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Laxative Potential of The Konjac Flour (*Amorphophallus muelleri* Blume) in Treatment of Loperamide Induced Constipation on Sprague Dawley Rats

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***Abstract*—**There is long history of konjac tubers being used as a cure for certain diseases in China and Japan. Konjac flour is prepared from konjac tubers and it contains high concentration of glucomannan. Konjac Glucomannan (KGM) is dietary fiber and the role of which has been demonstrated in weight reduction, lowering blood cholesterol and sugar level, promoting intestinal activity etc. Konjac glucomanan has a property of swelling by absorbing water, more than a hundred times its own weight. Therefore it helps increasing weight of feces, water content of feces, and promotes satiety feeling. Mode of actions of dietary fibre as laxatives agents includes holding water inside the bowel lumen, inhibition of water absorption in the colon and stimulating colonic motility. Number of fecal pellets did not effected in rats were fed on 300 and 600 mg/kg of konjac flour, as well as constipated control and Dulcolax treatment. Water content, weight of fecal pellets and gastrointestinal transit ratio were higher in rats treated with 600 mg/kg than 300 mg/kg of konjac flour. Rats were administered with Dulcolax showed the highest gastrointestinal transit ratio, followed by 600 mg/kg konjac flour. The lowest feed consumption was noted in 600 mg/kg konjac flour diet group.

***Keywords*—**Laxative, konjac flour, *Amorphophallus muelleri* Blume, glucomannan, constipation.

I. Introduction

CONSTIPATION is a common problem in public health related with infrequency, difficulty or discomfort of defecation process and sense of incomplete evacuation, which marked with feces remain in the colon for prolonged periods of time, leading to water absorption, hardening of stool and excessive straining [1]. An epidemiologic study of constipation in the United State identified it as an inability to evacuate feces completely and spontaneously three or more times per week [2]. Several conditions such as deficiency of dietary fiber, fluid, exercise, metabolic problem, increase use of medication and age can cause constipation. Constipation generally first appears between the ages of two and four years children. Up to one third of children ages 6 to 12 years report constipation [3]. Constipation is also common in older people and the number of persons reporting constipation increases with age [4].

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Laxatives drugs are agents that add bulk to intestinal contents, that retain water within the bowel lumen by virtue of osmotic effects, or that stimulate intestinal secretion or motility, thereby increasing the frequency and ease of defecation [5]. There are four main types of laxative drug: bulking agents, stool softeners, stimulant laxatives and osmotic ally active compounds [6]. The use of laxative drug is very common for constipation treatment especially for older people. But, repeated use of laxative drugs has side effects. Senna (anthraquinones) can cause allergic reactions, fluid and electrolyte depletion, and Melanesia coli. The side effect of bulking agents was bloating and flatulence depends on their doses. Diphenylmethane derivatives (bisacodyl) may cause cramping and electrolyte depletion when large doses are used. Diarrhea is a side effect of colchicine drug [5].

Side effects of the laxative drug encourage the research to find safer compound without side effects and derived from plants. Several researches reported that many plant could use as laxative agents, such as: apple fruit [7], figs fruit [8], kiwi fruit [9], [10], papaya fruit [11], watermelon fruit [12], flaxseed [13], *Aloe ferox* Mill leaves [14], *Aloe vera* leaves [15], tamarind leaves [16], agarwood leaves [17], [18], euphorbiaceae leaf [19] and konjac tubers [20].

Konjac glucomannan (KGM) is a dietary fiber that derived from *Amorphophallus konjac*. It has been shown to relieve constipation, which could be associated with increased stool bulk and improved colonic ecology [21]. Several researches also reported that konjac flour that contains glucomannan can used as laxative agent for children, pregnant women, and healthy man. Reference [22] found that glucomannan to be beneficial in the treatment of constipation in children with no significant side effects such as: abdominal pain, bloating, abdominal distention, excessive gas, diarrhea, or anaphylactic symptoms. Reference [23] reported that consumption of 1.45 grams per day of glucomannan in constipated pregnant women for 1-3 months induced a return to normal frequency of weekly number of evacuations (4.9-5.8 times/weeks). Moreover, supplementation of konjac glucomannan (4.5 gram per day) into low-fiber diets increased bowel movement frequency by 30% and improved the colonic ecology in slightly-constipated adults [24].

