interest in plant-based therapeutics continues to grow, studies like this one are essential to validate the efficacy and safety of medicinal plants, paving the way for their integration into modern healthcare practices (9).

MATERIAL AND METHODS

The plant Perovskia abrotanoides was collected in June from Hanna Urak in the Balochistan city of Quetta. The identification of the plant was confirmed by Dr. Mansoor Ahmad at the Research Institute of Pharmaceutical Sciences, Department of Pharmacognosy, Faculty of Pharmacy, University of Karachi, with a voucher specimen number M-195. To prepare the methanolic extract, the collected plants were washed, dried at room temperature (25°C) for ten days, and subsequently ground into a coarse powder using a grinder. This powder was stored in an airtight container until extraction. The extraction process involved maceration, where the powdered plant material was immersed in 99.9% methanol and periodically shaken and stirred for five days. Following filtration through Whatman filter paper, the methanol was evaporated using a rotary evaporator at 40°C, yielding a dark greenish semi-solid residue.

Phytochemical screening was conducted on the methanolic extract to identify various bioactive compounds. The presence of alkaloids was confirmed by dissolving 2g of the methanolic extract in 5ml of 2N HCl, filtering the solution, and adding Wagner and Mayer's reagents, which resulted in the formation of precipitates indicating alkaloids. Saponins were detected by diluting 50mg of the extract in 20ml of distilled water and shaking it for 15 minutes, which led to the formation of a 2cm thick foam. Flavonoids were identified by treating the extract with sodium hydroxide, which produced a bright yellow color that turned colorless upon the addition of diluted acid. The presence of glycosides was confirmed by mixing 3ml of glacial acetic acid, one drop of 5% ferric chloride, and 2ml of the extract, followed by the addition of concentrated sulfuric acid, which resulted in a blue coloration in the acetic acid layer. Tannins were detected by mixing the extract with a 1% gelatin solution containing sodium chloride, resulting in the formation of a white precipitate. Finally, terpenoids were identified by mixing the extract with chloroform and concentrated sulfuric acid, leading to the formation of a reddish-brown precipitate.

Animal studies were conducted following ethical guidelines approved by the Animal Ethics Committee of Balochistan University and in compliance with ARRIVE guidelines. Guinea pigs (500-600g) were used to assess the anti-asthmatic activity, while rabbits (1000-1400g) were employed for hepatoprotective and toxicological studies. The animals were housed in the animal facility at the Centre for Advanced Studies for Vaccinology and Biotechnology (CASVAB) under controlled conditions, including a temperature of 20ºC (±2), relative humidity of 55% (±5%), and a 12-hour light/dark cycle. A standard pellet diet was provided to all animals.

To evaluate chronic toxicity, two groups of rabbits were used. Group I served as the control and received 0.5ml/kg of normal saline orally, while Group II was treated with the methanolic extract at a dose of 30mg/kg daily for ninety days. The animals were monitored daily for clinical signs and mortality both prior to and immediately following dose administration and up to four hours before the next dose. On the 90th day, blood samples were collected using cardiac puncture and processed for biochemical analysis. The serum was separated by centrifugation and stored at -20°C until further analysis. Liver function tests, including measurements of glucose, urea, lipid profile, and creatinine levels, were performed using a standard reagent kit and an automated analyzer. A comprehensive hematological assessment, including hemoglobin, RBC count, MCV, hematocrit, MCH, total WBC count, platelet count, and MCH, was conducted using a Beckman Coulter HMX analyzer.

$$\%\ \boldsymbol{Growth\ Inhibition} = \frac{\boldsymbol{no.of\ fronds\ in\ test}}{\boldsymbol{no.of\ fronds\ in\ control}} \times \mathbf{100}$$

The anti-asthmatic activity of the methanolic extract was assessed using a histamine-induced bronchospasm model in guinea pigs. The animals were divided into three groups of six each. Group I received distilled water (5ml/kg), Group II was treated with the methanolic extract (300mg/kg), and Group III received the standard drug chlorpheniramine (1ppm). The pre-convulsive time (PCT), which is the time taken for the onset of dyspnea following histamine exposure, was recorded for each group before and after treatment. The percentage of protection provided by the treatments was calculated based on the PCT values.

