

Effects of Morphological Changes and Intestinal Transit time After Administration of Daesenggi-Tang in Rats

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This study was examined the effects of Daesenggi-Tang on intestinal mucosa and gastrointestinal transit time and plasma lipids in rats. Adult male rats were fed four weeks on diets containing no addition(basal diet group), 5 % cellulose(cellulose group) and Daesenggi-Tang group(Daesenggi-Tang group). The results were as follows; 1. The gastrointestinal transit times was significantly decreased in Daesenggi-Tang administered group compare to basal diet and cellulose groups. Carmine red mixed with Daesenggi-Tang, as a marker, was administered through a gastric tube for stomach or intracecally by a chronically implanted catheter for colon transit. Small intestinal transit and large intestinal transit time were significantly decreased in Daesenggi-Tang administered group compare to basal diet. 3. The height of jejunal villi was developed in Daesenggi-Tang administered group compare to basal diet. The thickness of mucosa and muscle layer of colonic mucosa were significantly developed in Daesenggi-Tang administered group compare to basal diet group. 4. The numerical change of goblet cell in colonic mucosa was increased acid mucin stained alcian blue in Daesenggi-Tang administered group compare to basal diet and cellulose group. 6. HDL-cholesterol of plasma lipid was increased in Daesenggi-Tang administered group compare to basal diet and cellulose groups. These results suggests that Daesenggi-Tang may be used in prevention and treatment of constipation resulting in increase of fecal weight, decrease of gastrointestinal transit time, development of intestinal villi, intensify of stainability of acid mucin in colon.

Key words : Daesenggi-Tang, Gastrointestinal transit, Intestinal mucosa, Constipation

Introduction

Constipation is a common clinical problem that comprises of symptoms included excessive straining, hard feces, feeling of incomplete evacuation and infrequent defecation. Although many conditions, such as metabolic problems, fiber deficiency, anorectal problem, an drug, can cause constipation¹.

Many patients fail to respond to the simple constipation remedies of increased fiber and fluid intake. Primary constipation - ie. constipation with no causative factor - is very common. When secondary to other conditions, medications, or disease processes, the focus of constipation management is correction of causative factors². Symptoms of constipation have been attributed to slow transit, irritable bowel syndrome, or pelvic floor

dysfunction resulting in dyssynergic defecation^{2,3}.

Patients with dyssynergic defecation usually respond to biofeedback therapy and pelvic muscle re-education. Constipation-predominant irritable bowel syndrome is best managed with dietary monitoring and modification, fiber therapy, and education regarding self-monitoring and self care². Patients with slow transit constipation may benefit from fiber therapy and increased activity, but most also will require laxative therapy². The consistency of faeces is the result of the transit rate of digest and/or changes intestinal absorption⁴. The transit rate is normally closely related to variations in the myoelectrical activity of the gut, whereas changes in water and electrolyte absorption are not necessarily caused by changes in motility⁴.

Feeding of dietary fiber affects gastrointestinal function and faecal output. In human, the addition of natural fibers to the diet normalizes the speed of intestinal transit⁵ as well as increasing faecal wet and dry weight⁶. Fiber also decreases nutrient and mineral assimilation but to a degree that varies

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with the type and physical composition of the fiber^{7,8)}. Studies of dietary fibers and their effects on bowel function have indicated various changes in stool output and composition, not all of which are solely attributable to water binding properties measurable in vitro⁹⁾. Research reports examining the effects of added dietary fibers on stool bulk and composition have been reviewed¹⁰⁾.

Sennosides, the main laxative components of various senna extracts, chemically belong to the anthraquinones. They are inert in the upper gastrointestinal tract. Anthraquinones induce fluid secretion exclusively in the colon when administered orally as senna glycosides¹¹⁾. Senna laxatives also cause changes in motility of the large intestine⁴⁾. have examined the effects of Daesenggi-Tang on intestinal mucosal changes, gastrointestinal transit time and plasma lipids compare to dietary fiber group in rats.

