

## **Ultrasonic emulsification of parenteral valproic acid-loaded nanoemulsion with response surface methodology and evaluation of its stability**

### **ABSTRACT**

Response surface methodology (RSM) was used to optimize the formulation of a nanoemulsion for central delivery following parenteral administration. A mixture of medium-chain triglyceride (MCT) and safflower seed oil (SSO) was determined as a sole phase from the emulsification properties. Similarly, a natural surfactant (lecithin) and non-ionic surfactant (Tween 80) (ratio 1:2) were used in the formulation. A central composite design (CCD) with three-factor at five-levels was used to optimize the processing method of high energy ultrasonicator. Effects of pre-sonication ultrasonic intensity (A), sonication time (B), and temperature (C) were studied on the preparation of nanoemulsion loaded with valproic acid. Influence of the aforementioned specifically the effects of the ultrasonic processing parameters on droplet size and polydispersity index were investigated. From the analysis, it was found that the interaction between ultrasonic intensity and sonication time was the most influential factor on the droplet size of nanoemulsion formulated. Ultrasonic intensity (A) significantly affects the polydispersity index value. With this optimization method, a favorable droplet size of a nanoemulsion with reasonable polydispersity index was able to be formulated within a short sonication time. A valproic acid loaded nanoemulsion can be obtained with 60% power intensity for 15 min at 60 °C. Droplet size of  $43.21 \pm 0.11$  nm with polydispersity index of 0.211 were produced. The drug content was then increased to 1.5%. Stability study of nanoemulsion containing 1.5% of valproic acid had a good stability as there are no significant changes in physicochemical aspects such as droplet size and polydispersity index. With the characterisation study of pH, viscosity, transmission electron microscope (TEM) and stability assessment study the formulated nanoemulsion has the potential to penetrate blood-brain barrier in the treatment of epilepsy.

**Keyword:** Ultrasonication; Valproic acid; Epilepsy; Blood-brain barrier; Central composition design; Nanoemulsion