Konjac flour which has been reported as a laxative agent was konjac glucomannan that originated from Japan (*Amorphophallus konjac*). In fact, there are another species of

konjac (*Amorphophallus muelleri* Blume) that have a high potential and prospects for development in Indonesia [25]. Therefore, this research will be conducted to determine the effect of konjac flour from Indonesia as laxative drug. Therefore this paper is, to report the laxative effect of konjac flour on loperamide-induced constipation rats. The konjac flour from *Amorphophallus muelleri* Blume was extracted by using multi-stage maceration method with ethanol solvent at three stages of concentration.

II. Materials And Methods

A. Preparation of Materials

The tubers of konjac (*Amorphophallus muelleri* Blume) were thoroughly washed with water, cut into thin slices and dried in the oven at 40^{o}C for 24 hours. The dried chips were grinded into powder with stamp mill for 16 hours, 30 minutes, 24 second at frequency 18.47. Then, konjac flour was sieved at 30 meshes and blower by using air classifier. 25 gram of materials was purified by multi stage maceration method with 233.77 ml ethanol 40%, 60% and 80% respectively, at 434.22 rpm for 4 hours, 16 minutes. Then, it was filtered by a filter paper and the precipitate was dried in an oven at 40^{o}C for 24 hours [26].

B. Animals

Male albino rats (*Rattus norvegicus*) of Sprague Dawley strain with a mean weight 175-250 gram. The animals were housed individually in plastic cage placed in a well ventilated house with optimum condition. They were acclimatized to the animal house condition for 7 days during which they were allowed free access to standard diet (AIN-93M) and tap water *ad libitum*.

C. Ethical Approval

All experiment procedures were approved by the Ethical Clearance Committee, University of Brawijaya, Malang, Indonesia.

D. Induction and Evaluation of Constipation

Constipation was induced in the animals by the oral administration of 1ml loperamide (3mg/kg body weight in water for 3 days), while the normal control were administered with the water only. The passage of reduced, hard and dry fecal pellets indicated constipation in the rats.

E. Experimental Design

The rats were grouped into five of three rats each, the animals in group 1 (normal control) and group 2 (constipated control) were not administered with konjac flour. Group 3 and 4 comprised constipated rats given 300 and 600 mg/kg body weight/day of konjac flour respectively, while group 5 were constipated rats administered with 0.75 mg/kg body weight of Bisacodyl (Dulcolax). The water intake and feed intake of all the rats were recorded during experiment period and treatment continued for 5 days. Then, the gastrointestinal transit ratio measurement was assessed on the sixth day.

F. Total Number, Dry Weight and Water Content of the Fecal Pellet

The excreted fecal pellets of individual rats were collected everyday at 15:00 throughout the duration of the experiment. Total number, weight and water content of the fecal pellets were determined and data taken from the average value of five days assessment. The water content was calculated as the difference between the wet and dry weight on the pellet.

G. Gastrointestinal Transit Ratio

Gastrointestinal transit ratio was measured according to the method in [16]. Before measurement of GIT ratio, rats were fasted for 18 hours but they allowed free access of water. Then, the rats were fed a standard diet. After 45 minutes, 1ml of norit (3 gram suspended in 25ml of water) was orally administered to the rats as a marker. 20 minutes after administering the marker, the animals were anesthetized and sacrificed. The abdomen immediately cut open to excise the whole small intestine. The small intestine from the pylorus to the caecum was quickly removed and the distance traveled by the norit and the total length of the intestine were measured. The GIT ratio was expressed as the percentage of the distance travelled by the norit relative to the total length of the small intestine.

H. Statistical Analysis

Data are presented as mean ± standard deviation of three replicates and were subjected to one way analysis of variance (ANOVA) followed by Tukey's Honestly Significant Difference (HSD) test to determine significant differences in all parameters. Values were considered statistically significant at $P<0.05$.

III. Results

A. Feed and Water Intake

To evaluate the laxative effect of konjac flour from *Amorphophallus muelleri* Blume, groups of rats were induction with loperamide 3mg/kg body weight for three days, except one group for normal control. After induction time, all the groups of rats were fed with diet containing konjac flour with the doses based on experimental design and also Dulcolax as a laxative drug control. The weight of feed intake and water intake was significantly reduced in constipated rat compared with normal control.

