

## Effect of Hydro-Alcoholic Extract of *Teucrium Polium* on Castor Oil-Induced Diarrhea in Male Rat

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Article information	Abstract
<p>Article history: Received: 23 Aug 2011 Accepted: 26 Apr 2012 Available online: 29 Oct 2012 ZJRMS 2013; 15(6): 54-57</p> <p>Keywords: Diarrhea Teucrium Polium Rat</p> <p>*Corresponding author at: Department physiology, Physiology-Pharmacology Center, Rafsanjan University of Medical sciences E-mail: mohammadatir@yahoo.com</p>	<p><b>Background:</b> Diarrhea is one of the world's health problems as the most common causes of death in children. In this study, the effect of <i>Teucrium Polium</i> (TP) extract on diarrhea induced by castor oil has been studied.</p> <p><b>Materials and Methods:</b> 30 male rats were divided into five equal groups containing extract with doses of 100, 200 and 600 mg/kg; diphenoxylate (5 mg/kg); and control group or vehicle (normal saline) groups. One hour after feeding the drugs or vehicle in the volume of 10 ml/kg, 2 ml of castor oil were fed to each animal through an oral-gastric catheter. Then excrements of animals were separately observed in the cages for 4 hours and their quality, frequency and stool weight were determined. Data analysis was performed using one-way ANOVA and Tukey post-test and <math>p &lt; 0.05</math> was considered as significant.</p> <p><b>Results:</b> Diphenoxylate and 600 mg/kg dose of TP reduced the percentage of the weight loss of animals, their excretion frequency and defecation index (<math>p &lt; 0.001</math>). The 600 mg/kg dose of TP decreased the fecal water content compared to the control group (<math>p &lt; 0.01</math>).</p> <p><b>Conclusion:</b> Based on our data, essential oil of TP has an effect similar to diphenoxylate on the reduction of osmotic diarrhea symptoms and also reduces the volume of excreted water</p>

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### Introduction

Today, diarrhea is defined based on a more than 200 grams increase in the stool weight per day which is associated with an increase in fecal waters, repeated defecation, urgency in defecation and irritation around the anus [1]. Diarrhea is one of the most important health problems, particularly in children around the world and it causes million deaths worldwide each year and is one of the most common causes of children mortality [2]. In Iran, diarrhea is the second leading cause of death in children next to respiratory infections [3]. Prolonged diarrhea can cause loss of water. This means that the body loses its fluid enough to function normally. Loss of water is especially dangerous for children and the elderly; therefore it should be promptly treated in order to prevent more serious problems [4]. The main treatment for diarrhea is to compensate water and electrolytes; and drugs are used to treat symptoms [5]. Infectious causes of diarrhea in children are often self-limiting.

Treatment of the most bacterial and viral causes of diarrhea primarily includes supportive measures such as correction of dehydration and electrolyte deficits and treatment of side effects due to the mucosal injury. Antibiotic treatment is recommended only for some bacterial and parasitic causes of diarrhea [2]. In recent years, tendency towards using herbal medicines and the use of these drugs in the treatment and prevention of

diseases has increased. Studies have shown that some plants have antispasmodic properties and delay or inhibit bowel movements and reduce its discharges. Among the plants with anti-diarrheal effects which have been identified by researches, *albizia lebeck* [6], thyme, *satureja* and *verbenaceae* herbs can be mentioned [2]. One of the plants which are somehow recommended in traditional medicine for improving gastrointestinal condition is TP (*Teucrium polium*) of *Laminaceae* species which is grown widely around the world.

TP is an herbaceous, perennial and shrub herb. History of using this plant is more than 2000 years [7, 8]. This plant is widely used by traditional practitioners for the treatment of inflammation, rheumatism, wound dressing and also as the lowering the blood sugar [8, 9]. In new researches, other properties have been also mentioned for this herb including anticonvulsant, anti-inflammatory, analgesic, antipyretic, wound healer, anti-microbial activity, antioxidant, anti-ulcer and lowering blood pressure properties [8-10]. According to the conducted studies, the use of this herb is effective in relieving headaches, weakness of gastrointestinal function, genital diseases - urinary and menstrual delay or interruption due to the overall weakness [8]. Also analgesic, antispasmodic and anticonvulsant effects have also been mentioned for this herb and it contains some amounts of tannin,

terpenoids, saponine, flavonoid, alpha glucoside, sterols, leucoanthocyanidin, betacarophyllene, humulene, caryophyllene, D-terpenoid, asparagine and resinous material [8, 9, 11, 12]. Considering the previous studies showing anti-contractile effects of TP on gastrointestinal smooth muscle and that it has decreased stomach and bowel movements frequency [8, 13], the effect of TP extract on diarrhea caused by castor oil has been studied in the present study.

