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# Effects of Chili on Abdominal Pain, Abdominal Burning and Rectal Sensation in Diarrhea Predominate Irritable Bowel Syndrome (IBS-D)

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## ABSTRACT

***Background:*** Visceral hypersensitivity is involved in the pathogenesis of irritable bowel syndrome (IBS). Ingestion of chili has been reported to induce abdominal pain and burning symptoms in IBS, possibly by way of capsaicin receptor (TRPV1) stimulation. Chronic ingestion of chili can improve symptoms of NERD and functional dyspepsia. However, there is no study in IBS-D patients.

***Objective:*** To determine the effects of chronic chili ingestion on abdominal pain, abdominal burning and rectal sensation in IBS-D patients.

***Methods:*** Ten IBS-D patients were included. All patients received capsules of placebo powder or chili powder (chili 2.1 gm/day, capsaicin 2.5 mg/day) orally in 3 divided doses before meals for 6 weeks, in a randomized double-blinded crossover fashion with a 4-week washout period. Gastrointestinal severity symptom and rectal sensation scores were assessed and compared between the placebo and the chili treatment groups at week 0, 1, 2, 4, and 6, using a 100-mm long visual analog scale. Rectal barostat was evaluated in all patients at the end of each treatment period. Gastrointestinal symptoms in response to spicy food were evaluated before and at the end of treatment.

***Results:*** All patients completed the study without serious adverse events. Compared to placebo, chronic chili ingestion had no significant effects on abdominal pain, abdominal burning, abdominal bloating, postprandial fecal urgency, diarrhea and incomplete evacuation symptom scores. Chronic chili ingestion appeared to significantly increase sensory threshold of rectal perception for the first rectal sensation (12 vs. 8 mmHg; $p = 0.03$) without significant effect on rectal compliance. After chronic chili ingestion, abdominal burning symptom score in response to a standard spicy meal was significantly decreased, compared with that after placebo ingestion ($4.3 \pm 2.4$ vs. $14.1 \pm 5.1$; $p = 0.02$).

***Conclusions:*** Chili ingestion for 6 weeks significantly increased the sensory threshold of rectal perception for the first rectal sensation in IBS-D patient, without significant effects on rectal compliance and IBS symptoms. In addition, abdominal burning after standard spicy meal was significantly decreased. The results suggested that 2.1 gm/day of chili ingestion for 6 weeks can desensitize the capsaicin receptors in the proximal gut and the rectum.

**Key words :** Chili, rectal sensation, irritable bowel syndrome, IBS, capsaicin

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## INTRODUCTION

Visceral hypersensitivity has long been considered a significant pathophysiologic mechanism in the irritable bowel syndrome (IBS). The capsaicin or transient receptor potential vanilloid type1(TRPV1) plays an important role in visceral nociception[1-3]. Increased TRPV1 receptors have been found in the gut mucosa of patients with functional gastrointestinal disorder with associated visceral hypersensitivity, including in the esophagus of non-erosive reflux disease (NERD) patients[4], in the colon of IBS patients[5], and in the rectum of rectal hypersensitivity patients[6].

Capsaicin, the pungent ingredient of chili, can stimulate TRPV1 receptors and mediate pain and burning sensation[7, 8]. It has been used as a valuable tool to evaluate the chemoreceptor-mediated visceral sensation in the human gut[9,10]. The average daily chili consumption for a Thai adult is about 5 grams per person[11]. Ingestion of chili can aggravate gastrointestinal symptoms in patients with functional dyspepsia and irritable bowel syndrome[12-15]. Recently, a study in 20 IBS-D patients demonstrated that acute ingestion of chili-containing meals produced higher abdominal pain and abdominal burning symptom scores compared with the respective scores in healthy volunteers after standard meal[15]. In addition, rectal hyperalgesia is also demonstrated in IBS patients after ingestion of chili-containing meals [12]. Such observations suggest that IBS patients exhibit gut hypersensitivity to chili.

