Case Report

Anti-diarrheal effects of wood creosote, Seirogan, in Japanese patients: a retrospective study

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Abstract: Seirogan, a wood creosote, is a nonprescription drug used to treat diarrhea. However, reports of its clinical use are rare. Here, we report on the efficacy of wood creosote (3 capsules daily) for the alleviation of diarrheal symptoms in 148 patients from 10 clinics in Japan. The wood creosote capsules were classified as remarkably effective (44 patients), effective (71 patients), and partially effective (13 patients) based on the degree of alleviation of diarrheal symptoms that were induced by a variety of causes. The antidiarrheal efficacy of the capsules did not differ between males and females, and young patients (21–30 years) showed greater improvement in diarrheal symptoms than did old patients (> 61 years). Although this report is based on the re-evaluation of old data that had been preserved by our company, the effectiveness and range of symptoms that were treatable with wood creosote has likely remained unchanged. To the best of our knowledge, this is the first public report on the clinical effectiveness of wood creosote capsules for the treatment of a wide range of diarrheal symptoms.

Keywords: diarrhea; wood creosote; Seirogan; retrospective study; capsule

1. Introduction

Wood creosote (Seirogan) capsule is a Japanese traditional anti-diarrheal medication [1]. In East Asian countries, wood creosote is used as a non-prescription drug (and as a supplement in the United States) for the treatment of patients with a variety of diarrheal symptoms [2]. Wood creosote is made from tar, which is prepared by distillation of stems of beech trees [3]. It is a colorless or light-yellow liquid with a peculiar smell. Although wood creosote shows only weak antibacterial effect, it shows no or very few adverse effects [4, 5]. Therefore, wood creosote has been approved as a non-prescription drug. Owing to its easy-to-use nature and efficacy and safety, wood creosote has captured more than 50% share of the anti-diarrheal market in Japan. However, reports on its clinical use for the treatment of diarrhea are scarce [6]. There has been a growing emphasis on the use of drugs from natural origin, which are considered safer than synthetic ones; thus, the clinical potential

of wood creosote in treating diarrhea should be explored.

Here, we summarize cases of 148 diarrhea patients who were treated with wood creosote capsules for 1–3 days. In >78% cases, diarrheal symptoms were decreased by treatment with wood creosote capsules. To the best of our knowledge, this is the first report on the anti-diarrheal efficacy of wood creosote on a variety of diarrheal symptoms.

2. Case presentation

2-1. Subjects

Primary care physicians in ten clinics in Japan made the diagnosis of diarrhea. Taiko Pharmaceutical Co., Ltd. covered all-expense of the treatment of patients during the survey. All doctors had no conflicts of interest in the survey. The protocol of the study was approved by the Ethics Committee of Taiko Pharmaceutical Co., Ltd. (No. 790716) and presented to individual hospitals or clinics (Miyaura Clinic, Yokota Clinic, Hotta Clinic, Terada-Manjyu Clinic, Kondo Clinic, Yasui Clinic, Ajinomoto Clinic, Toyama Red Cross Hospital, Osaka Gyomei-kan Hospital, and Asahi Osaka Clinic, see details in Supplementary materials. An original protocol written in Japanese and all data were submitted to "*data*".). According to the original protocol and contracts, we re-confirmed that all subjects had given their informed consent for inclusion prior to their participation in the study. The study had been conducted in accordance with the Declaration of Helsinki, which was re-approved by the Ethics Committee of Taiko Pharmaceutical Co., Ltd. (No. 190927).

Doctors eliminated patients with severe diarrheal symptoms and less than 15 years old from this survey. The patients (aged 15–85 years; n = 148 [71 males and 78 females]) were categorized into 22 groups according to diagnoses (Table 1). The age-wise distribution of patients is shown in Table 2. Pregnant patients were not recruited in this study.

Table 1. Number of patients and their diarrheal causes at diagnosis.

