

# Preparation and characterization of quercetin loaded polymeric nanoparticles

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## Introduction

Quercetin (QUE), 3,3',4',5,7-Pentahydroxyflavone is one of the most important flavonoids which has diverse biological actions including antioxidant properties, anti-inflammatory, antimicrobial, and anticancer activities. It is also reported to have an anti-proliferative effect on human ovarian, stomach, and breast cancer cells. Despite its valuable biological properties, the main drawback of QUE is that its insolubility in water, which impedes its use as an effective treatment against several diseases (Yadav et al., 2022). QUE has highly hydrophobic nature and its clinical use is restricted by its poor absorption. However, alternative strategies such as polymeric nanoformulations can improve its water solubility, bioavailability, and targeted delivery at the target site, which in turn enhances the therapeutic capability. Biodegradable polymers and non-ionic compounds such as various types of Pluronic are preferred, especially for incorporating poorly water soluble substances into nanoparticles (Kumar et al., 2015). For this reason, this study aims to develop QUE loaded polymeric nanoparticles in order to improve its solubility and sustained release. Newly developed polymer nanoparticles were prepared by emulsion-solvent evaporation method by using poly(l-lactide-co-caprolactone-co-glycolide) (PLCG), a copolymer of polylactic acid, polycaprolactone, and polyglycolic acid as biodegradable polymer. Pluronic F-127, non-ionic, biocompatible amphiphilic copolymer was also used for stabilization of water phase (Li et al., 2009). In-vitro characterization of nanoparticles was conducted by means of particle size, PDI, Zeta potential and in-vitro drug release studies. It is hypothesized that QUE loaded PLCG based nanoparticles would be capable of improving the solubility, release and biological effectiveness of QUE due to submicron size of the prepared particles.

## Materials and methods

Quercetin (QUE), Poly(L-lactide-co-caprolactone-co-glycolide) (PLCG) and Pluronic F-127 (PF-127) were purchased from Sigma-Aldrich. The chromatographic system used was Agilent 1100 series. The HPLC analyses were performed on a C18 column (150x4.6 mm, 5 µm particle size) with UV detection at 370 nm. The mobile phase was composed of methanol:water pH 2 (50:50, v/v) mixture, and flow rate was set to 1 mL/min.

Emulsion-solvent evaporation method was used to prepare QUE loaded PLCG nanoparticles. Beforehand, PLCG (20 mg) and QUE (2 mg) were dissolved in acetone. The oil phase was added to the aqueous phase containing 0.5% Pluronic F-127 (PF-127). Subsequently, the solution was ultrasonicated for 3 min on ice bath. The mixture was stirred using magnetic stirrer for the evaporation of organic solvent for 8 h. The formed nanoparticles were then washed with MilliQ water twice. Further, the nanoparticles were centrifuged at 20,000 rpm for 20 min. The average particle size and size distribution (PDI value) and also zeta potential of the PLCG nanoparticles were measured by zeta sizer (Nano ZS, Malvern Inst., UK). The encapsulation efficiency of QUE (EE%) was determined by indirect method.

In vitro drug release studies from optimized formulation were performed in the mixture of phosphate-buffered saline (PBS) (pH 7.4) and methanol (70:30) using dialysis bag method at 37°C ± 0.5°C. 2 mL of nanoparticle dispersion was transferred into a dialysis bag which was immersed in 25 mL. The release medium (1 mL) was taken out at predetermined time intervals and added with the same volume of fresh medium to adjust sink conditions. The content of QUE was determined by HPLC. Each test was carried out in triplicate.

## Results and discussion

The QUE loaded PLCG nanoparticles prepared as described in this study, were observed to be opalescent and yellowish. The mean particle size of nanoparticles was  $208.7 \pm 7.5$  nm with a polydispersity index (PDI) of  $0.128 \pm 0.042$ , indicating uniformity size distribution of optimized nanoparticles. The zeta potential of the nanoparticles was  $-21.5 \pm 1.91$  mV (Table 1). After QUE entrapment, nanoparticles showed a slight size increase compared to drug-free nanoparticles ( $176.9 \pm 0.128$  nm) (Table 1).

Table 1. Characterization of QUE loaded nanoparticles

	Size (nm)	Zeta potential	PDI	EE%
QUE np	$208.7 \pm 7.5$	$-21.5 \pm 1.91$	$0.128 \pm 0.042$	81

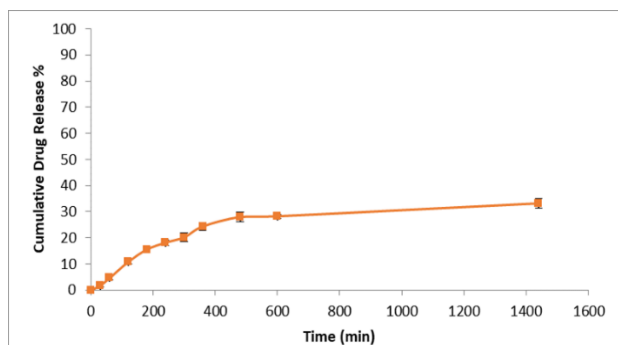


Fig. 1. Cumulative drug release

Encapsulation efficiency of QUE loaded nanoparticle formulation was 81% (Table 1) indicating improved loading of active ingredient within PLCG nanoparticles. Cumulative drug release of QUE from nanoparticles at 1440 min was approximately 33% emphasizing high entrapment of QUE within nanoparticles (Fig. 1).

## Conclusion

In this study QUE loaded PLCG nanoparticles were prepared by emulsion-solvent evaporation method. Based on the above mentioned in-vitro characteristics, we concluded that prepared nano-formulation is a promising nanoparticulate drug delivery system with high QUE loading capacity. For future studies, it is aimed to improve the release properties of QUE from nanoparticles.

## References

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