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Implication of Oxidative Stress in Small Intestine Disorders, Constipation and Diarrhea: A Mini Review

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Implication of Oxidative Stress in Small Intestine Disorders, Constipation and Diarrhea: A Mini Review

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Abstract
Diarrhea pathophysiology and constipation are multifactorial gastrointestinal (GI) disorders characterized by intestinal peristalsis disruption of and an irregularity in secretion/absorption process. Oxidative stress, as an imbalance in prooxidants/antioxidants, has recently been recognized as a significant player in these GI disturbances. In this respect, numerous studies were performed and have shown that the deleterious effects on GI tract were accompanied by accumulation of oxidants and depletion of antioxidant system. Antioxidant remedy is necessary in scavenging free radicals and reactive oxygen species preventing oxidative stress-induced GI interruptions.

Keywords: Gastrointestinal disorders; Diarrhea; Constipation; Oxidative stress.

1. INTRODUCTION

Gastrointestinal (GI) motility disorders are the most common GI disturbances in the general population [1]. Diarrhea is one of the major health threats to populations in tropical and subtropical countries. It is responsible for about 5 million deaths annually, of which 2.5 million are children aged less than 5 years [2, 3]. By definition, diarrhea is simply an altered movement of electrolytes and water through the intestinal mucosa. Various mechanisms are responsible for this pathophysiology, such as increased luminal osmolarity, hypersecretion, absorption reduction, and intestinal motility acceleration. These changes cause fluid accumulation in the digestive tract leading to an enteropooling process [4]. In this respect, several studies have used plant extracts and isolated compounds to treat or prevent diarrhea [5-7].

Conversely, an antagonist GI affection, which is characterized by opposite effects, notably, infrequent or difficult evacuation of feces is called constipation. It is a functional GI disorder, which affects 8-15% of the general population [8]. Synthetic drugs are widely used for treatment of constipation. Equally important, some medicinal plant extracts are known to exhibit laxative effects by accelerating the GI transit [9].

Numerous studies have shown that reactive oxygen species (ROS) generation is involved in the development of numerous affections. ROS are potent oxidants to many biomolecules, such as lipid, proteins, and DNA [10]. Consequently, in this review, we will discuss the interaction between oxidative stress and GI disorders, such as diarrhea and constipation.

2. OXIDATIVE STRESS IN THE PROCESS OF INTESTINAL HYPERSECRETION

2.1. Rotavirus and Bacterial Infections-induced Diarrhea

Many studies suggest the implication of oxidative stress in the complication of diverse perturbations, including infectious affections induced by germs in the GI tract. Rotavirus (RV) corruption engenders watery stools via multiple processes, such as oxidative stress. Indeed, the results obtained by Buccigrossi *et al*. [11] suggested a link between oxidative stress and RV-induced diarrhea. These findings demonstrate that RV causes an early production of ROS and depletion in the GSH (Glutathione)/GSSG (Glutathione disulfide) ratio.

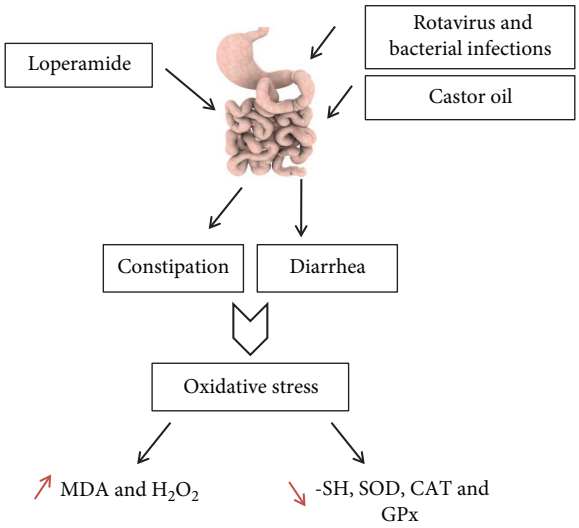
Identically, there is some evidence that hypersecretion induced by bacterial infections was accompanied by oxidative damage. In this context, during the stages of *Salmonella* infection, ROS are also generated and implicating ROS generation as an important host response to GI infection which provokes a depletion of glutathione (the main antioxidant of intestinal epithelial cells) [12].

2.2. Castor Oil–induced Diarrhea Associated with Oxidative Stress

Several studies have shown the intervention of oxidative stress in castor oil–induced diarrhea. Therefore, recent studies have shown that acute administration of castor oil increased the formation of malondialdehyde (MDA) in the GI tract mucosa indicating an increase in lipid peroxidation [13, 14]. This process presents a possible mechanism of tissue alteration by oxygen reactive derivatives.

Moreover, recent findings indicated that diarrhea is also associated with hydrogen peroxide (H_2O_2) production in intestinal mucosa. H_2O_2 by itself is relatively inactive but can lead to the formation of toxic (•OH). This later, thus generated, oxidize

Figure 1: Implication of oxidative stress in gastrointestinal disorders.



malondialdehyde (MDA), hydrogen peroxide (H_2O_2), superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx).

important cellular components and deplete glutathione. Oxidative degradation of lipids provokes a membrane fluidity alteration, disruption in ion exchange, loss of membrane integrity, and finally damage in cellular functions [15].

A more recent study reported that castor oil–induced diarrhea was able to induce a deleterious effect on the sulfhydryl (-SH) group. This alteration can be explained by the protein oxidation process, which leads to the dysfunction of many enzymes [16].

Enzymatic antioxidants including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) have an important role in the prevention of oxidative damage by ROS. SOD plays a crucial action in dismutation of superoxide radicals to H_2O and oxygen. On the other hand, CAT protects the cells from toxic effects of ROS by transforming H_2O_2 to H_2O and O_2 [17]. In this respect, numerous studies have reported that castor oil–induced diarrhea causes depletion of antioxidant activities of SOD, CAT, and GPx, which explains the overproduction of ROS [18].

3. OXIDATIVE STRESS IN CONSTIPATION

A recent study showed the intervention of oxidative stress in the loperamide-induced constipation in rats. In colonic mucosa, the oxidative stress conditions were assessed by an increase of MDA and H_2O_2 production. These effects were accompanied with perturbation of enzymatic and nonenzymatic antioxidants [19].

4. CONCLUSION

In conclusion, understanding the mechanisms by which various factors perturb the intestinal balance by oxidative stress installation open the way for designing new strategies based on the use of antioxidants as potential therapeutics for GI disorders (diarrhea and constipation).

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