

Table.3 The effect of histamine or histamine related ligands on epilepsy.

Ligands targets	Ligands	Seizure Model	Seizure	Reference
Histamine	Histamine	^a Amygdala Kindling; ^{b,c} Audiogenic seizure	Seizure (↓a); AGS (↓b,c)	^a (Ago, Ishikawa, Matsumoto, Ashequr Rahman & Kamei, 2006), ^b (Feng & Faingold, 2000), ^c (Feng, Naritoku, Randall & Faingold, 2001)
	Histidine	^{a,b,c} Amygdala Kindling; ^d Genetic epilepsy; ^e PTZ	Seizure onset (↓a,b,d); Seizure stage (↓b,e) (↑a) ; myoclonic jerks onset (↓e); Seizure (- c); forelimb clonus onset (↓a)	^a (Wada, Shiraishi, Nakamura & Koshino, 1996), ^b (Kamei, Ishizawa, Kakinoki & Fukunaga, 1998), ^c (Yoshida, Noguchi & Tsuru, 2000), ^d (Yawata, Tanaka, Nakagawa, Watanabe, Murashima & Nakano, 2004), ^e (Zhang, Shen, Jin, Hu, Zhao & Chen, 2004)
	Carcinine	^{a,b} PTZ; ^c Febrile seizure	Seizure onset (↓a,b); Seizure stage(↓a); Febrile seizure(↓c)	^a (Chen, Li, Zhu, Shen & Wei, 2002), ^b (Chen et al., 2004), (Dai et al., 2015)
HNMT inhibitor	Metoprine	^a Amygdala Kindling; ^b AGS; ^{c,d} Genetic epilepsy	Seizure onset (↓d); Seizure stage(↓a); clonic-tonic convulsions(↓b); spike wave discharge(↓c)	^a (Kamei, Ishizawa, Kakinoki & Fukunaga, 1998), ^b (Vinogradova, Shatskova & Tuomisto, 2007), ^c (Samotaeva, Birioukova, Midzyanovskaya, Kuznetsova, Bazyan & Tuomisto, 2012) ^d (Yawata, Tanaka, Nakagawa, Watanabe, Murashima & Nakano, 2004)
H1R antagonist	Antazoline	MES	electroconvulsive threshold(↓)	(Swiader, Wielosz & Czuczwar, 2004)
	Cetirizine	Amygdala Kindling	Seizure (-)	(Fujii, Tanaka, Harada, Hirai & Kamei, 2003)
	Chlorpheniramine	MES	EEG seizure(↓); tonic extensor seizure (↓); clonic seizures(-)	(Ishikawa et al., 2007)
	Cyproheptadine	MES	EEG seizure(↓); tonic extensor seizure (↓); clonic seizures(-)	(Ishikawa et al., 2007)
	Diphenhydramine	^a Amygdala Kindling; ^b MES; ^c Vestibular stimulation;	Seizure (↑ a,d); EEG seizure(↓b); tonic extensor seizure (↓b); clonic	^a (Fujii, Tanaka, Harada, Hirai & Kamei, 2003), ^b (Ishikawa et al., 2007), ^c (Sturman, Freeman & Quinn,

