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Suhaili Shamsi et al., J Pharm Drug Deliv Res 2017, 6:4 (Suppl)
DOI: 10.4172/2325-9604-C1-020

NanoCUR: formulation and its effect on major human cytochrome P450 enzymes

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Statement of the Problem: Curcumin (CUR) is a phenolic compound from turmeric with multiple beneficial pharmacological properties, many of which result from enzyme modulation. CUR is a potent inhibitor of the cytochrome P450 (CYP) family of enzymes that play a vital role in the metabolism of drugs, carcinogens and toxins. To improve its in vivo solubility, stability and bioavailability, CUR has been formulated into many types of nano-sized formulations. However, it is not known whether the transformation of CUR into nanoformulations would affect its enzyme activities or not. The aim of this study was to compare the cellular response and CYP enzyme inhibitory activities of CUR before and after its encapsulation in a nanocarrier.

Methodology & Theoretical Orientation: A micellar formulation of CUR (NanoCUR) was developed using thin film hydration method with Pluronic F127 as stabilizer. To determine particle integrity after processing, the mean size of NanoCUR was monitored by dynamic light scattering (DLS). Cytotoxicity, anti-cytoproliferative effect and cellular uptake of NanoCUR were evaluated in the human liver HepG2 cell line. The effects of NanoCUR on CYP1A2, CYP2C9, CYP2D6 and CYP3A4 in human recombinant enzyme systems and HepG2 cells were evaluated.

Findings: NanoCUR was amenable to lyophilisation, and retained its nano-sized spherical dimensions (17 – 33 nm) upon dilution with HBSS and EMEM. NanoCUR was a weaker cytotoxic agent against the HepG2 cells compared to CUR in solution (sCUR). This was due to a lower cellular uptake of CUR from NanoCUR than from sCUR. NanoCUR was a weaker inhibitor of CYP2C9 and CYP2D6 than sCUR. NanoCUR was, however, 1.76-fold more potent against the CYP3A4 (IC50 5.13 ± 0.91 μM) metabolic function. Both sCUR and NanoCUR had no effect on the CYP3A4 mRNA levels in the HepG2 cells.

Conclusion & significance: NanoCUR possessed the biological activities of CUR, albeit at a lower potency and response rate. The Pluronic F127 micellar structures in NanoCUR may impart synergism to the CUR-mediated inhibition of CYP3A4 metabolic function, which is an important consideration for further development and evaluation of NanoCUR as a potential adjuvant for anti-cancer chemotherapy.

Biography

Suhaili Shamsi graduated from the University of Western Australia, Australia with a PhD after completing her Bachelor of Science with First Class Honours in Biochemistry at Universiti Putra Malaysia. Her PhD thesis is entitled "Development and evaluation of curcumin-loaded Pluronic F127 nanoformulation" that focuses on the synthesis of a simple, cost-effective yet stable curcumin nanoformulation that maintained most of the biological activities of curcumin. Dr Suhaili Shamsi is currently a senior lecturer at the Department of Biochemistry, Faculty of Biotechnology and Biomolecular Sciences, Universiti Putra Malaysia. Her current research interest focuses on incorporating nanotechnology into the development of adjuvant, specifically for chemotherapy purpose, by utilizing the myriad of natural products found locally in Malaysia. Apart from that, Suhaili Shamsi is also interested in studying the mechanism of drug-drug/food interactions through the modulation of protein efflux transporters and cytochrome P450 enzymes.

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