ABSTRACT

Flavonoids which are widely spread in plants. This can be categorized as flavonols, flavanols, flavanones, flavones, anthocyanidin and isoflavones. Quercetin, Rutin and Silibinin accounts these three flavonoids used major proportion of flavonol intake in the diet as functional food. Among all other flavonoids, quercetin has many health care and disease-prevention benefits. However, it has limitation like poor soluble in water, P-gp efflux and unstable in gastric fluid which leads to a lower therapeutic efficacy and bioavailability. Polymer-based formulations, such as nano emulsions and solid lipid nanoparticles have been developed to increase the therapeutic efficacy of flavonoids. Recent drug delivery systems such as Dual Loaded Flavono Nanoparticulate System (DLFNP) have not yet been studied with Quercetin and bio enhancers (Rutin and Silibinin).

In present study, dual loaded flavono nanoparticulate System have been developed for oral delivery of quercetin to enhance its pharmacological activities. The fabrication of Dual Loaded Flavono Nanoparticles by nanoprecipitation technique. Prepared Dual Loaded Flavono polymeric nanoparticles were subjected to characterization and various pharmacological activities.

Enhancement of Pharmacological activities of prepared Quercetin-Rutin(Qu-Ru NPs),Quercetin-Silibinin(Qu-Si NPs) loaded polymeric nanoparticles polymeric nanoformulations than the pure compound might be due to

1. Natural bio-enhancers (Rutin and Silibinin) might have synergistically enhanced the Pharmacological activities of Quercetin.
2. Natural bio-enhancer rutin and silibinin might have suppressed the drug metabolizing enzyme cytochrome P450 3A, hepatic & intestinal glucuronidation and sulfation of the Quercetin.
3. Natural bio-enhancer Rutin and Silibinin along with Quercetin might have reversed the multidrug resistance by modulating ATP-binding cassette transporter proteins such P-gp, MDRP1, MDRP2 and BCRP and enhanced anti-cancer activity in multidrug resistant human cancer cells like (Ovkar3) cells, HeLa, HEPG2.
4. Nanosizing not only reduces the size but also increase the surface area, which in turn increased the aqueous solubility of the drug, which might have increased the Pharmacological activity of the prepared polymeric nanoformulation.
(5) Prepared Quercetin (Qu NPs), Rutin (Ru NPs), Silibinin(Si NPs), Quercetin-Rutin(Qu-Ru NPs), Quercetin-Silibinin(Qu-Si NPs) loaded poly(butyl methacrylate-co-(2-dimethylamino ethyl) methacrylate-co-methyl methacrylate polymeric nanoparticles released nanosized quercetin and natural bio-enhancers in gastric fluid, which might have increased the aqueous solubility and permeability. Hence, the movement of undissolved quercetin to the intestine might have prevented; thereby hydrolytic degradation of quercetin in the intestine might have prevented.

(6) Released nanosized quercetin and natural bio-enhancers might have targeted the affected cells by passive targeting mechanism via enhanced permeability and retention (EPR) effect and thereby enhance its pharmacological activities of Dual Loaded Flavono polymeric nanoparticles.

**GRAPHICAL ABSTRACT**