Chronic chili ingestion may desensitize TRPV1 receptors in the gastrointestinal tract. In a recent study, 30 functional dyspepsia patients were randomized to receive 2.5 g/day of red pepper powder or placebo for 5 weeks[16]. Significant improvement of epigastric pain was noted[16]. In another small study, 8 NERD patients received oral chili for 6 weeks. At the end of treatment, chili significantly improved heartburn and regurgitation symptoms compared to placebo[17]. The effect of chronic chili ingestion in patients with IBS-D is not known, however. The objective of the present preliminary study was to determine the effect of 6 weeks of chili ingestion on gastrointestinal symptoms generally, gastrointestinal symptoms in response to standard spicy meal, and rectal sensation in patients with IBS-D.

## MATERIALS AND METHODS

### Patients

Ten IBS-D patients [6 women, 4 men; mean age 47 ± 10.2 years; range 27-60 years; body mass index (BMI) 24.1 ± 3.8 kg/m$^2$] who fulfilled the Rome III criteria[18] were recruited from the out-patient clinic, King Chulalongkorn Memorial Hospital, Bangkok. All patients had a normal colonoscopy at least 1 year before the study inclusion. IBS-D patients with diabetes mellitus, major neurological disorders, psychological disorders, pregnancy, previous abdominal surgery, or history of severe gastrointestinal symptoms after spicy foods were excluded. Medications which may alter gastrointestinal motility and sensation, including antidiarrheal, anticholinergic drugs, smooth muscle relaxants, domperidone, metoclopramide, proton pump inhibitors and $H_2$ receptor antagonists, tricyclic antidepressants, selective serotonin reuptake inhibitors, calcium channel blockers, were discontinued for 7 days prior to the study. Patients were also asked to avoid chili and spicy food items for the preceding 7 days. The study was approved by the institutional review board of The Faculty of Medicine, Chulalongkorn University, Bangkok. All patients provided a written inform consent.

### Study design

This study was a randomized double-blinded crossover study. After a one-week run-in period, all patients went through the study of two treatment periods, separated by a four-week washout interval. Patients were given either oral capsaicin capsules or placebo capsules 3 times daily for 6 weeks. The randomized treatment assignments were sealed in envelopes.

### Study protocol

Patients were randomized in a double-blind manner to receive one gelatin and two enteric coated capsules containing either red chili or placebo 3 times a day for 6 weeks, with a four-week washout interval. Patients were asked to take the capsules 15 minutes before meals. Gastrointestinal symptoms and adverse events were evaluated at baseline, week 1, week 2, week 4 and week 6 of treatment. The capsules were prepared by the Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmaceutical Sciences, Chulalongkorn University. There were 2 kinds of capsules: i) a gelatin capsule designed to be dispersed in the stomach [the red chili powder (*Capsicum frutescens Linn*, 2.38 mg capsaicin per 2 g dry weight, Hand Brand No. 1, Nguan Soon Co., Ltd., Bangkok, Thailand) administered in opaque gelatin capsule con-

taining 0.5 g], and ii) an enteric coded capsule designed to be dispersed in the intestine [Kollicoat MAE; containing 0.7% sodium lauryl sulfate (USP) and 2.3% polysorbate80 (Ph. Eur.) as emulsifying agents, dissolves at a pH above 5.5, containing 0.1 g chili mixed with lactose 0.4 g]. An opaque gelatin capsule and enteric coded capsules containing 0.5 g of lactose powder served as placebos. Two grams of chili represented an amount of chili in a typical single serving Thai meal. It has also been reported that the average chili consumption by a Thai adult was about 5 g per day[11].

To determine the effect of chronic chili ingestion on rectal sensation, all patients underwent the rectal barostat at the end of treatment period. Gastrointestinal symptoms in response to a standard spicy meal were evaluated at baseline and at the end of both treatment periods.

