Pak. j. sci. ind. res. Ser. B: biol. sci. 2025 **68B**(2) 215-222

Effect of Prebiotic Supplemented Cookies on Rats with Chemically Induced Colitis

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(received January 22, 2024; revised May 25, 2024; accepted June 3, 2024)

Abstract. Inflammatory bowel disease develops in areas of the world where prebiotic intake is inadequate. Ulcerative colitis is a type of IBD symbolized by inflammation of the colon's mucosal lining. increased consumption of DF is linked to a decreased risk of inflammation. Anaerobic colonic bacteria transform prebiotics into short chain fatty acids. Okara is an emerging prebiotic derived from agro-food industrial waste that enhances human gut health. The current research was conducted to utilize nutrient rich residue Okara for the preparation of value added products in different proportions 0, 5, 10, 15 and 20% against GIT disorder. The severity of colitis was made less severe by Okara as seen by the lowering pH and decreased disease activity index. Short chain fatty acids values significantly ($P<0.05$) increase in both studies. Okara an agro-industrial waste helps to support the species of bacteria in the gut that make short-chain fatty acids and provide anti-inflammatory potentials. These patterns might encourage better gut health.

Keywords: Okara, cookies, prebiotic, short chain fatty acid, inflammation, ulcerative colitis

Introduction

The gastrointestinal tract undergoes both micro and macro changes in response to various factors such as diet, lifestyle, disease and medications. Micro changes: The GIT hosts a complex ecosystem of micro-organisms. Changes in diet, antibiotics, stress and other factors can alter the composition and diversity of the gut microbiota. Macro changes: The GIT undergoes rhythmic contractions known as peristalsis to propel food and waste material through the digestive tract. Nutrient absorption primarily occurs in the small intestine, where nutrients are absorbed into the blood stream for distribution to the body's cells. Inflammatory conditions such as inflammatory bowel disease (IBD) can cause mucosal ulceration and thickening of the intestinal wall. Overall, both micro and macro changes in the GIT can have significant implications for digestive health.

Inflammatory bowel disease is an autoimmune condition marked by chronic gastrointestinal tract inflammation and linked to a dys-regulated immune response and an over abundance of immune cells in the colon Juritsch and Moreau (2018). Nonetheless, in the twenty-first century, IBD has become more commonplace worldwide in terms of occurrence. Cases of IBD are increasing in Asia, even though they are still less than in western nations Park and Cheon (2021). Crohn's disease and Ulcerative colitis are the two most common chronic diseases associated with inflammatory bowel disease. CRP (C-reactive protein) is the most widely used serum indicator of inflammation in IBD. It is a pentameric protein made by the liver under certain conditions including (but not limited to) inflammation. CRP may be more sensitive than ESR (erythrocyte sedimentation rate) and correlates better with disease activity in inflammatory bowel disease (IBD). Both may be more useful in Crohn's disease (CD) than in ulcerative colitis (UC).

Patients with ulcerative colitis have a continuous stretch of inflammatory tissue in their colon and more commonly in the rectum or distal colon. Crohn's disease, on the other hand, can cause inflammation in any part of the gastrointestinal tract, including the oral cavity though it's most frequent in the ileocolic region Juritsch and Moreau (2018). Rectal bleeding or bloody diarrhea are common ulcerative colitis symptoms, whereas abdominal pain and weight loss are common Crohn's disease symptoms Podolsky (2002). Worldwide Crohn's disease is less common than ulcerative colitis. According to reports, there are 1.2-20.3 and 7.6-245 cases of UC

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per 100,000 people annually, respectively and in terms of overall incidence and prevalence. Genetics, environmental factors, autoimmune and gut microbiota are the main risk factors for ulcerative colitis. Bloody diarrhea with or without mucus, tenesmus, rectal urgency and varying degrees of stomach pain that are frequently relieved by feces are all features of the classic presentation of UC Gajendran *et al*. (2019).

