RESEARCH PAPER

Evaluation of Anti Epileptic Activity of Datura metel (Linn.) Leaves Against Maximal Electroshock and Isoniazid Induced Seizures in Mice

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Received: 28th Feb, 2026 | **Revised:** 14th Mar, 2026 | **Accepted:** 4th Apr, 2026 | **Available Online:** 20th Apr, 2026

ABSTRACT

The present report is an investigation of antiepileptic activity of Datura metel Linn. It is a well-known plant which is used in Indian traditional medicine for Asthma, Rheumatism, Tumors, Cough, Fever, Antimicrobials and Epilepsy. The aqueous extract of Datura metel were subjected to acute toxicity studies and then screened for antiepileptic activity by maximal electroshock (MES) and isoniazid (INH) induced seizures in albino mice. Acute toxicity studies of extract were toxic up to recommended dose 2000 mg/kg body weight orally as per OECD guidelines no.423. Animals were treated with aqueous extract of 200, 400 and 600 mg/kg body weight. Phenytoin was used as reference anticonvulsant drugs for comparison. The study reported the significant delay in clonic seizure induced by INH and dose dependent decrease in duration of hind leg extensor phase in MES model. In MES model, Datura metel showed significant reduction in duration of hind limb extension with 400 mg/kg dose and 600 mg/kg. Similar dose dependent results were obtained in PTZ model by delayed the onset of clonic convulsions. Aqueous extract of Datura metel showed anticonvulsant activity against MES and INH animal models. The aqueous extract of Datura metel deserves further investigation for detailed elucidation of active constituents and the mechanisms of action.

Keywords: Antiepileptic activity, Datura metel, Phenytoin, Maximal electroshock, Isoniazid.

How to cite this article: Pathak S, Alok K, Patel AK, Vishwakarma R, Singh VP, Pandey AK. Evaluation of Anti Epileptic Activity of Datura metel (Linn.) Leaves Against Maximal Electroshock and Isoniazid Induced Seizures in Mice. Int J Drug Deliv Technol. 2026;16(30s):863-870. DOI: 10.25258/ijddt.16.30s.86

Source of support: Nil.

Conflict of interest: The authors declare no conflict of interest.

Introduction:

Epilepsy is a relatively common neurological disorder. The term epilepsy is collectively designated for a group of chronic central nervous system (CNS) disorder characterized by spontaneous occurrence of seizures generally associated with the loss of consciousness and body movements (convulsion).[1] Epilepsy is often defined as the occurrence of at least two unprovoked seizures separated 24 hours apart but the latest international consensus definition only requires a single epileptic seizure as long as there is an enduring predisposition to generate epileptic seizures.[2] Many of the etiological factors leading to a first epileptic seizure in the elderly cause an enduring predisposition to seizures. There annual incidence of 50/100,000 per year. Approximately 5-10% of the population will have at least one seizure, with the highest incidence occurring in early childhood and late adulthood.[3] WHO estimates that eight people per 1000 worldwide have this disease. Over half of the 50 million people with epilepsy worldwide are estimated to live in Asia. Approximately, 85% of people affected with epilepsy live in developing countries. Accurately 60% of all epilepsies are idiopathic or cryptogenic.[4] It is estimated that there are 55, 00,000 persons with epilepsy in India, 20, 00,000 in USA and 3,00,000 in UK. The annual economic burden of epilepsy in India is 88.2%.[5], [6] Epilepsy is slightly more common in men as compare to

women because estrogen has a seizure-activating effect, whereas progesterone exerts a seizure protective effect.[7] Seizures occur because a group of cortical neurons discharge abnormally in synchrony. The neuronal membrane potential is regulated by an accurate balance between excitatory postsynaptic potential (EPSP) and inhibitory postsynaptic potential (IPSP). If this balance is compromised an epileptic seizure can be generated.[8] A test commonly used to diagnose epilepsy is called an electroencephalogram (EEG). The doctor may also request a brain scan by using magnetic resonance imaging (MRI), computed tomography (CT) and positron emission tomography (PET) scan in order to see structures inside the brain. Bromide was introduced in 1857 for treating epilepsy and Phenobarbital in 1912.[9], [10] Subsequently many other anticonvulsants were discovered. Carbamazepine and valproate are normally used in the treatment of epilepsy but can cause a lot of adverse effect, now most preferred drug are phenytoin and GABA analogue.[11], [12]

