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Original Article

Pharmacology Section

# Anti-Diarrhoeal Activity of the Aqueous Extract of the Bark of Cinnamomum Zeylanicum Linn in Mice

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## ABSTRACT

**Purpose:** The plant, *Cinnamomum zeylanicum* (Laureceae), is a small, ever green plant which is native to southern India and it has been reported to possess a number of medicinal properties. The purpose of the present study was to evaluate the anti-diarrhoeal activity of the aqueous extract of the bark of *Cinnamomum zeylanicum* which is used traditionally as folk medicine, by using a castor oil and MgSO4 (Magnesium Sulphate) induced diarrhoea model.

**Methods:** The aqueous extract of the bark of this plant at graded doses (100mg/kg, 200mg/kg body weight) was investigated for its anti-diarrhoeal activity in terms of the reduction in the rate of defaecation and the consistency of faeces in castor oil, Mgso4 induced diarrhoea. To understand the mechanism of its anti-diarrhoeal activity, its effect was further evaluated on the gastro-intestinal transit time with charcoal meal.

**Results:** The bark extract showed significant ($p<0.05$) inhibitory activity against castor oil and Mgso4 induced diarrhoea. There was a significant reduction in the gastro-intestinal motility which was observed by using the charcoal meal test in mice.

**Conclusion:** The results which were obtained in this study substantiated the anti-diarrhoeal effects of the aqueous extract of *Cinnamomum zeylanicum* Linn and its use by the traditional practitioners in the treatment of diarrhoea.


**Key Words:** Anti-diarrhoeal activity, Cinnamon bark, Castor oil, Mgso4, Char coal meal

## INTRODUCTION

Diarrhoea is characterized by an increased frequency of bowel movements, wet stools and abdominal pain [1]. It is a leading cause of malnutrition and deaths among children in the developing countries of the world today [2]. According to the World Health Report, diarrhoea is the cause of 3.3% of all the deaths worldwide. The worldwide distribution of diarrhoea accounts for more than 5-8 million deaths each year in children who were aged less than 5 years. The use of traditional medicine to combat the consequences of diarrhoea has been emphasized by the WHO in its diarrhoea control programme [3,4,5,6,7,8]. Many synthetic chemicals are available for the treatment of diarrhoea, but they have some side effects. The natural drugs are used as anti-diarrhoeal drugs, which are not always free from adverse effects [9].

The approach towards evaluating medicinal plants has been based on the chemical extraction of the plants which are then tested on various experimental models. Morphine, quinine, emetine, digitalis glycosides, ergot alkaloids and vinca alkaloids which are in wide use today, were originally obtained from plants. Several studies have shown the beneficial effects of traditional medicines on diarrhea [10,11,12,13].

In developing countries like India, a majority of people who live in the rural areas almost exclusively use traditional medicines in treating all sorts of diseases, including diarrhoea [7].

*Cinnamomum zeylanicum* is one of the oldest herbal medicines which are known, as it had been mentioned in Chinese texts as early as 4,000 years ago. It is often used for medicinal purposes due to its unique properties [14]. The genus, Cinnamomum, comprises of several hundred species which occur in Asia and Australia. These several species of cinnamon yield a volatile oil on distillation. The most important cinnamon oils which are used in world trade are those which are obtained from C. zeylanicum, C. cassia, and C. camphora. However, a number of other cinnamon species are distilled on a much smaller scale and the oils are used either locally or are exported [15].

*Cinnamomum zeylanicum* Linn (family. Lauraceae) is a small evergreen tree which is native to southern India and Sri Lanka, growing from sea level to nine hundred meters. The tree has a thick, reddish brown bark and small yellow flowers, and its leathery leaves have a spicy smell. It grows to a height of approximately 20 -60 ft (8 -18m) and is found primarily in tropical forests. The leaves are ovate-oblong in shape and 7-18 cm long. The flowers which are arranged in panicles have a greenish colour and a distinct odour. The fruit is a purple, one-centimeter berry which contains a single seed. The Chinese used it as a herbal medicine since 4000 years as a treatment for fever, diarrhoea, and menstrual problems.

*Cinnamomum zeylanicum* has a mildly astringent action and aromatic properties and it is used in European medicine. In the list of Johor medicines, it has a place for the treatment of colic and diarrhoea [16]. Among several plant materials of the genus, Cinnamomum which were examined, only the bark of Cinnamomum zeylanicum was found to contain a major phenolic metabolite of doubly linked proanthocyanidins [17].