For the hepatoprotective study, the rabbits were divided into three groups, each consisting of five animals. Group I received normal saline (0.5ml/kg) orally and served as the control. Group II was treated with CCl4 to induce hepatic damage and received 0.5ml/kg of distilled water followed by 0.5ml/kg of liquid paraffin (1:1) after 36 hours. Group III, which was treated with the methanolic extract, received 300mg/kg of the extract for 15 days. After the final dose of the extract, the same group was administered CCl4 (1 ± ml/kg liquid paraffin, 1:1) after a 36-hour interval. Blood samples were collected 36 hours after the last dose, and liver function tests, including measurements of direct bilirubin, total proteins, albumin, alkaline phosphatase (ALP), and SGPT levels, were conducted using an automated analyzer. Histopathological examination of liver tissues was

performed by sectioning the liver, staining the sections, and observing them under a microscope for any cellular alterations.

The antibacterial activity of the methanolic extract was evaluated using the Microplate Alamar Blue Assay (MABA) against various microorganisms, including Shigella flexenari, Bacillus subtilis, Salmonella typhi, Staphylococcus aureus, and Pseudomonas aeruginosa. Stock cultures of the organisms were maintained on agar, and nutrient broth was used to prepare inoculums. After dilution, the organisms were inoculated on soy agar petri plates, and wells were cut into the agar for the addition of the test extract. Amoxicillin was used as the standard drug, and 50% ethanol and water were kept as controls. The plates were incubated at 37°C for 24 hours, and the inhibition zones were measured to determine the antibacterial activity of the extract.

The phytotoxicity of the methanolic extract was assessed using a Lemna minor bioassay. E-medium was prepared and adjusted to pH 5.5 to 7.0. The extract was dissolved in methanol and evaporated before adding the E-medium and Lemna minor fronds. The flasks were incubated for seven days, and the percentage growth inhibition was calculated.

Anticancer activity was evaluated using Hela cells, 3T3 cells, and MU7 assays following the methodology outlined by Shafiq Ur Rahman. The methanolic extract was tested at various concentrations, and the percentage of inhibition was calculated. In all experiments, statistical analysis was performed using Dunnett's t-test, with results considered significant at $P < 0.05$ and highly significant at $P < 0.01$. This comprehensive methodology facilitated a thorough evaluation of the pharmacological properties of the methanolic extract of P. abrotanoides, allowing for a detailed assessment of its potential therapeutic applications.

RESULTS

The methanolic extract of Perovskia abrotanoides was subjected to a series of phytochemical tests, revealing the presence of several bioactive compounds. The results are summarized in Table 1. These results indicate that the methanolic extract of P. abrotanoides contains several important

Table 1: Phytochemical Tests of Methanolic Extract of P. abrotanoides

S. No.	Phytochemical Test	Result
01	Alkaloids	Absent
02	Saponins	Present
0	Flavonoids	Present
04	Tannins	Present
05	Glycosides	Absent
06	Terpenoids	Present
07	Volatile oils	Present

phytoconstituents, including saponins, flavonoids, tannins, terpenoids, and volatile oils, which are known for their therapeutic potential.

rabbits at a dose of 300 mg/kg for 90 days. Various biochemical and hematological parameters were evaluated, and the results are presented in Tables 2 and 3.

Table 2: Effect of Chronic Administration of Methanolic Extract of P. abrotanoides (300 mg/kg) on Biochemical Parameters in Rabbits

Parameter	Control (Mean ± SEM)	Drug Treated (Mean ± SEM)	Significance (P-value)
Urea (mg/dL)	77.2 ± 2.91	73.4 ± 0.81	< 0.05*
Blood Glucose (mg/dL)	100.2 ± 9.46	77.2 ± 1.16	< 0.05*
Serum Calcium (mg/dL)	Non-significant decline	Non-significant decline	Non-significant

Table 3: Effect of Chronic Administration of Methanolic Extract of P. abrotanoides (300 mg/kg) on Hematological Parameters in Rabbits

Parameter	Control (Mean ± SEM)	Drug Treated (Mean ± SEM)	Significance (P-value)
Platelet Count ($\times 10^9$/L)	321.6 ± 34.16	302.4 ± 1.37	< 0.05*

*Significant results ($P < 0.05$)

The chronic toxicity of the methanolic extract of P. abrotanoides was assessed by administering the extract to the results indicate a significant decrease in urea and random blood glucose levels in the treated group compared to the control group. However, no significant alterations were observed in serum calcium levels. The platelet count showed a significant decline in the treated group. The anti-asthmatic potential of the methanolic extract of P. abrotanoides was evaluated using a histamine-induced bronchospasm model in guinea pigs. The results are depicted in Figure 1.

