Original Research Article

Constipation-relieving effect of L-arabinose

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Abstract

Purpose: *To investigate the mitigating effect of L-arabinose on constipation in a mouse model of experimental constipation.*
Methods: *Kunming mice were used as experimental animals to establish a constipation model. Intestinal propulsion, first defecation time, number of defecation pellets, and the weight of defecation pellets in 5 h were measured. L-Arabinose was given at 3 dose levels, viz, low dose (0.5 g/kg/day), medium dose (0.75 g/kg/day), and high dose (2.5 g/kg/day), and their effects on constipation were compared with that of the model control group.*
Results: *Compared with the model control group, there were significant differences in ink propulsion (F = 22.67, p < 0.05); time taken for first black stool to appear (F = 19.51, p < 0.05), number of fecal pellets (F = 12.22, p < 0.05), and fecal weight (F = 5, p < 0.05) in the L-arabinose groups.*
Conclusion: *L-Arabinose relieves constipation symptoms in an experimental mouse model of constipation. Therefore, L-arabinose may be useful in the management of patients with constipation, but further studies in humans are required to ascertain this.*

Keywords: *L-Arabinose, Fecal pellets/grains, Constipation, Stool, Intestinal propulsion*

INTRODUCTION

Constipation is a common chronic digestive tract disease which affects individuals of all ages, and its global prevalence is between 2 and 27 % [1]. Serious disturbances in electrolyte and acid-base balance result in decline in quality of life and huge economic burden on the affected patients. Constipation refers to the reduction in defecation times or difficulty in defecation as a result of loss of normal defecation function. Clinically, constipation may result in multiple treatment failures [2].

Chronic constipation has negative psychological, social and behavioral effects on all patients, especially children [3]. In childhood, constipation can lead to a variety of symptoms such as rectal distention, fecal incontinence and fecal retention [4]. It is also particularly common among the elderly, with up to 40 % of community residents reporting constipation symptoms. Among the residents of sanatoriums, the reported prevalence is as high as 80 % [5-7]. Chronic constipation may lead to complications such as fecal obstruction, urinary retention, hemorrhoids, anal fissures and fecal incontinence [8]. These complications impact negatively on health-related quality of life.

Constipation is usually associated with changes in lifestyle, especially as one ages [9,10]. Indeed, constipation increases with age. In some studies, it was reported that the incidence of chronic constipation in women was significantly higher than that in men, with the male-to-female ratio ranging from 1:1.2 to 1:4.6 [11,12]. Some scholars have found that food affects all aspects of body functions, and it can be used for good health or prevention of disease [13]. Consumption of functional foods alleviates constipation and its symptoms [14]. In view of the unique efficacy of L-arabinose in alleviating constipation, the effect of L-arabinose on constipation in experimental constipation mouse model was investigated in this study. This was based on previous studies, with a view to providing scientific basis for the application of L-arabinose in health products.

EXPERIMENTAL

Materials

L-Arabinose (purity 99 %, HPLC grade) was provided by Dalian Sanyi Institute of Bioengineering. Compound Difenol Ester Tablets were purchased from Changchun Changhong Pharmaceutical Co. Ltd., (batch number: 20110702). Arabic gum powder was bought from Tianjin Komeo Chemical Reagent Co. Ltd., production batch number: 2011041. Activated Carbon (powder) was product of Tianjin Damao Chemical Reagent Factory.

This research was approved by the Animal Ethical Committee of Children's Hospital of Nanjing Medical University, No. 8, Jiangdong South Road, Jianye District, Nanjing (approval no. 20175090), and was carried out according to "Principles of Laboratory Animal Care" (NIH publication no. 85 - 23, revised 1985) [15].

Animals and feeding

Twenty-five male Kunming mice with initial body weight of 18 - 22 g were purchased from the Laboratory Animal Center of Dalian Medical University. The production license No. was SCXK (Liao) 2008-0002. The animals were kept in the animal laboratory room of Sanyi Institute of Bioengineering in Dalian, and were provided feed and drinking water *ad libitum* under natural illumination. The room temperature was 20 - 25 $^{\circ}$C, and humidity was 40 - 60 %.

Preparation of ink

Gum arabic (100 g) was weighed and added to 800 mL of water. The mixture was boiled until it became transparent. Then, 50 g of activated carbon powder was added to the solution, and the mixture was boiled. On cooling, the volume of the solution was made up to 1000 mL with water, and the solution was kept refrigerated at 4 $^{\circ}$C prior to use. It was shaken immediately before use.

