

## Formulation of the N-Acylethanolamine, Linoleoylethanolamide into Cubosomes for Delivery across the Blood-Brain Barrier

**Authors :** Younus Mohammad, Anita B. Fallah, Ben J. Boyd, Shakila B. Rizwan

**Abstract :** N-acylethanolamines (NAEs) are endogenous lipids, which have neuromodulatory properties. NAEs have shown neuroprotective properties in various neurodegenerative diseases including Alzheimer's disease, Parkinson's disease and ischemic stroke. However, NAEs are eliminated rapidly in vivo by enzymatic hydrolysis. We propose to encapsulate NAEs in liquid crystalline nanoparticles (cubosomes) to increase their biological half-life and explore their therapeutic potential. Recently, we have reported the co-formulation and nanostructural characterization of cubosomes containing the NAE, oleoylethanolamide and a synthetic cubosome forming lipid phytantriol. Here, we report on the formulation of cubosomes with the NAE, linoleoylethanolamide (LEA) as the core cubosome forming lipid. LEA-cubosomes were formulated in the presence of three different steric stabilisers: two brain targeting ligands, Tween 80 and Pluronic P188 and a control, Pluronic F127. Size, morphology and internal structure of formulations were characterized by dynamic light scattering (DLS), cryogenic transmission electron microscopy (Cryo-TEM) and small angle X-ray scattering (SAXS), respectively. Chemical stability of LEA in formulations was investigated using high-performance liquid chromatography (HPLC). Cytotoxicity of formulations towards human cerebral microvascular endothelial cell line (hCMEC/D3) was also investigated using an MTT (3-[4, 5- dimethylthiazol-2-yl]-2, 5-diphenyl tetrazolium bromide) assay. All cubosome formulations had mean particle size of less than 250 nm and were uniformly distributed with polydispersity indices less than 0.2. Cubosomes produced had a bicontinuous cubic internal structure with an Im3m space group but different lattice parameters, indicating the different modes of interaction between the stabilisers and LEA. LEA in formulations was found to be chemically stable. At concentrations of up to 20 µg/mL LEA in the presence of all the stabilisers, greater than 80% cell viability was observed.

**Keywords :** blood-brain barrier, cubosomes, linoleoyl ethanolamide, N-acylethanolamines (NAEs)

**Conference Title :** ICSRD 2020 : International Conference on Scientific Research and Development

**Conference Location :** Chicago, United States

**Conference Dates :** December 12-13, 2020