Poster

Use of brain organoids for the evaluation of toxicity and biodistribution of nanomedicines

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ABSTRACT

The evaluation of safety and efficacy is a crucial requirement in the development of new drugs. Traditionally, animal models, especially murine, have been the standard approach. However, growing evidence suggests that these models often fail to accurately replicate human physiology, a limitation that is particularly pronounced in the study of drugs targeting the central nervous system (CNS). This is due to significant molecular and cellular differences between the human brain and rodent models. Furthermore, animal experimentation entails high costs, requires specialized personnel, and is increasingly restricted by regulatory and funding agencies, driving the need for more predictive human-based models(García-Delgado et al., 2022).

Human 2D cell cultures offer an alternative, yet they present limitations, such as the inability to replicate the three-dimensional architecture of tissues and the complex cell-cell interactions found in vivo. In contrast, 3D in vitro models, like brain organoids, have emerged as powerful tools to better simulate human brain tissue and to explore novel therapies for neurological diseases. These multicellular models, typically derived from pluripotent stem cells, mimic the structural and functional complexity of the human brain more closely than traditional 2D cultures(Lancaster et al., 2013).

Nanoparticles (NPs) represent a promising approach in both therapeutic and diagnostic fields. Functionalized NPs loaded with bioactive compounds, such as cannabinoids, have shown anti-inflammatory, antioxidant, and antinociceptive effects without psychoactive properties, offering alternative mechanisms to currently available CNS drugs (Álvarez-Fuentes et al., 2012).

This study aims to develop cerebral organoids to assess the biodistribution and toxicity of PLGA-PEG polymeric nanoparticles loaded with cannabidiol (CBD), synthesized via nanoprecipitation (NPP). The evaluation of CBD-NP behavior within the CNS, using cerebral organoids, will provide insight into their potential therapeutic application.

For biodistribution analysis, NPs were labeled with the fluorophore Nile Red for visualization under fluorescence microscopy. Immunohistochemical staining was also performed on organoid sections to evaluate the biodistributión of NPs and assess potential cytotoxic effects.This approach aims to advance CNS drug delivery by combining cerebral organoids with nanoparticles, promoting safer and more effective therapies.

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