Animal grouping and treatment

Following 2 days of adaptive feeding, 25 mice were randomly divided into blank control group, model control group and three L-arabinose groups i.e. low dose (0.5 g/kg/day), medium dose (0.75 g/kg/day), and high dose (2.5 g/kg/day) groups. L-Arabinose was administered by gavage, and the doses were with reference to the recommended dose for humans. Purified water was used in the preparation of the required concentrations of the test substance. The blank group and the model control group were given equivalent volumes of purified water by gavage, in place of L-arabinose. Gastric perfusion was given once a day for 15 consecutive days.

Small intestinal movement test

After 15 days, mice in each group were fasted for 16 min. The model control group and the three arabinose dose groups were given compound diphenolate (5 mg/kg) by gavage, while the blank control group was given purified water. After 30 min, the L-arabinose groups were given the ink solution containing 5 % activated carbon powder and 10 % gum Arabic, while mice in the blank and model control groups were given equivalent amounts of ink via gavage. Immediately after 25 min, the animals were sacrificed using cervical dislocation, and the abdominal cavity was opened to separate the mesentery, cutting the intestinal portion from the pylorus. The lower end of the ileocecal part was placed on a tray, and the small intestine was gently pulled straight. The length of the intestine was designated 'total length of the small intestine', and the distance from the pylorus to the front of the ink was designated 'ink propulsion length'. The ink propulsion (%) was calculated as shown in equation 1:

$$IP = (IPL/(cm))/(T/(cm)) \times 100 \text{ %} \ldots\ldots (1)$$

where IP is ink propulsion, IPL is ink propulsion length, and T is total length of the small intestine.

Mice defecation studies

After 15 days, mice in each group were fasted for 16 h. The blank control group was given purified water. The model control group and the three L-

arabinose groups were given compound diphenolate (10 mg/kg) by gavage. After 30 min, mice in the blank control group and model control group were given ink by gastric lavage. The mice in the dose groups were given ink containing the sample. The animals were raised in a single cage and fed with normal feed and drinking water. After the ink infusion, the time taken for the first black stool to appear from each mouse, and the number and weight of black stool grains in 5 h were recorded.

The experiment showed that the weight of black stool, number of fecal particles, small intestine transit time, and defecation time were measurable within 5 h.

Statistical analysis

Data are expressed as mean ± SD. Intra-group comparison was made with analysis of variance (ANOVA), while LSD *t*-test was used for two-group comparisons. All statistical analyses were done using SPSS 17.0 statistical software. Statistical significance was fixed at $p < 0.05$.

RESULTS

Effect of L-arabinose on mouse small intestinal motion

The results of ink propulsion test in blank control group were significantly different from those in model control group ($p < 0.01$), indicating that the mouse model of constipation was successfully established. Compared with the model control group, the ink propulsion of the high and middle dose groups differed significantly ($p < 0.01$), and the ink propulsion of the high dose group was higher than that of the blank control group. The low L-arabinose dose did not have any effect on small intestinal peristalsis. These results indicate that only a certain critical dose of L-arabinose is capable of significantly enhancing small intestinal peristalsis function in mice (Table 1).

There were significant differences in time of the first defecation, number of fecal particles and fecal weight between the blank control group and the model control group ($p < 0.01$), which indicated that the mouse model of constipation was successfully established. Compared with the model control group, the results of test on time of first black stool showed statistical significance ($p < 0.01$). The number of fecal grains and the weight of feces were increased, but there was no significant difference. The reason may be that feces in the high dose group were sparse, and occasionally adhered to mice, making it difficult to count. The results showed that L-arabinose

significantly shortened the first defecation time of experimentally constipated mice, while increasing the number of fecal grains and the weight of feces.

Table 1: Effect of L-arabinose at different oral concentrations on small intestinal motility in mice (n = 25)

Group	Ink propulsion length (cm)	Total length of small intestine (cm)	Ink propulsion (%)
Blank control (n=5)	30.60 ± 3.86	38.40 ± 2.41	0.85 ± 0.03
Model control (n=5)	18.65 ± 3.71**	36.45 ± 3.74	0.55 ± 0.08**
High-dose (n=5)	31.85 ± 4.29##	38.05 ± 2.61	0.85 ± 0.05##
Medium-dose (n=5)	25.60 ± 3.01*##	34.55 ± 2.84	0.75 ± 0.06*##
Low-dose (n=5)	18.40 ± 3.93**	32.40 ± 3.40**#	0.60 ± 0.09**
F-value	14.18	3.41	22.67
P-value	<0.01	0.028	<0.01