The main properties of cinnamon are astringent, warming, stimulating, carminative, anti-septic, anti-fungal, anti-viral, blood purifying, and aiding digestion. All these properties of cinnamon make it a good medicinal plant. The sensorial qualities of cinnamon are slightly sweet, pleasant, warm and bitter, besides being strongly aromatic [18]. The barks from the branches of this tree without the epidermis and the subereous layer, is marketed as the commercial cinnamon, which has been used since long in perfumery, culinary, and native medicinal systems [19,20].

Cinnamon barks are widely used as a spice. They have been used to treat diarrhoea and other problems of the digestive system and as a component of the compounds which are used in Indian Ayurvedic medicine [21]. The cinnamon bark contains volatile oils (14%), cinnamaldehyde (60%), eugenol (up to 10%), trans cinnamic acids (51%); phenolic compounds (41%), condensed tannins, catechins, and proanthocyanidins; monoterpenes and sesqiterpenes (pinene); calcium monoterpenes oxalate; gum; mucilage; resin, starch, sugars, and traces of coumarin [22].

Hence, the present study was undertaken to evaluate the possible anti-diarrhoeal activity of the bark extract of Cinnamomum Linn which is used commonly in Indian traditional medicine, by using various validated models and to find out if the folk medicinal use has a scientifically justified basis.

## MATERIALS AND METHODS

### Plant Material Collection and Extraction

Cinnamon bark (Cinnamomum zeylanicum), which was taxonomically identified, was purchased from the local market at Guntur, A.P. A specimen has been preserved in our laboratory for further references. The bark was dried and finely powdered in a mechanical mixer. 10g of finely-powdered cinnamon was weighed and mixed with 100ml of water and this was kept on a water bath at 60ºC for two hours and filtered [23]. This extract was diluted with distilled water and was administered orally to mice.

### Animals

Albino mice (M/F) which weighed between 25-30 gms was used in this study. The cages of the animals were placed at room temperature with controlled cycles of 12 hours of light and 12 hours of of darkness. The relative humidity was maintained at 44-45 %. All the animals were fed with a standard pellet diet (Agro Corporation Private Limited, Bangalore, India) and water ad libitum. The standard pellet diet comprised of 21% protein, 5% lipids, 4% crude fiber, 8% ash, 1 % calcium, 0.6% phosphorous, 3.4% glucose, 2 % vitamin, and 55% nitrogen-free extract (carbohydrate) and it provided a metabolizable energy of 3600 kcal /kg. The study protocol was approved by the institutional animal ethical committee (Reg.no. 798/03/C/CPCSEA-2003) of NRI Medical College, Chinakakani. The animal beds in the cages were renewed thrice a week to ensure hygienic conditions and the maximum comfort of the animals.

### Phytochemical Screening

The phytochemical analysis of the crude extract was carried out to determine the active phytochemical constituents which were responsible for the anti-diarrhoeal activity [Table/Fig-4].

### Acute Toxicity Study

Different doses (50–2000mg/kg, p. o) of the aqueous extract of the bark of Cinnamomum zeylanicum were administered to groups of mice and they were observed continuously for 1 hour and then at half – hourly intervals for 4 hours, for any gross behavioural changes and further up to 72 hours, followed 14 days for any mortality as per the OECD Guideline 425. The bark extract of Cinnamomum zeylanicum was found to be non-toxic up to the maximum dose of 2000mg/kg body weight.

### Castor Oil Induced Diarrhoea

The method which was proposed by Galvez et al., was modified to suit the experimental needs [24,25]. The animals were kept in fasting for 24 hours before the test, with free access to water. The mice were divided in to 4 groups of 5 animals each. Diarrhoea was induced by administering 0.5ml of castor oil orally. Group I was taken as the control group (0.5ml of distilled water), Group II which received Loperamide (5mg/kg) served as the standard group, and Groups III and IV received the extract (100, 200 mg/kg, oral) 30 minutes before the castor oil administration. Each animal was placed in an individual cage, the floor of which was lined by blotting paper. The floor lining was changed every hour. The consistency of the faecal matter and the number of both the wet and the dry diarrhoeal droppings were counted every hour for a period of 4 hours. During an observation period of 4 hours, the total number of faeces which were excreted by the animals was recorded. The numerical score which was based on the stool consistency was assigned as follows; normal stool=1, semi solid=2, and watery stool=3 [26].