TABLE I
Effect of Konjac Flour of Feed Intake and Water Intake

Treatment (mg/kg body weight)	Feed intake (gram)	Water intake (ml)
Normal control	23.57 ± 2.26^{b}	15.73 ± 1.67^{ab}
Constipated control	16.74 ± 0.78^{a}	11.93 ± 1.01^{a}
Konjac flour 300	16.69 ± 0.45^{a}	14.00 ± 0.35^{a}
Konjac flour 600	14.96 ± 1.89^{a}	14.20 ± 1.00^{a}
Dulcolax 0.75	18.79 ± 0.71^{ab}	13.20 ± 0.60^{a}

Data are means ± SD (n=3): different letters from the control are significantly different ($P<0.05$)

Based on Table I, normal control group had the highest value of feed intake and significant different compare with

other control group. Addition of konjac flour doses had a tendency to reduce feed intake of constipated rats. Meanwhile, the water intake was highest in normal control group, but it had a different trend compare with feed intake parameter. This is due to the increased dosage of konjac flour would increase water consumption of constipated rats although there were no significant difference amongst konjac flour diet group ($P<0.05$). These result indicated that the administering of loperamide affected on feed and water intake.

B. Fecal Properties

In the control group, loperamide administration significantly decreased the number of fecal weight and fecal water content, suggesting the induction of loperamide-induced constipation ($P<0.05$). In the meantime, the number fecal pellet was no significant difference between control groups. It indicated that the administering of loperamide was not effect of number fecal pellet.

TABLE II
EFFECT OF KONJAC FLOUR ON FECAL PROPERTIES OF RATS

Treatment (mg/kg body weight)	Fecal pellet number	Fecal weight (gram)	Fecal water content (%)
Normal control	13.53 ± 0.95	1.46 ± 0.21^{ab}	56,.84 ± 5.20^{b}
Constipated control	8.93 ± 2.89	0.55 ± 0.09^{a}	34.42 ± 1.22^{a}
Konjac flour 300	10.40 ± 1.04	0.88 ± 0.01^{a}	53.64 ± 4.12^{b}
Konjac flour 600	12.00 ± 3.12	1.16 ± 0.44^{ab}	58.19 ± 5.38^{b}
Dulcolax 0.75	11.53 ± 1.27	0.88 ± 0.12^{a}	53.80 ± 5.63^{b}

Data are means ± SD (n=3): different letters from the control are significantly different ($P<0.05$)

In the constipated groups, when the konjac flour content in diet was increased, the water content and weight of fecal pellet increased dose-dependently, the increase being significant with the dose 600 mg/kg body weight in comparison with the constipated control group ($P<0.05$). Moreover, in the dose 600 mg/kg of konjac flour was the highest in fecal water content following with normal control group [Table II]. These result indicated that administration of 600 mg/kg of konjac flour could relieved constipation by increased of water content of fecal in comparison with Dulcolax (laxative drug).

Loperamide administration reduced the gastrointestinal motility in the untreated constipated rats [Fig. 1]. It was noted that no significant difference of ratio was observed between the constipated control and the normal control. It showed that the administering of loperamide had no effect on the gastrointestinal transit ratio. The konjac flour diet increased the gastrointestinal transit ratio with the increasing of the doses. Especially for the dose 600 mg/kg of konjac flour, the treatment of konjac flour increased the gastrointestinal movement which compared with Dulcolax, a standard laxative drug.

C. Gastrointestinal Transit Ratio

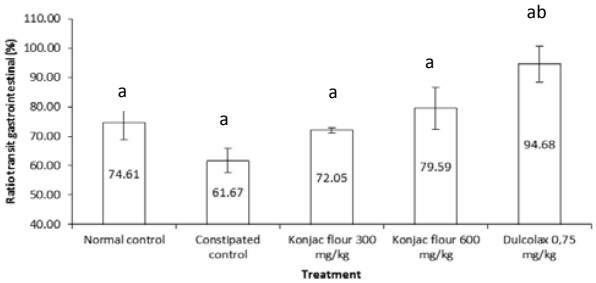

Fig. 1 Data is gastrointestinal transit ratio in normal, loperamide-induced rats + konjac flour and loperamide-induced rats + dulcolax-treated rats. Data are mean of three determination ± standard deviation bars with different letters from the control are significantly different ($P<0.05$)

