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RESEARCH ARTICLE

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The Effect of *Pelargonium sidoides* Extract on Penicillin-Induced Epileptic Activity

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Abstract

Objective: The aim of this study is to investigate the effects of *Pelargonium sidoides* extract on penicillin-induced epileptic activity. Epilepsy is a neurological disorder characterized by seizures due to abnormal electrical activity in the brain. *P. sidoides* is a medicinal plant known for its anti-inflammatory and antioxidant properties, making it a candidate for research into natural therapeutic alternatives. This study seeks to evaluate the potential effects of this plant on epileptiform activity, contributing to the exploration of effective options for epilepsy treatment. This study represents the first investigation into the relationship between *P. sidoides* and epileptiform activity

Methods: A total of 18 female Wistar albino rats, aged 16-20 weeks and weighing 220-350 g, were randomly divided into three groups: Control group (n=6) received intracortical penicillin-G, Vehicle group (n=6) received intracortical penicillin with physiological saline, and Experimental group (n=6) received intracortical penicillin-G combined with *P. sidoides* extract. The rats were treated daily for 10 days with physiological saline and *P. sidoides* extract at a dosage of 60 mg/kg via gavage. Last day of the experiment neuromuscular blockade was induced with urethane, and electrophysiological recordings were obtained from the cortex.

Results: Statistical analysis was performed using SPSS 15.0, and normality of the datas was confirmed for all groups using the Kolmogorov-Smirnov test. No statistically significant differences were found in average peak frequency or amplitude between the penicillin group and the *P. sidoides* group ($p>0.05$). The average peak frequency for the penicillin group was 59±1.5 spikes/min, while for the *P. sidoides* group, it was 56.3±4.3 spikes/min.

Conclusion: Although *P. sidoides* may suggest a potential influence on epileptiform activity, the results indicate that it does not provide effective or significant protection under the tested conditions. Further research is necessary to explore its therapeutic potential in the treatment of epilepsy.

Keyword: Epilepsy, *Pelargonium sidoides*, antiepileptic, electrophysiology, neuroprotection

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INTRODUCTION

Epilepsy is a complex neurological disorder characterized by seizures caused by abnormal electrical activity in the brain, which can lead to alterations in an individual's consciousness, behavior, memory, and sensory perception (1). The incidence of epilepsy varies significantly across different populations worldwide. For instance, in Asian countries, the annual incidence rate is approximately 52.5 per 100,000 person-years. It has been observed that the burden of epilepsy in Asia may be more widespread in countries like Turkey compared to China. In Asia, Turkey is reported to have the highest prevalence of active epilepsy (6.7 per 1,000 people), while China has the lowest prevalence (4.1 per 1,000 people) (2). Among the various types of epilepsy, one of the most challenging is drug-resistant epilepsy (DRE), which, according to research, occurs in approximately 13.7% of community-based populations and 36.3% of clinic-based cohorts (3). A common challenge posed by DRE is the inadequacy of current treatment options and the presence of diverse pathologies in different individuals.

Traditionally, the definition of epilepsy is based on the occurrence of two unprovoked seizures. However, international epilepsy organizations have proposed recommendations to broaden this definition for more specific cases (4). In this context, understanding the underlying mechanisms of epileptic seizures is of critical importance for developing treatment approaches and strategies. Alongside advanced therapeutic options and medications, there is an increasing interest in natural products and traditional medicine practices. Promising findings regarding the antiepileptic effects of herbal treatments have emerged in the existing literature (5).

P. sidoides is a widely used medicinal plant in traditional medicine, utilized for treating various health issues. However, there is a limited number of studies specifically investigating the effects of this plant on epilepsy. Current knowledge highlights the anti-inflammatory and antioxidant properties of *P. sidoides*, suggesting notable potential for these characteristics to influence epileptic activity (5). Furthermore, the contributions of its components to neurological protection emphasize the need for research into new and effective methods for epilepsy treatment.

The aim of this study is to investigate the effects of *P. sidoides* extract on penicillin-induced epileptic activity. The research seeks to evaluate the potential effects of *P. sidoides* on epilepsy, contributing to the exploration of natural and effective alternatives in epilepsy treatment.

METHODS

Using 18 female Wistar albino rats (aged 16 to 20 weeks, weighing 220 to 350 g), three groups were formed: (1) control group, (2) vehicle group, and (3) experimental group (n=6, for each of the three groups). First group received intracortical (ic) penicillin-G (500 IU), the second group received penicillin (ic) + physiological saline, and the experimental group received treatment with penicillin-G (500 IU) + *P. sidoides* extract. Physiological saline and *P. sidoides* extract were administered daily for 10 days via gavage at a dose of 60 mg/kg in a volume of 1 ml per 100 g. Subsequently, neuromuscular blockade was applied to the rats with urethane, and access was obtained from the skull to the cortex by drill using a screw technique, allowing for electrophysiological recordings to be taken for 2-3 hours.