## Symptom assessment

Gastrointestinal symptom severity was assessed by using a 100-mm-long visual analogue scale[19]. The VAS consisted of verbal anchors at each end (0 = no symptom, and 100 = the most severe symptom). The gastrointestinal symptoms evaluated were: (i) abdominal pain, (ii) abdominal burning, (iii) abdominal bloating, (iv) nausea, (v) heartburn, (vi) food regurgitation, (vii) belching, (viii) chest pain, (ix) early satiety, (x) urgency, (xi) diarrhea, and (xii) sense of incomplete rectal evacuation. Patients were interviewed for the number of days with abdominal pain, over the past one week. Similarly, stool pattern was assessed, using the Bristol Stool Form scale. Assessment of adverse effects was based on diary card and self-reported complaints at each visit. In addition, patients were allowed to contact the physician by phone for any treatment-related problem. Alum milk (240 mL) was prescribed as a rescue medication in case the patient experienced severe abdominal pain or burning. At each visit, the amount of leftover alum milk was recorded. Unused capsules were counted to evaluate the treatment compliance.

For evaluation of gastrointestinal symptoms in response to standard spicy meal ingestion, postprandial gastrointestinal symptoms were assessed at 5 minutes before meal, immediately after meal, and then every 15 minutes for 2 hours, using a 100-mm-long VAS at baseline and at the end of chili and placebo treatments.

## Rectal barostat study

Rectal barostat was evaluated at the end of treatment. On the study day, each patient visited the Gastrointestinal Motility Research Unit, King Chulalongkorn Memorial Hospital, at 8:00 am after an overnight fast. Fifteen minutes after a 200 mL tap water enema, patient lay on the left lateral position in a quiet private room. Barostat study was performed using a polyvinyl catheter (outer diameter 4.7 mm) incorporated with a 500 mL non-compliance polyethylene bag inflatable by a 2.8-mm central lumen and an electronic barostat (Distender series II; G&J Electronics, Inc., Toronto, ON, Canada). The barostat bag was placed between 5 and 15 cm from the anal verge. The bag was then inflated with 120 mL of air and deflated completely. After a 5-minute rest period, the perception and pressure-volume relationship in response to rapid phasic distention were studied by applying stepwise pressures (8, 12, 16, 20, 24, 28, 32, 36, 40, 44 and 48 mmHg) increasingly into the bag. For each distention, the bag was distended at the rate of 40 mL/s, maintained for 1 minute, with 1 minute interval to allow the intrabag pressure to fall to 0 mmHg.

Rectal sensation was evaluated by using a symptom description chart. The patients were explained with a standardized verbal explanation of our scores regarding of stool sensation and pain. Rectal sensation of stool perception was scored 0-4; score 0 = no sensation, score 1 = first sensation of stool, score 2 = first sensation of urgency of stool, score 3 = moderate urgency of stool, and score 4 = severe urgency of stool with intolerable need to pass stool. Rectal sensation of pain perception was scored 0-5; score 0 = no pain, score 1 = first sensation of pain, score 2 = mild pain, score 3 = moderate pain, score 4 = severe pain, and score 5 = intolerable pain. The patients were asked to record sensation at 50 seconds after the onset of each distension[20]. Pressure threshold was defined as the minimum pressure that induced the first perception of each sensation.

## Statistical Analysis

Data were given as mean ± SEM or median and range. The Kolmogorov-Smirnov test was used to determine the normality of data distribution. Comparisons of parametric data including symptom scores on questionnaire during treatment with chili or placebo were analyzed by analysis of variance for repeated measurements and paired student's *t*-test. Compari-

sons of non-parametric data including rectal sensation threshold for stool perception and pain between the two groups were analyzed by Wilcoxon's signed ranks tests. A two-tailed *p*-value less than 0.05 was considered statistically significant.

## RESULTS

All patients completed the study without serious adverse events. The baseline gastrointestinal symptoms reported by the patients before each treatment period are summarized in Table 1. There are no significant differences in baseline gastrointestinal symptoms between the two treatment periods. Five patients were randomized to receive chili first, and five patients received placebo first. The groups did not differ in mean age, (51 ± 1.8 vs. 41 ± 7.1 years; $p > 0.05$), sex distribution (female 60% vs. 60%; $p > 0.05$) or BMI (26 ± 0.6 vs. 20 ± 1.5 kg/m2; $p > 0.05$). All patients had longstanding IBS symptoms (mean duration 6.6 ± 1.9 years, range 1-19 years). Mean number of capsules used per patient in the chili and placebo treatment were 351 ± 2.1 (93%) and 349 ± 2.6 (93%) ($p > 0.05$). The total amounts of alum milk consumption in the chili and the placebo treatment groups were 63 ± 28.3 and 35 ± 19.2 mL, respectively ($p > 0.05$)