## Materials and Methods

**Animals and groups:** 30 male rats weighing 200-250 g were used in this experimental study [30]. They were kept at the temperature of 20-22°C, under 12 h light and 12 h dark condition with free access to the food and water. Ethical charter of working with laboratory animals approved by Rafsanjan University of Medical Sciences was observed during the tests. The animals were deprived of food 24 hours before the start of the study and then were divided randomly into 5 groups (N=6 in each group) as following: 1-Extract 100 (receiving 100 mg/kg), 2-Extract 200 (receiving 200 mg/kg), 3-Extract 600 (receiving 600 mg/kg), 4-Diphenoxylate (receiving 5 mg/kg) and, 5-The control group receiving only the vehicle.

All the drugs were dissolved in 0.9% saline and then the animals were fed as gavages (normal saline 10 ml/kg) [14, 15]. Diphenoxylate dose used in this study had no side effects such as mortality or respiratory weakness.

**Extraction:** fresh leaves of TP were collected in the late spring (second half of May onwards) from the mountainous region of the northwest of the city of Jiroft (Sardouyeh) in Kerman province and they were dried at laboratory temperature and then grounded after approval by a botanist. 250 grams of the resulted powder were incubated in 60% water and 40% ethyl alcohol (98%) for 48 hours in darkness and at 45°C and it was stirred twice per day. The obtained solution was placed on the aluminum sheets after filtration by ordinary filter paper; then it was left to be dried and condensed on a water bath with 45°C for 24 hours [16]. Solutions with concentrations of 100, 200 or 600 mg in 10 ml of normal saline were prepared after complete drying of the essential oil. The doses were chosen based on the previous studies [17] and our pilot experiments.

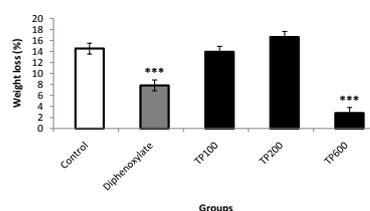
**Diarrhea induced model:** One hour after gavage with different doses of extract, drug or vehicle, animals were fed with 2 ml of castor oil through gavage. Then each animal was weighed and placed in a separate cage on the filter paper with the specified weight and were observed for four hours [14]. At the end of observation, all the animals were weighed twice to calculate the weight loss. Finally, data of excrement quality (including normal, soft, and watery), defecation frequency, defecation index and fecal water content were calculated and collected. Defecation index was determined by sum of defecation frequency and excrement quality. To determine the water content of the excrement, the fresh (wet) excrement was initially weighed, and then filter papers were incubated at

50°C for 24 h to make excrement to be dried. By determining the difference between the dry and wet excrements, water content of the excrement was measured. At the end of four hours, the animals were weighed and their weight loss was calculated [15].

SPSS-11 statistical software was used for data analysis. Data are reported as Mean±SD and were compared by Tukey post-test and one-way ANOVA statistical test and  $p < 0.05$  was considered as a significant difference.

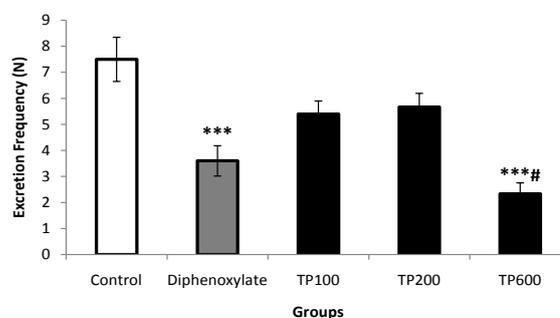
## Results

The weight loss of control group at the end of the 4 hour was  $14.53 \pm 2.03$  percent after 2.5 ml of castor oil gavages. This index in diphenoxylate and teucrium 600 groups was reduced to  $7.85 \pm 1.16$  and  $2.82 \pm 0.62$  respectively ( $p < 0.001$ ). The percentage of weight loss in other doses of Teucrium was not significantly different from control group (Fig. 1). Defecation frequency in different groups are shown in Figure 2, indicating a significant difference of teucrium 600 and diphenoxylate with the control group ( $p < 0.001$ ) and also between Teucrium 600 and the other two doses of plant ( $p < 0.005$ ). Comparison of the defecation index of different groups (Fig. 3) showed that this index was significantly decreased in Teucrium 600 and diphenoxylate groups compared to the control group ( $p < 0.001$ ). Also, this dose of the herb compared to the other doses also showed significant differences ( $p < 0.01$ )



**Figure 1.** The effect of *Teucrium* extract and diphenoxylate on the weight loss after castor oil-induced diarrhea.

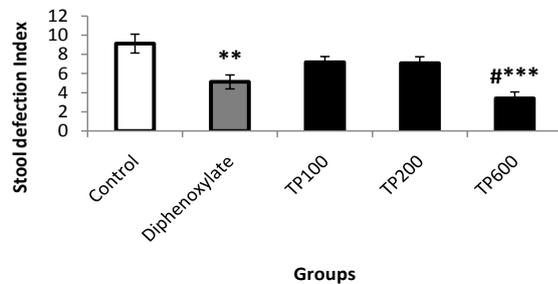
\*\*\* $p < 0.001$  compared to the control group. TP= *Teucrium polium*. N=6 in each group.



**Figure 2.** The effect of *Teucrium* extract and diphenoxylate on defecation frequency after castor oil-induced diarrhea.