Datura is mentioned in all the ancient scriptures of Ayurveda. In ancient flora it is used in the treatment of spasmodic asthma, fever with catarrhal symptoms, anesthetic cough and convulsion.[13] It grows in waste lands, along the roadside, gardens and railway lines, and in scrub, jungles throughout the tropical parts of India. *D.metel* can grow in very alkaline soil but is unable to grow in the shade.[14] A coarse, shrubby annual with large flower, 0.9-1.2 m high, alternate dark green leaves grows throughout India. The plant as a whole has narcotic, leaves are used as a local application for rheumatic swellings of the joints, lumbago, sciatica, neuralgia, and painful tumours. Seeds are used externally for piles.[15] Scopolamine has analgesic and sedative actions and produce amnesia. It also has anti-inflammatory and anti-nociceptive property. It is acrid, anti-hyperglycemic, hypolipidemic and antimycotic. Aqueous extract are reported to be used in the treatment of gastric pains and indigestion and may be useful for the treatment of organophosphate poisoning.[16] Several herbal medicines constitute a potentially important avenue leading to novel therapeutic agent for epilepsy that may not only prevent but also be safe, inexpensive, highly tolerated and convenient for many patients.[17] Every year a lot of plants from traditional medicinal system have been screened for their potential antiepileptic activity but only few of them are included in health care system after clinical research.[18]

MATERIALS AND METHODS

Plant collection

Fresh leaves of *Datura metel* Linn used for the study was collected from the waste lands, along the road side and bank of Ganges River of Varanasi district, Uttar Pradesh during August 2012. The sample drug has been identified and Authenticated by Dr. K. N. Dubey at Banaras Hindu University, Varanasi. The voucher specimen of the plant was deposited at the college for further reference.

Preparation of extract

Leaves were separated from other parts of the plant and stored in polythene bag. The Leaves was air dried in shade. The size were reduced and made to coarse powder and then further passed through the appropriate sieve number to obtain uniform particle size.[19] Dried powder was extracted by using water in Soxhlet apparatus. Coarse powdered was packed in soxhlet column with water at boiling point. Temperature was maintained at the level of boiling point and time taken approximate 18-19 hr, until the leaves was colourless. The extracts were concentrated on water bath and were kept in desiccators.[20]

Preliminary Phytochemical screening

The phytochemical examination of the aqueous extract of *Datura metel* was performed by the standard methods.[21]

Animals used

Albino male mice (20-30g) were purchased from Jamia Hamdard animal house, New Delhi. The animals were maintained in a well-ventilated room with 12:12 hour light/dark cycle in polypropylene cages.[22] The animals were fed with standard pellet feed and water was given ad libitum. Ethical committee clearance was obtained from Institutional Animal Ethics Committee (IAEC) of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA). All test animals are allowed free access to food and water ad libitum, both being withdrawn just prior to experimentation.[23], [24]

Drugs and Chemicals

Phenytoin was obtained as a gift sample from Akum Drugs and Pharmaceutical Company, Haridwar. Fresh drug solutions were prepared on each day of the experiments. Drugs were administered intraperitoneally (i.p.) in a volume of 2 ml/100 g of animal.[25] Control animals received equal volume of injections of the appropriate vehicle. The doses and pretreatment times

of the extract of the Leaves of *Datura metel* and the standard antiepileptic drugs used were obtained from preliminary studies in our laboratory. The pretreatment dose and the times following the administration of either isoniazid (300 mg/kg, s.c.) were *Datura metel* extract (200, 400 and 600 mg/kg, i.p.), and phenytoin (25 mg/kg,i.p.).[26]

Acute Toxicity Study

Toxicity is the degree to which a substance is able to damage an exposed organism. In screening drugs, determination of LD50 (the dose which has proved to be lethal to 50% of the tested group of animals) is usually an initial step in the assessment and evaluation of the toxic characteristics of a substance.[27] The acute toxicity of aqueous extract of *Datura metel* was determined as per the OECD guideline no. 423 (Acute Toxic Class Method). It was observed that the test extract was toxic even at 2000mg/kg dose. Hence, $1/10^{th}$ (200mg/kg), $1/5^{th}$ (400mg/kg) and another dose (600mg/kg) of this dose were selected for further study.[28]

