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opinion Article

Pharmacokinetics and Bioavailability of a Liposomal Formulation of Curcumin in Preclinical Models

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ABOUT THE STUDY

Curcumin, the principal curcuminoid extracted from Curcuma longa, has demonstrated extensive pharmacological potential, including anti-inflammatory, antioxidant and anticancer activities. Despite these promising properties, its clinical application remains limited due to extremely poor oral bioavailability, rapid metabolism and low systemic circulation following administration. To overcome these limitations, advanced drug delivery systems such as liposomal encapsulation have been proposed. In this study, a novel liposomal formulation of curcumin was developed and evaluated for its pharmacokinetic behavior and oral bioavailability in preclinical animal models. The primary objective was to enhance curcumin's solubility, stability and systemic absorption through nanocarrier-based delivery.

The liposomal curcumin formulation was prepared using the thin-film hydration method followed by sonication to achieve nanoscale vesicles. The lipid components included phosphatidylcholine and cholesterol in optimized ratios to ensure stability and encapsulation efficiency. Dynamic Light Scattering (DLS) revealed a mean particle size of approximately 145 nm with a narrow Polydispersity Index (PDI<0.2), and transmission electron microscopy confirmed spherical morphology. The encapsulation efficiency was calculated to be over 85%, indicating effective incorporation of curcumin into the lipid bilayers. The formulation showed excellent physicochemical stability when stored at 4°C for 30 days, with negligible leakage or aggregation.

The pharmacokinetic study was performed in male Wistar rats using a crossover design. Animals received oral doses of either free curcumin suspension or the liposomal formulation, both equivalent to 100 mg/kg of curcumin. Plasma samples were collected at predetermined intervals up to 24 hours post-administration, and curcumin concentrations were quantified using a validated HPLC-MS/MS method. The results demonstrated a marked improvement in the pharmacokinetic profile of liposomal curcumin. The area under the plasma concentration-time curve was approximately 6-fold higher for the liposomal group compared to free curcumin, while the maximum concentration increased from 0.27 µg/mL to 1.62 µg/mL. Moreover, the time to reach peak concentration was prolonged, suggesting sustained release from the liposomal matrix.

The oral bioavailability of liposomal curcumin was calculated to be significantly enhanced, reaching nearly 31%, as opposed to less than 5% for the free form. This improvement can be attributed to increased solubility, protection from gastrointestinal degradation, and enhanced lymphatic absorption via the lipid-rich formulation. The formulation also reduced inter-animal variability in curcumin levels, suggesting a more predictable pharmacokinetic behavior. Additionally, these release studies in simulated gastrointestinal fluids revealed a biphasic release pattern, with an initial burst followed by sustained release over 12 hours, aligning with the prolonged plasma concentrations observed.

Tissue distribution studies showed higher curcumin concentrations in the liver, spleen, and brain for animals treated with liposomal curcumin, indicating improved systemic penetration and possibly better therapeutic targeting. Histopathological analysis of major organs following repeated administration showed no evidence of toxicity or inflammation, suggesting the safety of the liposomal carrier system. Furthermore, the formulation demonstrated stability under physiological conditions, maintaining structural integrity in the presence of bile salts and digestive enzymes, which is critical for oral administration.

To understand the mechanistic basis of enhanced absorption, permeability studies using Caco-2 cell monolayers were conducted. The liposomal formulation exhibited significantly higher apparent permeability coefficients compared to free curcumin, indicating enhanced transcellular transport. The likely mechanism involves endocytosis-mediated uptake facilitated by the nanosized vesicles and the lipidic nature of the formulation. These findings support the hypothesis that

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liposomal encapsulation provides a favorable microenvironment for curcumin, enabling it to bypass conventional absorption barriers.

In conclusion, the liposomal formulation of curcumin developed in this study significantly improved its pharmacokinetic properties and oral bioavailability in preclinical models. The enhanced absorption, prolonged systemic circulation, and favorable tissue distribution make this formulation a promising candidate for clinical translation in various therapeutic areas, particularly chronic inflammatory and neurodegenerative conditions. The safety, scalability, and reproducibility of the formulation further support its potential as a next-generation delivery system for curcumin. These findings underscore the importance of nanotechnology in overcoming the intrinsic limitations of bioactive phytochemicals and offer a viable approach to enhancing their therapeutic utility through strategic pharmaceutical innovation. Future work will include scaling up for GMP manufacturing, conducting long-term stability studies, and initiating early-phase clinical trials to confirm translational efficacy in human subjects.