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Anti-Colitis Effects of Brown Rice Reported by Experimental Studies

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Abstract

Brown (unpolished) rice is a good source of vitamins, minerals, and dietary fiber and is consumed as a health food, particularly in Asian countries. Although a limited number of studies have investigated the anti-colitis effects of brown rice, including rice bran and treated brown rice, some have reported the protective effects of brown rice in animal models of dextran sulfate sodium-induced colitis in the following settings: 1) Rice bran oil, 2) Brown rice fermented by *Aspergillus oryzae*, 3) Enzyme-treated rice fiber, and 4) *Kurozu* (fermented vinegar made from brown rice). The possible mechanisms underlying the anti-colitis effects of brown rice include anti-oxidant effects, inhibition of proinflammatory cytokine production, myeloperoxidase activity, neutrophil infiltration in the colonic mucosa, activation of nuclear factor kappa B (NF-κB), and improvement of dysbiosis. However, the active components in dietary products derived from brown rice or treated brown rice have not yet been identified. This report summarizes the studies demonstrating the anti-colitis effects of brown rice or treated brown rice in animal models of colitis.

Keywords: Brown rice; Rice bran; Anti-colitis effect; Inflammatory bowel disease; Ulcerative colitis

Introduction

Both white and brown (unpolished) rice are widely consumed as a staple food item in many Asian countries, including Japan. Brown rice is whole-grain rice from which the outmost layer (husk or hull) is removed, leaving only the germ and bran [1]. White rice is produced from brown rice by a milling process wherein the bran and germ are removed, leaving behind the mostly starchy endosperm. Although there is no significant difference in the calorie content between brown and white rice, there are significant differences in processing and nutritional content. Brown rice contains an abundance of vitamins such as vitamin B1, minerals, and dietary fiber compared with white rice; therefore, it is regarded as a health food [2]. In Japan, the increased incidence of beriberi (or thiamin deficiency) in the late 1800s was attributed to, among other causes, the increased consumption of cooked white rice instead of brown rice.

Crohn's disease (CD) and ulcerative colitis (UC) are the two most commonly encountered forms of inflammatory bowel disease (IBD), which is characterized by chronic relapsing inflammation. Patients with IBD are at an increased risk of colorectal cancer because of chronic inflammation [3]. Although the causes of IBD have not been fully elucidated [4-6], intestinal microbiota has been shown to be involved in IBD in both human and animal models of colitis [5]. Dietary factors influence the composition of the intestinal microflora, which appear to play a major role in the development of IBD. Moreover, multiple genetic factors [7], dysregulation of mucosal immunological function, overproduction of pro-inflammatory cytokines [6,8,9], and oxidative stress [10,11] also play important roles in the development and severity of IBD. A recent systematic review indicated that the incidence of CD and UC in western and European countries was 90 and 505 vs. 319 and 322 per 100,000 persons, respectively [12,13].

Diet therapy may be useful to control inflammation in IBD patients because prolonged administration is associated with a very low incidence of severe adverse effects. Moreover, supplementation with probiotics or prebiotics has been reported to suppress colitis in IBD patients [5]. Therefore, the occurrence and severity of IBD may be influenced by dietary factors [14]. A multicenter case-control study in Japan proposed that a decrease in the daily consumption of rice may be related to the occurrence of IBD [14,15]. In contrast, daily consumption of meat and sugar has been associated with an increased incidence of both CD and UC in case-control studies [14]. Although brown rice is regarded as a health or functional food, no large-scale study till date has been conducted to determine whether the consumption of brown rice can attenuate colitis in IBD patients, and clinical evidence of the efficacy of brown rice against IBD remains unclear. However, Chiba et al. [16,17] reported that the consumption of a semi-vegetarian diet, in which brown rice is a staple food and animal fat is limited, was found to induce disease remission in two Japanese patients with CD. Although the active ingredients in a semi-vegetarian diet remain unclear, the potential efficacy of brown rice for the remission of CD has been reported.

Moreover, there have been relatively few studies pertaining to the anti-colitis effects of brown (unpolished) rice or dietary factors derived from brown rice in animal models of colitis [3,5,6,18,19]. In this report, studies demonstrating the anti-colitis effects of brown rice in animal models are summarized.