Diagnosis.	No. of Patients	Diagnosis	No. of Patients
Acute enteritis	71	Colitis	3
Infectious gastroenteritis	14	Chronic gastroenteritis	2
Uncomplicated diarrhea	12	Suspicion of food poisoning	2
Acute gastroenteritis	7	Chronic colitis	1
Acute colitis	6	Chronic diarrhea	1
Chronic enteritis	6	Nervous gastroenteritis	1
Irritable colitis	5	Habitual diarrhea	1
Gastrogenic diarrhea	3	Catarrhal colitis	1
Nervous diarrhea	3	Hemorrhagic gastritis	1
Gastroenteritis	3	Gastric ulcer	1
Ulcerous colitis	3	Acute pancreatitis	1
		Total	148

Table 2. Age-wise distribution of patients.

Age (Years)	Number
≤20	6
21–30	30
31–40	23
41–50	22
51–60	31
≥61	36
Total	148

2-2. Treatments

Because wood creosote has a typical smell, oral treatment with raw wood creosote is intolerable for most patients. Therefore, 166 mg of wood creosote was adsorbed onto 66 mg of magnesium aluminometasilicate and filled into capsules. The patients took 1 capsule after a meal (total 3 capsules per day) for 1–3 days. When patients were unable to take meals, they took wood creosote capsules at 9:00 am, 12:00 pm, and 18:00 pm. The patients who received other related medications, such as berberine-containing medicines, antibiotics, synthetic antibacterial agents, or antiflatulents, during the treatment with wood creosote capsules were excluded from this study.

2-3. Evaluation

Records of fecal score, frequency of defecation per day, and other symptoms before and after the treatment with wood creosote were documented using a score sheet (see Supplementary materials, Score sheet). Finally, primary care physicians evaluated the efficacy of wood creosote capsules as follows:

(1) Remarkably effective: diarrheal symptoms disappeared within 3 days after treatment initiation. Stool consistency normalized, and the patients felt comfortable.

(2) Effective: diarrheal symptoms improved within 3 days after treatment initiation. Stool consistency improved, and patients had no problem in performing daily activities.

(3) Partially effective: diarrheal symptoms partially improved within 3 days after treatment initiation. Stool consistency slightly improved.

(4) Not effective: symptoms persisted even 4 days after treatment initiation.

No data could be subjected to statistical analyses.

2-4. Results

Summary of the efficacy of wood creosote capsules on diarrheal symptoms is shown in Table 3. In more than 78% of the patients, diarrheal symptoms were improved effectively (remarkably effective + effective). No difference was observed in the efficacy of anti-diarrheal effect of wood creosote capsules between both sexes (Fig. 1).

Table 3. Summary of the efficacy of wood creosote capsules in treatment of diarrhea.

	Number	%
Remarkably effective	44	29.73
Effective	72	48.65
Partially effective	13	8.78
Not effective	19	12.84
Total	148	100

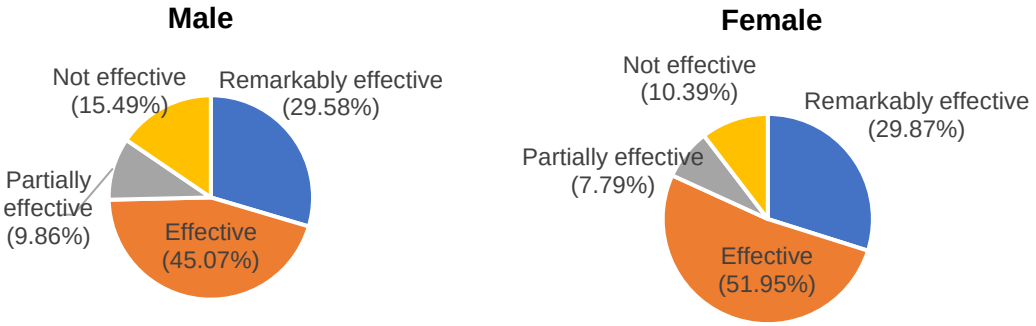

Figure 1. Comparison of anti-diarrheal efficacy of wood creosote capsules between male (n = 71) and female (n = 77) patients.