The extract significantly increased the pre-convulsive time (PCT) compared to the control group, indicating a protective effect against histamine-induced bronchospasm. The observed anti-asthmatic effect was comparable to that of the standard drug chlorpheniramine.

The hepatoprotective potential of the methanolic extract of P. abrotanoides was assessed in rabbits by inducing

Table 4: Effect of Methanolic Extract of P. abrotanoides on Liver Function Tests in Rabbits

Parameter	CCl_4 Treated (Mean ± SEM)	Extract Treated (Mean ± SEM)	Significance (P-value)
Direct Bilirubin (mg/dL)	Elevated	Significantly Reduced	< 0.05*
Total Proteins (g/dL)	Reduced	Significantly Increased	< 0.01**
Albumin (g/dL)	Reduced	Significantly Increased	< 0.01**

Table 5: Effect of Methanolic Extract of P. abrotanoides on Enzyme Levels in Rabbits

Parameter	CCl_4 Treated (Mean ± SEM)	Extract Treated (Mean ± SEM)	Significance (P-value)
SGPT (U/L)	Elevated	Significantly Reduced	< 0.05*
ALP (U/L)	Elevated	Significantly Reduced	< 0.05*

*Significant results (P < 0.05), **Highly significant results (P < 0.01)

hepatotoxicity with CCl_4. Liver function tests were performed, and the results are summarized in Tables 4 and 5. The methanolic extract significantly reduced elevated levels of direct bilirubin, SGPT, and ALP while increasing the levels of total proteins and albumin in the CCl_4-treated group. These results suggest a potent hepatoprotective effect of the extract.

The phytotoxic potential of the methanolic extract was assessed using a Lemna minor bioassay. The results are presented in Table 6.

Table 6: Phytotoxicity Bioassay of Methanolic Extract of P. abrotanoides

Concentration (µg/mL)	% Growth Inhibition	Positive Control (Paraquat) (µg/mL)
10	9.09%	0.015
100	100%	0.015
1000	100%	0.015

The extract exhibited significant phytotoxicity at higher concentrations, with complete inhibition of growth observed at 100 µg/mL and 1000 µg/mL concentrations. The antibacterial activity of the methanolic extract was evaluated against several bacterial strains. The results are summarized in Table 7.

Table 7: Antibacterial Activity of Methanolic Extract of P. abrotanoides

Bacterial Strain	% Inhibition by Extract (3000 µg/mL)	% Inhibition by Standard Drug (Ofloxacin) (3000 µg/mL)
Escherichia coli	No Inhibition	92.01%
Bacillus subtilis	No Inhibition	92.74%
Shigella flexenari	No Inhibition	-
Staphylococcus aureus	81.00%	96.17%
Pseudomonas aeruginosa	21.22%	93.51%
Salmonella typhi	No Inhibition	90.78%

The methanolic extract exhibited significant antibacterial activity against Staphylococcus aureus (81%) but showed limited or no activity against other tested organisms. The anticancer potential of the methanolic extract was evaluated using Hela cells, 3T3 cells, and MU7 assays. The results are presented in Table 8.

Table 8: Anticancer Activity of Methanolic Extract of P. abrotanoides

Assay	Treatment	Concentration (mg/ml)	% Inhibition	IC50 (mg/ml ± SD)
Hela Cell Assay	Doxorubicin	30 µg/ml	73%	1.4 ± 0.2
	Methanolic Extract	30 µg/ml	0.7%	Inactive
Cytotoxicity Assay (3T3)	Cycloheximide	30 µg/ml	71%	0.85 ± 0.07
	Methanolic Extract	30 µg/ml	11%	Inactive
MU7 Assay	Doxorubicin	50 µg/ml	73.94%	0.77 ± 0.04
	Methanolic Extract	50 µg/ml	25.02%	Inactive

The methanolic extract of P. abrotanoides did not demonstrate significant anticancer activity in the assays performed, with only minimal inhibition observed and no notable cytotoxic effects.