*$P < 0.05$, **$p < 0.01$, compared with the blank control group; #$p < 0.05$, ##$p < 0.01$, compared with the model control group

Table 2: Effect of L-arabinose at different oral concentrations on defecation time, fecal grains and fecal weight in mice

Group	Time taken for first black stool appearance (min)	Number of fecal grains	Stool weight (g)
Blank control (n=5)	106.84 ± 9.84	24.40 ± 2.21	0.40 ± 0.06#
Model control (n=5)	197.65 ± 22.36**	18.00 ± 2.96**	0.26 ± 0.04**
High-dose (n=5)	141.28 ± 28.91**##	17.60 ± 3.14**	0.34 ± 0.10
Medium-dose (n=5)	132.84 ± 12.46*##	26.80 ± 4.29##	0.42 ± 0.07##
Low-dose (n=5)	192.35 ± 20.03**	14.60 ± 3.37**	0.28 ± 0.07*
F	19.51	12.22	5.00
P-value	<0.01	<0.01	<0.01

*$P < 0.05$, **$p < 0.01$, compared with the blank control group; #$p < 0.05$, ##$p < 0.01$, compared with the model control group

DISCUSSION

In this study, Kunming mice were used as experimental animals, and the effect of L-arabinose administration for 15 days on constipation in experimental constipation mice was studied. It was found that L-arabinose at the

dose of 0.75 g/kg promoted intestinal motility, shortened the time of first defecation, and increased fecal weight and the number of fecal grains in mice. The results showed that L-arabinose significantly alleviated the constipation symptoms in the experimental constipation mice.

Some workers injected ^{14}C-labeled L-arabinose into human subjects through isotope labeling method and recovered their exhaled gas after 6 h. The results showed that the content of ^{14}C accounted for only 0.8 % of the total amount injected. In addition, the content of ^{14}C recovered from 24-h urine was about 85 %, indicating that L-arabinose is an indigestible sugar. Indigestible sugars also include fructose oligosaccharides, galacto-oligosaccharides and isomaltose oligosaccharides, all of which promote intestinal peristalsis and stimulate defecation [16,17]. They are used as functional foods for alleviation of constipation, and they are highly priced in the market. Animal experiments have shown that microbial degradation of L-arabinose occurs in the small intestine, with a good acidification effect on the intestine. The main organic acids produced in the intestine after L-arabinose degradation are acetic acid, propionic acid, lactic acid, succinic acid and malic acid [18-20].

Compound diphenoxylate, which was used to establish experimental constipation model, weakens intestinal peristalsis by inhibiting intestinal mucosal receptors and eliminating peristaltic reflex of local mucosa, delaying the passage of intestinal contents and facilitating the absorption of intestinal water. Therefore, it may be speculated that L-arabinose, as an indigestible sugar, is hardly absorbed in the small intestine. Thus, it has good biochemical stability, so that its effective concentration can be maintained in the small intestine. After being decomposed by intestinal microorganisms, it produces a large number of organic acids and gases such as CO_2 and H_2, which acidify the intestinal tract of mice.

Long-term acidic environment of the intestinal tract promotes the growth of probiotics and maintains their predominance in intestinal tract. The combined action of organic acids and probiotics improves the function of intestinal mucosa and enhances the self-regulation function of intestinal tract. The large number of organic acids and gases such as CO_2 and H_2 produced lead to the decrease in intestinal pH, and increase in osmotic pressure and peristaltic reflex. Increased intestinal peristalsis reduces the contact between intestinal contents and the intestinal mucosa, thereby reducing the absorption of intestinal water, softening the feces, enhancing intestinal peristalsis, and alleviating constipation.

L-Arabinose, a proliferating factor for probiotics, plays an important role in regulating the bacterial flora of *Bifidobacteria* and *Lactobacillus*. Its development into functional sugar food for alleviating constipation needs further studies.

CONCLUSION

L-Arabinose, a proliferating factor for probiotics, plays an important role in the regulation of the bacterial flora of *Bifidobacteria* and *Lactobacillus*. It relieves constipation symptoms in an experimental mouse model of constipation. Therefore, L-arabinose may find therapeutic use in the management of patients with constipation. However, its development into functional sugar food for alleviating constipation needs further studies.

DECLARATIONS

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the author(s) named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. All authors read and approved the manuscript for publication. Bin Jiang conceived and designed the study, Hao Wang, Wenxian Zhang, Bin Jiang collected and analysed the data, while Hao Wang wrote the manuscript.

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