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ORIGINAL ARTICLE

# Evaluation of Antipropulsive Activity of *Decachaeta incompta* (DC) King and Robinson and its Sesquiterpene Lactones on Induced Hyperperistalsis in Rats

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## ABSTRACT

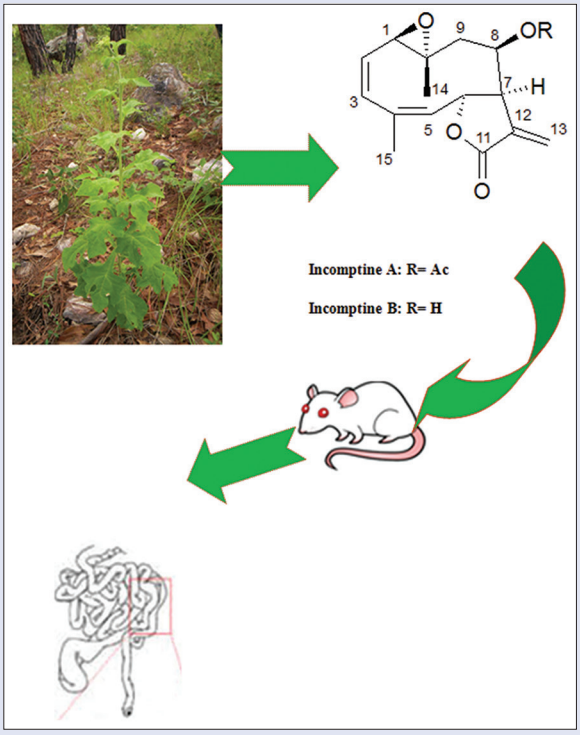
**Background:** *Decachaeta incompta* (DC) King and Robinson (*Asteraceae*) is a plant used in Mexico especially in rural communities in the State of Oaxaca by traditional medicine practitioners to treat diarrhea. However, scientific evidence does not exist in any literature on antipropulsive activity of *D. incompta* and its sesquiterpene lactones that explain in part the traditional use of this plant. **Objectives:** The present study was undertaken to evaluate a possible antipropulsive activity of the dichloromethane crude extract and two sesquiterpene lactones from *Decachaeta incompta*. **Materials and Methods:** Charcoal-gum acacia, lactose and castor oil-induced hyperperistalsis assays were used to assess the antipropulsive activity of the crude extract from *D. incompta* and its sesquiterpene lactones, incomptines A and B. **Results:** The antipropulsive activity of *D. incompta* was investigated by studying the effect of the aerial parts dichloromethane extract and incomptines in three models of induced hyperperistalsis in rats. Dichloromethane extract showed significant inhibition of charcoal-gum acacia and castor oil-induced hyperperistalsis with values of $ID_{50}$ 31.70 and 27.31 mg/kg, respectively. Incomptine A, showed significant inhibition of charcoal-gum acacia, lactose and castor oil induced hyperperistalsis with values of $ID_{50}$ 21.10, 14.20 and 16.20 mmol/kg, respectively. In contrast, incomptine B showed inhibition of charcoal-gum acacia and lactose-induced hyperperistalsis with values of $ID_{50}$ 11.90 and 9.60 mmol/kg, respectively. **Conclusion:** The results indicate that dichloromethane extract of *D. incompta* and its sesquiterpene lactones have antipropulsive activity. Furthermore, these results give additional support to the reports of the traditional use of *D. incompta* for the treatment of diarrhea.

**Key words:** Antipropulsive activity, *Decachaeta incompta,* Diarrhea, incomptine A, sesquiterpene lactones

## SUMMARY

- *Decachaeta incompta* is a plant used in the State of Oaxaca, Mexico by traditional medicine practitioners to treat diarrhea. However, scientific evidence does not exist in any literature on antipropulsive activity of *D. incompta* and its sesquiterpene lactones that explain in part the traditional use of this plant. Charcoal-gum acacia, lactose and castor oil-induced hyperperistalsis assays were used to assess the antipropulsive activity of the crude extract from *D. incompta* and its sesquiterpene lactones, incomptines A and B. Dichloromethane extract showed significant inhibition of charcoal-gum acacia and castor oil-induced. Incomptine A, showed significant inhibition of charcoal-gum acacia, lactose and castor oil induced hyperperistalsis. In contrast, incomptine B showed inhibition of charcoal-gum acacia and lactose induced hyperperistalsis. The results indicate that dichloromethane extract of *D. incompta* and its sesquiterpene lactones have antipropulsive activity. Furthermore, these results support the reports for the traditional use of *D. incompta* for the treatment of diarrhea.