Colonic SCFAs deficiency, particularly butyrate, may result in chronic colonic damage. UC patients with active disease have lower SCFAs concentrations in the intestinal lumen than normal people. This suggested a link between SCFAs deficiency and UC. Butyrate enemas, on the other hand, have had mixed outcomes in the treatment of active UC Wong *et al*. (2006). Prebiotics as treatments for human IBD are still in the early stages of development. Okara is believed to normalize bowel movement and function and might be used as an immobilization carrier to promote cell survival in the GIT environment, lowering and decreasing the risk of colon disease development Nishibori *et al*. (2018).

Okara is a gluten-free soybean pulp or dietary fiber leftover produced after the aqueous fractions have been extracted during soy milk production Kamble *et al*. (2019). When 1 Kg of soybean is used to make soymilk, more than of 1 Kg Okara is produced, resulting in a large amount of residue Davy and Vuong (2020). Okara is primarily composed of DF. Okara's nutritional profile lends it potential prebiotic properties that interact with gut bacteria Pérez-López *et al*. (2016). It's important to include Okara (residue) in food products to reduce the environmental impact of their disposal and also improve the nutritional profile of the item Wu *et al*. (2012). Cookies are the most popular snack in the world due to their diversity, extended shelf life, ease of availability and low prices Abdel-Moemin (2015). Okara supplemented cookies encourage people to consume agro industrial waste as a functional food to boost the nutritional worth of the product and to substitute wheat in the bakery industry which can assist with medical issues. Since dietary fiber is the most widely recognized part of Okara, its supplemented items can be utilized as a prebiotic treatment for serious ailments.

Materials and Methods

Soybean was purchased from Ayub Agriculture Research Institute (AARI), Faisalabad. Cookie ingredients were procured from the local market and all chemicals used in the study for various analyses were acquired from Sigma-Aldrich (St. Louis, MO, USA).

Animals. Investigational rats were used in the efficacy trials to evaluate the ulcerative colitic potential of cookies made from different Okara and wheat flour fractions. For this purpose, 120 male Sprague Dawley rats were purchased and caged. In the animal modeling, five groups of rats were formed in two major groups assigning 12 rats to each group (Table 1).

Diet. The rats were first accustomed to being fed a basic diet for one week. Normal and colitic rats were fed Okara supplemented cookies powder. T_0 (wheat cookies) and other groups were fed Okara supplemented cookies powder 5, 10, 15 and 20% (Table 2). Rats were sacrificed after three weeks.

Colitis induction. In trial II, rats were given 2.5% colitis-grade dextran sulfate sodium DSS (w/v) in their drinking water for one week to cause ulcerative colitis Bibi *et al*. (2017) to see what effect it had.

Colon length and weight. The rats were sacrificed after being anesthetized. Blood was drawn with a syringe and centrifuged for 15 min at 3,000 rpm before being stored at -20 °C. Colons were collected after dissection, washed and measured.

Rats' fecal pH and SCFAs. The cecal content was diluted in water 1:3 (w/v) and the pH was measured with a pH meter. To determine SCFA, the diluted samples were centrifuged (9,000 g, 15 min, 4 °C) and the supernatants were employed in (GLC) Jiménez-Escrig *et al*. (2013).

Assessment of inflammation. Stool consistency, blood in the stool and body weight are the three parameters. To define the disease activity index (DAI) in each group, these clinical variables were evaluated independently, combined and then split by three criteria Table 3 Mchenga *et al*. (2008).

Statistical analysis. The analysis was performed in triplicates and results were presented as mean values The obtained data was designed to analyze for analysis of variance (ANOVA), LSD and two-factor factorial Steel *et al*. (1999).

Results and Discussion

The fecal pH of normal and colitic rats is shown in (Fig. 1). Trial I pH ranged from 6.53±0.00 to 6.35±0.01 and trial II pH ranged from 7.01±0.01 to 6.87±0.01 PH

significantly (P<0.05) decreased in both studies. The lowest pH values were seen in T_4 in both studies.