### Effect of chronic chili ingestion on gastrointestinal symptoms in IBS-D patients

The mean overall symptom, abdominal pain, abdominal burning, abdominal bloating, postprandial fecal urgency, diarrhea and incomplete evacuation scores at the end of 6 weeks decreased similarly from baseline in the chili and the placebo treatment groups ($p > 0.05$). (Figure 1-3) Heartburn, nausea, food regurgitation, acid regurgitation, belching, early satiety and chest pain after chili treatment were not significantly different from those after placebo treatment. Chili had no significant influence on the number of days with abdominal pain and on the Bristol stool form scale[21]. The impact of IBS symptoms on daily life was also not significantly different between the two treatments.

With regard to the side effects observed in the chili treatment, postprandial fecal urgency symptom score was significantly higher only at the first week of chili ingestion compared to placebo ($p = 0.04$), whilst there was no significant difference at week 2, week 4 and week 6 of treatment. (Figure 4) This symptom improved after 1 week of treatment, and no patient stopped the treatment because of the symptom. Abdominal burning symptom score also increased and was significantly higher than placebo ($p = 0.03$) only during week 2, and this symptom was also progressively improved after the second week of treatment. Abdominal warmness sensation was transiently developed within an hour after chili capsule ingestion was also reported.

### Effect of chronic chili ingestion on gastrointestinal symptoms in respond to standard spicy meal

There were no significant differences in baseline

**Table 1.** Baseline gastrointestinal symptom scores before capsaicin and placebo treatment period in 10 patients.

| Baseline symptom scores | Before chili period | Before placebo period | *p*-value |
|---|---|---|---|
| Abdominal pain | 36.4 ± 9.8 | 35 ± 11.7 | 0.873 |
| Abdominal burning | 42.3 ± 9.7 | 31.5 ± 12.2 | 0.371 |
| Abdominal bloating | 34 ± 10.1 | 32.2 ± 11.7 | 0.891 |
| Postprandial fecal urgency | 38.1 ± 10.5 | 31.9 ± 11.6 | 0.58 |
| Diarrhea | 19.9 ± 9.1 | 16.9 ± 11.4 | 0.789 |
| Incomplete evacuation | 32.3 ± 11 | 33.4 ± 11.8 | 0.935 |
| Heartburn | 16.2 ± 6.3 | 20.6 ± 8.6 | 0.721 |
| Nausea | 23.6 ± 10.8 | 18.3 ± 9.1 | 0.629 |
| Early satiety | 36.2 ± 10.4 | 30.6 ± 12.1 | 0.667 |
| Food regurgitation | 20.8 ± 7.9 | 22 ± 9.9 | 0.92 |
| Acid regurgitation | 11 ± 6.6 | 18.4 ± 9.9 | 0.59 |
| Belching | 30.71 ± 9.2 | 28.14 ± 12 | 0.672 |
| Chest pain | 14 ± 6.1 | 11.5 ± 7.6 | 0.683 |
| Global GI symptom | 52.6 ± 9.1 | 58 ± 12.3 | 0.681 |
| Interrupt of normal life | 60.2 ± 10.7 | 51.5 ± 13 | 0.513 |

