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New oral delivery systems for treatment of inflammatory bowel disease

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Abstract

Inflammatory bowel disease (IBD) is often localized to specific sites in the gastrointestinal tract (GIT). As a result, this disease can be treated with oral site-specific (targeted) drug delivery systems. Targeted delivery systems for treatment of IBD are designed to increase local tissue concentrations of antiinflammatory drugs from lower doses compared with systemic administration. This review addresses the impact disease has or may have on oral targeted delivery for treatment of IBD as well as a number of delivery approaches currently used in marketed products or under investigation. Delivery systems reviewed rely on temporal control, changes in pH along the GIT, the action of local enzymes to trigger drug release, and changes in intraluminal pressure. Dissolution of enteric polymer coatings due to a change in local pH and reduction of azo-bonds to release an active agent are both used in commercially marketed products. Newer approaches showing promise in treating IBD are based on polysaccharides. These materials are most effective when used as compression coatings around core tablets, which contain the active agent. More complex polymeric prodrugs systems are also under investigation. If the dose of the drug is sufficiently low, this approach may also prove useful in improving treatment of IBD.

Keywords: Oral targeted drug delivery; Large intestine; Colon; Inflammatory bowel disease; Anti-inflammatory

Contents

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1. Introduction

Inflammatory bowel disease (IBD) is a localized inflammation of the small and large intestine. Since intestinal inflammation is confined to specific mucosal or transmural locations, it is possible to deliver drugs specifically to the site(s) of inflammation. In site-specific (targeted) drug delivery it is possible to reduce the total amount of drug administered thus reducing side effects. Broadly speaking, the foregoing has been the basis for using drug delivery to treat IBD.

Many IBD patients experience inflammation in the colon and as a result, much of the literature focuses on colon-specific delivery systems. Many reviews are available on this topic [1–14]. The intent of this review is to focus on novel lower intestinal delivery systems that are, or potentially can be, used to treat IBD. A challenge in developing therapeutically effective products for IBD is the impact disease on the delivery system. As noted below, a range of mechanisms is available to trigger release of a drug in the human gastrointestinal tract (GIT). These mechanisms generally depend on one (or more) of the following variables: time, GIT pH, enzyme activity, oxidation–reduction potential, and intraluminal pressure. Many of these variables are directly impacted by active IBD. For instance, active disease normally leads to altered transit times, most significantly through the colon. Thus, a delivery system relying on the passage of time to control the site of drug release needs to function effectively in patients who demonstrate stasis in one region and rapid and variable transit through other parts of the colon. Similar considerations must be addressed with systems relying on other mechanisms used to control the site of drug delivery.

This review examines various approaches to delivery of drugs in the GIT (primarily those that lead to delivery to the distal small intestine or colon) for treatment of IBD. This examination is made in light of the diseased patient in both the active and quiescent state. Historically, most research on targeted delivery systems has been performed in normal (undiseased) animals and healthy human volunteers.

2. IBD and the GIT

2.1. Site of disease

An immediate issue for targeted delivery systems is site of the disease in the patient. IBD is comprised of two specific conditions: ulcerative colitis (UC) and Crohn's disease (CD). The location of inflammation along the GIT in UC and CD at diagnosis is shown in Fig. 1 [15]. In UC, sites of inflammation extend to the more proximal regions of the colon over time. In CD, the predominate site of inflammation is the distal ileum; between 30% and 40% of patients also have significant colonic involvement. Thus, a delivery system for patients with UC will probably differ from one used to treat CD. The subset of CD patients with colonic involvement will probably benefit from a formulation designed to treat UC.