**Supplementary Table 1**. Summary of anticonvulsant effect(s) of plant extracts and purified drugs isolated from plant material in different rodent models of seizures/epilepsy.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Species** | **Drug/**  **extract studied**  (active dose, route of administration, pretreatment time) | **Model**  **of seizures/epilepsy** | **EEG recording** | **Behavioral measure**  **of convulsions** | **Other findings** | **Suggested mechanism of anticonvulsant action** | **Ref.** |
| *Berberis sp.* | berberine  (20 mg/kg; ip;  30 min) | PTZ-induced seizure test in mice | – | ***NS*** latency and duration of myoclonic jerks  ***NS*** occurrence of seizure  ***NS***  mortality | – | – | (Bhutada et al., 2010) |
| MES test in mice | – | **** HLTE duration  **** HLTE occurrence  **** mortality | – | – |
| KA-induced seizure test in mice | – | **** latency to tonic-clonic seizures  **** mortality | – | – |
| berberine  (5 mg/kg; ip;  30 min) | PTZ-induced seizure test in mice | – | ***NS*** seizure occurrence |  |  | (Shanbhag et al., 1970) |
| MES test in mice | – | ***NS*** seizure occurrence | – | – |
| berberine  (400 mg/kg; ip; 30 min) | PTZ-induced seizure test in rats | – | ***NS*** MCS occurrence  ****latency to MCS  ***NS*** GTCS occurrence  ****latency to GTCS  ***NS*** mortality | – | – | (Sadeghnia et al., 2011) |
| berberine  (50-200 mg/kg; ip; 40 min) | 4-AP-induced seizure model in rats | – | **** latency to the generalized seizures | **** aspartate release from hippocampus  **** glutamate release from hippocampus | due to reduction of the excitatory (aspartate and glutamate) neurotransmission | (Sadeghnia et al., 2017) |
| berberine  (50-100 mg/kg;  ip; daily, for 1 week before KA-injection) | KA-induced temporal lobe epilepsy in rats | – | **** seizure severity within 24 h  **** number of spontaneous seizures after 2 weeks | **** hippocampal nitrite level  **** hippocampal MDA level | at least partially due to the antioxidant activity | (Mojarad and Roghani, 2014) |
| berberine  (25-50 mg/kg; po; daily; 1 week before KA administration and 1 week after KA administration) | KA-induced temporal lobe epilepsy in rats | – | **** incidence rate of status epilepticus during first 24 h after KA injection  **** occurrence of spontaneous recurrent seizures at 6th week after KA tretment | **** reactive oxygen species, caspase 3 in hippocampus  **** GSH, Nrf2, heme oygenase 1 level, catalase activityin hippocampus  **** NFκB, toll-like receptor 4, TNF-α, IL-1b in hippocampus  **** degeneration and neuronal loss in CA3 region of hippocampus  **** mossy fiber sprouting in CA3 region of hippocampus | due to suppression of oxidative stress, neuroinflammation and apoptosis processess | (Sedaghat et al., 2017) |
| berberine  (25-100 mg/kg; ig; once daily, 7 days before PILO administration) | PILO-induced temporal lobe epilepsy in rats | – | **** latency to the first seizure  **** time to SE  **** percentage of SE  **** mortality | ***NS*** superoxide dismutase activity in hippocampus  **** catalase, glutathione level in hippocampus  **** lipid peroxidation in hippocampus  **** degeneration of neurons in CA1 region of hippocampus  **** memory impairments 2 weeks after pilocarpine-induced SE | due to antioxidant properties | (Gao et al., 2014) |
| methanolic extract from *B. integerrima* roots  (140-200 mg/kg; ip; 30 min) | PTZ-induced seizure test in mice | – | **** HLTE latency  ***NS*** mortality after 30 min and 24 h | – | – | (Hosseinzadeh et al., 2013) |
| methanolic extract from *B. integerrima* roots  (200 mg/kg; ip; 30 min) | MES test in mice | – | **** HLTE occurrence  ***NS*** HLTE duration  ***NS*** mortality after 30 min and 24 h | – | – |