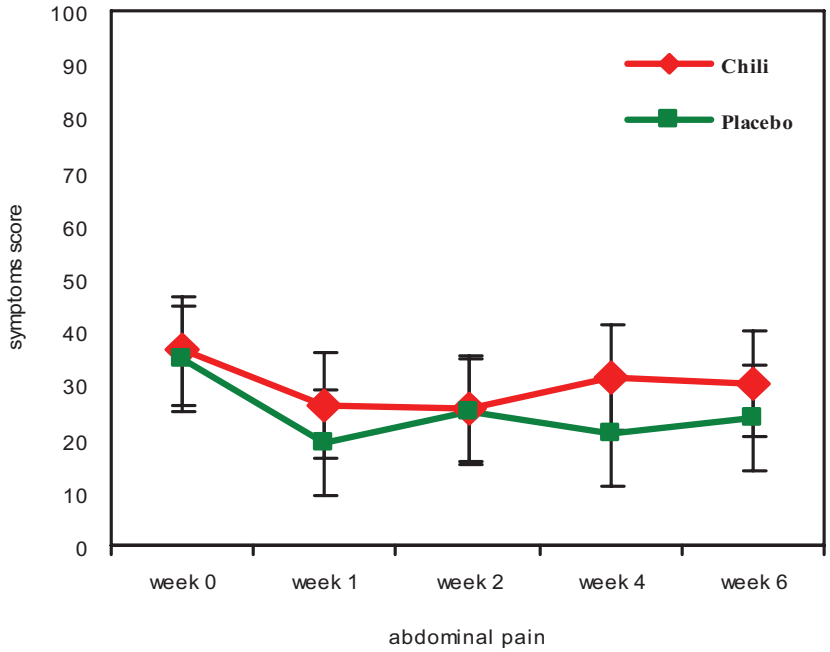


**Figure 1.** Course of the weekly mean abdominal pain score during chili and placebo ($p > 0.05$)

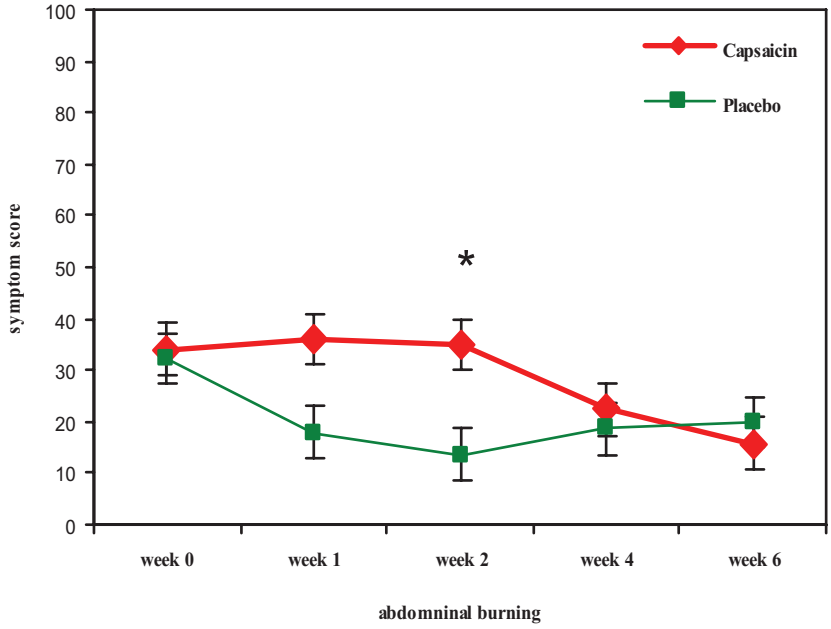


**Figure 2.** Course of the weekly mean abdominal burning score during chili and placebo whilst asterisks indicate a statistically significant difference between the two groups (*$p = 0.03$)

gastrointestinal symptoms in response to spicy meal between the two treatments. After 6 weeks of chili ingestion, the maximum abdominal burning symptom score after standard spicy meal ingestion was significantly deceased compared to placebo (4.3 ± 2.4 vs. 14.1 ± 5.1; $p = 0.02$). The other postprandial gastrointestinal symptoms in response to standard spicy meal were not significantly different between the two groups. (Figure 5)

## Effect of chronic chili ingestion on rectal sensation in IBS-D patients

After chronic chili ingestion, chili significantly increased the sensory threshold in response to balloon