**Abbreviations used:** IMSS: Instituto Mexicano del Seguro Social; $ID_{50}$: 50% inhibitory dose; TLC: Thin layer chromatography; NMR: Nuclear magnetic resonance.

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## INTRODUCTION

Diarrhea is a gastrointestinal disease characterized by an increase in stool frequency and a change in stool consistency. It causes several million of deaths worldwide annually. It remains as one of the major health problems to populations in developing countries where there are poor sanitary conditions. It caused around 1.7 billion cases of childhood diarrheal diseases every year. Also, it is the second-leading cause of death in children under 5 years old and responsible for killing nearly 525,000 children every year.[1] In Mexico, (https://pubmed.ncbi.nlm.nih.gov/31314211/) 3.4 per 100 000 people died due to diarrhea in 2016.[2]

Traditional medicine practitioners in the State of Oaxaca, Mexico have been known to treat various human ailments such as diarrhea and stomach ache with several medicinal plants, one of which being *Decachaeta incompta* (DC) King and Robinson.[3,4] The plant belongs to the family, *Asteraceae*, which also includes other *Decachaeta* species such as *Decachaeta thieleana* (Klatt ex Klatt) King and Robinson and *Decachaeta ovatifolia* (DC) King and Robinson. *Decachaeta thieleana*, in specific showed anticancer and anti-inflammatory properties.[5,6] In the case of *D. incompta* showed important antiprotozoal and antibacterial activities.[3,7] The leaves of these species have been shown to contain sesquiterpene lactones and flavonoids.[3-8]

*D. incompta* is an erect herb that can grow 3 m tall at an altitude of 900–2000 m above sea level. The flowers are white or yellow, and its leaves are usually alternate. It is found in the different States of Mexico, such as Oaxaca, Michoacán, Jalisco, Puebla, and Veracruz.[9] In local traditional medicine of Oaxaca, the aerial parts of this species are used for the treatment of diarrhea. Previous chemical studies of this plant led to the isolation of sesquiterpene lactones incomptines A-D.[3,7] Pharmacological investigations revealed that extracts of *D. incompta* and its sesquiterpene lactones have antiamoebic, antigiardial, trypanocidal, phytotoxic, spermatic and antibacterial activity.[3,7,10] However, scientific evidence does not exist in literature on antipropulsive activity. The main aim of the present work was, therefore, to investigate the antipropulsive activity of the aerial parts dichloromethane extract of *D. incompta* and its sesquiterpene lactones incomptines A and B to give additional support to its traditional use for the treatment of diarrhea.

## MATERIALS AND METHODS

### Plant material

*Decachaeta incompta* (DC) King and Robinson (*Asteraceae*) was collected by Dr. Alfredo Ortega in Portillo Nejapa de Madero (16°36'00"N, 95°59'00"O) State of Oaxaca, Mexico. The identification of the plant was done by the MS Abigail Aguilar Contreras taxonomist of the Instituto Mexicano del Seguro Social (IMSS). A voucher specimen (15311) was deposited in the institutional Herbarium IMSSM.

### Preparation of the aerial parts dichloromethane extract of *Decachaeta incompta*

The method previously described by Calzada *et al*.[3] was used. The aerial parts of the plant species were washed with distilled water and dried at 35°C for 4 days. The dried aerial parts were ground to fine powder and a yield of 25 g was obtained. The plant material was extracted by percolation at room temperature with dichloromethane (350 mL). After filtration, the extracts were combined and evaporated *in vacuo* to yield 2.0 g of red residue.

### Isolations of sesquiterpene lactones from *Decachaeta incompta*

Incomptines A and B were isolated from the dichloromethane extract of *D. incompta* according to the method of Calzada *et al*.[3] Briefly, the dichloromethane extract (2 g) was subjected to column chromatography (Silica gel G, 20 g, 70–230 mesh, Merck) using a step gradient of hexane and dichloromethane-MeOH to give incomptine A (100 mg) and incomptine B (550 mg). Both compounds were identified by comparison of the spectroscopic data (nuclear magnetic resonance) and thin layer chromatography. With authentic samples disposable in our laboratory.