| chloroform fraction of methanolic extract from *B. integerrima* roots  (200 mg/kg; ip; 30 min) | PTZ-induced seizure test in mice | – | **** HLTE latency  ***NS*** mortality after 30 min and 24 h | – | – |
| MES test in mice | – | ***NS*** HLTE occurrence  ***NS*** HLTE duration  ***NS*** mortality after 30 min and 24 h | – | – |
| hydromethanolic fraction of methanolic extract from *B. integerrima* roots  (200 mg/kg; ip; 30 min) | PTZ-induced seizure test in mice | – | **** HLTE latency  **** mortality after 30 min  ***NS*** mortality after 24 h | – | – |
| MES test in mice | – | ***NS*** HLTE occurrence  ***NS*** HLTE duration  ***NS*** mortality after 30 min and 24 h | – | – |
|  | hydroalcoholic extract from *B. vulgaris* (400 mg/kg; ip; 30 min) | PTZ-induced seizure test in rats | – |  latency to the onset of seizures  rate of mortality**** | – | – | (Khosravi Dehaghi et al., 2017) |
|  | methanol fraction of hydroalcoholic extract from *B. vulgaris* (200 mg/kg; ip; 30 min) | – |  latency to the onset of seizures  rate of mortality**** | – | – |
| *Cannabis sativa* | CBD  (ip; 60 min) | MES test in mice | – | ED50 = 80 mg/kg  (95% CI = 65.5‐96.0) | – | – | (Patra et al., 2019) |
| CBD  (ip; 2 h) | MES test in mice | – | ED50 = 83.5 mg/kg  (95% CI = 68‐101) | – |  | (Klein et al., 2017) |
| CBD  (20-200 ng/mouse; icv; 10 min) | MES test in mice | – | ****seizure occurrence | * paxilline (potassium BK channel blocker) does not affect anticonvulsant action | – | (Shirazi-zand et al., 2013) |
| CBD  (50-100 mg/kg; ip; 60 min) | MEST test in mice | – | ****seizure threshold | – | partially due to interaction with TRPV1 receptors | (Gray and Whalley, 2020) |
| CBD  (100 mg/kg; ip; 60 min) | MEST test in TRPV1 knockout mice | – | ****seizure threshold | – |
| CBD  (ip; 60 min) | sc PTZ test in mice | – | ED50 = 120 mg/kg  (95% CI = 98.5‐146) | – | – | (Patra et al., 2019) |
| CBD  (ip; 2 h) | sc PTZ test in mice | – | ED50 = 159 mg/kg  (95% CI = 102‐225) |  |  | (Klein et al., 2017) |
| CBD  (60 mg/kg; ip; 30 min) | sc PTZ test in mice | – | **** seizure latency  **** seizure duration |  |  | (Vilela et al., 2017) |
| CBD  (60 mg/kg; ip; 30 min) | ip PTZ test in mice | **** latency to first seizure  **** total seizure duration | **** seizure latency  **** seizure duration | **** IL-6 level in PFC vs. vehicle+PTZ-treated group  ***NS*** IL-6 level in PFC vs. vehicle+PTZ-treated group  ***NS*** IL-2,IL-4, IL-10, IL-17, TNF-α, IFN-γ level in PFC and HIP vs. vehicle+PTZ-treated group   * CB1, CB2 and TRPV1 receptor antagonists (i.e., AM251, AM630 and SB366771, respectively) reversed anticonvulsant effect | Due to indirect  CB1 and CB2 receptor facilitation and TRPV1 channel desensitization |
| CBD  (60 mg/kg; ip; 30 min) | iv PTZ test in mice | – | **** threshold for the forelimb clonus |  |  |
| CBD  (200 ng/mouse; icv; 10 min) | iv PTZ test in mice | – | ***NS*** myoclonic and clonic seizure threshold  ****tonic seizure threshold | Co-administration of paxilline (potassium BK channel blocker) and CBD attenuated its anticonvulsant effect | part due to the decrease in intracellular Ca levels that is likely mediated by BK channels | (Shirazi-zand et al., 2013) |
| CBD  (60 mg/kg; ip; every other day; 30 min before each PTZ injection) | PTZ-induced kindling in mice | – | ****kindling progression | – | – | (Vilela et al., 2017) |
| CBD  (ip; 60 min) | 6 Hz test (32 mA) in mice | – | ED50 = 144 mg/kg  (95% CI = 102‐194) | – | – | (Patra et al., 2019) |
| CBD  (ip; 60 min) | 6 Hz test (44 mA) in mice | – | ED50 = 173 mg/kg  (95% CI = 136‐213) | – | – |