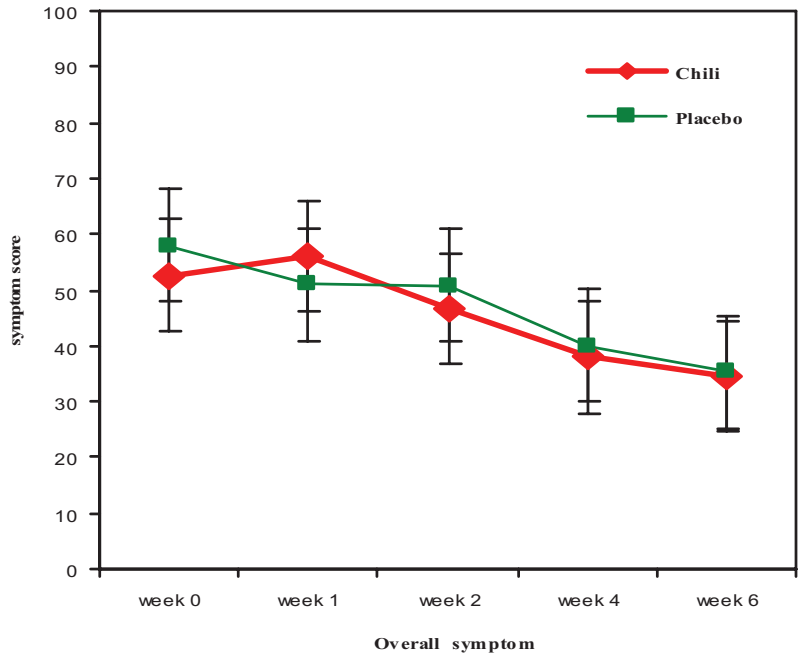


**Figure 3.** Course of the weekly mean overall symptom score during chili and placebo ($p > 0.05$)

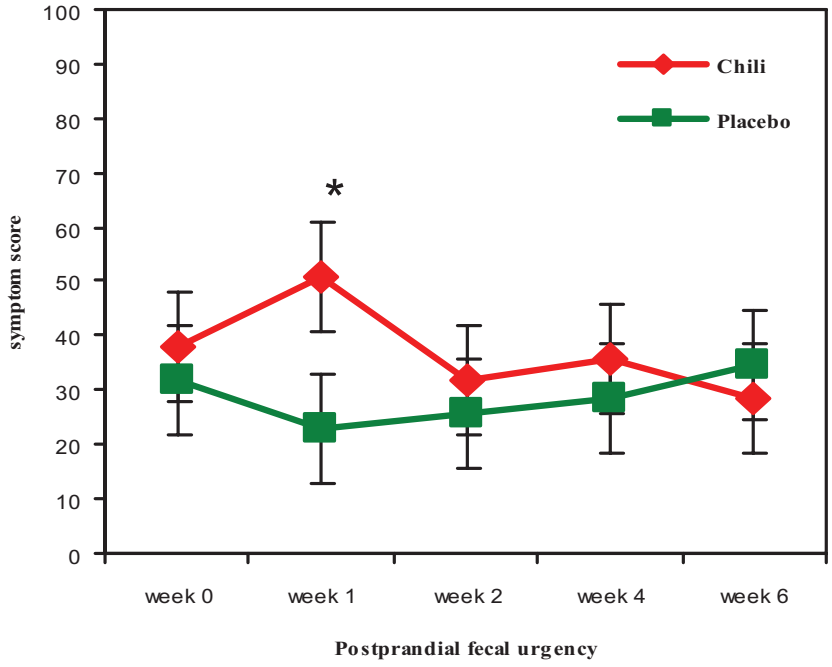


**Figure 4.** Course of the weekly mean postprandial fecal urgency score during chili and placebo, whilst asterisks indicate a statistically significant difference between the two groups (*$p = 0.04$)

distension for first rectal sensation compared to placebo ($p = 0.03$), with no significant effect on first sensation of urgency, moderate urgency and severe urgency (Figure 6). There were no patients with first sensation of pain within the range of distension in this study. In addition, the rectal compliance was not different when comparing the two groups (Figure 7).