ANTIEPILEPTIC ACTIVITY

Effect on Maximal electroshock (MES) induced seizures

Vehicle control mice developed tonic flexion of the limb followed by tonic extension of hind limb (THLE) after the MES test.[29], [30] There was significant ($P<0.05$ and $P<0.001$) and dose dependent reduction in duration of convulsion in mice treated with *Datura mettel*(400 mg/kg) as compare to vehicle control mice.[31] It also significantly and dose dependently ($P<0.05$ and $P<0.01$) attenuated incidence of convulsion induced after MES test. Mice treated with *Datura metel* significantly decreased the mortality induced after MES test.[32] Mice treated with phenytoin (25 mg/kg) significantly decreased duration of THLE as well as MES induced mortality and incidence of convulsion in mice as compare to vehicle control mice.[33]

Effect on Isoniazid (INH) induced seizures

Isoniazid (300 mg/kg s.c.) elicited tonic-clonic convulsions followed by THLE and mortality in mice. Mice treated with test drug significantly delayed onset of convulsion as compared to INH control mice. There was significant reduction in the duration of clonic and tonic convulsion in test drug treated mice as compared to INH treated mice.[34] Test drug treated mice showed significant reduction in convulsion as compared to INH treated mice[35]. Mice treated with test drug (200mg/kg) failed to produce any significant reduction in tonic convulsion as compared to INH treated mice.[36]

Statistical analysis

The results of this study were expressed as mean ± standard error of mean (mean±SEM). The significance of differences among the groups was assessed by using one way ANOVA and followed by Dunnet's test. Significance is established when probability value (p value) is less than 0.05. P values are denoted as $*P<0.05$ as significant, $**P<0.01$ as highly significant and $***P<0.001$ as very highly significant.

RESULTS

Phytochemical screening

The results of preliminary phytochemical screening of the aqueous extract of *Datura metel* revealed that presence of alkaloids, glycosides, tannins, terpeniods, phenols, amino acids and absence of steroids, flavonoids and carbohydrates.

Effects of Datura metel on MES Induced Epilepsy

The duration of tonic hind limb extension in mice treated with vehicle was 11±0.73 seconds. The *Datura metel* at doses of 400 mg/kg were protect animals from seizures and significantly ($p<0.01$) reduced the duration of tonic hind limb extension (Fig-1). Whereas, the standard drug phenytoin treated animals exhibits abolished tonic hind limb extension.[37] Phenytoin treated animals have shown 83.33% protection against MES induced seizures where as *Datura metel* 600 mg/kg have shown 50% protection respectively (Table-1).

Effect of Datura metel on INH Induced Epilepsy

Isoniazid (300 mg/kg s.c.) elicited tonic-clonic convulsions followed by THLE and mortality in mice. Mice treated with *Datura metel* significantly delayed ($P < 0.05$ and $P < 0.001$ respectively) onset of convulsion as compared to INH control mice (Fig-2). There was significant reduction in the duration of clonic and tonic convulsion ($P < 0.05$ and $P < 0.01$ respectively) in 400 and 600 mg/kg treated mice as compared to INH control mice (Fig-3). *Datura metel* (600mg/kg) treated mice showed significant reduction ($P < 0.05$) in tonic convulsion as compared to INH treated mice.[38] Mice treated with *Datura metel* (200mg/kg) failed to produce

any significant reduction in clonic-tonic convulsion as compared to INH control mice. As depicted in table 2, treatment with *Datura metel* (200mg/kg) significantly protect (P <0.05 and P < 0.001 respectively) against convulsions induced by single dose of INH as compared to INH control mice.

