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Intranasal delivery of amphotericin B to the cerebrospinal fluid using a discoidal nano system

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Cryptococcal meningitis is a severe fungal infection in which the fungus invades the body and enters the cerebrospinal fluid (CSF). Intravenous amphotericin B (AmB) remains a first-line treatment. However, systemic AmB achieves limited CSF exposure because of poor water solubility and unfavourable distribution. Intrathecal administration can increase CSF concentrations, but it is associated with significant risk and technical complexity.

The proposed study investigates the feasibility of delivering AmB to the CSF via intranasal administration using a discoidal nanoscale delivery system (nanodiscs). AmB can be incorporated into a lipid bilayer, mainly composed of lecithin and cholesterol, stabilised at the edges by various copolymers. Nanodiscs would be prepared by lipid film hydration to form multilamellar vesicles, followed by controlled disruption into bilayer discoidal nanoparticles.

The methodology relies on colloidal and nasal applicability studies. Particle size and size distribution would be characterised by dynamic light scattering, transmission electron microscopy (TEM), and small-angle X-ray scattering (SAXS), alongside the determination of zeta potential as a relevant nanoparticle characteristic. Structural investigations via thermoanalysis and X-ray powder diffraction would also be carried out, alongside the determination of nanoparticle–active substance interactions using vibrational spectroscopy. *In vitro, ex vivo,* and *in vivo* nasal applicability studies would also be performed.

With ongoing research and the determination of the correlation between nanoparticle characteristics and permeability profile, an enhanced drug delivery system would be developed to address such unmet clinical needs.