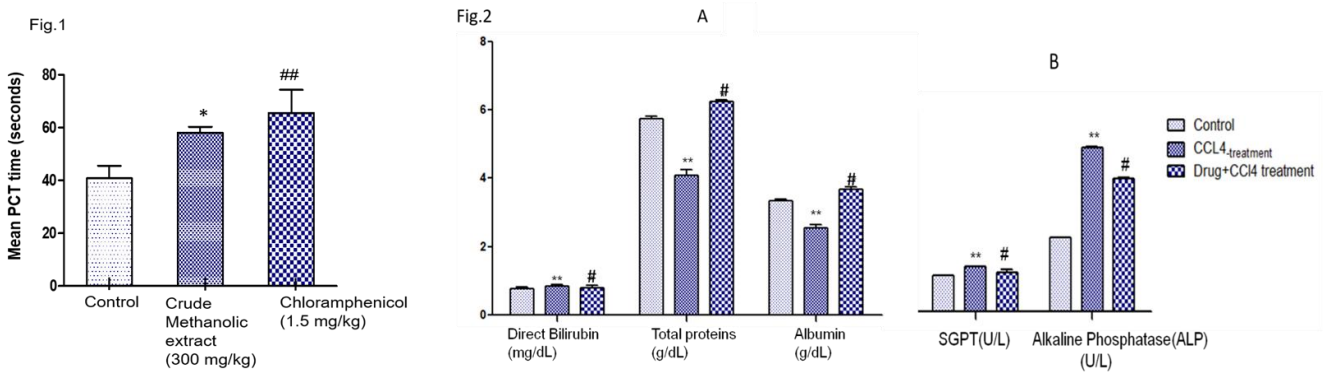

Figure 1 Assessment of anti-asthmatic activity and liver function tests of crude methanolic extract of P. abrotanoides. Values are mean ± SEM; n=5; * = P < 0.05, ** = P < 0.01

Overall, the results indicate that the methanolic extract of P. abrotanoides possesses significant hepatoprotective and anti-asthmatic properties, along with notable antibacterial and phytotoxic activities.

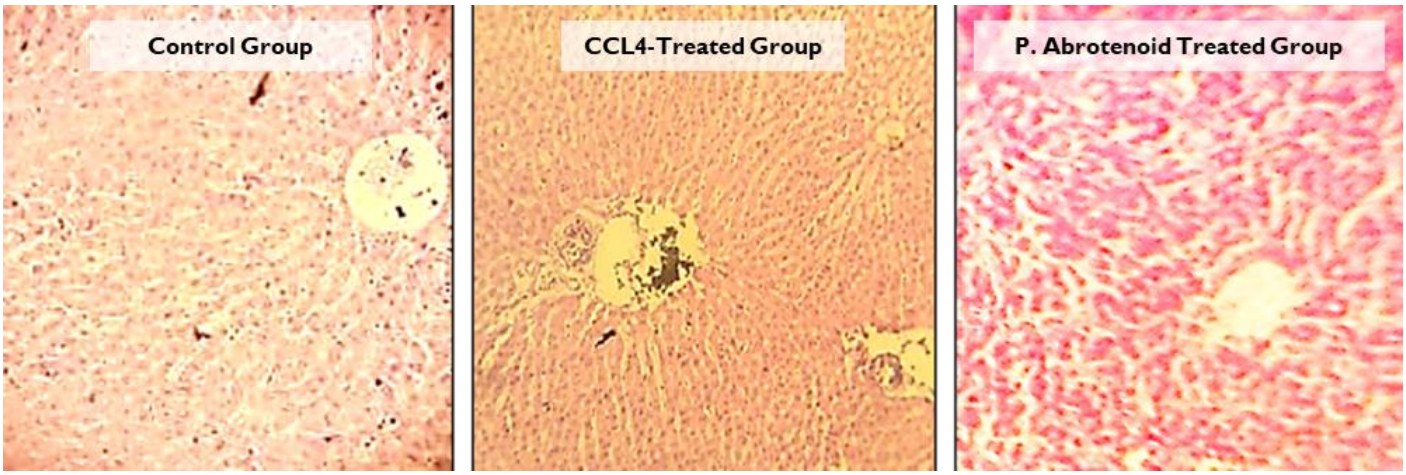

Figure 2 Photomicrograph of rabbit liver showing central vein and hepatocytes

However, the extract did not exhibit anticancer potential in the assays conducted. These findings suggest that P. abrotanoides could be a valuable candidate for the development of therapeutic agents targeting liver disorders, respiratory conditions, and bacterial infections. Further research is warranted to isolate and identify the specific bioactive compounds responsible for these effects.

