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Mixed Poloxamer Nanomicelles for the Anticonvulsant Lamotrigine Drug: Solubility, Micellar Characterization, and *In-Vitro* Release Studies

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Recently the applications of Poloxamers in drug development is promising as it facilitated the drug molecule for delivering to the correct place, at the correct time and in the correct amount. Poloxamers can form nanomicelles to encapsulate hydrophobic drugs in order to increase solubility, stability and facilitate delivery at target. In this context, the solubilization of anticonvulsant lamotrigine (LMN) drug in a chain of Poloxamers containing different polyethylene oxide and polypropylene oxide moieties were examined. The results showed better solubilization of LMN in Poloxamers contain low CMTs while poor with Poloxamers having high CMTs. Systematic investigation of two mixed Poloxamer nanomicelles (P407:P403 and P407:P105) for LMN bioavailability at body temperature (37 °C) were investigated. The solubility of LMN was enhanced in mixed P407:P403 nanomicelles with the amount of P403 and reduced in mixed P407:P105 nanomicelles with the amount of P105. LMN encapsulated mixed Poloxamer nanomicelles were found spherical in shape with ∼25 nm D_h sizes. The *in-vitro* release profiles of mixed Poloxamer nanomicelles demonstrated the biphasic model with initial burst release and then slowly release of LMN. Better biocompatibility of LMN in the mixed P407:P403 nanomicelles was confirmed with stability data. The results of this work were proven the mixed P407:P403 nanomicelles as efficient nanocarriers for LMN.

Keywords: Mixed Poloxamer Nanomicelles, LMN Solubility, *In-Vitro* Release, Bioavailability.

1. INTRODUCTION

The healthcare industry has currently faced many challenges to develop formulations for a hydrophobic drug that has very low aqueous solubility which results in poor bioavailability. The bioavailability of hydrophobic drugs is often enhanced through micellar solubilization using surfactants [1–3]. Surfactant micellar based solubilization is an important approach due to the adequately high quantity in water and easy movement through membranes, which has to facilitate for better pharma formulations. Such approach mainly depends on the drug's nature that will have particular and individual interactions and compatibility with given micelles of surfactant [4]. At present, the major challenge in pharma formulations is to design and deliver potent surfactant micelles with nano in size [5]. Several surfactants nanomicelles were investigated for improved drug absorption and efficacy. Amongst them, the polymeric surfactant nanomicelles emerged as the most favourable approach. The polymeric surfactant nanomicelles are capable of enhancing the stability and solubility of drugs, increasing cellular uptake and attaining *in-vivo* benefits [6, 7]. In recent years, the mixture of two or more polymeric surfactants to form a mixed polymeric surfactant nanomicelle was a wonderful approach to make better soft assemblies with unique properties [8]. These mixed polymeric surfactant nano micelles enhance thermodynamic and kinetic stabilities, good drug encapsulation efficiency, accurate control on particle size and changing the surface with various moieties [9].

The focus of current research was on triblock copolymeric non-ionic surfactants consisting of a middle hydrophobic polypropylene oxide (PPO) block (at above 20 °C) that connects to hydrophilic polyethylene

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