### Magnesium Sulphate-Induced Diarrhoea

A similar protocol, as the one which was used for castor oil-induced diarrhoea, was followed. Diarrhoea was induced by the oral administration of Magnesium sulphate at a dose of 2g/kg to the animals, 30 minutes after the pre-treatment with distilled water to the control group, after the pre-treatment with Loperamide (5mg/kg) to the positive control group and after the pre-treatment with the aqueous extract at the doses of 100 and 200 mg/kg to the test groups. All the administrations were carried out through the oral route [27].

### Effect on Gastrointestinal Transit Time

The mice were kept in fasting for 24 hours and were divided into four groups of five mice each and each animal was given 0.1ml of 1% charcoal suspension orally, 60 min after an oral dose of the test drug, the standard and the vehicle. Group I was administered 0.5ml distilled water, Group II received Loperamide 5mg/kg and Groups III and IV received the extract at the dose of 100mg/kg and 200mg/kg body weight respectively. The faecal boluses which were expelled were collected. Each faecal bolus was pressed on a white sheet of paper to examine the presence of the charcoal meal. The time for the appearance of the 1st faecal bolus with the charcoal meal was recorded.

### Statistical Analysis

The data which was obtained in the studies were subjected to one way analysis of variance (ANOVA) for determining the significant difference. The inter group significance was analyzed by using Dunnet's t-test. A p value of $< 0.05$ was considered to be significant. All the values were expressed as mean ± SEM.

## RESULTS AND DISCUSSION

In the castor oil-induced diarrhoea experiment, the extract of the bark of Cinnamomum zeylanicum produced a marked anti-diarrhoeal effect in the mice, as shown in [Table/Fig-1].

At doses of 100 and 200 mg/kg , the extract significantly decreased ($p<0.05$) the total number of faeces which was produced upon the administration of castor oil (54.12 % at 100mg/kg, 65.74% at 200mg/kg ) as compared to that in the control group. Similarly, the extract, at 100 and 200 mg/kg dose levels, significantly ($p<0.05$) reduced the extent of the diarrhoea (71.7%, 80.4%) in the test animals in the magnesium sulphate-induced diarrhoea test [Table/Fig-2]. However, both the doses were shown to reduce the total number of faeces in the test groups as compared to that in the control.

| ANOVA | | | | | | |
|---|---|---|---|---|---|---|
| Source of Variation | SS | df | MS | F | P-value | F crit |
| Between Groups | 790.55 | 3 | 263.5167 | 45.63059 | 4.57E-08 | 3.238872 |
| Within Groups | 92.4 | 16 | 5.775 | | | |
| Total | 882.95 | 19 | | | | |

Castor oil in induced diarrhea in mice.
Values are presented as mean ± SEM, (n=5); ** p<0.05, Dunnet's t-test as compared to Control.

| Groups | Treatment | No. of faecal droppings in4 h | %Inhibition of defecation |
|---|---|---|---|
| I (Control) | Castor oil (0.5ml,p.o) + Distilled water(0.5ml, p. o) | 21.6±0.24 | - |
| II (Standard) | Castor oil (0.5ml, p .o) + Loperamide (5mg/kg, p. o) | 5.4±1.66** | 75** |
| III | Castor oil (0.5ml,p.o) + AECB (100mg/kg, p .o) | 9.8±0.91** | 54.12** |
| IV | Castor oil (0.5ml, p .o) + AECB (200mg/kg, p .o) | 7.4±0.97** | 65.74** |

AECB: Aqueous extract of Cinnamon bark

| ANOVA | | | | | | |
|---|---|---|---|---|---|---|
| Source of Variation | SS | df | MS | F | P-value | F crit |
| Between Groups | 738.75 | 3 | 246.25 | 128.4783 | 2.19E-09 | 3.490295 |
| Within Groups | 23 | 12 | 1.916667 | | | |
| Total | 761.75 | 15 | | | | |

