OXIDANT DEFENSE MECHANISMS IN THE HUMAN COLON

MATTHEW B. GRISHAM, RICHARD P. MACDERMOTT, and EDWIN A. DEITCH

Departments of Physiology and Biophysics and Surgery
Louisiana State University Medical Center
Shreveport, Louisiana
Gastroenterology Section
University of Pennsylvania School of Medicine
Philadelphia, Pennsylvania

Abstract—Reactive oxygen metabolites have been implicated as important mediators of inflammation-induced intestinal injury associated with ischemia (and reperfusion), radiation, and inflammatory bowel disease. Because the colonic mucosa may be subjected to significant oxidant stress during times of acute and chronic inflammation, knowledge of the oxidant defense mechanisms in the colon is of biologic and potential clinical importance. Therefore, the objective of this study was to quantify the specific activities of superoxide dismutase (SOD), catalase, and GSH peroxidase in the normal human colon. We found low, but significant, amounts of all three enzymes in the mucosa, submucosa, and muscularis/serosa of the human colon. However, the mucosal levels of SOD (3.6 ± 0.3 units/mg protein), catalase (11 ± 3 units/mg), and GSH peroxidase (15.2 ± 0.8 mU/mg) represented only 8%, 4%, and 40%, respectively, of those values determined for human liver. Colonic epithelial cells derived from mucosal biopsies exhibited significantly higher specific activities for SOD (12 ± 0.5 units/mg) and catalase (26 ± 6 units/mg) when compared to whole mucosa, suggesting most of the mucosal activity was associated with the epithelial cells and not the lamina propria. In a comparative study, we found that a human colonic carcinoma cell line (CaCo-2) contained significantly lower SOD (6 ± 0.5 units/mg) and catalase (6 ± 0.6 units/mg) activities when compared to colonic epithelial cells. Taken together, our data suggest that: (1) the colonic mucosa is relatively deficient in antioxidant enzymes when compared to liver, and (2) most of the protective enzyme activity is localized within the epithelium and not the mucosal interstitium.

INTRODUCTION

The colonic mucosa plays an important role in maintaining proper fluid and solute exchange as well as providing a restrictive barrier to the immigration of

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potentially noxious bacteria, bacterial products (lipopolysaccharide, N-formylated peptides), and luminal antigens. The mucosal epithelium in known to be injured in a variety of pathophysiological conditions such as ischemic colitis, radiation enteritis, necrotizing enterocolitis, and inflammatory bowel disease (IBD). The enhanced mucosal permeability that results from injury to the epithelium may facilitate the entry of luminal components such as bacteria and bacterial products into the mucosal interstitium and ultimately the systemic circulation. Recent work suggests that the gut ischemia induced by either hemorrhage or endotoxin results in mucosal injury that coincides with translocation of luminal bacteria into the mucosal interstitium (1, 2). These data have prompted investigators to suggest that a breech in the mucosal barrier may play an important role in the initiation and exacerbation of multiorgan failure (MOF) (3).

There is a growing body of experimental evidence to suggest that inflammation-induced intestinal injury associated with ischemia (and reperfusion), radiation, and IBD is mediated in part by reactive oxygen metabolites (ROM) generated by the parenchyma and/or inflammatory phagocytes (4, 5). Most tissues are protected from the injurious effects of these cytotoxic species by the action of certain antioxidant enzymes such as superoxide dismutase (SOD), catalase, and GSH peroxidase. The levels of these enzymes vary greatly from tissue to tissue, with the liver and spleen containing high concentrations and other tissues such as heart and skeletal muscle containing very low levels of these antioxidant enzymes. Virtually nothing is known regarding the levels of antioxidants in the human colon. Indeed, the relative paucity of antioxidant enzymes in certain tissues has prompted some investigators to suggest that these tissues may be easily overwhelmed by enhanced ROM production and thus more sensitive to oxidant injury (6). Since the colonic mucosa may be subjected to significant oxidative stress during times of hypoperfusion or inflammation and thus susceptible to mucosal injury, knowledge of the oxidant defense systems of the gut is of biological and potential clinical importance. Therefore, as a first step in clarifying the intrinsic oxidant defenses in the human colon, we measured the levels of SOD, catalase, and GSH peroxidase in segments of the human colon, in mucosal biopsies, and from a human colonic carcinoma cell line.

**MATERIALS AND METHODS**

*Collection of Tissue and Preparation of Colonic Epithelial Cells (7–9).* Colonic specimens were collected from a total of six patients undergoing elective colon resections for adenocarcinoma of the distal bowel including the descending and sigmoid colon as well as the rectum. For one set