Table-1: Effect of aqueous extract of *Datura metel* on Maximum electroconvulsive shock (MES) induced seizures in mice

S. No.	Treatment		Time (sec) in various phases of convulsion (MEAN±SEM)					
1.	Drug	Dose (mg/kg)	Flexon	Extension	Clonus	Stuper	No. of animals convulsed	% of Animals Protected
2.	Normal Saline + MES	2 ml/100g	3±0.36	11±0.73	12.5±0.76	30.5±12.5	6/6	0
3.	Phenytoin + MES	25	0	0	11±0.57	0	1/6	83.33
4.	Test drug + MES	200	2.5±0.42**	11.16±0.98**	12.83±0.7 NS	35.16±6.5*	4/6	33.33
		400	0.83±0.4 NS	1.83±1.16 NS	4.6±2.3*	23.83±16.9 NS	4/6	33.33
		600	2.5±0.76**	16.16±2**	9.8±2 NS	20.33±18.5 NS	3/6	50

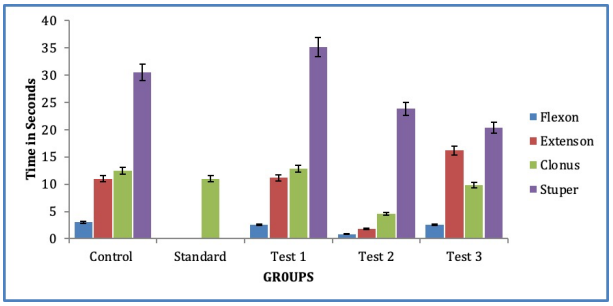
Values are expressed as mean ± SEM by using one way ANOVA and followed by Dunnet's test.
n=6, *P<0.05, **P<0.01, ***P<0.001, NS-not significant

Table-2: Effect of aqueous extract of *Datura metel* on isoniazid (INH) induced seizures in mice

S. No.	Treatment		Time (sec) in various phases of convulsion (MEAN±SEM)				
1.	Drug	Dose (mg/kg)	Latency	Tonic	Clonic	No. of animals convulsed	% of Animals Protected
2.	Normal Saline + INH	2 ml/100g + 300	139.83±8.1	3.16±0.4	4±0.5	6/6	0
3.	Phenytoin + INH	5 + 300	0	0	0	0/6	100
4.	Test drug + INH	200 + 300	133.8±9.9**	2.83±.60**	1.3±0.2 NS	4/6	33.33
		400 + 300	172.5±4.7**	1.16±0.3 NS	1.5±0.4 NS	3/6	50
		600 + 300	147.6±7.2**	3±0.3**	4±0.5**	1/6	83.33

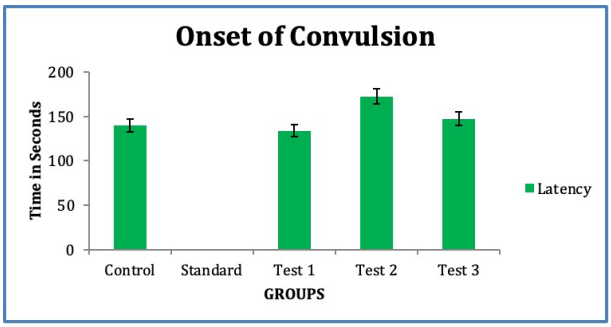
Values are expressed as mean ± SEM by using one way ANOVA and followed by Dunnet's test.
n=6, *P<0.05, **P<0.01, ***P<0.001, NS-not significant

Fig-1: Effect of aqueous extract of *Datura metel* Linn. on Maximal electroconvulsion shock (MES) induced seizures in mice.



Values are expressed as mean ± SEM by using one way ANOVA and followed by Dunnet's test.
n=6, *P<0.05, **P<0.01, ***P<0.001, NS-not significant

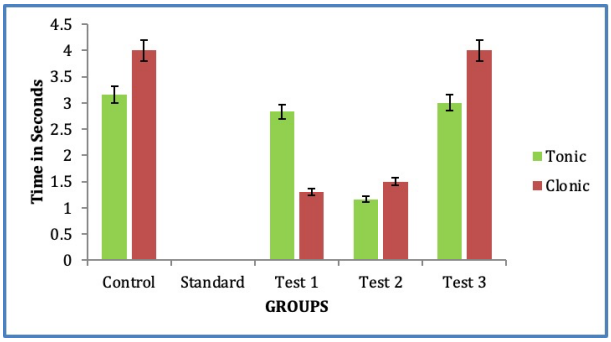
Fig- 2: Effect of aqueous extract of *Datura metel* Linn. on Isoniazid (INH) induced seizures in mice.



