

**Development and Evaluation of Polyphenol Nanoparticles as a  
Hepatoprotective Nanomedicine against Diclofenac-Induced  
Hepatotoxicity**

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**Abstract**

Curcumin (CUR) and morin are polyphenolic compounds that have anti-inflammatory, antioxidant, antimicrobial and hepatoprotective properties. The aim of the current study was to formulate these polyphenols into a polymeric nanoscale formulation to examine their potential hepatoprotective activity in an animal model of diclofenac-induced hepatotoxicity. The optimal polyphenol nanoformulation was found to be CUR-loaded poly(ethylene glycol)-polycaprolactone nanoparticles (PEG-PCL NPs). The NPs were around 67 nm in size with more than 82.4% loading efficiency. CUR NPs were evaluated against diclofenac-induced hepatotoxicity in mice, by studying the histopathological changes and gene expression of drug-metabolizing *cyp450* (*cyp3a11*, *cyp2c29*, and *cyp2d9*) and *ugt* (*ugt2b1*) genes in the livers of the animals. Our findings revealed that free CUR and CUR NPs have a hepatoprotective effect based on histological investigation, but that there is no significant effect of free CUR and CUR NPs on drug metabolizing enzymes.

**Keywords:** Curcumin, diclofenac, hepatotoxicity, nanoparticles, NSAIDs.