Material and Methods

1. Measurement of body weight, daily food intake, faecal output, whole gut transit, plasma lipid and morphological studies

1) Animals

Male Sprague-Dawley rats weighing 180-190 g were fed a nonpurified diet for five days, then experimental diet(Table 1). The rats were maintained at 22 ± 2 °C and 60 ± 5 % relative humidity in a room temperature with a 12hours light : dark cycle and given free access to food and water ad libitum. Rats were divided into 3 groups of eight or six rats each. They were fed diets containing fiber-free(basal diet), 5 % cellulose and extracts of Daesenggi-Tang(2 ml/day) for 4 weeks.

Table 1. Composition of experimental diets (Unit: g/kg)

Ingredients	Basal diet	5 % Cellulose	Daesenggi-Tang
Casein	200	200	200
DL-methionine	3	3	3
Sucrose	552	552	552
Corn starch	150	100	150
Corn oil	50	50	50
AIN-76 mineral	35	35	35
AIN-76 vitamin mix	10	10	10
Dietary NSP ²⁾			
5 % Cellulose	0	50	0
Daesenggi-Tang	0	0	2 ml/day

1. American Institute of Nutrition (1977)

2. NSP : Non-starch Polysaccharide

2) Diets

The diets used in these studies consisted of the following ingredients in g/100 g diet : 20 g casein, 0.3 g DL-methionine, 55.2 g sucrose, 15 g corn starch, 5 g corn oil, 3.5 g AIN-76 mineral(American Institute of Nutrition), 1 g AIN-76 vitamin mix, and 2-5 g test substances substitute for corn starch(Table 1). The test substances(dietary non-starch polysaccharide(NSP))

included 5 g cellulose(5 %), and Daesenggi-Tang(2 ml/day).

Table 2. Contents of Daesenggi-Tang.

Scientific Name	Dose(g)
Rheum palmatum L.	16
Magnolia officinalis	8
Citrus aurantium	8
Crystalline sodium sulfate	8
Total amounts	40

3) Preparation of Medical Decoction and Administration

The composition of Daesenggi-Tang is shown in Table 2. Most herbs for the prescription in this study were purchase from the Woosuk Oriental Medical Hospital. Ten dose of medicine was boiled with 1 ℓ of distilled water, and fine filtered decoction was extracted until the volume was reduced to 200 ml in a rotary vacuum evaporator. Experimental rats were oral-administered daily with 2 ml of decoction.

4) Measurement of body weight, daily food intake and faecal output

Rats were monitored daily for general health and body weight changes were determined weekly. Food intake and food efficiency were monitored weekly for 4 weeks. The daily food intake data obtained for 4 weeks.

5) Faecal output

During the experiment the rats were kept individually in cages with a wire-meshed floor through which faeces fell onto drawing paper. After administration of the test substances mixed with basal diet, Daily faecal output(dry weight) was obtained by freeze-drying.

6) Whole gut transit

After administration of basal diet(control) and test substances, transit times were determined in separate animals by measurement of the initial appearance of dye in the faeces after intragastric intubation of 2 ml aqueous 1.5 % carmine red dyes. During the experiment, the animals were kept individually in a wire meshed cage to enable the faeces to fall through onto drawing paper. The time until appearance of the first coloured faeces was measured.

7) Measurement of plasma lipid

At the termination of the study, rats were deprived of food for 16 hours and blood was taken by cardiac puncture from all animals under anesthesia, and assayed for total plasma cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides.

8) Morphological studies

After anesthesia with ethyl ether, the mid-region of the small intestine(jejenum) and mid-colon were removed, split longitudinally and pinned flat, mucosal side uppermost in 0.1M phosphate buffer(pH 7.3). The tissue was fixed in 3 % phosphate buffered glutaraldehyde (pH 7.35), and during

fixation, gently brushed with a sable brush to remove surface debris. At the end of 2 hours the tissue was cut into approximately 1 cm pieces and rinsed in phosphate buffer. Samples processed for scanning electron microscopy (SEM) were rinsed in distilled water, dehydrated through a graded series of acetone and critical point dried. Fed animals anesthetized with ethyl ether, and Two 1 cm segments were obtained from jejunum and colon. The tissue samples, fixed in 10 % neutral buffered formalin, were sliced into rings and dehydrated successively in 70 % ethanol, 95 % ethanol, 100 % ethanol, and 100 % xylene. Tissues were embedded in paraffin and 7 μ m sections were cut and stained with hematoxylin and eosin. The coded slides were observed for blind analysis and viewed at 40 \times magnification in Zeiss microscope fitted with a micrometer (1 \times 1 mm). Twenty-five villi were selected randomly from each tissue section for measurement. Villus length (crypt to tip) was measured on the right side of each villus. The number of goblet cells per villus was determined by counting at least three villi from each slide.