Values are expressed as mean ± SEM by using one way ANOVA and followed by Dunnet's test.

n=6, *P<0.05, **P<0.01, ***P<0.001, NS-not significant

Fig- 3: Effect of aqueous extract of *Datura metel* Linn. on Isoniazid (INH) induced seizures in mice.



Values are expressed as mean ± SEM by using one way ANOVA and followed by Dunnet's test.

n=6, *P<0.05, **P<0.01, ***P<0.001, NS-not significant

DISCUSSIONS AND CONCLUSIONS

Currently available antiepileptic drugs are able to efficiently control epileptic seizures in about 50% of the patient, another 25% may shoe improvement, whereas the remaining 25% of antiepileptic drugs do not benefit significantly.[39] Furthermore, undesirable side effect from the drugs used clinically often render treatment difficult so that a demand for new types of antiepileptic exists. One of the approaches to search for new antiepileptic drugs is to investigate the naturally occurring compounds, which may belong to new structural classes.[40] In the present study, for the screening of aqueous extract of *Datura metel* for antiepileptic activity, two standard methods namely maximal electroshock (MES) and Isoniazid (INH) methods have been used.[41] In traditional medicine system, many plants and herbs claimed to have antiepileptic activity without any scientific basis. The aim of the present study was to carry phytochemical investigation and evaluation of putative antiepileptic activity of leaves of *Datura metel.* The parameters observed were the duration of tonic hind limb flexion, tonic hind limb extension, clonus, stupor and incidence of recovery and death. MES method has a high degree of productivity for drugs useful in the management of tonic- clonic seizures in man. The second group of mice received a subcutaneous injection of isoniazid (300mg/kg). Isoniazid is used widely for the treatment and chemoprophylaxis of Tuberculosis, but can have serious effect on the central nervous system causing seizures and comas. The factor responsible for INH-induced epileptic seizures is the decreased of GABA below the critical level in some neurons. Phenytoin treated group showed 100% protection of the animals. INH-induced epileptic seizures in mice significantly delayed the onset of seizures. The test group treated showed protection of the animals from convulsion. The induction of seizure with isoniazid (INH) results from the action of pyridoxine.[42] The precipitating mechanism of seizure is not exactly known but it may relate to INH-induced pyridoxine deficiency.

In conclusion the result of the present study revealed significant antiepileptic potential of the aqueous extract of *Datura metel.* At a dose of 400 and 600 mg/kg body weight, the test drug has shown statistically significant anticonvulsant effect against both MES and INH convulsions.[43] It is therefore possible that antiepileptic activity of the plant may be exerted by the various Phytoconstituents present in the plant i.e. alkaloids, flavonoids, steroids, tannins, glycosides, triterpenes, protein and amino acid and justify its use as a traditional folk remedy for central nervous system related activities. However, further studies are necessary to ascertain its clinical effectiveness and the mechanism of action of the extract and its active compound.[44]

REFERENCE:

[1] P. Pandey *et al.*, "Identification of Datura metel phytochemicals as potential EGFR inhibitors in lung cancer," *Sci. Rep.*, vol. 15, no. 1, Dec. 2025, doi: 10.1038/s41598-025-23982-0.

[2] B. L. Rajbongshi and A. K. Mukherjee, "Drugs from poisonous plants: Ethnopharmacological relevance to modern perspectives.," *Toxicon X*,

vol. 25, p. 100215, Mar. 2025, doi: 10.1016/j.toxcx.2025.100215.

[3] M. Asif *et al.*, "Synthesis and Characterization of Chemically and Green-Synthesized Silver Oxide Particles for Evaluation of Antiviral and Anticancer Activity.," *Pharmaceuticals (Basel).*, vol. 17, no. 7, Jul. 2024, doi: 10.3390/ph17070908.

[4] H. Khalid *et al.*, "Computer-assisted discovery of natural inhibitors for platelet-derived growth factor alpha as novel therapeutics for thyroid cancer.," *Front. Pharmacol.*, vol. 15, p. 1512864, 2024, doi: 10.3389/fphar.2024.1512864.

