Research Paper

Double Coated Tablets of Nimesulide for Colon Targeting

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ABSTRACT: The present study was aimed at developing oral colon targeted drug delivery system for Nimesulide utilizing recently designed and patented system called CODESTM, which consisted of a lactulose containing core overcoated with both Eudragit E and Eudragit L designed to rapidly disintegrate in the colon, in order to give a new life for an existing banned drug. CODESTM tablets were prepared by tabletting Nimesulide and lactulose, followed with film coating of Eudragit. The prepared tablets were evaluated on the basis of in vitro dissolution study and in vivo disintegration study was performed by gamma scintigraphic evaluation in rats. The onset of Nimesulide release was found to dependent on the coating level of Eudragit E, and at Eudragit E coating level of 8% (coating weight gain), the onset of in vitro drug release was found to be optimum. When the same was subjected on scintigraphic evaluation for in vivo disintegration study, there was a reasonable agreement between the in vitro/in vivo data. It is concluded that Nimesulide can be targeted to hindgut by a novel approach of CODESTM.

KEYWORDS: Nimesulide; NSAIDs; Colorectal Cancer; Colon Specific Delivery; Polymethacrylate polymers; Gamma Scintigraphy.

Introduction

Oral site-specific drug delivery systems, especially colon-specific drug delivery systems, have attracted a great deal of interest recently for the local treatment of a variety of bowel diseases (Yang et al., 2002) and also for improving systemic absorption of drugs susceptible to enzymatic degradation in the upper G.I.T such as peptides and proteins (Tozaki et al., 1997).

Colorectal Cancer (CRC) is one of the representatives for colon specific diseases and is a leading cause of death in the world (Fukutake et al., 1998). This malignancy is also one of the most serious complications of Inflammatory Bowel Disease (IBD) including Ulcerative Colitis (UC) and Crohn’s disease (Eaden et al., 2001). Long-term UC patients have an increased risk of developing CRC compared with the general population (Ekrom et al., 1990). The precise mechanisms of the IBD-related carcinogenesis process are largely unclear, although it is generally assumed that IBD-related carcinogenesis occurs as a result of chronic inflammation (Weitzman et al., 1990).

Since colorectal carcinomas develop over a period of many years, tumor prevention has been a subject of great interest (Giovannucci et al., 1995). Accumulating evidence indicates that NSAIDs could lower the incidence of colorectal carcinomas (Angulo et al., 2002). The anti-neoplastic property of NSAIDs has been shown in epidemiological studies with human (Reddy et al., 2000), clinical studies of the human disease familial adenomatous polyposis (FAP) (Steinbach et al., 2000) and in experimental carcinogenesis studies with animals (Fukutake et al., 1998). However, long-term uses of non-selective NSAIDs can lead to gastrointestinal toxicity from sustained inhibition of COX-1 (Angulo et al., 2002). Such drawbacks, however, can be overcome by formulating them as colon-specific drug delivery systems, which can deliver drugs to the lower gastrointestinal tract without releasing them in the upper GI-tract, can be expected to increase the quality of life for patients suffering from colon specific diseases. Treatment might be more effective if

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