Editorial

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Therapeutic Perspectives of Brivaracetam Against Epilepsy

Ankur Kumar, Rohit Bhatia and Pooja A Chawla*

Department of Pharmaceutical Chemistry, ISF College of Pharmacy, India

***Corresponding author:** Pooja A Chawla, Department of Pharmaceutical Chemistry and Analysis, ISF College of Pharmacy, Moga-142001, Punjab, India

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ABSTRACT

Abbreviations: FDA: Food and Drug Administration; GAERS: Genetic Absence Epilepsy Rat from Strasbourg; AEDs: Anti-Epileptic Medications

Perspective

Seizure is the fourth leading neuro disease affect about 85 million people worldwide. The symptoms of seizures are due to an aberrant synchronized activation of excitatory neurons, characterizes this disorder [1]. A pulse of voltage termed as a paroxysmal depolarisation shift happens when neurons fire simultaneously. During this time, the neurons' resistance to firing decreases, resulting in numerous nerve impulses which produce abnormal high electronic impulses in brain [2]. Brivaracetam, it is propyl counterpart of levetiracetam, an anticonvulsant and racetams compound, was approved as an add-on medication by FDA in February 2017. It is approved for the treatment of POS in adolescents and adults and old age people [3] (Figure 1).

Pharmacology, Toxicology and Safety

Brivaracetam examined *in vitro* activity in rat hippocampus slice after spread with a high potassium-low calcium solution values ranging from 1–10 μM. Brivaracetam at promiscuity dosage reduced the spontaneous bursts, but LEV don does not react against these drug-resistant marker of epileptiform activity [4]. Brivaracetam has been widely researched in *in vivo* epilepsy and convulsion model. The corneally ignited mouse is a partial epilepsy model. Brivaracetam at doses several orders of magnitude lower than those required LEV for prevent animal to secondary generalised motor seizure (ED_{50} value 1.2 versus 7.3 mg/kg, i.p.). Brivaracetam suppressed both severity of motor seizure and then liberation length more profoundly than LEV in another model of focal epilepsy, the subcortical structures of rat. Brivaracetam's action was also studied in models with generalised seizures. Brivaracetam effectively protected mice genetically predisposed to audiogenic seizures from chronic convulsions (ED_{50} value 2.4 versus. 30 mg/kg, i.p.) [5]. Brivaracetam suppressed spike-wave discharges more completely in compare to LEV in a model without epilepsy, the genetic non-epilepsy rat from Strasbourg (GAERS).

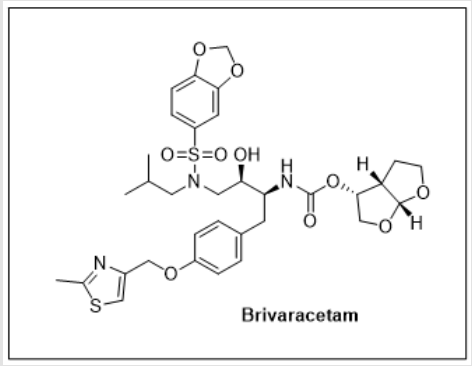

Figure 1.

Chronic pre-treatment before to corneal stimulation with LEV or 10 times lower dose of brivaracetam two times daily (1.7-54 mg/kg i.p. versus 0.21-6.8 mg/kg i.p.) suppressed kindling development in the same corneal kindling model. Most significantly, discontinuing therapy with sustained corneal stimulation led in a more dramatic and long-lasting suppression of the kindling process than LEV. Brivaracetam's action versus partially drug-resistant self-sustaining status epilepticus (SSSE) in rats was tested to determine its anticonvulsant characteristics in an acute seizure paradigm [6]. The model demonstrated the stimulating excitatory pathway may result in reverberating limbic circuits in which seizures are self-sustaining, causing brain injury. Once started, this process is resistant to common anticonvulsants i.e., diazepam and phenytoin. Explicit path stimulation generated SSSE in adult male rats.

At 20 and 300 mg/kg, the aggregate duration of active seizures was reduced to 11% and 0.8 percent of controls, respectively [7]. Brivaracetam's oral acute toxicity demonstrated to minimal in rat, mice, and dog, with short time CNS effect typically arising at dose of 100 mg/kg or above in a dose-dependent manner. Under continuing medication, these effects subsided after a few days. There have been no severe cardiovascular, respiratory, or gastrointestinal problems noted (UCB, data on file). Based on clinical symptoms, the maximal nonlethal oral single dose in rats was over 1000 mg/kg, and in male and female rat a no-effect limit at 500 mg/kg was determined. Dogs, rats, and monkeys were tested for chronic toxicity [8].

Pharmacokinetics

Brivaracetam bioavailability is quick and nearly complete after oral dosing. At a dose range of 10-600 mg, drug exhibits linear pharmacokinetics. At supratherapeutic doses, brivaracetam metabolic clearance increases in a time-dependent manner; a constant stage is attained within one week of treatment repeated. Plasma protein binding is modest (20%), with a volume of distribution near to total body water (0.6 L/kg). Brivaracetam's terminal half-life of elimination is about eight hours and does not change with administered dose [9]. The Brivaracetam absorption profile was examined using pharmaco-scintigraphy (UCB, data on file). Brivaracetam uniformly absorbed in Gastrointestinal system and demonstrated by comparative AUC (completely bioavailable in stomach) values of 97, 98, and 101 % in the different part of stomach and intestines [10].

Future Directions

With the increase in new AEDs since 1994, a new AED must either demonstrate significantly improved safety and performance or address a market demand. Claiming a far greater safety profile is a risky endeavour, as safety problems are often identified after the drug has been provided to tens of hundreds of patients. Certain novel medicines are definitely more effective in some people than others in terms of efficacy, although the efficacy profiles among most new drugs appear to be comparable [11]. For these reasons, the Brivaracetam development programme focused on unmet needs. Infantile spasms are a prime example of an unsatisfied demand, as there is presently no FDA-approved therapy for this illness. Although epilepsy affects both men and women equally, it is believed over one million American women of reproductive age suffer from it [12]. Many women's health problems are exacerbated by epilepsy, particularly those of reproductive age.

Exacerbations of seizures have been connected to a decline in endogenous progesterone levels during the perimenstrual phase, and research suggests that exogenous progesterone therapy can lower seizure frequency [13]. Brivaracetam may be especially beneficial against catamenial seizures since it is a neuroactive synthetic equivalent of allopregnanolone, a naturally occurring progesterone metabolite [14]. Brivaracetam's minimal teratogenicity makes it an excellent therapy option for women hoping to have children. Brivaracetam's safety, tolerability, pharmacokinetics, and anticonvulsant efficacy as just a contribute therapy in women with catamenial epilepsy who are uncontrollable on their current AED regimen are being studied [15].

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