## DISCUSSION

The results of this study indicated that in patients with IBS-D, chronic chili ingestion the significantly increased sensory threshold of rectal perception for first rectal sensation without significant effect on rectal compliance. In addition, at week 6 of chili treatment, ab-

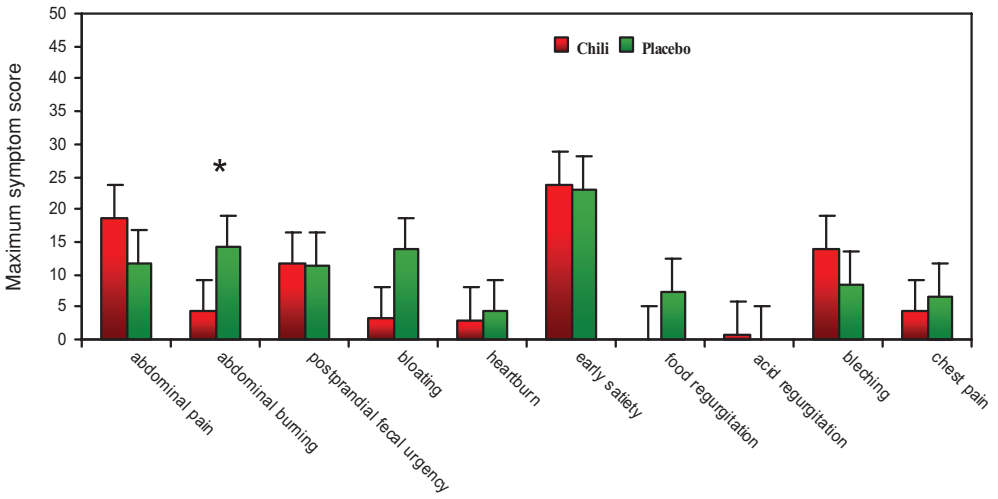


**Figure 5.** Gastrointestinal symptoms scores in response to a standard spicy meal after 6 weeks of chili and placebo treatments. NS = $p > 0.05$, *$p = 0.02$

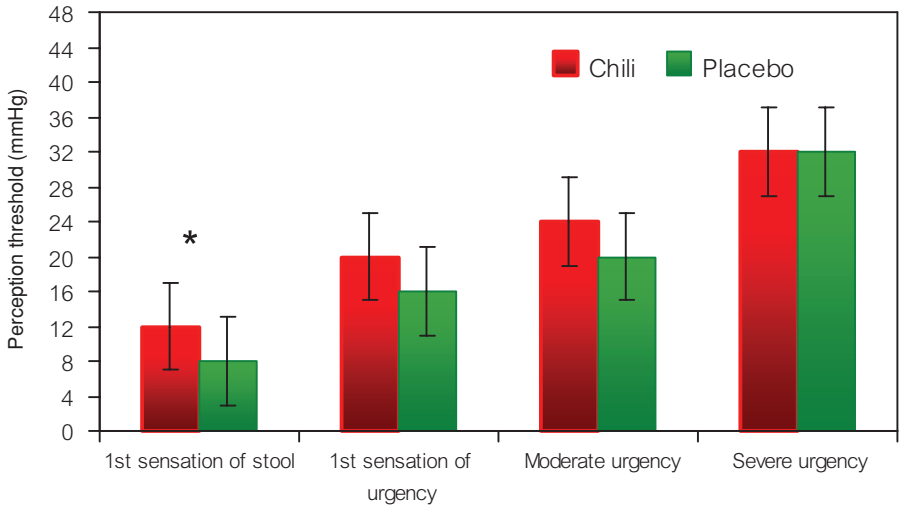


**Figure 6.** Sensory threshold of rectal perception in response to balloon distention after chili and placebo capsule ingestion. NS = no significance; NS = $p > 0.05$, *$p = 0.03$