IV. DISCUSSION

Oral administration of loperamide (3mg/kg body weight) for three days induced constipation on normal rats by decreasing of fecal pellet weight and water content. This is related to that loperamide enhances absorption of water, electrolytes, and glucose from an isotonic buffer containing glucose, and partially reversed the effects of PGE_2 (prostaglandin E_2) on water and electrolytes transport. PGE_2 induced secretion of fluid in the rat intestinal tract and its action might be related to an effect on intestinal motility [27]. When secretion was induced by PGE_2, loperamide significantly reduced that secretion [28]. The drug also suppresses the peristaltic contraction caused by distension of the intestinal lumen [29]. Moreover, loperamide may reverse the elevation of hydrostatic tissue pressure that opposes normal absorption, when secretory stimuli increase mucosal tension. This anti secretory effect at the mucosal is accompanied by motor effects when loperamide reaches the mesenteric muopiate receptors [30]. The reduction in the water consumed by the constipated animals may also be due to the effect of the drug which probably accounted for the reduction in water content of the fecal pellets [14].

The administration of konjac flour of *Amorphophallus muelleri* Blume to the constipated rats was effective in influencing increased water content, weight of fecal pellet and intestinal motility. These are indication of the laxative property of the plant. This may be due to the high concentration of glucomannan as dietary fiber. Konjac glucomanan has a property of swelling, by absorbing 138-200% of water [31]. Hence, konjac have beneficial effect to relieve constipation because of its capacity to absorb and retain water in the gut.

High content of dietary fiber on diet relates to fecal consistency, because fecal consistency depends on the ratio of the water holding capacity of the insoluble solids, such as dietary fibers. When there are sufficient water holding solids or little no bound water, stools remain thick or formed. On the other hand, if there are too few of these water holding solids to bind all of the water present, stool consistency becomes loose, eventually to the point of being like water [32].

Dietary fiber is fermented by micro flora in the colon. The result of this is to stimulate microbial growth and to increase microbial mass [33]. The additional mass in the colon that occurs with adequate fiber diets eases distal propulsion of luminal contents, and this decreased transit time means less time for interaction between the enterocyte and luminal contents [34]. Dietary fiber fermentation by micro flora was also to lead the production of SCFAs that lower colonic pH and result in a significant prebiotic effect in which the growth of beneficial intestinal micro flora. The formation of SCFAs helps to improve laxation and regularity by increasing fecal bulk and weight and increasing the water holding capacity (and thus the hydration) of feces [35]. Intraluminal administration of SCFAs provoked contractions at the proximal colon, which migrated to the transversal and distal colon. SCFAs caused a significant increase in the luminal concentration of 5-HT of the vascular isolated and luminal perfused rat colon ex vivo. 5-HT (5-hydroxytryptamine) plays an important role in regulating colonic motility [36].

In this study, Dulcolax (bisacodyl) was used as the laxative drug control. Generally, the effect of the treatment with the konjac flour compared favorably well to that of bisacodyl. This is an indication that the konjac flour was effective in ameliorating constipation, thereby increasing the motility in the intestine and ease of defecation. Based on the data, Dulcolax treatment was higher on gastrointestinal transit ratio, but lower on water content and weight of fecal pellet than 600 mg/kg konjac flour diet group. It was indicated that both of them have difference mechanism to relieve constipation. It is well-known that, bisacodyl is a laxative drug that classified in stimulant agent. It has been called “stimulant” laxative because it was thought to work by stimulating intestinal motility. It is hydrolyzed in the small intestine and colon by endogenous esterase to its free form and has effects in the small intestine and colon [5]. The drug act by stimulating peristalsis, sensory nerve endings (hence the frequent side effect of colic) and possibly interfering with electrolyte flux to inhibit water absorption in colon [6].

V. Conclusion

Oral administration of konjac flour from *Amorphophallus muelleri* Blume exhibited laxative activity in loperamide induced constipated rats. The result suggested that, the beneficial effect of the dietary fiber is in improving bulky feces and intestinal motility. Rats were administered with 600 mg/kg body weight showed the better laxative action than the lower dose.

The administering of loperamide affected on feed and water intake of konjac flour treated rats and dulcolax-treated rats. Numbers of fecal pellet was not affected amongst all treatments and normal control rats, although fecal weight and fecal water content of loperamide-induced + konjac flour and loperamide-induced plus dulcolax treated rats were affected at $P<0.05$, by treating rats with administering konjac flour at 300 and 600mg/kg body weight and for dulcolax-treated rats at 0.75mg/kg body weight.