### Animals

Male Sprague-Dawley rats (200–250 g) were obtained from the animal house of the IMSS. These studies were conducted with the approval of the Specialty Hospital Bio-Ethical Committee of the National Medical Center "Siglo XXI" from IMSS (Approval No.: R-2016-3601-193). Investigation using experimental animals was conducted in accordance with the official Mexican norm NOM-0062-ZOO-1999 entitled Technical specifications for the production, care and use of laboratory animals.[11] They were fasted overnight, but tap water was available *ad libitum* until the start of the experiments.

### Effect on charcoal-gum acacia-induced hyperperistalsis

The method, described by Calzada *et al*.,[12] was adopted to study the effect of the compounds on hyperperistalsis in rats. The test rats were divided into the control group and test groups containing six animals in each group. Rats were treated orally with pure compounds or extract (0.01, 0.1, 1.0 and 10 or 10, 20, 40 mg/kg in 1 mL of a 2% dimethyl sulfoxide (DMSO) solution in water), or vehicle (1 mL of a 2% DMSO solution in water) or loperamide hydrochloride or atropine sulfate (Sigma) (0.01, 0.1, 1.0 and 10, or 10, 20, 40 and 60 mg/kg in 1 mL of a 2% DMSO solution in water). After 20 min, each of these animals was given 1 mL of the charcoal meal (10% charcoal suspension in 5% aqueous Arabic gum) by the oral route. All animals were sacrificed after 30 min; the stomach and small intestine were removed and extended on a clean glass surface. The distance moved by the charcoal meal from the pylorus was measured and then expressed as a percentage of the distance from the pylorus to the cecum. After, the plot of the percentage of inhibition against concentration was made; the best straight line was determined by regression analysis and the 50% inhibitory dose ($ID_{50}$) values were calculated. The regression coefficient, its level of significance ($p$) and correlation coefficient were calculated.

### Effect on lactose-induced hyperperistalsis

Lactose-induced hyperperistalsis test was executed in the same way as for the charcoal-gum acacia-induced hyperperistalsis; however, in this case, 1 mL of the lactose-methylene blue meal (300 mg of lactose-5 mg of methylene blue in 1 ml of water) was used by the oral route. The distance moved by the lactose-methylene blue meal from the pylorus was measured and then expressed as a percentage of the distance from the pylorus to the caecum.

### Effect on castor oil-induced hyperperistalsis

Castor oil-induced hyperperistalsis assay was executed in the same way as for the charcoal-gum acacia-induced hyperperistalsis; however, in this case, 1 mL of castor oil-charcoal meal (1 mL castor oil-15 mg of charcoal) was used by the oral route. The distance moved by the castor oil-charcoal meal from the pylorus was measured and then expressed as a percentage of the distance from the pylorus to the cecum.

### Statistical analysis

The experiments were performed six times for each concentration. $ID_{50}$ values are mean ± standard error of the mean. $P < 0.05$ (one-way

ANOVA followed by Dunnett's *post hoc* test), GraphPad Prism version 5.03 (GraphPad Software Inc., La Jolla, CA, USA) was used.

## RESULTS AND DISCUSSION

Diarrhea is a common symptom of gastrointestinal disorder; it is characterized by an increase in stool frequency and gut motility. Diarrhea is a common and major public health problem in developing countries and remains a leading cause of morbidity and mortality. Diarrheal disease is the leading cause of childhood death and the second most common cause of death worldwide. Worldwide of diarrhea accounts for an estimated 525,000 deaths each year among children <5 years of age.[1,13] In Mexico, 3.4/100,000 people died due to diarrhea in 2016.[2,14] In this context, herbal treatments in traditional medicine remain as important remedy to treat diarrhea in rural communities of Oaxaca, Mexico.[15,16]

