Pharmaceutical Regulatory Affairs 2012: Brain targeting potential of carbamazepine SNEEDS- BITS, Pilani, INDIA

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Abstract

The delivery of novel drug delivery systems to epileptic brain would be an attractive strategy [1]. Carbamazepine (CBZ) SNEDDS was developed using medium chain triglycerides, polysorbate 80, lecithin and ascorbyl palmitate. Ternary phase diagrams were constructed to identify the self nano-emulsified region. The SNEDDS were subjected to visual observation, size and zeta potential, scanning electron microscopic studies, Fourier transformed infrared spectroscopy, pharmacokinetics and brain distribution studies analyzed by HPLC. It was found that oil to surfactant ratio had an impact on the physical characteristics of the nano-emulsion formed. The brain levels of CBZ from optimized SNEDDS (108±1.2 nm - 25.6±3.5 mv) were significantly high at all time points when compared to solution. The initial levels of CBZ from SNEDDS was 8.023mcg/ml thereafter the levels were consistently high till 8 hrs and the initial levels of CBZ from plain solution was 3.62mcg/ml followed by a gradual decline till 4hrs evidently showing that the clearance of CBZ from SNEDDS was reduced. The brain targeting index of SNEDDS and solution were 3 and 2 respectively. The brain enhancement factor value was found to be 22.29 at 15 mins revealing a very rapid penetration of CBZ into brain. The role of GABAB receptor-mediated mechanisms in the pathogenesis of seizures depends upon neural networks involved, which determine the seizure type. Generalized seizures involve diffuse, bi-hemispheric neuronal networks, while focal seizures involve regional brain networks. GABAB receptor agonists have been shown to diminish seizure activity in mouse models of both generalized convulsive and focal seizures. However, generalized non-convulsive seizures such as typical and atypical absence seizures (AASs) characteristically are exacerbated by GABAB receptor agonists and blocked by GABAB receptor antagonists. The reason for this dichotomy is the involvement of thalamic circuitry in both typical and atypical absence seizures. Food and Drug Administration and. as a result, the treatment options for children and adults with epilepsy have been expanded considerably. These new generation antiepileptic drugs offer equal efficacy with improved tolerability, pharmacokinetic properties, and side effect profiles compared with the traditional drugs. With many new medications available, the clinician treating children with epilepsy must be well versed in the application of these drugs to their patient population. This manuscript will review the indications, mechanism of action, pharmacokinetics, adverse effects, and dosing of the new generation of anticonvulsant medications.