DISCUSSION

The findings of this study demonstrated that the methanolic extract of Perovskia abrotanoides exhibited significant pharmacological activities, particularly in its anti-asthmatic, hepatoprotective, antibacterial, and phytotoxic effects. These results aligned with previous studies that have identified the therapeutic potential of various plant-derived compounds. The anti-asthmatic activity observed in this study was consistent with earlier research, which highlighted the role of flavonoids and other bioactive compounds in modulating inflammatory pathways and oxidative stress, key factors in asthma pathogenesis (1). The significant increase in pre-convulsive time in guinea pigs treated with the extract suggested that P. abrotanoides could offer a protective effect against bronchospasm, potentially through its antioxidant properties, which counteracted the oxidative stress known to exacerbate asthma symptoms (2).

The hepatoprotective activity of the extract was evident in the significant improvement of liver function markers in rabbits subjected to CCl_4-induced hepatotoxicity. This effect was likely due to the presence of flavonoids and terpenoids, which have been previously reported to possess hepatoprotective properties by inhibiting lipid peroxidation and stabilizing hepatic cell membranes (3). The histopathological analysis further supported this conclusion, as the extract reversed the hepatic cellular damage caused by CCl_4, restoring normal liver architecture. These findings were in line with studies that have demonstrated the protective effects of plant-derived antioxidants in liver injury models (4).

The study also revealed that the methanolic extract of P. abrotanoides had significant antibacterial activity, particularly against Staphylococcus aureus. This was consistent with prior research indicating that essential oils and other extracts from the Lamiaceae family, to which P. abrotanoides belongs, possess broad-spectrum antimicrobial properties (5). The high efficacy against Staphylococcus aureus suggested that the extract could be a promising candidate for the development of new antibacterial agents, especially in the face of rising antibiotic resistance. However, the extract's limited activity against other bacterial strains highlighted the need for further studies to identify the specific components responsible for this selective antibacterial effect.

Despite these promising results, the extract did not exhibit significant anticancer activity in the cell lines tested. This contrasted with previous findings where other species within the Lamiaceae family showed cytotoxic effects against various cancer cell lines (6). The absence of anticancer activity in P. abrotanoides might be due to the concentration of active compounds being insufficient or the specific bioactive molecules present in this species not targeting the pathways involved in cancer cell proliferation (10-1). Further research could focus on isolating individual compounds from the extract to evaluate their specific anticancer potential, possibly in combination with other therapeutic agents (6-9).

The strengths of this study included the comprehensive evaluation of multiple pharmacological activities using well-established in vivo and in vitro models. The inclusion of histopathological analysis provided a deeper understanding of the extract's hepatoprotective effects, while the phytochemical screening offered insights into the potential bioactive constituents responsible for the observed activities. However, the study also had several limitations (26-27). The exact mechanisms underlying the pharmacological effects of the extract were not fully elucidated, and the study was limited by the use of crude extract rather than isolated compounds. Additionally, the chronic toxicity assessment, although informative, did not cover long-term effects or potential toxicity at higher doses (10-17).

Future studies should aim to isolate and characterize the specific bioactive compounds within P. abrotanoides that contribute to its pharmacological activities. Investigating the molecular mechanisms involved in the anti-asthmatic and hepatoprotective effects could provide valuable insights into their therapeutic potential (15, 21). Moreover, expanding the scope of antibacterial testing to include a broader range of bacterial strains and resistance profiles could help identify the spectrum of antimicrobial activity. Given the lack of anticancer effects observed in this study, further research could explore the possibility of synergistic effects with other known anticancer agents or alternative methods of extraction to enhance the yield of potential cytotoxic compounds (18-25).

CONCLUSION

In conclusion, the methanolic extract of Perovskia abrotanoides demonstrated significant anti-asthmatic, hepatoprotective, and antibacterial activities, supporting its potential as a therapeutic agent for respiratory and hepatic disorders as well as for bacterial infections. However, the absence of anticancer activity highlighted the need for further investigation. These findings contributed to the growing body of evidence supporting the medicinal use of plant-derived compounds, while also emphasizing the importance of continued research to fully realize their therapeutic potential.

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