

New Technology Platforms: New Formulations and Delivery Systems

Optimal care of patients with epilepsy must include therapies for long-term management as well as acute treatment of seizure emergencies. In both situations the ideal delivery system would direct drug to the site of action while limiting exposure elsewhere in the central nervous system and the rest of the body. Although progress has been made in targeting drug delivery for other conditions, this technology has not yet been successfully applied to epilepsy. Many immediate-release antiepileptic drugs (AEDs) formulations cause side effects when levels exceed minimum toxic concentrations and have the potential for breakthrough seizures when levels fall below minimum effective concentrations. Overcoming these problems requires more frequent daily dosing, but decreased medication compliance may obviate any benefits from frequent daily dosing. Controlled-release formulations permit once or twice daily dosing with the potential for improved outcomes. New technologies permit better control of oral drug release and can accommodate larger doses. Controlled-release products in easy-to-swallow formulations such as liquids and beads may be particularly useful for children and the elderly. Innovative technology platforms are also proving invaluable in the development of new therapies utilizing alternate routes of administration. In general, antiepileptic drugs are poorly water-soluble and some are unstable in aqueous solutions. In the past, these physical-chemical characteristics have necessitated the use of toxic organic solvents or pH adjustments to adequately solubilize and stabilize injectable AED formulations. Approaches such as microemulsions, nanocrystals and cyclodextrins now permit the development of injectable formulations for a larger number of AEDs and other CNS medications. For example, carbamazepine, which is virtually insoluble in water, and topiramate, which is only moderately water soluble and unstable in aqueous solutions, can be formulated as intravenous products using cyclodextrins. The clinical and commercial success of rectal diazepam gel has attracted increasing interest in the development of formulations to treat seizure emergencies outside the hospital. The challenge in this therapeutic category is designing formulations with long shelf lives that contain high concentrations of unionized drug in non-toxic solubilizing agents. New developments in intramuscular injection technology combined with advances in formulations may permit expanded use of intramuscular injections. In terms of formulation challenges, many of the same technological advances useful for intravenous formulations are also advantageous in developing new products for other non-oral routes of administration. Recent development activity has focused on intranasal formulations of benzodiazepines that offer the prospect of safe, effective, and easily administered therapies for seizure emergencies as an alternative to rectal administration. Technological advances in drug delivery have increased the potential opportunity for better products to treat epilepsy and related disorders.