

## Liquid chromatographic separation of phenobarbitone, ethosuximide, phenytoin and carbamazepine on a polystyrene-divinyl benzene column

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Epilepsy is a common cause of morbidity and social stigmatization in Kenya. Phenobarbitone, ethosuximide, phenytoin and carbamazepine are the most commonly used drugs for epilepsy management in Kenya. Liquid chromatography is recognized as the most rapid, specific, precise, sensitive and cost effective method of analysis in multiple drugs. There is no compendial method for the simultaneous analysis of the four drugs. However, several silica based reversed phase liquid chromatographic methods have been reported for their analysis (Szabo & Browne 1982; Torra et al 2000). Although such reversed phase stationary phases still dominate the liquid chromatographic field, polymeric columns are increasing in popularity as their retention characteristics and applications become better understood. One such material, polystyrene-divinylbenzene, is stable in a wide pH range (pH 1–13). A validated liquid chromatographic method for the simultaneous separation of phenobarbitone, ethosuximide, phenytoin and carbamazepine on a polystyrene-divinyl benzene column in 15 min is described. The method was developed by the systematic study of different types of co-polymer materials, type and concentration of organic modifiers, buffer pH and concentration and column temperature. A PLRP-S 100 Å 8-mm column maintained at 60°C and a mobile phase consisting of acetonitrile-tertiary butanol-phosphate buffer (pH 7.6, 0.2 M)-water (25:5:10:60, v/v) were used. The flow rate was 1 ml/min with ultraviolet detection at 220 nm. The detector response was linear for all the compounds ( $R > 0.999$ ) in the concentration ranges of 0.005–3.1, 0.05–25, 0.005–3.1 and 0.003–1.6 mg for phenobarbitone, ethosuximide, phenytoin and carbamazepine, respectively. The within-day and between-day coefficients of variation ranged from 1.1 to 2.0 and 1.4 to 6.9 %, respectively. The limits of detection were 2.0, 15.6, 6.4 and 2.0 ng while the limits of quantitation values were 7.5, 62.5, 32.5 and 15.6 ng for phenobarbitone, ethosuximide, phenytoin and carbamazepine, respectively. By studying the effect of small changes in acetonitrile concentration, pH and column temperature, the method was found to be robust. Satisfactory peak symmetry, selectivity and column stability was maintained over the 7 months study period at the high column temperature without any aggressive column solvent clean up. This method has been used for analysis of pharmaceutical raw materials, finished products and dissolution studies of the drugs in commercial samples on the Kenyan market (Orwa et al 2004). This paper therefore reports the development of a cost effective liquid chromatographic method on a polymer column for the analysis of the four commonly used anticonvulsant drugs in resource-poor countries.

### References:

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