2. Measurement of whole gut, small intestine and large intestine transit

1) Animals

Male Sprague-Dawley rats weighing 180-190 g were fed a nonpurified diet for five days, then basal (fiber free) diet for 7 days (Table 1). The rats were maintained at 22 \pm 2 $^{\circ}$ C and 60 \pm 5 % relative humidity in a room temperature with a 12 light : dark cycle and given free access to food and water ad libitum. Rats were divided into 3 groups of six rats each.

2) Whole gut transit

After administration of basal (fiber free) diet for 7 days, carmine red (1.5 %) suspended in 2 ml aqueous solution added 200 mg experimental diets (test substances) or 2 ml of Daesenggi-Tang was administered through a stomach tube at a fixed time (PM 2:00). During the experiment, the animals were kept individually in a wire meshed cage to enable the faeces to fall through onto drawing paper. The time until appearance of the first coloured faeces was measured.

3) Small intestine transit

Carmine red (1.5 %) suspended in 2 ml aqueous solution added 200 mg experimental diets (test substances) was administered through a stomach tube at a fixed time. 20 min after application of this marker and 200 mg experimental diets, the animals were killed by an over dose of ether. The stomach and the whole small intestine were removed, gently stretched on filter paper and the length of the small intestine as well as the length of the coloured part measured and calculated as percentage of the length of the whole small intestine.

4) Large intestine transit

Under anesthesia, a silicone rubber-catheter was chronically implanted into the caecum with the distal end fixed on the animal's neck where it was fixed to facilitate injection of the marker. During the experiment, the animals were kept individually in a wire meshed cage to enable the faeces to fall through onto drawing paper. Carmine red (1.5 %) suspended in ml aqueous solution added 200 mg experimental diets (test substances) was injected into caecum through the catheter. The time until appearance of the first coloured faeces was measured. Whole gut transit, small intestine transit and large intestine transit were studied in the same animals.

3. Statistical analysis

All data are expressed as mean \pm SEM. Statistical significance was calculated by student's t test for paired data. Probability values of $p < 0.05$ were considered significance. Each experimental group is only compared with the control to determine the effect of supplementing the diet with fiber and extracts of Daesenggi-Tang.

Results

1. Body weights, food intake and food efficiency

Animals in all dietary groups gained weight at similar rates (Table 3). Daesenggi-Tang group tended to be lighter than the basal diet group, none of these differences reached significance. It can be seen from Table 2 that the rats consumed equivalent amounts of the diets. But food efficiency of Daesenggi-Tang group (0.283 \pm 0.10 (gain/g food)) was reduced compared to basal diet (0.340 \pm 0.08 (gain/g food)) and 5 % cellulose groups (0.314 \pm 0.08 (gain/g food)).

Table 3. Food intake and growth in rats fed basal diets, 5 % cellulose and Daesenggi-Tang for 4 weeks

Dietary groups	Initial body weight	Weight gain	Food intake	Food efficiency
Units	g	g/day	g/day	gain/g food
Basal diet	182.0 \pm 6.3	5.54 \pm 1.34	16.29 \pm 1.38	0.340 \pm 0.08
5 % Cellulose	182.6 \pm 7.8	5.32 \pm 1.21	16.97 \pm 1.62	0.314 \pm 0.08
Daesenggi-Tang	182.9 \pm 3.0	4.93 \pm 2.12	16.79 \pm 2.54	0.283 \pm 0.10

1. Values are mean \pm SEM, n=8

2. Whole gut transit time

Addition of 5 % cellulose and administration of Daesenggi-Tang influenced transit time. The mean transit time was 16.75 hours for basal diet group, 11.31 hours for 5 % cellulose group and 6.93 hours for Daesenggi-Tang group (Table 4). The gastrointestinal transit time was significantly decreased 2 times in Daesenggi-Tang administered group compare to basal diet and 5 % cellulose groups.