Mgso4 in induced diarrhea in mice

**[Table/Fig-1]:** Effect of aqueous extract of bark of C. zeylanicum on castor oil (0.5ml) induced diarrhea in mice

| Groups | Treatment | No. of faecal droppings in 4 h | % Inhibition of defecation |
|---|---|---|---|
| I (Control) | Mgso4 2g / kg p.o) + Distilled water(0.5ml, p. o) | 18.4±0.81 | - |
| II (Standard) | Mgso4 2 g/ kg , p .o) + Loperamide (5mg / kg, p. o) | 2.4±0.4** | 86.9** |
| III | Mgso4 2g/ kg ,p .o) + AECB (100mg / kg, p .o) | 5.2±0.86** | 71.7** |
| IV | Mgso4 2g/ kg , p .o) + AECB (200mg / kg, p .o) | 3.4±0.4** | 80.4** |

Values are presented as mean ± SEM, (n=5); ** p<0.05, Dunnet's t-test as compared to Control.
AECB: Aqueous extract of Cinnamon bark.

| ANOVA | | | | | | |
|---|---|---|---|---|---|---|
| Source of Variation | SS | df | MS | F | P-value | F crit |
| Between Groups | 53512.19 | 3 | 17837.4 | 577.3399 | 3.1E-13 | 3.490295 |
| Within Groups | 370.75 | 12 | 30.89583 | | | |
| Total | 53882.94 | 15 | | | | |

Gastro-intestinal transit time

**[Table/Fig-2]:** Effect of Aqueous extract of bark of C. zeylanicum on Mgso4 (2g/kg p.o) induced diarrhea in mice

| Groups | Treatment | Dose (p. o) | Time(minutes) for the appearance of 1st faecal bolus with Charcoal meal |
|---|---|---|---|
| I (Control) | Distilled water | 0.5ml | 59±2.16 |
| II (Standard) | Loperamide | 5mg/kg | 220±3.91** |
| III | AECB | 100mg/kg | 128±2.2** |
| IV | AECB | 200mg/kg | 169.8±2.31** |

**[Table/Fig-3]:** Effect of Aqueous extract of bark of C. zeylanicum on Char coal meal stimulated gastro-intestinal transit.
Values are presented as mean ± SEM, (n=5); **p<0.05, Dunnet's t-test as compared to Control.
AECB: Aqueous extract of Cinnamon bark.

In the gastro-intestinal transit test, the extract, at the doses of 100 and 200 mg/kg, retarded the gastro-intestinal transit of the charcoal meal in mice, where a significant (p<0.05) retardation of the intestinal transit was observed at the doses of 100 and 200 mg/kg dose as compared to that in the control [Table/Fig-3].

## DISCUSSION

Diarrhoea results from an imbalance between the absorptive and secretory mechanisms in the intestinal tract, which is accompanied by an excess loss of fluid in the faeces. In some types of diarrhoea, the secretory component predominates, while other types of diarrhoea are characterized by hyper motility. Castor oil causes

| Chemical constituents | Aqueous extract |
|---|---|
| Tannins | + |
| Alkaloids | + |
| Flavonoids | + |
| Sugars | + |
| Glycosides | + |
| Terpenes | + |
| Starch | + |

**[Table/Fig-4]:** Chemical constituents of aqueous extract of Cinnamomum zeylanicum bark

diarrhoea due to its active metabolite, ricilonic acid [28,29], which stimulates the peristaltic activity in the small intestine, leading to changes in the electrolyte permeability of the intestinal mucosa. Its action stimulates the release of endogenous prostaglandins [30]. In this study, the aqueous extract of *Cinnamomum zeylanicum* exhibited a significant anti-diarrhoeal activity. The aqueous extract of *Cinnamomum zeylanicum* significantly reduced the intestinal transit, as was observed by a decrease in the intestinal motility of the char coal meal. Phytochemical screening revealed the presence of alkaloids, glycosides, sugars, terpenes and flavonoids. Earlier studies have shown that the anti-dysenteric and anti-diarrhoeal properties of medicinal plants were due to the presence of tannins, alkaloids, saponins, flavonoids, sterols and/or tri terpenes and reducing sugars [25,31,32,33]. Hence, tannins, reducing sugars, sterols and/or tri terpenes may be responsible for the mechanism of action of the anti-diarrhoeal activity of Cinnamomum zeylanicum. This could be due to the fact that the extract increased the re-absorption of water by decreasing the intestinal motility, as was observed by the decrease in the intestinal transit in the charcoal meal test.

## CONCLUSION

The results of this investigation revealed that the aqueous extract of Cinnamomum zeylanicum contained pharmacologically active substances with anti-diarrhoeal properties. Further research has to be carried out to fractionate and purify the extract, in order to find out the molecule which is responsible for the anti-diarrhoeal activity which was observed.

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