Statistical Analysis

All datas were statistically analyzed using SPSS 15.0. The normality of the dataset was assessed with the Kolmogorov-Smirnov test, and it was found that all groups exhibited a normal distribution. To evaluate differences in spike frequency and amplitude across each period among the groups, One-Way ANOVA followed by a post-hoc Tukey test was employed. Furthermore, all results are expressed as means ± standard error of the mean (SEM), with $p < 0.05$ considered to indicate statistical significance.

RESULTS

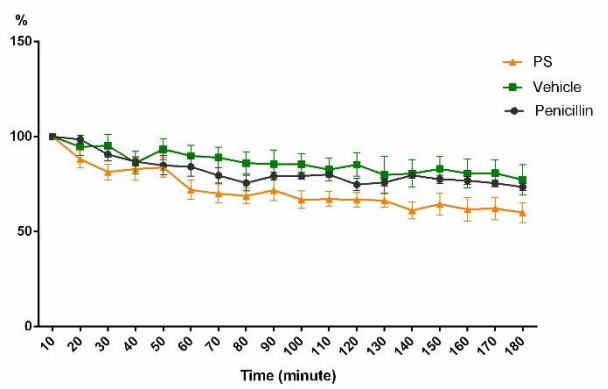

Figure 1. There was no significant difference in spike frequency between all groups. Frequency Value= 100 x The mean of spike frequency after substance administered/ The mean of spike frequency before substance administered

Our results indicate that there is no statistically significant difference in the average peak frequency between the penicillin group and the *P. sidoides* group ($p>0.05$). The average peak frequency in the penicillin group was found to be 59±1.5 spikes/min, while the average peak frequency in the *P. sidoides* group was determined to be 56.3±4.3 spikes/min (Figure 1). Another finding of our study is that there was also no significant difference in the average amplitude values among the penicillin, vehicle, and *P. sidoides* groups ($p>0.05$). These factors suggest that although *P. sidoides* may create an impression of a potential effect on epileptiform activity, it does not provide effective or significant protection under the current conditions. Figure 2 presents the representative ECoG recordings for all groups at the 90th minute: (A) Penicillin (500 IU, i.c.); (B) Vehicle group (Serum physiologic; 1 ml/100 g

p.o. for ten days); (C) *P. sidoides* (60 mg/kg p.o. for ten days).

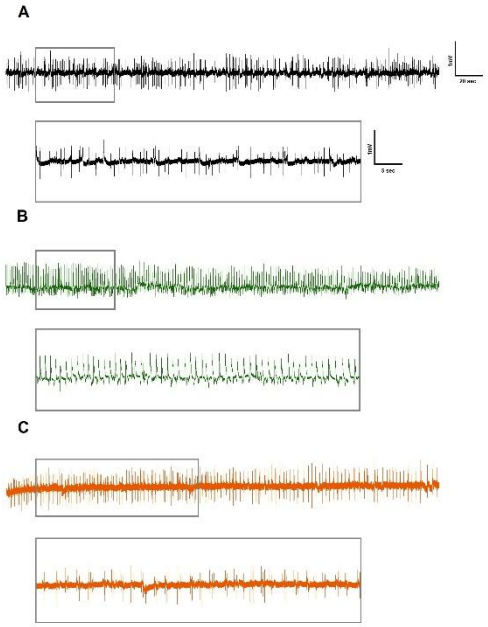

Figure 2. Representative ECoG recordings for all groups at 90th minute: (A) Penicillin (500 IU, i.c.); (B) Vehicle group (Serum physiologic; 1ml/100g p.o. for ten days); (C) Pelargonium sidoides (60mg/kg p.o. for ten days p.o.)

DISCUSSION

Epilepsy is a multifaceted neurological disorder demanding a comprehensive understanding of its etiology and effective treatment strategies. The symptomatic relief provided by antiseizure drugs (ASDs) is mediated through interactions with various cellular targets. The primary objectives of this research include the modulation of voltage-gated ion channels, the enhancement of GABA inhibition, the direct modulation of synaptic release, and the inhibition of synaptic excitation mediated by ionotropic glutamate receptors (6). The intricate mechanisms of these interactions aim to reduce the intrinsic excitability of neurons and hinder the synchronization of abnormal firing, ultimately mitigating seizure activity.

Antibiotics, specifically penicillin, have been documented to induce seizure activity due to neurotoxicity, representing one of the most thoroughly studied examples of antibiotic-induced seizures (7). GABA-evoked Cl^- currents in the context of penicillin show that penicillin blocks both postsynaptic and presynaptic inhibition mediated by GABAA receptors (8,9). This blockade may interfere with normal synaptic function, potentially exacerbating seizure susceptibility. Notably, the enhancement of GABAergic inhibition through ASDs can counteract these adverse effects, emphasizing the significance of targeting GABA receptors in seizure management.

P. sidoides, a medicinal plant known for its therapeutic properties, has garnered interest in the context of epilepsy treatment. The plant's extract exhibits anti-inflammatory and immunomodulatory effects and may influence neuronal excitability (10). Although research has shown that derivatives of *P. sidoides* can exhibit antiproliferative effects on cancer cells (11), its potential role in modulating GABAergic activity remains an area ripe for exploration. Given that penicillin-induced seizure models exhibit disruption in GABAergic transmission, it is plausible that *P. sidoides* may aid in restoring the balance of

inhibitory signaling, thereby contributing to seizure control.