3. Mean faecal weight

The mean faecal weight was 0.314±0.18(g dry/day) for basal diet group, 1.324±0.25(g dry/day) for 5 % cellulose group and 0.325±0.10(g dry/day) for Daesenggi-Tang group. The mean faecal weight was increased 4 times in 5 % cellulose group compare to basal diet and Daesenggi-Tang groups(Table 3). In 5 % cellulose group, these increment depends on nondigestible dietary fiber fed cellulose. Faeces of Daesenggi-Tang groups were soft faeces.

Table 4. Gastrointestinal transit time (oral to anus) and faecal weight in rat fed basal diets, 5 % cellulose and Daesenggi-Tang for 4 weeks

Dietary groups	Time (hours)	Faecal weight (g dry/day)
Basal diet	16.75	0.314±0.18
5 % Cellulose	11.31	1.324±0.25
Daesenggi-Tang	6.93	0.325±0.10

1. Values are mean ± SEM, n=8

4. Whole gut transit time using the test substance

Whole gut transit time as measured by faecal excretion in rats pretreated orally with basal diets, 5 % cellulose and Daesenggi-Tang for 4 weeks(200 mg cellulose or 2 ml Daesenggi-Tang + 3 ml carmine red marker). The whole gut transit time until appearance of the first coloured faeces was 14.33 hours for basal diet group, 11.66 hours for 5 % cellulose group and 5.42 hours for Daesenggi-Tang group(Table 5). The whole gut transit time was significantly decreased 2-3 times in Daesenggi-Tang administered group compare to basal diet and 5 % cellulose groups.

Table 5. Whole gut transit time as measured by faecal excretion in rats pretreated orally with basal diets, 5 % cellulose) and Daesenggi-Tang for 4 weeks(200 mg cellulose or 2 ml Daesenggi-Tang + 3 ml carmine red marker)

Dietary groups	Whole gut transit time(hours)
Basal diet	14.33
Cellulose	11.66
Daesenggi-Tang	5.42

1. Values are mean ± SEM, n=6

5. Small intestine transit using the test substances

Small intestine transit shown as percentage of the total small intestine length in its pretreated orally with basal diet, 5 % cellulose and Daesenggi-Tang for 4 weeks (administered 200 mg test substances or 2 ml Daesenggi-Tang + 3 ml carmine red marker). Small intestine transit was 22 % for basal diet group, 28.9 % for 5 % cellulose group and 89.9 % for Daesenggi-Tang group(Table 6). Daesenggi-Tang group accelerated more rapidly small intestine transit compare to basal diet and 5 % cellulose groups.

Table 6. Small intestine transit shown as percentage of the total small intestine length in its pretreated orally with basal diet, 5 % cellulose and Daesenggi-Tang for 4 weeks (administered 200 mg test substances or 2 ml Daesenggi-Tang + 3 ml carmine red marker)

Dietary groups	Small intestine transit (%)
Basal diet	22.0
Cellulose	28.9
Daesenggi-Tang	89.9

1. Values are mean ± SEM, n=6

6. Large intestine transit time using test substance

Large intestine transit as measured by faecal excretion of an intracaecally administered colour marker in rats pretreated orally with basal diet, 5 % cellulose and Daesenggi-Tang for 4 weeks (200 mg test substances or 2 ml Daesenggi-Tang + 3 ml carmine red marker). Large intestine transit time until appearance of the first coloured faeces was 17.3 hours for basal diet group, 15.3 hours for 5 % cellulose group and 1.7 hours for Daesenggi-Tang group(Table 7). Large intestine transit time was significantly decreased 9-10 times in Daesenggi-Tang administered group compare to basal diet and 5 % cellulose groups. Daesenggi-Tang group accelerated more rapidly small intestine transit compare to basal diet and 5 % cellulose groups.