Methods

In this report, we reviewed the English and Japanese literature and summarized the findings of retrieved studies that demonstrated the anti-colitis effects of brown rice in animal models. A literature search was performed using the following keywords: (1) "brown (unpolished) rice" and "colitis", (2) "rice bran" and "colitis", (3) "brown (unpolished) rice" and "inflammatory bowel disease", (4) "rice bran" and "inflammatory bowel disease", and (5) "fermented brown rice". Searches of the English and Japanese literature were performed using the PubMed (http://www.ncbi.nlm.nih.gov/pubmed/) and Japana Centra Revuo Medicina (Igaku Chou Zasshi) (http://search.jamas.or.jp/) databases, respectively.

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Animal models used in studies of IBD

Animal models are commonly used to study IBD. The symptoms and histopathological findings of 2,4,6-trinitrobenzenesulfonic acid (TNBS)-induced colitis in animal models resemble those observed in CD patients [20]. On the other hand, symptoms of dextran sulfate sodium (DSS)-induced colitis in animal models, such as bloody feces, weight loss, and mucosal ulceration, resemble those observed in UC patients [19,21]. Therefore, TNBS- and DSS-induced animal colitis models are often used to study CD and UC, respectively.

Anti-colitis effects of rice bran oil

Brown rice retains the bran component, and rice bran oil (RBO) is an abundant source of bioactive phytochemicals with antioxidant activities, such as gamma-oryzanol, and contains a number of phenolic compounds, such as phytosteryl ferulate [6,19,22]. Sierra et al. [23] reported that RBO reinforced Th1-dominant immune responses *in vitro*. RBO has been reported to confer health-related benefits in patients with several chronic diseases, including cancer, hyperlipidemia, and heart disease [19].

Moreover, Islam et al. [19] investigated the anti-colitis effects of RBO in a DSS-induced colitis model and reported that oral administration of RBO attenuated the histological findings of colitis and inhibited the production and activities of myeloperoxidase (MPO), pro-inflammatory cytokines, cyclooxygenase-2, and nuclear factor kappa B (NF-κB). They also suggested that phytosteryl ferulate was the key active ingredient of RBO. Reddy et al. [6] also investigated the anti-colitis effects of RBO as an antioxidant and reported that the consumption of RBO attenuated the histopathological changes of colitis and MPO activity and decreased neutrophil infiltration as well as the symptoms of diarrhea, body weight loss, and bloody feces in a DSS-induced colitis model.

Anti-colitis effects of brown rice fermented by Aspergillus oryzae

Fermented brown rice by *Aspergillus oryzae* (FBRA) is processed by fermenting brown rice and rice bran by *A. oryzae*. FBRA contains a large amount of dietary fiber [5,24], while *A. oryzae* contains a high content of enzymes with a strong ability to convert starches, proteins, and lipids to a variety of bioactive compounds [25]. Moreover, *A. oryzae* does not generate aflatoxin, a strong carcinogen associated with the occurrence of hepatocellular carcinoma [25]. Among the animal models [5] and clinical trials [26,27] reviewed in this study, no FBRA-associated toxicity was observed.

Ochiai et al. [28] reported the preventive effects of a hydrous ethanol extract of FBRA on gastrointestinal damage in a methotrexate (MTX)-treated animal model. FBRA extract contains nucleobases and low dietary fiber content, although FBRA generally contains abundant dietary fiber. Moreover, MTX treatment of an animal model resulted in malabsorption syndrome through severe malabsorption of nutrients and diarrhea [28]. They reported that oral administration of FBRA extract attenuated diarrhea, increased protein content in the small intestine, and improved survival [28].

Moreover, Kataoka et al. [5] reported ameliorating effects of FBRA on DSS-induced colitis in a rat model. They indicated that the consumption of a diet containing 5% and 10% FBRA attenuated colitis, as confirmed by macroscopic and histological findings, while that of a diet containing 10% FBRA also decreased the activity of MPO, which can serve as a marker of neutrophil infiltration in the colonic mucosa [5]. This group also reported that dietary FBRA increased the number of resident lactobacilli in the intestine of a rat model of DSS-induced colitis, although it did not change the proportion of lactobacilli spp., which also contains FBRA [24]. Selected strains of lactobacilli are beneficial to human health as probiotics and have been reported to suppress IBD [24].

