Contents lists available at SciVerse ScienceDirect

Chemical Engineering Research and Design

journal homepage: www.elsevier.com/locate/cherd

Formulation and statistical optimization of multiple-unit ibuprofen-loaded buoyant system using 2^3-factorial design

Jadupati Malakar[a], *Amit Kumar Nayak*[b,*]

[a] *Department of Pharmaceutics, Bengal College of Pharmaceutical Sciences and Research, Durgapur 713212, West Bengal, India*
[b] *Department of Pharmaceutics, Seemanta Institute of Pharmaceutical Sciences, Mayurbhanj 757086, Orissa, India*

ABSTRACT

This present investigation deals with the development and optimization of buoyant beads containing ibuprofen by emulsion-gelation method for gastroretentive delivery. The effect of three independent process variables like amount of sodium alginate, magnesium stearate, and liquid paraffin on drug entrapment, density, and drug release of buoyant beads containing ibuprofen was optimized using 2^3 factorial design. The observed responses were coincided well with the predicted values, given by the optimization technique. The optimized beads showed drug entrapment efficiency of 83.07 ± 3.25%, density of 0.89 ± 0.11 g/cm^3, cumulative drug release of 35.02 ± 1.24% after 8 h, and floated well over 8 h in simulated gastric fluid (pH 1.2) with 4.50 min buoyant lag-time. The average size of all buoyant beads ranged from 1.43 ± 0.05 to 1.82 ± 0.14 mm. The buoyant beads were characterized by SEM and FTIR spectroscopy for surface morphology and excipients–drug interaction analysis, respectively. All these beads showed prolonged sustained release of ibuprofen over 8 h in simulated gastric fluid (pH 1.2). The ibuprofen release profile from these buoyant beads followed Korsmeyer–Peppas model over a period of 8 h with anomalous (non-Fickian) diffusion mechanism for drug release.

Keywords: Ibuprofen; Sodium alginate; Magnesium stearate; Buoyant beads; Sustained release; Optimization; Factorial design

1. Introduction

Oral administration is always the preferred means of drug delivery to the systemic circulation due to low cost of therapy, ease of administration, patient compliance, *etc.* Many attempts have been made to develop sustained release oral dosage forms with better clinical effects and reduced dosing frequency. However, the success of these conventional sustained release dosage forms for oral use is limited due to the inability to increase their residence time in the stomach and proximal portion of the small intestine (Sriamornsak et al., 2005). The variable and too rapid gastrointestinal transit can result incomplete drug release from the dosage form at the absorption site in the gastrointestinal tract (GIT) leading weaken efficacy of the administered dose. To overcome this restrictions, in various oral sustained release dosage forms have been designated to be retained in the gastric region for prolonged period and released incorporated drugs to increase their bioavailability (Nayak et al., 2010b). Many approaches have been reported in the literature for improved gastroretention for oral sustained release dosage forms, *viz.* floatation (Nayak and Malakar, 2011), bio- or mucoadhesion (Nayak et al., 2010a), sedimentation (Rouge et al., 1998), unfoldable, expandable, or swellable systems (Klausner et al., 2003), super porous hydrogel systems (Chen et al., 2000), magnetic systems (Fujimori et al., 1994), *etc.* Every approach has its own limitations. For example, swelling and expanding systems may show a hazard of permanent retention in the desired site and bioadhesive systems may result in irritation of mucous layer due to high-localized concentration of the incorporated drugs (Singh et al., 2010). In addition, single-unit gastroretentive systems such as tablets or capsules may exhibit the all-or-none emptying phenomenon (Kanivva et al., 1988). On the other hand, multiple-unit dosage forms may be an alternative since they have been shown to reduce the inter- and intra-subject variabilities in drug absorption as well as to lower the possibility of

* *Corresponding author*. Tel.: +91 9583131603.
E-mail address: amitkrnayak@yahoo.co.in (A.K. Nayak).
Received 6 December 2011; Received in revised form 23 January 2012; Accepted 16 February 2012
0263-8762/$ – see front matter © 2012 The Institution of Chemical Engineers. Published by Elsevier B.V. All rights reserved.
doi:10.1016/j.cherd.2012.02.010