Next, we examined the anti-diarrheal efficacy of wood creosote capsules according to age of patients (Fig. 2). Younger patients (21–30 years) showed more improvement in diarrhea symptoms as compared with elderly patients (>61 years).

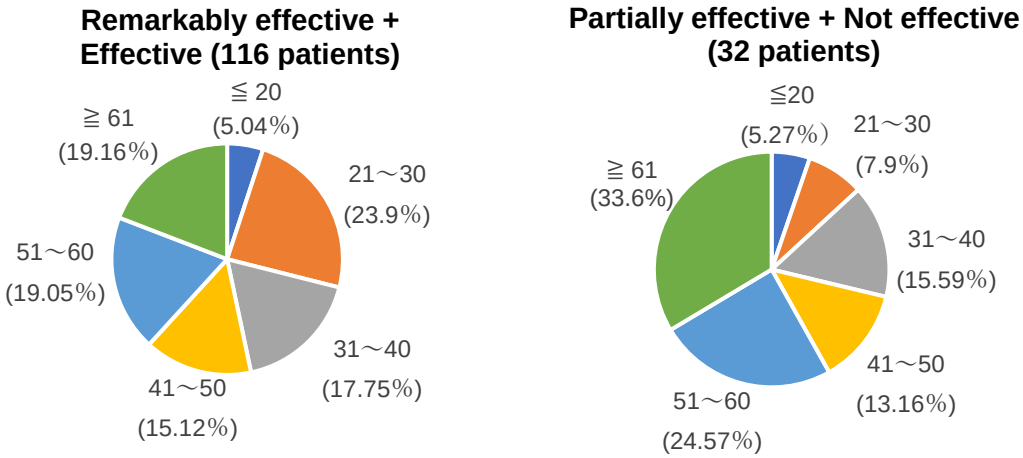

Figure 2. Anti-diarrheal efficacy of wood creosote capsule in younger patients. Patients were classified according to their age and improvement rate (%), which was calculated for the total number of patients (116 for remarkably effective + effective or 32 for partially effective + not effective) in each group.

Table 4. Efficacy of wood creosote capsules against each diarrheal cause.

	Number of patients							
Diagnosis	**Remarkably Effective**	**(%)**	**Effective**	**(%)**	**Partially Effective**	**(%)**	**Not Effective**	**(%)**
Acute enteritis	25	35.2	30	42.3	8	11.3	8	11.3
Acute gastroenteritis	1	14.3	5	71.4	0	0	1	41.3
Acute colitis	1	16.7	5	83.3	0	0	0	0
Chronic enteritis	0	0	3	50	2	33.4	1	16.7
Chronic gastroenteritis	0	0	0	0	1	50	1	50
Chronic colitis	0	0	0	0	0	0	1	100
Chronic diarrhea	0	0	1	100	0	0	0	0
Infectious gastroenteritis	2	14.3	10	71.4	1	7.1	1	7.1
Uncomplicated diarrhea	9	75	3	25	0	0	0	0
Irritable colitis	3	60	2	40	0	0	0	0
Gastrogenic diarrhea	0	0	3	100	0	0	0	0
Nervous diarrhea	2	66.7	1	33.3	0	0	0	0
Gastroenteritis	1	33.3	1	33.3	0	0	1	33.4
Nervous gastroenteritis	0	0	1	100	0	0	0	0
Ulcerous colitis	0	0	2	66.6	0	0	1	33.3
Habitual diarrhea	0	0	1	100	0	0	0	0
Catarrhal colitis	0	0	1	100	0	0	0	0
Colitis	0	0	1	33.3	0	0	2	66.7
Hemorrhagic gastritis	0	0	0	0	0	0	1	100
Gastric ulcer	0	0	0	0	1	100	0	0
Acute pancreatitis	0	0	1	100	0	0	0	0
Suspicion of food poisoning	0	0	1	50	0	0	1	50
Total number	44		72		13		19	