In this study, the dichloromethane extract and incomptines A and B [Figure 1] from *D. incompta* significantly protected rats against induced hyperperistalsis [Table 1]. In specific incomptine A showed important activity on charcoal-gum acacia, lactose and castor oil-induced hyperperistalsis with values of $ID_{50}$ 21.10, 14.20 and 16.20 mmol/kg, respectively. The activity of incomptine A was close to that of the loperamide, but far less than atropine, drugs used as the positive control. In the case of incomptine B exhibited antipropulsive activity in charcoal-gum acacia and lactose-induced hyperperistalsis assays. The extract was active in charcoal-gum acacia and castor oil-induced hyperperistalsis. In this sense, castor oil has laxative and irritant properties, it is hydrolyzed in the upper small intestine to ricinoleic acid which causes irritation and inflammation of the intestinal mucosa, leading to release of prostaglandins and nitric oxide which stimulate the intestinal motility, secretion and diminish the reabsorption of NaCl and water.[17,18] On the other hand, lactose intolerance occurs about 30 min after the consumption of meals caused diarrhea. Furthermore, undigested lactose becomes thick as it through the small intestine and causes an intraluminal osmotic effect resulting in diarrhea.[19] In the case of charcoal-gum acacia meals increase gut motility by the mechanic and osmotic mechanism.[20] *D. incompta* extract and its sesquiterpene lactones inhibited the induced hyperperistalsis in three models. It is probable that their effects may be exerting by the mechanic and osmotic properties as well as inhibitory properties on prostaglandins and nitric oxide effects.

The results of the present study, along with the antiprotozoal and antibacterial properties previously described from dichloromethane extract and incomptines A and B, could suggest that mechanism by which *D. incompta* inhibit diarrhea involves antiamoebic, antigiardial, antibacterial and antipropulsive effects. Furthermore, it justifies the use of decoction of the plant for the treatment of diarrhea in the local traditional medicine of Oaxaca and Michoacan, Mexico.[3,4]

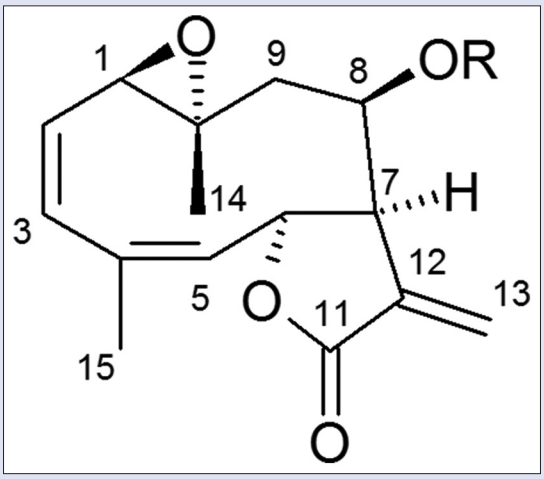


**Figure 1:** Structure of incomptines A and B from *Decachaeta incompta*. Incomptine A: R = Ac, Incomptine B: R = H

**Table 1:** Effect antipropulsive of *Decachaeta incompta* products on charcoal-gum acacia-induced hyperperistalsis, castor oil-induced hyperperistalsis and lactose-induced hyperperistalsis models in rat

| Treatment | $ID_{50}$ mmol/kg±SD[a] | | |
|---|---|---|---|
| | Charcoal-gum acacia | Lactose | Castor oil |
| Extract[b] | 31.7±0.060* | 314.6±0.025* | 27.31±0.040* |
| Incomptine A | 21.10±2.34* | 14.20±1.13* | 16.20±2.65* |
| Incomptine B | 11.90±2.50 | 9.64±2.40 | 79.30±1.23 |
| Loperamide HCl[c] | 1.00±2.44 | 55.94±3.65 | 6.50±3.56 |
| Atropine $H_2SO_4$[c] | 2.01±0.477 | 0.647±2.53 | 1.23±2.35 |

[a]Results are expressed as mean ($n$=6) ± SD, [b]mg/kg, [c]Positive controls, $r^2$>0.9800, *$P$<0.05 vs Positive controls. $ID_{50}$–50% inhibitory dose; SD: Standard deviation

## CONCLUSION

The data obtained indicate that the aerial parts extract of *D. incompta* and its sesquiterpene lactones incomptines A and B have antipropulsive activities that explain in part its use in the traditional medicine of the States of Oaxaca and Michoacan, Mexico. However, further investigation on the acute toxicity and on the mechanism of the Anti-diarrheal effect of the plant species needs to be carried out.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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