Short chain fatty acids of normal and colitic rats are shown in (Fig. 2, 3 and 4). Trial I acetate ranged from 36.05±0.00 to 58.99±0.01 (µmol/g) and trial II acetate ranged from 27.41±0.01 to 34.47±0.01 (µmol/g). Whereas propionate values of trial I ranged from 22.01±0.01 to 33.91±0.01 (µmol/g) and trial II propionate values ranged from 6.82±0.00 to 37.27±0.01 (µmol/g) and butyrate values of trial I ranged from 28.01±0.01 to 44.81±0.01 (µmol/g) and trial II butyrate values ranged from 6.97±0.01 to 30.35±0.02 (µmol/g). Short chain fatty acids values significantly (P<0.05) increase in both studies. The highest SCFA values were seen in T_4 in both studies.

The colon length and weight of normal and colitic rats are shown in (Fig. 5 and 6). Trial I colon length and weight ranged from 10.02±0.01 to 10.04±0.00 cm and 0.23±0.00 to 0.26±0.00 g respectively. Trial II colons from DSS-treated mice (T_0) were significantly shorter than those from DSS + Okara supplemented cookies fed groups but were significantly heavier, colon length and weight ranged from 5.82±0.01 to 9.11±0.01 cm

Table 1. Group of rats used to evaluate the colitic potential

	Trial I					Trial II				
	Normal rats					Colitic rats				
Groups	1	2	3	4	5	1	2	3	4	5
Feed	T_0	T_1	T_2	T_3	T_4	T_0	T_1	T_2	T_3	T_4

Table 2. Treatment plan of Okara supplemented cookies preparation

Treatment	Okara %	Wheat %
T_0	-	100
T_1	5	95
T_2	10	90
T_3	15	85
T_4	20	80

Table 3. Assessment of inflamination in stool consistency and blood stool

Score	Weight loss%	Stool consistency	Blood stool
0	None	Normal	No blood
1	0-5	Normal	Normal
2	5-10	Loose stools	Occult blood
3	10-20	Loose stools	Occult blood
4	20>	Diarrhea	Gross bleeding

The DAI is defined as the sum of weight loss stool consistency, and blood in stool

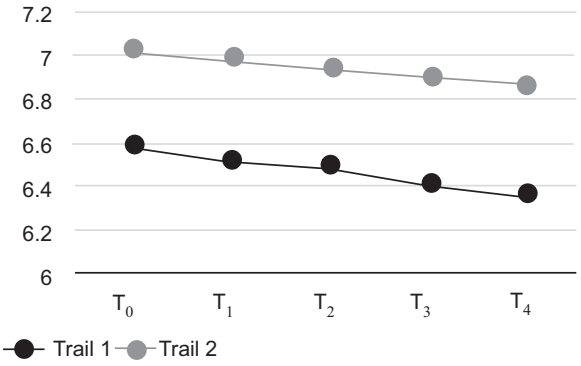

Fig. 1. Fecal pH of both studies.

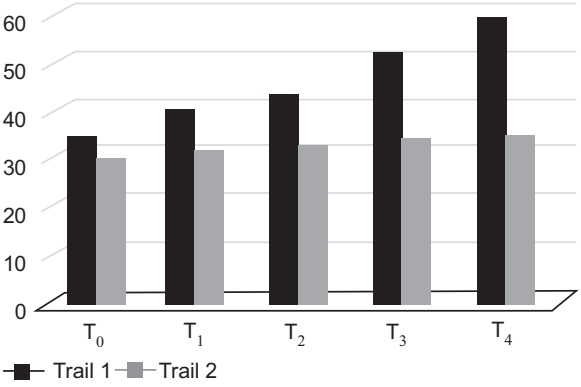

Fig. 2. Acetate (C_2) µmol/g.