[5] T. C. M. L. Rodrigues *et al.*, "Multi-target Phenylpropanoids Against Epilepsy," *Curr. Neuropharmacol.*, vol. 22, no. 13, pp. 2168–2190, Jun. 2024, doi: 10.2174/1570159x22666240524160126.

[6] J. Liu, A. R. Sternberg, S. Ghiasvand, and Y. Berdichevsky, "Epilepsy-on-a-chip system for antiepileptic drug discovery," *IEEE Trans. Biomed. Eng.*, vol. 66, no. 5, pp. 1231–1241, May 2019, doi: 10.1109/TBME.2018.2871415.

[7] W. Tahir, S. M. Fatima, S. F. Moin, M. Moin, and H. Waheed, "Datura alba seed proteins effect on snake venom enzymes with antioxidant and antibacterial activities.," *J. Taibah Univ. Med. Sci.*, vol. 20, no. 1, pp. 81–88, Feb. 2025, doi: 10.1016/j.jtumed.2025.01.005.

[8] Y. Gao *et al.*, "Discovery of Novel Antiepileptic Agents Targeting the α1β2γ2 GABAAReceptor," *J. Med. Chem.*, vol. 68, no. 16, pp. 17971–17989, Aug. 2025, doi: 10.1021/acs.jmedchem.5c01770.

[9] K. K. Borowicz-Reutt and M. Banach, "Acute and chronic treatment with moclobemide, a reversible MAO-inhibitor, potentiates the antielectroshock activity of conventional antiepileptic drugs in mice," *Pharmacol. Biochem. Behav.*, vol. 201, Feb. 2021, doi: 10.1016/j.pbb.2021.173110.

[10] T. C. M. L. Rodrigues *et al.*, "Epileptic Targets and Drugs: A Mini-Review," *Curr. Drug Targets*, vol. 24, no. 3, pp. 212–224, Sep. 2022, doi: 10.2174/1389450123666220927103715.

[11] Y. Cheng *et al.*, "Integrated serum metabolomics and network pharmacology approach to reveal the potential mechanisms of withanolides from the leaves of Datura metel L. on psoriasis," *J. Pharm. Biomed. Anal.*, vol. 186, Jul. 2020, doi: 10.1016/j.jpba.2020.113277.

[12] R. Guo, Y. Liu, Z. P. Xu, Y. G. Xia, B. Y. Yang, and H. X. Kuang, "Withanolides from the leaves of Datura metel L.," *Phytochemistry*, vol. 155, pp. 136–146, Nov. 2018, doi: 10.1016/j.phytochem.2018.08.005.

[13] X. Ji *et al.*, "Investigating potential molecular mechanisms of antiepileptic drug-induced depression through network toxicology and molecular docking," *Neuroscience*, vol. 577, pp. 25–36, Jun. 2025, doi: 10.1016/j.neuroscience.2025.05.015.

[14] Y. Su, F. Zhang, L. Wu, H. Kuang, Q. Wang, and G. Cheng, "Total withanolides ameliorates imiquimod-induced psoriasis-like skin inflammation," *J. Ethnopharmacol.*, vol. 285, Mar. 2022, doi: 10.1016/j.jep.2021.114895.

[15] C. L. Bellera and A. Talevi, "Quantitative structure–activity relationship models for compounds with anticonvulsant activity," *Expert Opin. Drug Discov.*, vol. 14, no. 7, pp. 653–665, 2019, doi: 10.1080/17460441.2019.1613368.

[16] X. Sang, H. Bi, X. Si, Y. Wang, X. Shi, and F. Wu, "Efficacy of extracts from Datura Metel L. for Psoriasis: a meta-analysis of case series and single-arm studies," *BMC Complement. Med. Ther.*, vol. 23, no. 1, Dec. 2023, doi: 10.1186/s12906-023-04159-6.

[17] N. Y. Khalil, H. K. AlRabiah, S. S. AL Rashoud, A. Bari, and T. A. Wani, "Topiramate: Comprehensive profile," *Profiles Drug Subst. Excipients Relat. Methodol.*, vol. 44, pp. 333–378, Jan. 2019, doi: 10.1016/bs.podrm.2018.11.005.