| CBD  (ip; 2 h) | 6 Hz test (44 mA) in mice | – | ED50 = 164 mg/kg  (95% CI = 124‐200) | – | – | (Klein et al., 2017) |
| CBD  (ip; 60 min) | Corneal  kindled mice | – | ED50 = 115 mg/kg  (95% CI = 77.5‐169) | – | – | (Patra et al., 2019) |
| CBD  (ip; 2 h) | Corneal  kindled mice | – | ED50 = 119 mg/kg  (95% CI = 89‐150) |  |  | (Klein et al., 2017) |
| CBD  (ip; 60 min) | MES test in rats | – | ED50 = 53.2 mg/kg  (95% CI = 39.1‐67) | – | – | (Patra et al., 2019) |
| CBD  (ip; 2 h) | MES test in rats | – | ED50 = 88.9 mg/kg  (95% CI = 69‐124) | – | – | (Klein et al., 2017) |
| CBD  (10 mg/kg; iv; 60 min) | PILO‐induced status epilepticus rat model | – | **** maximum seizure severity | – | – | (Patra et al., 2019) |
| CBD  (200 mg/kg; po; 8 weeks) | RISE‐SRS model of TLE in rats | – | **** seizure burden ratio | **** motor comorbidities  **** reference memory and working memory | – |
| CBD  (10-30 mg/kg; ip; 15 min) | Cocaine-induced seizure test in mice | – | **** seizure latency  **** seizure duration | – | – | (Vilela et al., 2015) |
| CBD  (15-90 mg/kg; ip; 30 min) | Cocaine-induced seizure test in mice | – | **** seizure duration  **** seizure latency (only 30 mg/kg) | **** glutamate release in hippocampal synaptosomes   * neither CB1 receptor antagonist (i.e., AM251) nor the CB2 receptor antagonist (i.e., AM630) revert anticonvulsant effect; * mTOR inhibitor (i.e., rapamycin) reversed anticonvulsant effect | due to activation of mTOR with subsequent reduction in glutamate release | (Gobira et al., 2015) |
| CBD  (100-200 mg/kg; ip; 60 min) | Scn1a+/- mice  (Dravet syndrome model) | – | **** seizure duration and severity  **** spontaneous seizures frequency | **** autistic-like social deficits  **** GABAA receptor-mediated inhibition  **** excitation/inhibition ratio  **** action potential firing of excitatory neurons | due to the inhibition of the lipid-activated G protein-coupled receptor GPR55 | (Kaplan et al., 2017) |
| CBD  (100-300 mg/kg; ip; 2h) | Lamotrigine-resistant amygdala kindled rat | – | no effect | – | – | (Klein et al., 2017) |
| CBD (25/mg/kg; po; 60 min) | repeated 6 Hz corneal stimulation test | ***NS*** duration of the ictal ECoG recordings  ***NS*** changes in power band spectrum | ***NS*** GTCS occurrence | ***NS*** FosB/∆FosB immunoreactivity in the l CA1 region of HIP and in the subiculum | – | (Costa et al., 2021) |
| CBN  (150 mg/kg; po; 30 min) | iv PTZ test in mice | – | ***NS*** threshold for clonic seizures | – | – | (Chesher and Jackson, 1974) |
| CBN  (50-200 mg/kg; po; 60, 120, 180, 240 min) | MES test in mice | – | ***NS*** HLTE duration | – | – |
| LN;  (350 mg/kg; ip; 30 min) | sc NMDA-induced seizures in mice | – | **** clonic seizure latency  ***NS*** clonic seizure occurrence | – | – | (Elisabetsky et al., 1999) |
| LN  (15-30 mM; icv; 5 min) | Quinolinic acid-induced seizures in mice | – | **** clonic seizure occurrence | – | – |
| LN  (2.2-2.5 g/kg; po; 30 min; 6 injections every third day) | PTZ-induced kindling in mice | – | **** % of convulsions > 3 s  **** kindling progression | ***NS*** L-[3H]glutamate binding to cortex membranes | – |
| LN (ip; 30 min) | sc PTZ test in mice | – | ***NS*** clonic seizure occurrence | ****anticonvulsant effect of diazepam and valproic acid | – | (Elisabetsky and Brum, 2003) |
| MES test in mice | – | ***NS*** HLTE occurrence | ****anticonvulsant effect of phenytoin and valproic acid | – |
| THC;  (1-80 mg/kg; po; 30 min) | iv PTZ test in mice | – | ***NS*** threshold for clonic seizures | – | – | (Chesher and Jackson, 1974) |