Furthermore, current efforts in epilepsy research are directed toward understanding the pharmacological properties of natural products, particularly their mechanisms of action. *P. sidoides* has been observed to possess immunomodulatory activity (5), which may also play a role in managing inflammation-related seizure activity. Investigating the interaction of *P. sidoides* with GABA receptors could provide insights into its therapeutic potential for epilepsy.

In a recent study, we demonstrated that *P. sidoides* inhibits cell proliferation, induces apoptosis by increasing oxidative stress and genotoxicity, and thereby promotes cancer cell death in a neuroblastoma cancer cell line (12). This study may identify a pathway of *P. Sidoides* that could potentially be effective in epilepsy.

Despite being a traditional remedy, the scientific evaluation of *P. sidoides* has highlighted the need for well-designed clinical studies to confirm its efficacy and safety profile. The lack of comprehensive datas on its toxicological properties necessitates thorough investigation, especially given its increasing popularity in modern medical systems in Europe. The potential of *P. sidoides*-based products as alternative therapies could address the urgent need for safer and more effective treatment options, especially in the context of drug-resistant epilepsy or in individuals who are reluctant to use chemical medications as alternatives to antiseizure drugs.

This study has several limitations, including a small sample size of 18 rats, which may affect the generalizability of the findings. Additionally, the focus on a single dosage and treatment duration of *P. sidoides* may not adequately capture its therapeutic potential. Furthermore, the study did not investigate the underlying mechanisms of action, and additional research in diverse seizure models is needed to validate the results and assess safety and efficacy.

CONCLUSION

In conclusion, the exploration of *P. sidoides* as an adjunctive treatment for epilepsy, especially in penicillin-induced seizure models, warrants further research. Understanding its interactions with GABAergic systems could unveil new therapeutic pathways for managing epilepsy, providing hope for patients who are not well-controlled by conventional ASDs. However, the potential toxicological effects and optimal dosing of *P. sidoides* must also be thoroughly investigated to ensure safety and efficacy. Integrating traditional knowledge with modern pharmacological research may lead to innovative treatment strategies that enhance the quality of life for individuals living with epilepsy.

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REFERENCES

1. Huff JS, Murr NI. Seizure. [Updated 2023 Feb 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430765/
2. Safeer VSM, Sahu JK, Madaan P, Winter S F, Baker GA, Bansal D. Estimating the active and lifetime prevalence and incidence of epilepsy in Asian Countries: A systematic review and meta-analysis. Epilepsy & behavior: E&B, 2024;154: 109739.
3. Sultana B, Panzini M A, Veilleux Carpentier A, Comtois J, Rioux B, Gore G. et al. Incidence and Prevalence of Drug-Resistant Epilepsy: A Systematic Review and Meta-analysis. Neurology, 2021;96(17):805–817. https://doi.org/10.1212/WNL.0000000000011839
4. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE., et. Al.ILAE official report: a practical clinical definition of epilepsy. Epilepsia, 2014;55(4): 475–482. https://doi.org/10.1111/epi.12550
5. Moyo M, Van Staden J. (2014). Medicinal properties and conservation of Pelargonium sidoides DC. Journal of Ethnopharmacology, 2014;152(2):243–255. https://doi.org/10.1016/j.jep.2014.01.009
6. Rogawski M A, Loscher W, Rho JM. Mechanisms of Action of Antiseizure Drugs and the Ketogenic Diet. Cold Spring Harbor Perspectives in Medicine, 2016;6(5):a022780.
7. Wallace KL. Antibiotic-induced convulsions. Critical Care Clinics, 1997;13(4): 741–762.
8. Katayama N, Tokutomi N, Nabekura J, Akaike N. Penicillin-induced triphasic modulation of GABAA receptor-operated chloride current in frog sensory neuron. Brain Research, 1992;595(2):249–255.
9. Yamamoto S, Yoshimura M, Shin MC, Wakita M, Nonaka K, Akaike N. GABA (A) receptor-mediated presynaptic inhibition on glutamatergic transmission. Brain Research Bulletin. 2011;84(1):22–30.

https://doi.org/10.1016/j.brainresbull.2010.10.007

10. Papies J, Emanuel J, Heinemann N, Kulić Ž, Schroeder S, Tenner B, et. al. Antiviral and Immunomodulatory Effects of Pelargonium sidoides DC. Root Extract EPs® 7630 in SARS-CoV-2-Infected Human Lung Cells. Frontiers in pharmacology, 2021;12:757666. https://doi.org/10.3389/fphar.2021.757666
11. Pereira A, Bester M, Soundy P, Apostolides Z. Anti-proliferative properties of commercial Pelargonium sidoides tincture, with cell-cycle G0/G1 arrest and apoptosis in Jurkat leukaemia cells. Pharmaceutical biology, 2016;54(9):1831–1840.
12. Aslan A, Seçme M. Effects of Pelargonium Sidoides Extract on Apoptosis and Oxidative Stress in Human Neuroblastoma Cells. Medicina (Kaunas, Lithuania), 2024;60(12):2110 https://doi.org/10.3390/medicina60122110