Table 7. Large intestine transit as measured by faecal excretion of an intracaecally administered colour marker in rats pretreated orally with basal diet, 5 % cellulose and Daesenggi-Tang for 4 weeks (200 mg test substances or 2 ml Daesenggi-Tang + 3 ml carmine red marker)

Dietary groups	Large intestine transit time(hours)
Basal diet	17.3
Cellulose	15.3
Daesenggi-Tang	1.7

1. Values are mean ± SEM, n=6

7. Jejunal villus heights and colonic mucosal thickness

The histological measurements of the jejunal villus heights and colonic mucosal thickness are shown in Table 8. Jejunal villus heights in 5 % cellulose and Daesenggi-Tang administered group for 4 weeks were higher than in basal diet group. Colonic mucosal thickness administered 5 % cellulose and Daesenggi-Tang for 4 weeks were higher than in basal diet group.

Table 8 . Jejunal villus heights and colonic mucosal thickness in rats fed basal diets, 5 % cellulose and Daesenggi-Tang for 4 weeks

Dietary groups	Jejunum	Colon
	Villus Height (µm)	Mucosal thickness (µm)
Basal diet	530.0±15.6	205±14.5
Cellulose	665.7±19.9	285±24.1
Daesenggi-Tang	594.4±14.5	254±17.1

1. Values are mean ± SEM, n=8

8. Numerical and histochemical changes of goblet cells in jejunum

In mid jejunum section that was used for histology, Basal

diet group had 20.4±3.6 goblet cells whereas the Daesenggi-Tang group had 32.4±5.7 in alcian blue stain. In PAS and AB-PAS stain, Jejunal mucosal goblet cell were more increased than in basal diet group (Table 9). The histochemical difference observed an increase in the proportion of goblet cells stained alcian blue in colonic mucosa of Daesenggi-Tang group (Table 10).

Table 9. Numerical and histochemical changes of goblet cells in jejunum in rats fed basal diets, 5 % cellulose and Daesenggi-Tang for 4 weeks

Dietary groups	Jejunum		
	AB ¹	PAS ²	AB-PAS ³
Basal diet	20.4±3.6	23.8±2.1	21.0±2.1
Cellulose	20.8±3.6	26.7±1.3	23.7±2.5
Daesenggi-Tang	32.4±5.7	36.3±2.4	28.2±2.6

1. Values are mean ± SEM, n=8
 1. AB, Alcian blue, 2. PAS, Periodic Acid-Schiff reagents
 3. AB-PAS, Alcian blue-Periodic Acid-Schiff reagents

9. SEM of jejunum and colon

SEM of jejunum in the basal diet group reveal the typical leaf-shaped villi of the rat small intestine, and mucus material extruded from goblet cells is less clearly evident in the intervillous cleft. The location of the mucin-secreting goblet cells is identified as the oval or round indentations in the otherwise smooth topography of the mucosal surface. The colonic mucosal surface of basal diet group consists of densely packed microvilli and the goblet cells were reduced. SEM of jejunum in the 5 % cellulose group, Continuous normal cell loss is usually observed as an occasional, intact, protruding cell at the villus tip. Mucus material extruded from goblet cells is clearly evident in the intervillous cleft. Greater quantities of mucus were usually observed to be associated with the villi. SEM of jejunum in the Daesenggi-Tang administration group, Continuous normal cell loss is usually observed as an occasional, intact, protruding cell at the villus tip. Mucus material extruded from goblet cells is clearly evident in the intervillous cleft. Greater quantities of mucus were usually observed to be associated with the villi.

Table 10. Numerical and histochemical changes of goblet cells in colon in rats fed basal diets, 5 % cellulose and Daesenggi-Tang for 4 weeks

Dietary groups	Colon
	AB/PAS/AB-PAS density
Basal diet	++/++/+++
Cellulose	++/++/+++
Daesenggi-Tang	++++/++/+++

1. Stain density: +, Weak, ++, Medium, +++ , Strong, ++++, Heavy strong

10. Changes of plasma lipids

The plasma concentrations of cholesterol, HDL cholesterol, LDL cholesterol and triglyceride did differ among three

groups. Cholesterol concentration of Daesenggi-Tang group was higher than control and 5 % cellulose group. HDL cholesterol concentration in Daesenggi-Tang group was higher than control and 5 % cellulose groups.

