Antidiarrhoeic effect of *Eugenia dysenterica* DC (Myrtaceae) leaf essential oil

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Essential oil from *Eugenia dysenterica* leaves was able to inhibit both the diarrhoea and enteropooling induced by castor oil; however, the distance travelled by charcoal meal in the intestine was not change. These data suggest that the antidiarrhoeic effect of the essential oil from *E. dysenterica* leaves is related to its ability to inhibit intestinal secretion and/or to increase intestinal absorption.

**Keywords:** diarrhoea; castor oil; essential oil; *Eugenia dysenterica*

1. Introduction

While *Eugenia dysenterica* (known in Brazil as ‘cagaita’) fruit has traditionally been used as a cathartic agent, the leaves have been used to treat diarrhoeic diseases (Almeida et al. 1998; Acton 2013). For the latter purpose, people usually imbibe decoctions or hydroalcoholic preparations, generally made of plant materials and a distillate beverage (such as brandy produced from cane sugar distillation); such preparations are known in Brazil as ‘garrafadas’ (Camargo 2011; Filho 2011). Preliminary phytochemical analysis of different kinds of ‘garrafadas’ had evidenced the presence of assorted secondary metabolites, including terpenic compounds (Quaresma & Marques 2010).

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The antidiarrhoeic effects of aqueous or hydroalcoholic extracts of *E. dysenterica* leaves have been previously studied (Lima et al. 2011); however, during the preparation of these extracts, their volatile content is presumably lost due to rotary evaporation or lyophilisation processes. Therefore, considering that one of the popular remedies produced from *E. dysenterica* leaves could contain volatile pharmacological principles, in this study we evaluated the effects of *E. dysenterica* leaf essential oil, in addition to the effects of the aqueous extract of the leaf on castor oil-induced diarrhoea.

2. Results and discussion

Castor oil increased both the diarrhoeic and the total number of stools (Supplementary Figure S1 – online only). Loperamide and the essential oil from *E. dysenterica* leaves significantly decreased the diarrhoea induced by castor oil (Supplementary Figure S1 – online only). The intestinal transit of charcoal meal was decreased by loperamide, but not by the essential oil from *E. dysenterica* leaves (Supplementary Figure S2(A) – online only). Castor oil increased intestinal content, and clonidine or the essential oil from *E. dysenterica* leaves inhibited this increase (Supplementary Figure S2(B) – online only). The major components of the essential oil from *E. dysenterica* leaves were *cis*-β-ocimene, (*E*)-caryophyllene, caryophyllene oxide, *a*-humulene, linalool and *trans*-β-ocimene (Supplementary Table S1 – online only).

Pancreatic lipases release ricinoleic acid from castor oil, which appears to induce intestinal anion secretion and intestinal fluid accumulation (enteropooling) (Iwao and Terada 1962, Racusen and Binder 1979). Therefore, inhibition of enteropooling processes represents a potential target for antidiarrhoeic compounds, and the essential oil from *E. dysenterica* leaves was able to decrease the enteropooling produced by castor oil administration, similarly to that observed with the standard treatment with clonidine (Musch et al. 2009). This observation strongly suggests that the antidiarrhoeic effect of the essential oil from *E. dysenterica* leaves is related to its ability to inhibit intestinal secretion and/or to increase intestinal absorption. Ricinoleic acid appears to be an agonist of the EP3 subtype of the prostanoid receptors, which increase intestinal motility under activation (Tunaru et al. 2012). In our study, loperamide (a classical antidiarrhoeic agent) decreased both the intestinal motility and castor oil-induced diarrhoea, which pointed out the importance of hypermotility in this model. However, the essential oil from *E. dysenterica* leaves did not alter the distance travelled by charcoal meal in the intestine, suggesting that inhibition of gastrointestinal motility is not involved in its antidiarrhoeic effect.

The major constituents of essential oil from *E. dysenterica* leaves observed in our investigation were *cis*-β-ocimene, (*E*)-caryophyllene, caryophyllene oxide, *a*-humulene, linalool and *trans*-β-ocimene. In general, these data are in agreement with previous reports (Costa et al. 2000; Duarte et al. 2009), the main differences being concerned with the high levels of *cis*-β-ocimene and caryophyllene oxide in our samples, which may be related to many factors, such as seasonality (Duarte et al. 2009). To date, only caryophyllene isomers, their oxidised product and *α*-humulene were properly pharmacologically characterised in the gastrointestinal tract. Despite the fact that (*E*)-caryophyllene, but not its oxide or *α*-humulene, has been shown to bind to the CB2 subtype of the cannabinoid receptors (Gertsch et al. 2008), (*E*)-caryophyllene is unlikely to be involved in the antidiarrhoeic effect of *E. dysenterica* leaf essential oil, at least through CB2 activation. Two pieces of evidence support this suggestion: (1) the CB2 receptor is weakly expressed or even absent on the enterocyte (Wright et al. 2008), but the essential oil altered the enterocyte physiology, as suggested by its effect on enteropooling; (2) CB2 activation decreases intestinal motility in some conditions, but the essential oil did not decrease intestinal transit. However, further
studies are necessary to clarify the molecular mechanism of the antidiarrhoeic effect of E. dysenterica leaf essential oil.

We have recently reported that the aqueous extract of E. dysenterica leaves possesses condensed tannins among other polyphenolic compounds (Prado et al. 2014); however, these water-soluble substances appear to have little or no contribution to the antidiarrhoeic effect of E. dysenterica leaves. Indeed, like that described by Lima et al. (2011) concerning the effects of aqueous extract of E. dysenterica leaves on rats, we did not observe any effect of this extract in castor oil-induced diarrhoea in mice (data not shown). Therefore, our study strongly suggests that the antidiarrhoeic effect of E. dysenterica leaves is related to their volatile components.

3. Conclusion
The essential oil from E. dysenterica leaves possesses an antidiarrhoeic effect that appears to be linked to its ability to alter the intestinal secretion and/or absorption processes.

Supplementary material
Experimental details to this paper are available online alongside Figures S1 and S2 and Table S1. http://dx.doi.org/10.1080/14786419.2015.1043633

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