[18] W. Alam, H. Khan, S. A. Khan, S. Nazir, and E. K. Akkol, "Datura metel: A Review on Chemical Constituents, Traditional Uses and Pharmacological Activities," *Curr. Pharm. Des.*, vol. 27, no. 22, pp. 2545–2557, May 2020, doi: 10.2174/1381612826666200519113752.

[19] T. Islam *et al.*, "Ethnobotanical uses and phytochemical, biological, and toxicological profiles of Datura metel L.: A review," *Curr. Res. Toxicol.*, vol. 4, Jan. 2023, doi:

10.1016/j.crtox.2023.100106.

[20] Y. Zeng *et al.*, "Ilepcimide inhibited sodium channel activity in mouse hippocampal neurons," *Epilepsy Res.*, vol. 170, Feb. 2021, doi: 10.1016/j.eplepsyres.2020.106533.

[21] J. Li *et al.*, "Three New α-Pyrone Derivatives with Antiepileptic Activity from the Marine Actinomycete Nocardiopsis sp. NBUDK19," *Mar. Biotechnol.*, vol. 27, no. 3, Jun. 2025, doi: 10.1007/s10126-025-10462-9.

[22] M. Inaji and T. Maehara, "[Initial Management of Status Epilepticus].," *No Shinkei Geka.*, vol. 51, no. 6, pp. 1069–1077, Nov. 2023, doi: 10.11477/mf.1436204853.

[23] K. Socała *et al.*, "Effect of Tadalafil on Seizure Threshold and Activity of Antiepileptic Drugs in Three Acute Seizure Tests in Mice," *Neurotox. Res.*, vol. 34, no. 3, pp. 333–346, Oct. 2018, doi: 10.1007/s12640-018-9876-4.

[24] A. U. Khan *et al.*, "Awareness and current knowledge of epilepsy," *Metab. Brain Dis.*, vol. 35, no. 1, pp. 45–63, Jan. 2020, doi: 10.1007/s11011-019-00494-1.

[25] M. Maguire, "Epilepsy and music: Practical notes," *Pract. Neurol.*, vol. 17, no. 2, pp. 86–95, Apr. 2017, doi: 10.1136/practneurol-2016-001487.

[26] U. Geronzi, F. Lotti, and S. Grosso, "Oxidative stress in epilepsy," *Expert Rev. Neurother.*, vol. 18, no. 5, pp. 427–434, May 2018, doi: 10.1080/14737175.2018.1465410.

[27] S. A. Hamed, "The effect of antiepileptic drugs on the kidney function and structure," *Expert Rev. Clin. Pharmacol.*, vol. 10, no. 9, pp. 993–1006, Sep. 2017, doi: 10.1080/17512433.2017.1353418.

[28] H. B. Newton and J. Wojkowski, "Antiepileptic Strategies for Patients with Primary and Metastatic Brain Tumors," *Curr. Treat. Options Oncol.*, vol. 25, no. 3, pp. 389–403, Mar. 2024, doi: 10.1007/s11864-024-01182-8.

[29] Z. Soleimani Meigoni, F. Jabari, M. Motaghinejad, and M. Motevalian, "Protective effects of forced exercise against topiramate-induced cognition impairment and enhancement of its antiepileptic activity: molecular and behavioral evidences," *Int. J. Neurosci.*, vol. 132, no. 12, pp. 1198–1209, 2022, doi: 10.1080/00207454.2021.1873979.

[30] K. K. Borowicz-Reutt, M. Popławska, M. Banach, and D. Wróblewska, "Influence of propafenone on the anticonvulsant activity of various novel antiepileptic drugs in the mouse maximal electroshock model," *Pharmacol. Reports*, vol. 70, no. 3, pp. 481–487, Jun. 2018, doi: 10.1016/j.pharep.2017.11.014.

[31] S. Carsten and S. Erwin-Josef, "Antiepileptic effects of cobalt, manganese and magnesium on bicuculline-induced epileptiform activity in hippocampal neurons," *Brain Res.*, vol. 1732, Apr. 2020, doi: 10.1016/j.brainres.2020.146684.