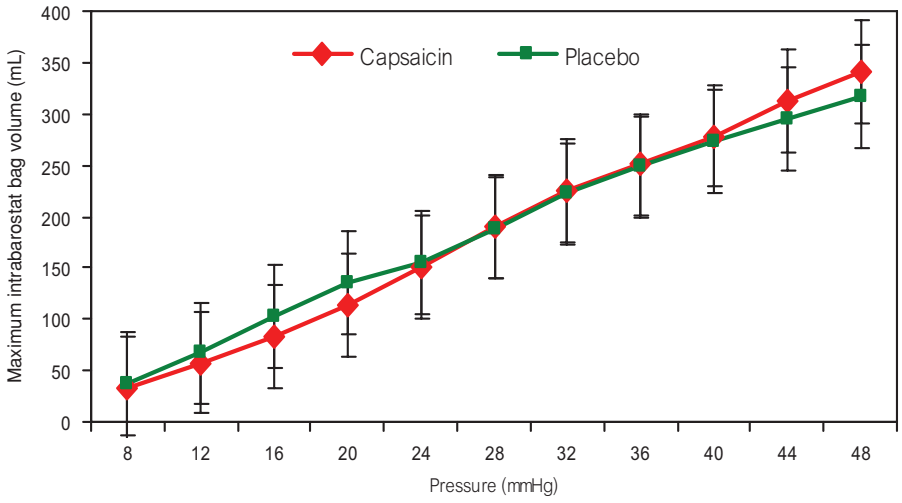


**Figure 7.** Rectal compliance after chili and placebo ingestion, $p > 0.05$

dominal burning induced by the standard spicy meal was significantly reduced compared to placebo. Six weeks of chili ingestion in IBS-D patients had no significant effect on abdominal pain, abdominal burning, abdominal bloating, postprandial fecal urgency, diarrhea and incomplete evacuation symptom scores. With regard to the course of the effect on symptoms, postprandial fecal urgency and abdominal burning significantly increased compared to placebo during week 1 and week 2 of chili ingestion and gradually decreased over time. However, there was no significant difference at the end of treatment.

The observation that postprandial fecal urgency and abdominal burning were aggravated at the initial chili ingestion in this study can be explained by sensitization of capsaicin receptor by chili. These results indicated that repeated exposure of the gut mucosa to capsaicin-containing chili ingestion induced the sensitization at the beginning followed by desensitization of the proximal gut and the rectal mucosa by capsaicin stimulation.

It has been reported that capsaicin receptor (TRPV1) was expressed throughout the human gastrointestinal tract[22,23]. In animal models, capsaicin mediated gut sensation by activation of capsaicin receptor at vagal afferent c-fibers of gut. Furthermore, intraluminal capsaicin infusion into human duodenum and jejunum induces abdominal pressure, abdominal pain, cramps and nausea[24]. In addition to proximal gut hypersensitivity, rectal sensation threshold in healthy humans decreased after a single 5-grams of capsaicin-containing chili ingestion[25]. Likewise, some previous studies showed that capsaicin-containing chili could stimulate gastrointestinal symptoms and rectal sensation in IBS patients[12,15].

Following capsaicin receptor stimulation, changes in the membrane permeability to calcium ion sensorial neuron with consequent depolarization lead to the release of many neuropeptides. Subsequently, the fibers become unresponsive to nociceptive stimuli. The increased threshold of rectal sensation after chili ingestion in our study suggested that the increase might be related to a desensitization effect of capsaicin. Although abdominal burning and postprandial fecal urgency decreased at the end of chili ingestion, there was no significant improvement. According to previous studies, capsaicin receptor was found at different levels throughout the human gut[22,23] Indeed the different levels of the human gut are also associated with different capsaicin dose effects, such that duodenal capsaicin induces sensations at lower doses than jejunal capsaicin[24] Capsaicin is a lipophilic substance and mucosal absorption in the upper gastrointestinal tract is fast[26] Either ingested capsaicin reaching the distal intestine or gastrointestinal absorption of capsaicin taking place is uncertain. Therefore the capsaicin dose, form of administration, and duration of capsaicin ingestion should be considered.

In conclusion, this study explored the 6-week effect of capsaicin-containing chili ingestion on gastrointestinal symptoms and sensation in IBS-D patient. Chronic chili ingestion significantly reduced abdominal burning induced by a standard spicy meal ingestion and increased sensory threshold of rectal perception for first rectal sensation in IBS-D patient compared to placebo, without significant effect on rectal compliance. The result suggested that there was a capsaicin desensitization effect in the gastrointestinal tract of IBS-D patients after 6 weeks of chili ingestion.

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