| THC;  (5-10 mg/kg; ip; 15 min) | Cocaine-induced seizure test in mice | – | **** seizure latency  **** seizure duration | * CB1 and CB2 antagonists (i.e., AM251 and AM630, respectively) did not abolish anticonvulsant effect * Combination of CB1 and CB2 antagonists at high doses attenuated anticonvulsant effect | Restoration of glycine receptor dysfunction | (Zou et al., 2020) |
| THC  (0.1-0.3 mg/kg; ip; 30 min) | hypertherrmia-induced acute seizures in Scn1a+/- mice (Dravet syndrome model) | – | **** threshold temperature for GTCS | – | – | (Anderson et al., 2020) |
| THC  (10-28.5 mg/kg/day; sub-chronic supplementation in chow) | hypertherrmia-induced spontaneous seizures in Scn1a+/- mice (Dravet syndrome model) | – | ***NS*** occurrence of spontaneoushypertherrmia-induced GTCS  ***NS*** frequency of spontaneoushypertherrmia-induced GTCS  ***NS*** mortality | – | – |
| CBD + THC  (0.1 mg/kg + 12 mg/kg; ip; 30 min) | hypertherrmia-induced acute seizures in Scn1a+/- mice (Dravet syndrome model) | – | **** threshold temperature for GTCS | – | – |
| CBD + THC  (500 mg/kg/day + 10 mg/kg/day; sub-chronic supplementation in chow) | hypertherrmia-induced spontaneous seizures in Scn1a+/- mice (Dravet syndrome model) | – | ***NS*** spontaneoushypertherrmia-induced GTCS occurrence  ***NS*** spontaneoushypertherrmia-induced GTCS frequency  **** seizure severity and mortality | – | – |  |
| CBD + THC  (50 mg/kg + 50 mg/kg; po; 120 min) | MES test in mice | – | ***NS*** HLTE duration | – | – | (Chesher and Jackson, 1974) |
| CBD + CBN  (50 mg/kg + 50 mg/kg; po; 120 min) | MES test in mice | – | ***NS*** HLTE duration | – | – |
| CBN + THC  (50 mg/kg + 50 mg/kg; po; 120 min) | MES test in mice | – | ***NS*** HLTE duration | – | – |
| CBN + CBD + THC  (50 mg/kg + 50 mg/kg + 50 mg/kg; po; 120 min) | MES test in mice | – | ****HLTE duration | – | – |
| *C. sativa* oil without volatile components  (at CBD dose of 25/mg/kg; po; 60 min) | Repeated 6 Hz corneal stimulation test | ***NS*** duration of the ictal ECoG recordings  ***NS*** changes in power band spectrum | **** GTCS occurrence | ***NS*** FosB/∆FosB immunoreactivity in the l CA1 region of HIP and in the subiculum | – | (Costa et al., 2021) |
|  | *C. sativa* oil with volatile components;  (at CBD dose of 25/mg/kg; po; 60 min) | Repeated 6 Hz corneal stimulation test | ***NS*** duration of the ictal ECoG recordings  ****power of delta rhythm  ****power of theta rhythm | **** GTCS occurrence | ***NS*** FosB/∆FosB immunoreactivity in the l CA1 region of HIP  **** FosB/∆FosB immunoreactivity in the subiculum | – |
| *Curcuma longa* | curcumin  (100-200 mg/kg; po; 3 days prior to PILO administration) | Lithium-PILO-induced SE in rats | – | ****seizure latency  ****seizure occurrence  ****SE latency  ****mortality | ****SE-iduced cognitive dysunctions  ****lipid peroxidation content in HIP and straitum  ****GSH level in HIP and striatum | – | (Ahmad, 2013) |
| curcumin  (50-200 mg/kg; po; 60 min) | PTZ-induced kindling in mice | – | ****kindling progression | ****malenodialdehyde level in brain  ****glutatione level in brain | – | (Agarwal et al., 2011) |
| curcumin  (80 mg/kg; po; 45 min) | iv PTZ test in mice | – | ***NS*** threshold for myoclonic and generalized clonic seizures  ****threshold for tonic seizures | * Anticonvulsant effect prevented by revented by non-selective adenosine receptor antagonist (i.e., 8-phenyltheophylline) and adenosine A1 receptor antagonist (i.e., 8-cyclopentyl-1,3-dipropylxanthine) but not by adenosine A 2A receptor antagonist (i.e., -(3-cholorostryl)caffeine); * Anticonvulsant action potentiated by non-selective A 1 /A 2 receptor agonist (i.e, 5′-N-ethylcarboxamidoadenosine) and adenosine A1 receptor agonist (N6 –cyclohexyladenosine) but not by adenosine A2A receptor agonist (i.e.,5′-(N-cyclopropyl) carboxamidoadenosine) | direct or indirect activation of adenosine A1 receptor | (Akula and Kulkarni, 2014) |
