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Enhanced Solubility and Oral Bioavailability of Hydrophobic Drugs Using Pluronic Nanomicelles: An In-Vitro Evaluation

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This communication is dedicated to Late Yogesh Chamkure for his forever memories in Dr Rakesh K. Sharma's research laboratory.

Poor drug solubility and oral bioavailability is a significant challenge with many effective drug candidates. Pluronic micelles are effective solutions for improved solubility, stability, and delivery of the hydrophobic drug to the right area, at the right time, and in the right amount. Solubilization of three drugs, namely curcumin (CUR), quercetin (QCN), and lamotrigine (LTG), were explored using Pluronics with varying molecular characteristics. All the drugs showed better solubility in Pluronic solutions. The tendency of augmentation in solubility was QCN > CUR > LTG. Results showed better solubilization of drugs in Pluronics which form micelles and have low CMTs. With an objective to enhance the oral bioavailability of drugs, the drug-loaded Pluronic P123 nanomicelles (PLC for CUR, PLQ for QCN, and PLL for LTG) have been prepared and characterized using UV-VIS, DLS, SANS, CPT, and TEM measurements. The drug-loaded P123 nanomicelles having particle sizes range from 18 to 22.5 nm and spherical in shapes. In the in-vitro release study, CUR and QCN showed slow release,while LTG exhibited a faster release profile. The PLC and PLQ assessed their anti-oxidant potential had confirmed the oxidation resistance more significantly than the free drug. Considering the pharma uses of CUR, QCN, and LTG drugs and observing the application of Pluronics in drug delivery systems, the present work facilitates insight into the possible formulations of these drugs.

1. Introduction

More than the past twenty years, triblock copolymers of polyoxyethylene (POE) and polyoxypropylene (POP) with the structure of POE-POP-POE (generally known as Poloxamers or Pluronic® or Synperonic®) accepted great recognition in the area of pharmaceutical as well as cosmetics, petroleum, paints, coatings, energy and food industries.[1–6] These linear triblock copolymers, Pluronics, are not much expensive and available commercially, some of which are approved by the FDA.[7,8] When Pluronic dissolved in water, it self-assembles into nano-sized spherical micelle, which constructed with POP as hydrophobic inner core and POE as hydrophilic outer corona.[9–11] The prominent role of these Pluronics is to solubilize the hydrophobic drugs within the POP core of micelles as drug delivery nanovehicles. Another advantage of using POE as the hydrophilic shell of Pluronic micelles shields the drug present in the core from the outside medium.[12–15] The selection of any Pluronic for a specific application is mainly driven by their various micellar assemblies formed.[16] The micellar behavior of the Pluronics is entirely dependent on the molecular constitution, like the lengths of their POE and POP parts and their EO-PO ratio[17,18] Extensive studies were carried out on the structure of Pluronics at different concentrations, temperatures, and pH environments display a large influence on their phase and micellar behaviour.[19–22] Pluronics were currently widely utilized to prepare thermodynamically stable nanomicellar systems in aqueous media that can be solubilized by hydrophobic pharmaceutically active ingredients[8,11] and lipophilic oils.[23] The solubilized hydrophobic compounds can also influence the structure of Pluronic through increasing the micellar size, the aggregation number, and the volume fraction of micellized polymer.[24–26]

Pluronics were used to enhance the bioavailability of various drugs and furnish metabolic stability with increasing

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