Anti-colitis effects of enzyme-treated rice fiber

Enzyme-treated rice fiber (ERF) is a prebiotic product made from raw rice bran by treatment with heat-resistant amylase, protease, and hemicellulose [3]. ERF is a heterogeneous mixture of dietary fiber and protein and a very good source of dietary fiber compared with rice bran [3]. Komiyama et al. [3] investigated the preventive effects of ERF in an animal model of DSS-induced colitis and indicated that ERF attenuated associated symptoms such as diarrhea and body weight loss as well as histological findings of colitis such as serum and mucosal cytokine levels and T cell activation in the spleen and mesenteric lymph nodes. These findings suggested that the anti-inflammatory effects of ERF were significantly superior to those of raw rice bran [3]. They also reported possible mechanisms of colitis attenuation by the oral administration of ERF, the preventive effect of dysbiosis (a decrease in *Clostridium* and *Eubacterium* spp.), promotion of short-chain fatty acid production, and attenuation of overwhelming immune responses [3]. Moreover, short-chain fatty acids are energy sources for the colonic epithelium and exhibit anti-inflammatory properties [3,29]. For example, butyrate reportedly has the ability to downregulate NF-κB activation [3].

Anti-colitis effects of Kurozu (Kurosu)

Kurozu (*Kurosu*) is traditional Japanese black vinegar made from brown (unpolished) rice that is widely used in the preparation of Japanese foods. It is manufactured by fermentation for more than a year in earthenware jars. The supernatant, known as *Kurozu*, contains acetic acid as well as an abundance of organic materials, minerals, and amino acids not found in other vinegars [18]. *Kurozu* also contains metabolites generated by lactobacillus and koji bacillus, among other microbes.

We previously demonstrated the protective effects of *Kurozu* in a rodent model of DSS-induced colitis [18]. Oral administration of *Kurozu* significantly attenuated DSS-induced colitis as well as symptoms of bloody feces, body weight loss and decreased nitrotyrosine levels in the colonic epithelium, possibly by antioxidant activities. Acetic acid, the main component of *Kurozu*, has been reported to improve hyperlipidemia in humans and animal models [30]. However, our study indicated that acetic acid did not ameliorate DSS-induced colitis [18].

Anti-colitis effects of brown rice or dietary factors derived from brown rice correlated with oxidative stress

In inflammatory conditions such as IBD, the generation of superoxide and nitric oxide (NO) is generally accelerated [18,31]. Superoxide is cytotoxic and associated with tissue damage in many diseases, and excessive NO production can aggravate inflammatory conditions [18]. Moreover, these molecules rapidly react with each other to form highly reactive peroxynitrite [32] that causes tissue damage via nitration of protein tyrosine residues to form nitrotyrosine, which is considered a marker of oxidative and nitration stress [18,33]. Therefore, peroxynitrite may have played a key role in the induction of colitis in these studies.

With regard to the MPO pathway, MPO is mainly released by neutrophils, so it is possible that RBO or treated brown rice may block MPO release by neutrophils in colonic tissues, as reported in other studies [18]. Nitrotyrosine is produced by at least two pathways: a reaction between superoxide and NO and a reaction between nitrite and MPO [18,32]. Therefore, the possibility that RBO or treated brown rice suppresses the reaction between MPO and nitrite, which leads to a decrease in nitrotyrosine formation, cannot be ruled out.

Conclusions

The anti-colitis effects of brown rice, including rice bran and treated brown rice, have been summarized in several studies that employed experimental colitis models. The anti-oxidative and inhibitory effects of pro-inflammatory cytokines, MPO activity, and activation of NF-κB have been identified as the major mechanisms underlying these anti-colitis effects. Moreover, the improving effects of dysbiosis may be related to the anti-colitis effects. However, the active components in dietary factors derived from brown rice have not yet been identified. At present, there is no clear evidence supporting the anti-colitis effects of brown rice in IBD. Therefore, clinical studies of this widely used dietary food are warranted.

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