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Formulation and processing of solid self-emulsifying drug delivery systems (HME S-SEDDS): A single-step manufacturing process via hot-melt extrusion technology through response surface methodology

Venkata Raman Kallakunta [a,1], Narendar Dudhipala [a,1], Dinesh Nyavanandi [a,1], Sandeep Sarabu [a,1], Karthik Yadav Janga [a,1], Srinivas Ajjarapu [a,1], Suresh Bandari [a,1], Michael A. Repka [a,b,*,1]

[a] Department of Pharmaceutics and Drug Delivery, University of Mississippi 38677, USA
[b] Pii Center for Pharmaceutical Technology, University of Mississippi 38677, USA

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ABSTRACT

The objective of the current study is the formulation development and manufacturing of solid self-emulsifying drug delivery systems (HME S-SEDDS) via a single-step continuous hot-melt extrusion (HME) process. For this study, poorly soluble fenofibrate was selected as a model drug. From the results of pre-formulation studies, Compritol® HD5 ATO, Gelucire® 48/16, and Capmul® GMO-50 were selected as oil, surfactant and co-surfactant respectively for manufacturing of HME S-SEDDS. Neusilin® US2 was selected as a solid carrier. The design of experiments (response surface methodology) was employed to prepare formulations via a continuous HME process. The formulations were evaluated for emulsifying properties, crystallinity, stability, flow properties and drug release characteristics. The prepared HME S-SEDDS showed excellent flow properties, and the resultant emulsions were stable. The globule size of the optimized formulation was 269.6 nm. The DSC and XRD studies revealed the amorphous nature of the formulation and FTIR studies showed no significant interaction between fenofibrate and excipients. The drug release studies showed significant ($p < 0.05$) improvement in solubility compared to the pure drug ($DE_{15} = 45.04$ for the optimized formulation), as >90% of drug release was observed within 15 min. The stability studies for the optimized formulation were conducted for 3 months at 40 °C/75% RH.

1. Introduction

Most new chemical entities (70–90%) and 30% of commercially available products exhibit poor water solubility and poor bioavailability (Nikolakakis and Partheniadis, 2017). The low solubility and reduced poor gastrointestinal (GI)-stability leads to poor bioavailability, high intra-subject/inter-subject variability and deficiency of dose proportionality (Bernkop-Schnürch, 2013; Lipinski, 2002). Thus, the poor solubility of the drug causes hindered dissolution, which is a rate-limiting step in absorption (Palmer, 2003). Various strategies such as complexation with cyclodextrin (Ammar et al., 2006), solid dispersions (Farmoudeh et al., 2020; Mande et al., 2017; Weuts et al., 2004), and lipid-based drug delivery systems (Odeberg et al., 2003) have been reported in the literature to improve the solubility to overcome the challenge of the poor solubility of the drugs. Among the lipid-based drug delivery systems (LBDDS), self-emulsifying drug delivery systems (SEDDS) acquired special attention as they have been efficient in improving the oral bioavailability of many poorly water-soluble drugs and improving the pharmacokinetic profiles (Nielsen et al., 2008).

SEDDS improve the solubility of poorly soluble drugs by preserving the drug in the solubilized state and in the form of finely dispersed droplets in the transit through the gastrointestinal tract (GIT), thus improving the bioavailability (Pouton, 2000). SEDDS typically consists of an isotropic mixture of oils (vehicle) and surfactants, optionally co-surfactants capable of forming fine oil in water (o/w) emulsions with the help of mild agitation from peristaltic movements in the GIT

* Corresponding author at: Department of Pharmaceutics and Drug Deliver, Pii Center for Pharmaceutical Technology, School of Pharmacy, University of Mississippi, University, MS 38677, USA.
E-mail address: marepka@olemiss.edu (M.A. Repka).
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