		^d Genetic epilepsy	seizures(-b); convulsive seizures(↓c)	2001), ^d (Yawata, Tanaka, Nakagawa, Watanabe, Murashima & Nakano, 2004)
	Epinastine	Amygdala Kindling	Seizure (-)	(Yokoyama, Sato, Iinuma, Onodera & Watanabe, 1996)
	Ketotifen	^{a,b} Amygdala Kindling; ^{c,d,e} MES	Seizure (↑a,b,d); electroconvulsive threshold(↓c); EEG seizure(↓e); tonic extensor seizure (↓e); clonic seizures(- e)	^a (Yokoyama, Sato, Iinuma, Onodera & Watanabe, 1996), ^b (Fujii, Tanaka, Harada, Hirai & Kamei, 2003), ^c (Swiader, Wielosz & Czuczwar, 2004), ^d (Yamada, Takizawa, Tamura & Kanda, 2012), ^e (Ishikawa et al., 2007)
	Loratadine	Amygdala Kindling	Seizure (-)	(Fujii, Tanaka, Harada, Hirai & Kamei, 2003)
	Mepyramine	Vestibular stimulation	convulsive seizures(↓)	(Sturman, Freeman & Quinn, 2001)
	Pyrilamine	^{a,b} Amygdala Kindling	Seizure (↑ a,b)	^a (Yokoyama, Sato, Iinuma, Onodera & Watanabe, 1996), ^b (Fujii, Tanaka, Harada, Hirai & Kamei, 2003)
	Triprolidine	KA	Seizure (↑)	(Kukko-Lukjanov et al., 2010)
H2R agonist	Amthamine	PTZ and picrotoxin	Seizure stage(↓)	(Seeley & Sturman, 2001)
H2R antagonist	Cimetidine	PTZ	Seizure (-)	(Swiader, Porebiak, Swiader, Wielosz & Czuczwar, 2006)
H3R antagonist	ABT-239	KA	Seizure stage(↓); Seizure onset (↓)	(Bhowmik, Saini & Vohora, 2014)
	AQ0145	Amygdala Kindling	Seizure stage(↓)	(Harada, Fujii, Hirai, Shinomiya & Kamei, 2004)
	DL77	PTZ, MES, STR	Convulsion (-PTZ and STR, ↓PTZ);	(Sadek, Saad, Subramanian, Shafiullah, Łazewska & Kieć-Kononowicz, 2016)
	Clobenpropit	^{a,b} Amygdala Kindling, ^b MES, ^c PTZ	Seizure stage(↓a,b,c)	^a (Harada, Fujii, Hirai, Shinomiya & Kamei, 2004), ^b (Harada, Hirai, Fujii, Harusawa, Kurihara & Kamei, 2004), ^c (Zhang, Chen, Huang, Hu, Wei & Yanai, 2003)
	E177	^a PTZ; ^b Pilocarpine	Seizure stage(↓a); Seizure onset (↓b)	^a (Alachkar et al., 2020), ^b (Alachkar et al., 2019)

	Iodophenpropit	^{a,b} Amygdala Kindling; ^b MES	Seizure stage(↓a,b)	^a (Harada, Fujii, Hirai, Shinomiya & Kamei, 2004), ^b (Harada, Hirai, Fujii, Harusawa, Kurihara & Kamei, 2004)
	Thioperamide	^{a,b,c} Amygdala Kindling; ^c MES; ^d Genetic epilepsy	Seizure (-a); Seizure stage(↓b,c); Seizure onset (↓d)	^a (Yoshida, Noguchi & Tsuru, 2000), ^b (Harada, Fujii, Hirai, Shinomiya & Kamei, 2004), ^c (Harada, Hirai, Fujii, Harusawa, Kurihara & Kamei, 2004), ^d (Yawata, Tanaka, Nakagawa, Watanabe, Murashima & Nakano, 2004)
	VUF5514	Amygdala Kindling and MES	Seizure stage(↓)	(Harada, Hirai, Fujii, Harusawa, Kurihara & Kamei, 2004)
	VUF5515	Amygdala Kindling and MES	Seizure stage(↓)	(Harada, Hirai, Fujii, Harusawa, Kurihara & Kamei, 2004)
	VUF4929	Amygdala Kindling and MES	Seizure stage(↓)	(Harada, Hirai, Fujii, Harusawa, Kurihara & Kamei, 2004)
	Novel compounds	^{a-h} PTZ; ^{c,d,e,f} STR; ^{b,c,d,e,f,g,h,i} MES; ^g 6-Hz stimulation	Seizure stage(↓a,g); Convulsion (↓a,b,c,d,e,f,h,i,j); Convulsion (- in b MES,in h PTZ); Seizure (↓g)	^a (Chen, Ren, Zhang & Hu, 2012), ^b (Sadek et al., 2014b), ^c (Sadek et al., 2016), ^d (Sadek, Saad, Schwed, Weizel, Walter & Stark, 2016), ^e (Alachkar et al., 2018a), ^f (Alachkar et al., 2018b), ^g (Łażewska et al., 2018), ^h (Song, Yan, Zhang, Guo, Zhou & Deng, 2020), ⁱ (Sadek et al., 2013), ^j (Bastaki, Abdulrazzaq, Shafiullah, Więcek, Kieć-Kononowicz & Sadek, 2018)
H1R agonist/ H3R antagonist	Betahistine	^a Amygdala Kindling ^b PTZ	ADD (↓a); Tonic-clonic seizure (↓b)	^a (Yoshida, Noguchi & Tsuru, 2000), ^b (Yazdi, Doostmohammadi, Pourhossein Majarshin & Beheshti, 2020)