**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 indirectCB1 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) | Cornealkindled mice | – | ED50 = 115 mg/kg(95% CI = 77.5‐169) | – | – | (Patra et al., 2019) |
| CBD (ip; 2 h) | Cornealkindled 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 firingof 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 amygdalakindled 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 receptoragonist (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 andlikely 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 latency50% 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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