[32] X. Gao *et al.*, "Rapid antiepileptic activity identification of isopimpinellin using a multi-model of epilepsy based on behavior-biomarker-BBB screening pipeline," *Phytomedicine*, vol. 150, Jan. 2026, doi: 10.1016/j.phymed.2025.157636.

[33] A. Tokariev *et al.*, "Impact of In Utero Exposure to Antiepileptic Drugs on Neonatal Brain Function," *Cereb. Cortex*, vol. 32, no. 11, pp. 2385–2397, Jun. 2022, doi: 10.1093/cercor/bhab338.

[34] A. A. Shukralla, E. Dolan, and N. Delanty, "Acetazolamide: Old drug, new evidence?," *Epilepsia Open*, vol. 7, no. 3, pp. 378–392, Sep. 2022, doi: 10.1002/epi4.12619.

[35] M. Tomić, U. Pecikoza, A. Micov, S. Vučković, and R. Stepanović-Petrović, "Antiepileptic drugs as analgesics/adjuvants in inflammatory pain: current preclinical evidence," *Pharmacol. Ther.*, vol. 192, pp. 42–64, Dec. 2018, doi: 10.1016/j.pharmthera.2018.06.002.

[36] S.-J. Wang, M.-Y. Zhao, P.-C. Zhao, W. Zhang, and G.-W. Rao, "Research Status, Synthesis and Clinical Application of Antiepileptic Drugs," *Curr. Med. Chem.*, vol. 31, no. 4, pp. 410–452, Jan. 2023, doi: 10.2174/0929867330666230117160632.

[37] Y. Gao, H. Yan, R. Jin, and P. Lei, "Antiepileptic activity of total triterpenes isolated from Poria cocos is mediated by suppression of aspartic and glutamic acids in the brain," *Pharm. Biol.*, vol. 54, no. 11, pp. 2528–2535, Nov. 2016, doi: 10.3109/13880209.2016.1168853.

[38] D. Nieoczym, K. Socała, P. Jedziniak, E. Wyska, and P. Wlaź, "Effect of Pterostilbene, a Natural Analog of Resveratrol, on the Activity

of some Antiepileptic Drugs in the Acute Seizure Tests in Mice," *Neurotox. Res.*, vol. 36, no. 4, pp. 859–869, Nov. 2019, doi: 10.1007/s12640-019-00021-1.

[39] X. Wang *et al.*, "A Novel Compound QO-83 Alleviates Acute and Chronic Epileptic Seizures in Rodents by Modulating KV7 Channel Activity," *CNS Neurosci. Ther.*, vol. 31, no. 3, Mar. 2025, doi: 10.1111/cns.70334.

[40] S. M. Manchishi, "Recent Advances in Antiepileptic Herbal Medicine," *Curr. Neuropharmacol.*, vol. 16, no. 1, May 2017, doi: 10.2174/1570159x15666170518151809.

[41] S. S. S. Manna, "Dual effects of anandamide in the antiepileptic activity of diazepam in pentylenetetrazole-induced seizures in mice," *Behav. Pharmacol.*, vol. 33, no. 8, pp. 527–541, Dec. 2022, doi: 10.1097/FBP.0000000000000700.

[42] J. K. Salminen, T. L. J. Tammela, A. Auvinen, and T. J. Murtola, "Antiepileptic drugs with histone deacetylase inhibition activity and prostate cancer risk: a population-based case–control study," *Cancer Causes Control*, vol. 27, no. 5, pp. 637–645, May 2016, doi: 10.1007/s10552-016-0737-2.

[43] Y. Ito *et al.*, "Antiepileptic Drugs Modulate Alzheimer-Related Tau Aggregation in a Neuronal Activity-Independent Manner," *Dement. Geriatr. Cogn. Disord.*, vol. 52, no. 2, pp. 108–116, Jun. 2023, doi: 10.1159/000529915.

[44] G. Gupta *et al.*, "Aqueous extract of wood ear mushroom, auricularia polytricha (Agaricomycetes), demonstrated antiepileptic activity against seizure induced by maximal electroshock and isoniazid in experimental animals," *Int. J. Med. Mushrooms*, vol. 21, no. 1, pp. 29–35, 2019, doi: 10.1615/IntJMedMushrooms.2018029113.