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# Design of tailor-made biocompatible nanocarrier for novel pyrazoloquinolinone ligand (CW-02-79) based on comprehensive evaluation of critical physicochemical descriptors

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The poor water solubility of novel patent-protected ligand of the pyrazoloquinolinone chemotype (CW-02-79), with significant binding affinity for sigma-2 receptors in the brain, restricts the development of conventional parenteral formulations and consequently, extensive pharmacological studies during the preclinical investigation. Therefore, we aimed to develop a biocompatible nanocarrier tailored to specific physicochemical properties of CW-02-79, to improve its transport across the blood-brain barrier and achieve the optimal brain disposition. In this context, a detailed analysis of lipophilicity (via log P and log D determination), solubility in various solvents/excipients (using shake-flask method) and crystalline state of CW-02-07 (using X-ray powder diffraction (XRPD), differential scanning calorimetry (DSC) with melt quenching approach and polarization microsocopy) was performed. After the analysis of key "input" physicochemical descriptors, based on the developed decision tree, nanoemulsions were selected as promising carriers for CW-02-79. The nanoemulsions were prepared using the high pressure homogenization method, varying the process (number of cycles, temperature and pressure) and formulation parameters (the content of the oil phase, the stabilizer mixture composition). Additionally, the influence of the sterilization process (thermal sterilization/aseptic filtration) on the nanoemulsion physicochemical properties was investigated, including droplet size and size distribution, zeta potential, pH, electrical conductivity and osmolality. The obtained results showed that it was possible to formulate CW-02-79-loaded nanoemulsions with 20% oil phase (medium chain triglycerides:castor oil at ratio 1:1), stabilized with the biocompatible emulsifiers (lecithin/polysorbate 80), exhibiting the nano-sized droplets (<200 nm) with narrow size distribution (polydispersity index < 0.2), zeta potential (> |-30| mV), pH (~ 5.7) and osmolality (295 mOsm/kg). The sterilization process did not remarkably affect the physiochemical properties of nanoemulsions, making them suitable for the parenteral administration. Owing to sastifying solubilization capacity for CW-02-79, physicochemical properties and preliminary stability, the nanoemulsions are the promising carriers worth exploring further to support the preclinical evalution of CW-02-79.

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