| curcumin  (150 mg/kg; ip; 25 min) | iv PTZ test in mice | – | **** seizure latency  ****latency to tonic-clonic seizure  ****duration of tonic and tonic-clonic seizures****  ***NS*** mortality, falling** | ****HTR7 receptor mRNA expression   * 5-HT1A, 5-HT2C and 5-HT4 antagonists diminished anticonvulsant effect * 5-HT7 antagonist strengthen anticonvulsant effect | By increasing the serotonin levels in the brain that influence receptors, including 5-HT1A, 5-HT2C, and 5-HT4 and  likely through the reduction of 5-HT7 gene expression | (Arbabi Jahan et al., 2018) |
| curcumin  (300 mg/kg; po; 60 min) | *ip* PTZ test in rats | – | ****myoclonic jerk latency  50% protection againstGTCS occurrence | **** MDA level in the brain  ****GSH level in brain | – | (Reeta et al., 2011) |
| curcumin  (300 mg/kg; po; 60 min) | MES test in rats | – | 33% protection against HLTE | **** MDA level in the brain  ****GSH level in brain   * anti-convulsant activity of sub-therapeutic doses of valproate, phenytoin, phenobarbitone and carbamazepine in rats | – | (Reeta et al., 2011) |
| α,β-turmerone  (50 mg/kg; iv; 10 min) | iv PTZ test in mice | – | ****threshold for ear twitch, myoclonic twitch, tail twitch  ****threshold for forelimb clonus  ****threshold for falling  ****threshold for HLTE  ****threshold for death | – | – | (Orellana-Paucar et al., 2012) |
| ar-turmerone (100 mg/kg; iv; 10 min) | iv PTZ test in mice | – | ****threshold for ear twitch, myoclonic twitch, tail twitch  ****threshold for forelimb clonus  ****threshold for falling  ****threshold for death | – | – |
| ar-turmerone  (1 and 20 mg/kg; iv; 10 min) | iv PTZ test in mice | – | ****threshold for HLTE  (only 1 mg/kg)  ****threshold for death | ***NS*** motor function/balance | – | (Orellana-Paucar et al., 2013) |
| ar-turmerone  (0.1-50 mg/kg; ip; 30 min) | 6 Hz psychomotor seizure test in mice | – | **** seizure occurrence**** | – | – |
| ar-turmerone (50 mg/kg; ip; 24 h) | – | **** seizure occurrence | – | – |
| aqueous extract of *Curcuma longa*;  (ip; at 14-16 postnatal day) | ip PTZ test in mice | – | ****latency to first seizure | – | – | (Sharma and Rauniar, 2016) |
| aqueous extract of *Curcuma longa*;  (200 mg/kg; po; daily by 21 days) | MES test in mice | – | ****duration of HLTE | – | – |
| *Curcuma longa* oil  (50-100 mg/kg; iv; 10 min) | iv PTZ test in mice | – | ****threshold for ear twitch, myoclonic twitch, tail twitch  ****threshold for forelimb clonus  ****threshold for falling (only 100 mg/kg)  ****threshold for HLTE (only 100 mg/kg)  ****threshold for death | – | – | (Orellana-Paucar et al., 2012) |
| *Indigofera arrecta* | methanol extract from aerial part of *I. arrecta* (250-1000 mg/kg; ip; 30 min) | sc PTZ test in mice | – | ****seizure latency  ***NS*** seizure occurrence  ***NS*** mortality | – | – | (Adejoke et al., 2020) |
| Indirubin (2-10 mg/kg; ip; 30 min) | 6 Hz-induced seizure test | \_ | ****number of mice protected | – | glycogen synthase kinase (GSK)-3 inhibition | (Aourz et al., 2019) |
| Indirubin (2-10 mg/kg; ip; 30 min) | iv PTZ test in mice | – | ***NS*** seizure threshold for myoclonic twitch, forelimb clonus, falling, tonic hindlimb extension and death | ­– |
| Indirubin (2-10 mg/kg, ip; 30 min) | PILO-induced seizures in rats | ­– | ****seizure severity | ­– |