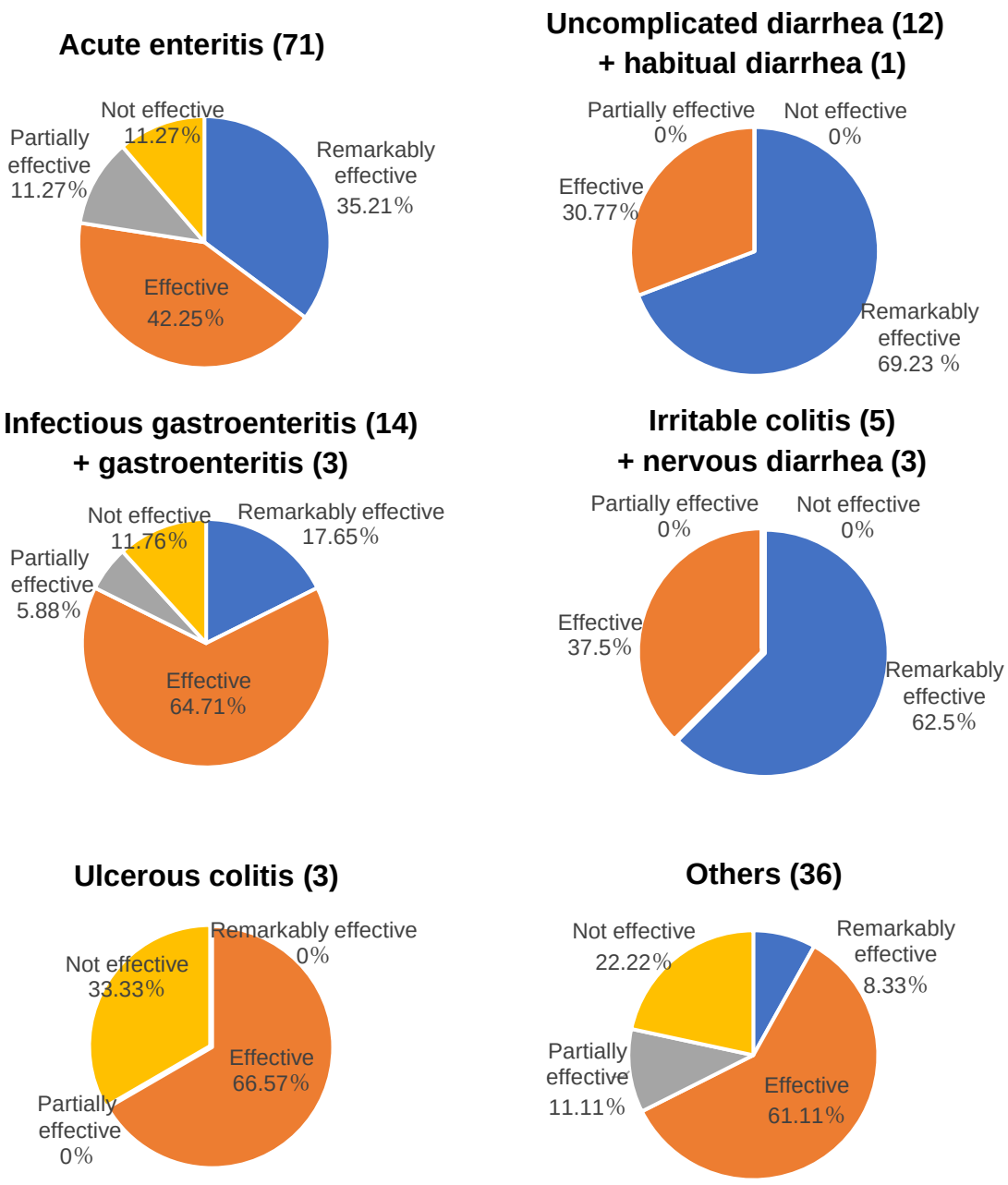

Figure 3. Re-evaluation of the efficacy of wood creosote capsules after classification based on diarrheal causes. Numbers in brackets indicate the number of patients.