Table 11. Plasma cholesterol, HDL cholesterol, LDL cholesterol and triglyceride concentrations in rats after fed basal diet, 5 % cellulose and Daesenggi-Tang for 4 weeks

Dietary groups	Cholesterol (mg/dl)	HDL Cholesterol (mg/dl)	LDL Cholesterol (mg/dl)	Triglyceride (mg/dl)
Basal diet	53.8±10.5	13.8±2.7	8.1±1.6	56.8±11.4
Cellulose	56.10±4.7	14.5±1.4	9.0±3.0	45.80±6.6
Daesenggi-Tang	65.80±8.9	18.4±1.8	10.0±2.0	47.0±10.3

1. Values are mean ± SEM, n=8

Discussion

Constipation is a symptom but can generally be defined as less than 2 bowel movements per week. The history and physical examination should be evaluated for stool size, frequency, and straining and discomfort on defecation. The influence of age, gender, and society should be considered. The etiologies of constipation can be classified as dietary; drug induced; metabolic; neurologic; or anatomic. If hard or small stools are part of the initial evaluation, then a dietary approach of increased dietary fiber intake can be used as a therapeutic trial. If it does not succeed or the history and physical evaluation indicate an ecology other than dietary, then barium-contrast enema, flexible sigmoidoscopy, colonoscopy, transit time, or anorectal manometry can be used selectively in further evaluation¹²⁾.

Detailed methods of treatment are described, such as how to increase fiber intake by use of dietary history and recommendation of appropriate fiber, food or supplement intake. Methods of using behavioral changes such as laxation and toilet-training programs are described. In selected situations pharmacologic therapy and rarely, surgical intervention, can be useful.

These experiment were designed to evaluate the effects of Daesenggi-Tang on intestinal mucosal changes, gastrointestinal transit time measurement (carmines red markers) and plasma lipids in rats. In these experiments, the histological measurements of the jejunal villus heights in 5 % cellulose and Daesenggi-Tang administered group for 4 weeks were higher than that of basal diet group. Colonic mucosal thickness administered 5 % cellulose and Daesenggi-Tang for 4 weeks were higher than that of basal diet group.

The mechanisms responsible for the structural and functional responses to prolonged fiber feeding are not known.

It is widely accepted that cell turn over in the crypts of LieberKuhn is an important determinant of villus morphology¹³⁾ and that this process is regulated in part by the gastrointestinal peptide hormones¹³⁾. Thus it is of interest to note that fiber feeding has been shown to modify the secretions of several of these peptides, suggesting that the structural response may be hormonally mediated.

In previous studies, it has been founded that prolonged administration of high levels of dietary fiber was associated with depressed solute absorption in vivo or improved metabolic tolerance. Factor contributing to such changes may include delayed gastric emptying¹⁴⁾, interference with solute diffusion or sequestration of solute in the luminal bulk phase so that presentation of solute to absorbing surface is retarded¹⁵⁾, improved intestinal transit resulting in decreased time of exposure of nutrient at the site of absorption¹⁶⁾, depression of transport at the enterocytes¹⁵⁾, or delayed clearance of nutrients from the villus after absorption.

The differential measurement of small and large bowel transit time is important in the investigation of the mechanism underlying diarrhea and constipation. Daesenggi-Tang administered group accelerate whole gut transit time and small intestinal transit compare to control and cellulose groups. An augmented excretion of normal faecal pellets begins 5.42 hours after Daesenggi-Tang administration. *Rheum palmatum* L. is a potent laxative. The hydrolysis products of the glucosides emodin and sennidin are the active principles. They stimulate the large intestine and increase the movement of luminal contents toward the anus, resulting in defecation. This herb has antispasmodic effects, and is about four times more potent than papaverine, an alkaloid isolated from opium. It has been observed to lower blood pressure and plasma cholesterol levels. It is a stomachic, stimulating the appetite. In addition, it displays antibacterial, antihelmintic, and anticancer properties¹⁷⁾.

This laxative effects may be ascribed predominantly to motility changes, causing a faster passage, being able to accelerate the release of already present normal faecal pellets and to increase the moisture content of the stool corresponding to conditions present in the proximal colon or cecum¹⁸⁾. An accelerated passage shortens the contact time between intestinal contents and absorptive surface thus reducing fluid absorption. Sennosides markedly reduce the total contraction frequency in the colon as investigated in an electromyographic study in rats and dogs^{4,19)}. In man, oral treatment with senna diminishes intraluminal colonic pressure significantly²⁰⁾.