| *Magnolia officinalis* | magnolol  (40-80 mg/kg; ip; 30 min) | ip PTZ test in mice | **** seizure latency  **** total number of seizure spikes | **** myoclonic jerk latency  **** generalized clonus latency  ****seizure severity | **** *c-fos* expression in the HIP and priform cortexx   * selective GABAA/benzodiazepine antagonist (i.e. flumazenil) abolished anticonvulsant effect | mediated by the GABAA/benzodiazepine receptor complex | (Chen et al., 2011) |
| honokiol  (1-5 mg/kg; ip; 30 min) | NMDA-induced seizures in mice | – | **** threshold for rrunning and bouncing clonic seizures  **** HLTE threshold (5mg/kg) | – | – | (Lin et al., 2005) |
| honokiol  (1mg/kg/day; po; for 2 constitutive days before the seizure test) | NMDA-induced seizures in mice | – | **** generalized seizure occurrence  **** generalized seizure latency  ****seizure score | ****NMDA-induced motor impairment  **** reactive oxigen species formulation in the brain structures  **** synaptosomal Na, K-ATPase nad Mg2+-ATPace activity | – | (Chang-Mu et al., 2010) |
| *Magnolia officinalis extract* (as vegetable capsules; 300 mg/kg; po; every 24 h for 10 days after the last KA treatment) | KA-induced recurrent SE in immature rats. | **** afterdischarge threshold  **** relative power of delta, theta, alpha, gamma bands  **** relative power of beta band | **** seizure intensity | **** NeunN-immunoreactive neurons in the dorsal HIP | – | (Vega-García et al., 2019) |
| ethanol extract of the Magnolia dealbata leaves(300 mg/kg; ip; 30 min) | ip PTZ test in mice | – | ***NS***myoclonus latency  **** clonus latency  **** tonus latency | – | – | (Martínez et al., 2006) |
| ethanol extract of the Magnolia dealbata leaves (300 mg/kg; po; 30 min) | – | ****myoclonus latency  **** clonus latency  **** tonus latency | – | – |
| *Moringa oleifera* | *Moringa oleifera* seed ethanol extract (2 g/kg; ig; 30 min; for 14 days) | ip PTZ test in mice | – | ****mortality | ****GABA concentration in HIP  ****glutamate concentration in HIP  ****expression ofGAD65 and α1 subunit off GABAA receptor in HIP  ***NS*** expression of GAD67 and γ2subunit of GABAA receptor | GABAergic system activation | (Liu et al., 2022) |
| kaempferol  (2 mg/kg; ig; 30 min; for 14 days) | – | ****mortality |
|  | naringenin  (200 mg/kg; ip; 30 min) | MES test in mice | – | ****HLTE duration | – | – | (Khodayar et al., 2016) |
| ip PTZ test in mice | – | ****seizure latency****  ****Straub’s tail latency  ****myoclonic seizure duration (200 mg/kg) | – | – |
| naringenin  (100 mg/kg; ip; daily injection for 8 days starting the day before KA injection) | KA-induced seizure model in mice | – | ****seizure latency | **** granule cell dispersion in the dentate gyrus  **** mammalian target of rapamycin complex 1 (mTORC1) activation in the dentale gyrus  **** TNFα and IL-1β expression in the dentale gyrus | – | (Park et al., 2016) |
| naringenin  (20-80 mg/kg; ip; by 7 days before PTZ administration) | ip PTZ test in mice | – | ****myoclonic jerks latency  ****GTCS latency (dose 80 mg/kg completely abolished GTCS)  **** GTCS duration | **** PTZ-induced cognitive impairment  ****GSH level in the brain  **** MDA level in the brain  **** TNF-alpha level in the brain | – | (Golechha et al., 2014) |
| naringenin (20-40 mg/kg; po; or 15 days) | PILO-induced seizure in mice | – | ****seizure severity  **s**eizure latency | ****SOD and CAT activity  **** lipid peroxidation  ****Glutathione reductase level   * neurons morphology improvement in Histologic examination of hippocampal sections |  | (Shakeel et al., 2017) |
|  | NRG-DM  (6.25-25 mg/kg; ip; 30 min) | iv PTZ test in mice | – | ****tail twitch, falling and HLTE threshold (12.5 mg/kg)  ****threshold for death | – | – | (Copmans et al., 2018) |