Number of patients and the improvement rate (%) in each diarrheal cause group is summarized in Table 4. Wood creosote capsules were effective in patients with acute enteritis, uncomplicated diarrhea, infectious gastroenteritis, and irritable colitis. In addition, wood creosote capsules were also effective in patients with nervous diarrhea and irritable colitis. The efficacy of wood creosote was re-evaluated after classification based on diarrheal causes and is shown in Fig. 3.

Wood creosote capsules efficiently decreased diarrheal symptoms (frequency of defecation and fecal score) occurring due to different causes. Although some patients did not respond to the treatment, no specific cause of ineffectiveness was found. Some patients experienced adverse effects:

bloating sensation (1 patient), nausea (1 patient), and cardialgia (1 patient). Except for one patient, however, these adverse effects disappeared during the treatment without abrupt withdrawal of the medication.

3. Discussion

Wood creosote (capsules) was remarkably effective (44 patients), effective (71 patients), and partially effective (13 patients) in alleviating diarrhea symptoms. Although younger patients (21–30 years) showed more improvement than elderly patients (>61 years), wood creosote capsules showed anti-diarrheal effect in all patients. Notably, it was more effective against acute diarrhea than chronic diarrhea. In addition, the present survey suggests that wood creosote could be applicable to patients with a wide range of diarrheal symptoms. Especially this medication shows high efficacies against mild to moderate symptoms, but not that with organic disorders.

Wood creosote, referred to as medicinal creosote, is called Seirogan (a trade name) in Japan [1]. Wood creosote is a mixture of phenolic compounds (including creosol, o-cresol, guaiacol, and 4-ethylguaiacol), which are the major components responsible for its anti-diarrheal activities [2]. Wood creosote normalizes bowel peristalsis and suppresses excess water leakage from epithelial cells [3]. Moreover, it inhibits L-type Ca^{2+} channels, which leads to lowered Ca^{2+} influx in smooth muscle cells. The decrease in Ca^{2+} ion levels suppresses contraction of smooth muscle, leading to the normalization of bowel peristalsis [4].

Moreover, wood creosote has been reported to directly inhibit the Cl^- channel, cystic fibrosis transmembrane conductance regulator (CFTR), on the apical membrane. The inhibition of the Cl^- channel induces osmolality change, which suppresses water leakage [5]. Because hyper-active Cl^- channel is associated with different types of diarrhea [6], wood creosote may be effective against a wide range of diarrheal symptoms. Use of wood creosote was less effective against diarrheal symptoms caused by organic disorders in the digestive tract, such as colitis, as compared with those associated with Cl^- channel-related diarrhea, suggesting that Cl^- channels may be the target of wood creosote.

Besides modulating these ion channel-mediated effects, wood creosote has been reported to prevent hyper colonic motility caused by the 5-HT3 receptor and 5-HT4 receptor in the proximal colon and distal colon, respectively [7]. Wood creosote has been shown to prevent the increase in colonic motility induced by stress stimulation via 5-HT receptors in the colon, suggesting that it might be effective in treating stress-induced diarrhea with abdominal pain [8].

Loperamide, an opioid receptor agonist, is used to treat acute diarrhea worldwide. It also shows high efficacy against a variety of diarrheal symptoms, except those of infectious diarrhea. A double-blind study showed that the anti-diarrheal efficacy of wood creosote was almost similar to that of loperamide [9]. Besides improving other symptoms of diarrhea, wood creosote improved or resolved abdominal cramping, whereas loperamide only improved diarrhea. It suggested that wood creosote could treat diarrhea with wider range of symptoms than loperamide [10], although further detailed comparative tests are needed.

4. Conclusions

Wood creosote capsules are effective in treating diarrhea occurring due to various causes. To the best of our knowledge, this is the first report on the efficacy of wood creosote capsules against diarrhea in clinical practice.

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Conflicts of Interest: M.T., M.I., H.M., T.M., K.O., T.S. are employed by Taiko Pharmaceutical Co., Ltd.. M.S. and H. T. have nothing to declare. All doctors supported this survey had no conflicts of interest. Taiko Pharmaceutical Co., Ltd. covered all-expense of the treatment of patients (approximately $1,000 pre patient) during this survey.

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