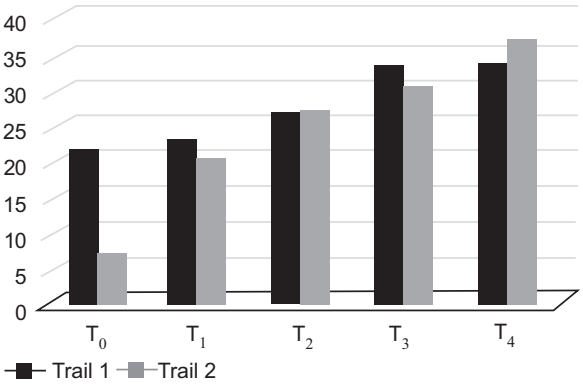

Fig. 3. Propionate (C_3) µmol/g.

and 0.46±0.05 to 0.24±0.01 g respectively. This pattern represents acute DSS treatment effects on colon length and weight. Colon length significantly (P<0.05) increased in both studies, whereas the weight of the colon increased significantly (P<0.05) in trial I and decreased significantly in trial II.

DAI values ranged from 2.54±0.01 to 1.69±0.01 (Fig. 7). DAI was significantly lowest in the (T_4) DSS + 20% Okara supplemented cookies treatment fed group. The colitis group without treatment (T_0) presented significantly increased inflammatory parameters and reduced body weight.

Prebiotics alter the microbial ecology of the gut by encouraging the development of commensal defense bacteria and boosting resistance to bacterial colonization that causes illness, which helps to prevent colitis (Sartor, 2004). In a study conducted by Pérez-López *et al*. (2018) on healthy rats, cecal pH showed only a small statistical change between the groups fed a 20% Okara-supplemented diet against the control diet (5.97 to 5.95). Common beans improve bowel health. According to Monk *et al*. (2017) findings, cooked chickpea flour significantly decreased the cecal luminal pH by 20% as compared to the basal diet (BD: 8.35 0.07, CK: 8.13 0.35). The pH of the cecal fluid in rats with DSS colitis was nearly neutral Videla *et al*. (2001). Pereira *et al*. (2011) claim that several variables, including the substrate type and strain used, initial pH and temperature, affect the growth of micro-organisms. A diet based on plants has a naturally greater fibre content, which helps to support the species of bacteria in the gut that make SCFAs and provides phytochemicals with anti-inflammatory qualities. Short-chain fatty acid levels are frequently reported to be lower in fecal samples from people with IBD Parada Venegas *et al*. (2019). Bean flour supplementation has been shown to modify the fecal microbiota. In the rats, beans reduced the fecal microbial abundance of the families Lactobacillaceae, Clostridiaceae, Peptococcaceae, Peptostreptococcaceae, Rikenellaceae and Pophyromonadaceae Monk *et al*. (2016).

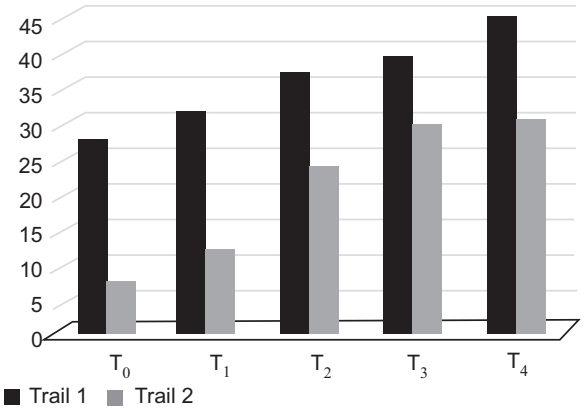

Fig. 4. Butyrate (C_4) µmol/g.

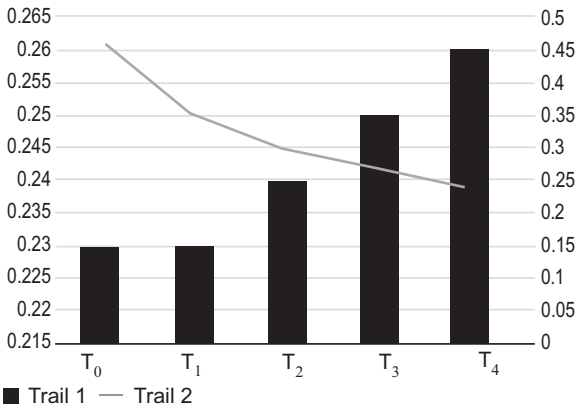

Fig. 6. Rat's colon weight (g).