Since constipation usually is a specific colon motility problem and the production of a hard stool is the consequence

of a prolonged retention time in the large intestine, a laxative preferentially should normalize colon motility and not only stimulate fluid secretion, at least not in the small intestine.

Crystalline sodium sulfate is not absorbed from intestinal mucosa. therefore, ingested salt will remain lumen and produce an osmotic effect to prevent the absorption of fluid. Luminal contents will increase and stimulate the peristaltic movement of the intestine, resulting in a purgative effect¹⁷⁾. The bitter taste of *Magnolia officinalis* can stimulate salivation, gastric secretion, and reflexive intestinal peristalsis¹⁷⁾. *Citrus aurantium* was commonly used to treat indigestion. It was also prescribed to relieve abdominal distension and ptosis of the anus or uterus¹⁷⁾.

Gastrointestinal mucus covers most of the mucosal surfaces of the gastrointestinal tract and has a protective capacity owing to lycoprotein components, mucin. Small intestinal goblet cells are mucus-secreting cells that are present throughout the epithelium with increasing relative frequency from the proximal jejunum to the distal ileum²¹⁾. Among the functions ascribed to intestinal mucus are lubrication, cytoprotection, interactions with selected bacterial enzymes^{22,23,24)}, secretion in response to toxins and parasites, cooperation with secretory IgA, residence for the normal bacterial flora, and substrate for luminal protease and endogenous flora. Since secreted mucin plays a central role in mucosal protection, dietary factors that affect the production of mucin, alter its composition, or enhance its degradation have the potential to impair its function.

In this experiments, mid-jejunum section that was used for histology, Basal diet group had 20.4±3.6 goblet cells whereas the Daesenggi-Tang group had 32.4±5.7 in alcian blue stain. In PAS and AB-PAS stain, Jejunal mucosal goblet cells were more increased than in basal diet group. The histochemical difference observed an increase in the proportion of goblet cells stained alcian blue in colonic mucosa of Daesenggi-Tang group.

It has been postulated that mucus contributes to the apparent thickness of the unstirred layer in the intestine²⁵⁾ and affords protection to the mucosal surface. Animals producing more mucus could have a slower absorption rate, especially for lipid-soluble compounds²⁶⁾.

Conclusions

Constipation is a common clinical problem that comprises of symptoms included excessive straining, hard faeces, feeling of incomplete evacuation and infrequent defecation. Although many conditions, such as metabolic problems, fiber deficiency,

anorectal problem, an drug, can cause constipation. This study was examined the effects of Daesenggi-Tang on intestinal mucosal changes, gastrointestinal transit time and plasma lipids in rats. Adult male rats were fed four weeks on diets containing no addition(basal diet group), 5 % cellulose (cellulose group) and extracts of Daesenggi-Tang (Daesenggi-Tang group).

The results were as follows; The mean faecal weight was significantly increased 2 times in Daesenggi-Tang administered group compare to basal diet group. The gastrointestinal transit times was significantly decreased in Daesenggi-Tang administered group compare to basal diet and cellulose group. Carmine red mixed with Daesenggi-Tang, as a marker, was administered through a gastric tube for stomach or intracecally by a chronically implanted catheter for colon transit. Small intestinal transit and large intestinal transit time were significantly decreased in Daesenggi-Tang administered group compare to basal diet and cellulose group. The height of jejunal villi was developed in Daesenggi-Tang administered group compare to basal diet. The thickness of mucosa and muscle layer of colonic mucosa were significantly developed in Daesenggi-Tang administered group compare to basal diet group. The numerical change of goblet cells in colonic mucosa was increased acid mucin stained alcian blue in Daesenggi-Tang administered group compare to basal diet and cellulose groups. HDL-cholesterol of plasma lipid was increased in Daesenggi-Tang administered group compare to basal diet and cellulose groups.

Theses results suggests that Daesenggi-Tang may be used in treatment of constipation resulting in increase of faecal weight, decrease of gastrointestinal transit time, development of villi, intensify of stainability of acid mucin in colon.

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