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References

[1] Mostafa SM, Bhandari S, Ritchie G, Gratton N, and Wenstone R. 2003. Constipation and its implications in the critically ill patient. *British Journal of Anaesthesia*. 91 (6): 815-19.
[2] Lembo A, and Camilleri M. 2003. Chronic constipation. *The New England Journal of Medicine*. 349 (4): 1360-1368.
[3] Biggs WS, and Dery WH. 2006. Evaluation and treatment of constipation in infants and children. *American Family Physician*. 73 (3): 469-477.
[4] Hsieh C. 2005. Treatment of constipation in older adults. *American Family Physician*. 72 (11): 2277-2284.
[5] Schiller LR. 2001. Review article: the therapy of constipation. *Alimentary Pharmacology and Therapeutics*. 15: 749-763.
[6] Emmanuel AV, Tack J, Quigley EM, and Talley NJ. 2009. Pharmacological management of constipation. *Neurogastroenterology and Motility*. 21 (2): 41-54.
[7] Niwa T, Nakao M, Hoshi S, Yamada K, Inagaki K, Nishida M, and Nabeshima T. 2002. Effect of dietary fiber on morphine-induced constipation in rats. *Bioscience, Biotechnology and Biochemistry*. 66 (6): 1233-1240.
[8] Oh HG, Lee HY, Seo MY, Kang YR, Kim JH, Park JW, Kim OJ, Back HI, Kim SY, Oh MR, Park SH, Kim MG, Jeon JY, Hwang MH, Shin SJ, and Chae SW. 2011. Effects of Ficus carica paste on constipation induced by high protein feed and movement restriction in beagles. *Laboratory Animal Research*. 27 (4): 275-281.
[9] Rush EC, Patel M, Plank LD, and Ferguson LR. 2002. Kiwifruit promotes laxation in the elderly. *Asia Pasific Journal of Clinical Nutrition*. 11 (2): 164-168.
[10] Chan AOO, Leung G, Tong T, and Wong NYH. 2007. Increasing dietary fiber intake in terms of kiwifruit improves constipation in Chinese patients. *World Journal of Gastroenterology*. 13 (35): 4771-4775.
[11] Widyastuti TEW, Srianta I and Lestari LA. 2008. Papaw flour (Carica papaya) as laxative agent on Sprague Dawley rats measured in caecum and feces. Medicinal Plant Journal. 7 (1): 76-83.
[12] Sharma S, Paliwal S, Dwivedi J, and Tilak A. 2011. First report on laxative of *Citrullus lanatus*. *Pharmacology*. 2: 790-797.
[13] Xu J, Zhou X, Chen C, Deng Q, Huang Q, Yang J, Yang N, and Huang F. 2012. Laxative effects of partially defatted flaxseed meal on normal and experimental constipated mice. *BMC Complementary and Alternative Medicine*. 12 (14).
[14] Wintola OA, Sunmoru TO, and Afolayan AJ. 2010. The effect of *Aloe ferox* Mill. in the treatment of loperamid-induced constipation in Wistar rats. *BMC Gastroenterology*. 10 (95): 1-5.
[15] Ashafa AOT, Sunmonu TO, Abass AA and Oghe AA. 2011. Laxative potential of the ethanolic leaf extract of Aloe vera (L.) Burm. f. in wistar rats with loperamide-induced constipation. *Journal of Natural Pharmaceuticals*. 2 (3): 158-162.
[16] Sudari D and Winarno MW. 2010. Effect of laxative juice of (*Tamarindus indica* Linn.) leaf on Wistar rats induced by Gambier fruit extract (*Uncaria gambir* Roxb). Health Research and Development Media. 20, (3): 100-103.
[17] Kakino M, Tazawa S, Maruyama H, Tsuruma K, Araki Y, Shimazawa M, and Hara H. 2010. Laxative effect of agarwood on low-fiber diet-induced constipation in rats. *BMC Complementary and Alternative Medicine*. 10 (68): 1-8.
[18] Hara H, Ise Y, Morimoto N, Shimazawa M, Ichinashi K, Ohyama M, and Iinuma M. 2008. Laxative effect of agarwood leaves and its mechanism. *Bioscience, Biotechnology and Biochemistry*. 72 (2): 335-345.
[19] Meite S, Bahi C, Yeo D, Datte JY, Djaman JA, and N’nguessan DJ. 2010. Laxative activities of Mareya micrantha (Benth) Mull. Arg.