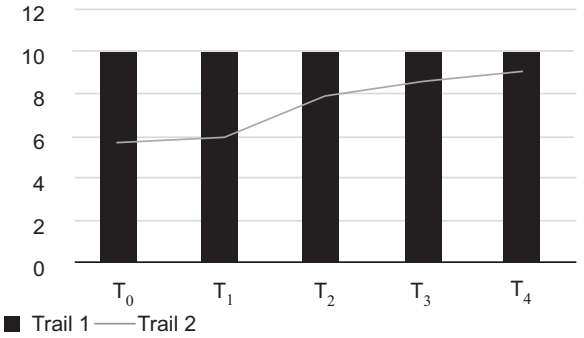

Fig. 5. Rat's colon length (cm).

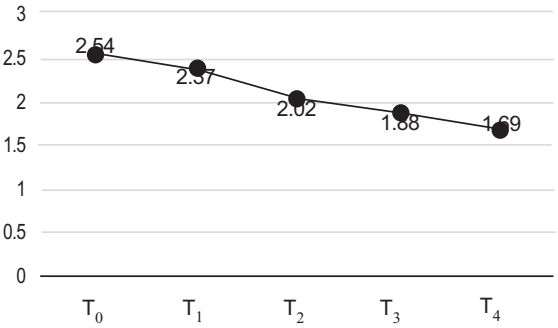

Fig. 7. Disease activity index.

DSS caused some changes in the SCFA molar ratio and a slight drop in the concentration of short chain fatty acids in the caecum Moreau *et al*. (2002). The main composition of short chain fatty acids is propionate, acetate and butyrate at a ratio of roughly 20:60:20, respectively. Daily 500-600 mmol of SCFAs are produced in the gut, depending on the diet's fiber content, the microbiota's makeup and the length of the gut's transit Silva *et al*. (2020).

The colonic physiological function is boosted by anti-inflammatory processes of SCFA-mediated signaling, which promote gut health and reduce the degree of colitis related inflammatory damage Monk *et al*. (2017). Clinically, it appears that treating colitis with more fermentable DF or SCFAs is advantageous Cabre and Domenech (2012). By controlling lipid balance and reducing oxidative stress and inflammation, SCFAs were essential in preventing metabolic syndrome Wang *et al*. (2021). The chemical composition of DF has a significant impact on its fermentability. Generally speaking, soluble polysaccharides ferment more quickly and thoroughly than insoluble polysaccharides Hamaker and Tuncil (2014).

In addition to increasing colonic butyrate production, fiber supplements also encouraged colonic epithelial cells to utilize butyrate which was inhibited in experimental colitis which is comparable to what has been documented in IBD in humans. These acids-especially acetate, butyrate and propionate-acidify the bowel and give the host's metabolism energy Schaafsma (2008). In comparison to standard rodent chow, 10% Okara decreased cecal acetate and increased cecal butyrate concentration in female rats for one month Jiménez-Escrig *et al*. (2008).

Length of colon can be used to detect colitis because the inflamed colon becomes thicker and shorter described as the result of a muscular contraction Santiago *et al*. (2007). According to Sayer *et al*. (2002), DSS-treated mice displayed considerable wasting and shortening of the colon compared to control by the conclusion of the 8-day study period.

Weight loss, diarrhea and rectal bleeding were all associated with acute histological changes in colitis brought on by DSS. The histological findings paralleled the macroscopically visible damage. Histological findings were consistent with remarkable morphological changes in DSS-treated rats compared to DSS + T_4-treated rats. For clinical assessment, DAI was determined to express the severity of colitis Sudirman *et al*. (2018). According to an analysis by Rose and Strombom (2020), eating a lot of fat increases the likelihood of developing ulcerative colitis.

A red seaweed (*Eucheuma cottonii*) extract that is high in dietary polysaccharides reduces the intestinal inflammation brought on by DSS, making it a promising colitis therapy option. Following a seven day course of treatment, taking EC extracts prevented weight loss, decreased the colon's weight-to-length ratio and also lessened colonic damage Sudirman *et al*. (2018).