| 6 Hz test in mice | – | ****psychomotor seizure occurrence  ****psychomotor****seizure duration (6.25 mg/kg) | – | – |
|  | pterostilbene  (100-200 mg/kg; ip; 30 min) | iv PTZ test in mice | – | ****threshold for the first myoclonic twitch  ****threshold for GTCS  ****threshold for forelimb tonus | – | – | (Nieoczym et al., 2019) |
| MEST test in mice | – | ****HLTE threshold | – | – |
| 6 Hz-induced psychomotor seizure threshold test in mice | – | ****psychomotor seizure threshold | – | – |
| pterostilbene  (200 mg/kg; ip; 30 min) | PTZ kindling in mice | – | ****seizure severity  **** kindling progression | **** GABA concentration in PFC and HIP  ***NS*** glutamate concentration in PFC and HIP |  | (Nieoczym et al., 2021) |
| *Solanum torvum* | methanolic extract from *Solanum torvum* seeds  (10-100 mg/kg; ip; 30 min) | ip PTZ test in mice | – | ****Straub's tail latency  ****extensor latency (10-30 mg/kg)  ****myoclonic jerk latency  ****clonic convulsion latency  ****stupor latency (10 and 100 mg/kg) | – | facilitation of GABAergic transmission | (Momin and Mohan, 2011) |
| *Zingiber purpureum* | banglene (50/50 ratio of trans-banglene and cis-banglene) | ip PTZ test in mice | – | ****seizure score  ****mortality | – | – | (Brillatz et al., 2020) |
| *Zingiber officinale* | hydroethanolic extract from *Zingiber oficinale* roots  (25-100 mg/kg; ip; 2 and 24 h) | iv PTZ test in mice | – | **** first myoclonic seizure threshold  **** generalized clonic seizure threshold (100 mg/kg and 50 mg/kg with 24 h pretreatment)  **** forelimb tonic extension threshold (50 and 100 mg/kg with 2 h pretreatment; 25-100 mg/kg with 24 h pretreatment) | – | – | (Hosseini and Mirazi, 2014, 2015) |
| hydroethanolic extract from *Zingiber oficinale* roots  (25-100 mg/kg; ip; daily for 7 days) | iv PTZ test in mice | – | **** first myoclonic seizure threshold  **** generalized clonic seizure threshold (50-100 mg/kg)  **** forelimb tonic extension threshold (50-100 mg/kg) | – | – |
| essential oil of *Z. officinale*  (50-100 mg/kg; ip; daily for 7 days; 30 min) | PILO-induced seizures in mice | – | ****seizure latency  ***NS*** mortality | – | – | (Felipe et al., 2008) |
| hydroalcoholic extract of *Z. officinale*  (100 mg/kg; ip; daily for 10 days before kindling procedure onset and then administration 60 min before each PTZ injection) | PTZ-induced kindling in mice | – | ****seizure severity  ****myoclonic jerk latency  ****generalized tonic-clonic seizure latency  ****generalized tonic-clonic seizure duration | ****NeuN expressing neurons (i.e., mature neurons) in CA3 region of HIP  ****astrocyte activation in CA3 region of HIP | – | (Naeimi et al., 2018) |

4-AP – 4-aminopyridine; CBD – cannabidiol; CBDVA ­– cannabidivarinic acid; CBGA – cannabigerolic acid; CBGVA – cannabigerovarinic  
acid; CBN – cannabinol; CI – confidence interval; GSH – glutathione; GTCS – generalized tonic-clonic seizures; HIP – hippocampus; HLTE – hindlimb tonic extension; ip – intraperitoneally; iv – intravenous; KA – kainic acid; KFD – kaempferide (4'-*O*-methyl kaempferol); KFL – kaempferol; LFP – local field potential; LN – linalool; MCS – minimal clonic seizures; MDA – malondialdehyde; MES – maximal electroshock; MEST – maximal electroshock threshold test; MNDA – NRG – naringenin; NRG-DM – naringenin 4',7-dimethyl ether; NRG-M – naringenin 7-*O*-methyl ether; *NS* – not statistically significant; PFC – prefrontal cortex; PILO – pilocarpine; po – *per os*;PTZ – pentetrazole; RISE-SRS – reduced intensity status epilepticus–spontaneous recurrent seizures; SE – status epilepticus; THC – *delta*(9)-tetrahydrocannabinol

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