Valproate: 
Past, Present, and Future

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ABSTRACT

Preclinical studies have been carried out during the past four decades to investigate the different mechanisms of action of valproate (VPA). The mechanisms of VPA which seem to be of clinical importance include increased GABAergic activity, reduction in excitatory neurotransmission, and modification of monoamines. These mechanisms are discussed in relation to the various clinical uses of the drug. VPA is widely used as an antiepileptic drug with a broad spectrum of activity. In patients, VPA possesses efficacy in the treatment of various epileptic seizures such as absence, myoclonic, and generalized tonic-clonic seizures. It is also effective in the treatment of partial seizures with or without secondary generalization and acutely in status epilepticus.

The pharmacokinetic aspects of VPA and the frequent drug interactions between VPA and other drugs are discussed. The available methods for the determination of VPA in body fluids are briefly evaluated.

At present, investigations and clinical trials are carried out and evaluated to explore the new indications for VPA in other conditions such as in psychiatric disorders, migraine and neuropathic pain. Furthermore, the toxicity of VPA, both regarding commonly occurring side effects and potential idiosyncratic reactions are described. Derivatives of VPA with improved efficacy and tolerability are in development.