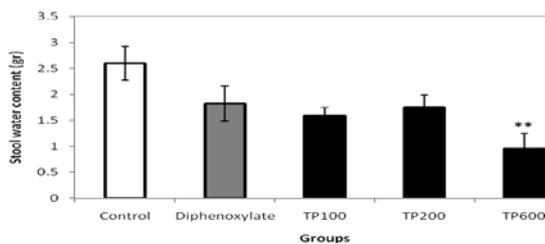
\*\*\* $p < 0.001$  compared to the control group and # $p < 0.005$  compared to TP 100 and TP 200. TP= *Teucrium polium*. N=6 in each group.

Although water content of the excrement was reduced in all groups compared to the control group, this reduction was significant only at the dose of 600 mg of Teucrium ( $p < 0.01$ , Fig. 4). The average water contents in the different groups were as follows: Control group:  $2.6 \pm 0.32$  g, Diphenoxylate:  $1.83 \pm 0.33$  g, extract 100 mg/kg:  $1.58 \pm 0.17$  g, extract 200 mg/kg:  $1.75 \pm 0.25$  g, and extract at a 600 mg/kg:  $0.96 \pm 0.28$  g.



**Figure 3.** The effect of Teucrium extract and diphenoxylate on defecation index after castor oil-induced diarrhea.

\*\*\* $p < 0.001$  compared to the control group and # $p < 0.01$  compared to TP 100 and TP 200. TP= *Teucrium polium*. N=6 in each group.



**Figure 4.** The effect of *Teucrium* extract and diphenoxylate on the water content of the excrement after castor oil-induced diarrhea.

\*\* $P < 0.01$  compared to the control group. TP= *Teucrium Polium*. N=6 in each group.

## Discussion

In this study, the effect of Teucrium herb on castor oil-induced diarrhea was examined for the first time. Results showed that Teucrium, at a dose of 600 mg/kg, has an effect similar to that of diphenoxylate on reducing the percentage of body weight loss of the animal, defecation frequency and defecation index and this herb has reduced the water content of the excrement compared to the control group.

The dried leaves of Teucrium herb is one of the rare herbs widely used in the southern parts of the country, especially in the provinces of Kerman, Hormozgan and Sistan & Baluchistan to treat diarrhea, especially in children. The purpose of this study is to examine the effect of hydroalcoholic extract of Teucrium on the improvement of diarrhea in the rats. The results showed that the extract at a dose of 600 mg/kg has an effect similar to the effect of 5 mg/kg diphenoxylate in reducing defecation frequency and weight loss due to the diarrhea. Teucrium also reduced the defecation index, which is an exact criterion in the evaluation of the effect of a drug on bowel evacuation and control of diarrhea [18]. Results

from other studies are consistent with our results. For example, in a study conducted on the effect of aqueous extract of Teucrium on the contraction frequency and intragastric pressure at baseline conditions and vagus nerve stimulation, it was observed that the extract of this herb reduces intragastric pressure in the condition of vagus nerve stimulation and the frequency of gastric contractions, both at the baseline and vagal stimulation conditions [8].

In another study, it was observed that the aqueous extract of TP reduces the KCl and acetylcholine-induced contractions of the small intestine outside the body in a concentration-dependent manner. These effects are independent from the inhibiting effects of alpha and beta noradrenergic and opioid receptors and even nitric oxide [13]. On the other hand, as the effect of the extract on the inhibition of ileum contractions induced by acetylcholine has been observed [19], therefore it may have anticholinergic effects as well. In addition; it was observed that the aqueous extract of Teucrium had significant analgesic and antispasmodic effects, although its analgesic effect is less than the effect of morphine [19]. Therefore, the observed inhibitory effects of this herb on gastrointestinal activity in this study and other above-mentioned similar studies can justify the traditional use of this herb in the treatment of the gastrointestinal tract disorders.

One of the outstanding results of this study was the reduction in the water content of the excrement when using 600 mg/kg TP extract, so that even diphenoxylate with the same dose used in clinical practice, had no such an effect. This result indicates that probably Teucrium has increased water absorption from the gastrointestinal tract. However, further studies are needed to confirm the effect of Teucrium plant through studying the effect of this herb on the water absorption in the body.

It has been reported that the high doses of TP have caused liver complications in diabetic rats [20], but it is not known whether this effect also occurs in normal animals. If this herb does not have any adverse effect or no serious adverse effects of its active ingredients on gastrointestinal movement are found, therefore, it can be suitable substitute for the opiates such as diphenoxylate (which are mostly exposed to the drug abuse) in controlling non-infectious diarrhea.

In conclusion, the findings of this study showed that leaves extract of Teucrium at the dose of 600 mg/kg has an effect similar to the effect of diphenoxylate on improving symptoms of casor oil-induced diarrhea. In addition, this herb also reduces the amount of water excreted in the excrement. Therefore, it may also be involved in the water absorbed from the gastrointestinal tract which needs further studies.

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**Authors' Contributions**

All authors had equal role in design, work, statistical analysis and manuscript writing.

**Conflict of Interest**

The authors declare no conflict of interest.

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