In rats with DSS-induced colitis, germinated barley foodstuff (GBF) oral supplementation which is low in lignified hemicelluloses and high in glutamine boosted mucosal protein and RNA contents and reduced mucosal damage in comparison to the control group, according to Araki *et al*. (2007). Moreover, it was demonstrated that GBF inhibited mucosal mast cells, protecting the intestinal submucosa from injuries. In a pilot study conducted by Hallert *et al*. (2003), 22 UC patients in retardation (median time from last relapse, one year prior to the intervention) had the safety and effectiveness of a high fiber diet assessed. For three months, it was advised that the patients increase their intake of oat bran by 60 g/day. The fecal SCFA concentration, particularly butyrate, increased statistically significantly as a result of the oat bran supplementation. The experiment showed that individuals with UC who were in remission had a good tolerance for the oat bran intervention and that it was effective in raising fecal SCFA concentrations.

Germinated barley meals which are high in hemicellulose-rich dietary fiber and glutamine-rich protein, have demonstrated prebiotic qualities in the DSS model of rat colitis by reducing the incidence of mucosal damage and bloody diarrhea Younis *et al*. (2015). Also, compared to a probiotic combination of *C. butyricum* and *lactobacilli* germinated barley meals had a better potential to lessen the signs and symptoms of DSS colitis Fukuda *et al*. (2002). Two additional prebiotics that can reduce DSS colitis in rats are lactulose and goat's milk oligo-saccharides. On the other hand, rats treated with FOS had no defense against inflammation, as demonstrated by its effects on DSS colitis. These contradictory findings may result from variations in the colitis model or from adjustments to the FOS delivery, which then alters fermentation rates and subsequently SCFA production Younis *et al*. (2015).

In a mouse model, Winkler *et al*. (2007) look at the decrease in colonic damage and disease activity. C57BL/6 mice were given DSS to induce colitis, and FOS treatment was administered twice a day for 19 days. Fructose oligo-saccharides treatment minimized colonic crypt loss, histological damage and disease activity index in rats. When compared to diets based on casein or whey, a soy only diet (20%, wt/wt) in mice was similarly observed to diminish colonic edema brought on by DSS-induced colitis, avoid colon shortening and attenuate GI histological abnormalities of IBD Jiang *et al*. (2011). Patients with IBD can benefit from using symbiotics as a treatment. In a trial on ulcerative colitis, a month-long regimen of a *Bifido bacterium* strain isolated from healthy rectal samples and FOS (12 g/d) the number of inflammatory markers and tissue inflammation were reduced and the clinical scores improved Furrie *et al*. (2005).

Conclusion

The current study has contributed significantly to the understanding of how dietary interventions can positively impact colitis, with a particular focus on the role of SCFA and pH modulation in the gut micro-environment. Discovered attributes of okara as a prebiotic source, highlighting its previously underutilized potential. By elevation the growth of friendly bacteria and promoting SCFA production, Okara has shown promise in justifying colitis symptoms and inflammation. Additionally, the pH modulation attained by okara's dietary fibers pays to the maintenance of a healthier gut environment which is critical in colitis management.

Key shortcomings of the study. Okara, being a rich source of dietary fiber, can promote the growth of beneficial gut bacteria when fermented in the colon. These bacteria produce metabolites like SCFAs, which have been associated with maintaining a healthy colon environment. SCFAs may help regulate colonic PH and create a slightly acidic environment that is conducive to the growth of beneficial bacteria while inhibiting the growth of harmful pathogens. SCFAs, particularly butyrate, have been associated with various health benefits, including promoting gut barrier function, reducing inflammation and providing energy for colonocytes. Okara's rich fiber content and potential to promote the growth of beneficial gut bacteria suggest it may have anti-inflammatory properties that could be beneficial in colitis. As always, it's essential to consume Okara as part of a balanced diet especially if you have specific health concerns like GIT aliments.

Conflict of Interest. The authors declare that they have no conflict of Interest.

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