(Euphorbiaceae) leaf aqueous extract in rats. *BMC Complementary and Alternative Medicine*. 10 (7).
[20] Passaretti S, Comin M, Donzelli R, Rocca F, Colombo E, Ferrara A, Dinelli M, Prada A, and Curzio M. 1991. Action of glucomannans on complaints in patients affected with chronic constipation: a multicentric clinical evaluation. *Italy Journal Gastroenterology*. 23 (7): 421-425
[21] Chen HL, Cheng HC, Liu YJ, Liu SY, and Wu WT. 2006. Konjac acts as a natural laxative by increasing stool bulk and improving colonic ecology in healthy adults. *Nutrition*. 22 (11): 1112-1119.
[22] Baucke VL, Miele E, and Staiano A. 2004. Fiber (Glucomannan) is beneficial in the treatment of childhood constipation. *Pediatrics*. 113 (3).
[23] Signorelli P, Croce P, and Dede A. 1996. A clinical study of the use of a combination of glucomannan with lactulose in the constipation of pregnancy. *Minerva Ginecology*. 48 (12): 577-582.
[24] Chen HL, Cheng HC, Wu WT, Liu YJ and Liu SY. 2008. Supplementation of konjac glucomannan into a low-fiber Chinese diet promoted bowel movement and improved colonic ecology in constipated adults: a placebo-controlled, diet-controlled trial. *Journal of the American College of Nutrition*. 27 (1): 102-108.
[25] Sumarwoto. 2005. Iles-iles (*Amorphophallus muelleri* Blume); Description and other properties of Iles-iles. *Biodiversity*. 6 (3): 185-190.
[26] Widjanarko, S.B, Faridah, A and Sutrisno, A. 2011. Effect of Multi-level ethanol leaching on physic-chemical properties of konjac flour (*Amorphophallus oncophillus*). Asean Food Conference 2011. BITEC, BANGKOK, Thailand June 16-18, 2011.
[27] Shandu BK, Tripp JH, Candy DCA, and Harries J T. 1981. Loperamide: studies on its mechanism of action. *Gut*. 22: 658-662.
[28] Hughes S, Higgs NB, and Turnberg LA. 1984. Loperamide has antisecretory activity in the human jejunum in vivo. *Gut*. 25: 931-935
[29] Sohji Y, Kawashima K and Shimizu M. 1978. Pharmacological studies of loperamide, an anti-diarrheal agent. *Nihon Yakurigaku Zasshi*. 74 (1): 155-63.
[30] Awouters F, Mengens A, Verlinden M, Schuurkes J, Niemegeers C, and Janssen PA. 1993. Loperamid: survey of studies on mechanism of its anti-diarrheal activity. *Digestive Diseases and Sciences*. 38 (6): 977-995.
[31] Sumarwoto. 2006. Review: Mannan content of Iles-iles tuber (*Amorphophallus muelleri* Blume). *Biotechnology*. 4 (1): 28-32.
[32] Saito T, Mizutani F, Iwanaga Y, Morikawa K, and Kato H. 2002. Laxative and Anti-diarrheal Activity of Polycarbophil in Mice and Rats. *Japanese Journal of Pharmacology*. 89 (2): 133-41.
[33] Cummings JH. 1984. Constipation, dietary fiber and the control of large bowel function. *Postgraduate Medical Journal*. 60: 811-819.
[34] Kurasawa S, Haack VS, and Marlett JA. 2000. Plant residue and bacteria as bases for increased stool weight accompanying consumption of higher dietary fiber diets. Journal of the American College of Nutrition. 19 (4): 426–433.
[35] Slavin JL, Savarino V, Paredes-Diaz A, and Fotopoulos G. 2009. A review of the role of soluble fiber in health with specific reference to wheat dextrin. Journal of International Medical Research. 37 (1): 1-17.
[36] Fukumoto S, Tatewaki M, Yamada T, Fujimiya M, Mantyh C, Voss M, Eubanks S, Harris M, Pappas TN, and Takahashi T. 2003. Short-chain fatty acids stimulate colonic transit via intraluminal 5-HT release in rats. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*. 284: R1269-R1276.