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• **Research Article**

Protective effect of ginger volatile oil against acetic acid–induced colitis in rats: a light microscopic evaluation

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OBJECTIVE: Ulcerative colitis is a chronically recurrent inflammatory bowel disease of unknown origin. In the present study, the effect of ginger (rhizome of *Zingiber officinale* Roscoe) volatile oil on a rat model of colitis was evaluated.

METHODS: Volatile oil of ginger with doses of 100, 200, and 400 mg/kg, prednisolone (4 mg/kg), or vehicle were administered orally to groups of male Wistar rats (n = 6) for 5 d. Animals were randomly divided into 6 groups, each group consisting of 6 rats. Colitis was induced by intracolonic instillation of 2 mL of 4% (v/v) acetic acid solution. All rats were sacrificed 24 h later and the tissue injuries were assessed macroscopically and histopathologically.

RESULTS: Ginger volatile oil with all doses reduced colon weight/length ratio ($P < 0.01$) and the effects were similar to the reference drugs. Higher oral doses of volatile oil (200 and 400 mg/kg) reduced ulcer severity ($P < 0.05$ and $P < 0.01$), ulcer area ($P < 0.01$) and ulcer index ($P < 0.01$). On the other hand, evaluation of microscopic scores showed that the dose of 400 mg/kg of volatile oil was effective to reduce inflammation severity ($P < 0.01$) and inflammation extent ($P < 0.05$) compared to the control group.

CONCLUSION: It is concluded that ginger volatile oil could effectively reduce symptoms of experimental colitis in a dose-dependent manner.

KEYWORDS: ginger; *Zingiber officinale*; oils, volatile; acetic acid; colitis; rats

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1 Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory condition affecting the gastrointestinal tract. It is divided into two major categories: ulcerative colitis and Crohn's disease. Ulcerative colitis is a disease of the colon mainly while Crohn's disease is a condition affecting all parts of

gastrointestinal tract. The cause of inflammatory bowel disease is unknown but several factors have been implicated. These include environmental factors, genetic factors, microbial pathogens, defects in immunoregulation and altered levels of inflammatory mediators[1-3]. Inflammatory mediators such as cytokines, eicosanoids and reactive oxygen metabolites play a crucial role in the development and persistence of the disease[4-6].

Glucocorticoids and aminosalicylates have been used for the treatment of IBD, but the side effects remain a major clinical problem. Various experimental colitis models have been established to screen drug effectivity against IBD and acetic acid-induced colitis. This research includes any animal model which mimics some of the acute inflammatory responses in ulcerative colitis[7-9].

Dietary supplements containing botanical products are used by the public for a wide range of health-related problems, including chronic inflammatory diseases such as chronic obstructive pulmonary disease, asthma and rheumatoid arthritis. A number of these botanical supplements have been used for centuries in Ayurvedic medicine, and it has been proposed that they have anti-inflammatory actions. Ginger, powdered rhizome of the herb *Zingiber officinale*, is widely used as a spice throughout the world. In Ayurvedic medicine, ginger has traditionally been used in the treatment for rheumatism, nervous disease, gingivitis, toothache, asthma, stroke, constipation and diabetes[10].

Ginger extract has been reported to have anti-inflammatory[11] and antioxidant effects[12,13]. Volatile oil of ginger has the capability to modulate the function of lymphocytes and cellular immune response. These results suggest that the volatile oil of ginger influences both cell-mediated immune response and nonspecific proliferation of T lymphocytes, and may exert beneficial effects in a number of clinical conditions such as chronic inflammation and autoimmune diseases[14]. In the present study, the effects of ginger (rhizome of *Zingiber officinale* Roscoe) volatile oil on a rat model of colitis was evaluated.

2 Materials and methods

2.1 Animals

Male Wistar rats (180-200 g) were obtained from the Animal Center, Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran. A 12-h light, 12-h dark cycle was maintained. The animals, being kept under standard conditions, had access to a standard diet and clean drinking water.

2.2 Preparation and the main components of ginger volatile oil

Dried rhizome of ginger was provided by the Herbarium Center of Goldaru Co. Ltd., Isfahan, Iran. The essential oil was isolated by hydrodistillation of the air-dried powdered rhizome of the plant for 3 h according to the method recommended in the *European Pharmacopoeia* (2002)[15]. Tween-80 solution (1%) in distilled water was used to solubilize the volatile oil of ginger as a suspension before being used.

2.3 Analysis of the essential oil

The essential oil was analyzed by gas chromatography-mass spectrometry (GC/MS) on a Hewlett Packard 6890 MS selective detector coupled with Hewlett Packard 6890 gas chromatograph equipped with a crosslinked 5% phenyl-methy siloxane, HP-5MS capillary column (30 m × 0.25 mm; film thickness 0.25 μm) operated under the following conditions: carrier gas, helium with a flow rate of 2 mL/min; column temperature, 60-275 ℃ at 4 ℃/min; injector and detector temperature, 280 ℃; volume injected, 0.1 μL of the oil; split ratio, 1:50. The MS operating parameters were as follows: ionization potential 70 eV, ionization current 2 A, ion source temperature 200 ℃, resolution 1 000.

Identification of oil components was based on computer matching with the Wiley 275 L. library as well as comparison of the fragmentation patterns of mass spectra with those reported in the literature[16-18]. The relative percentage of the oil constituents was calculated from the peak areas.

2.4 Chemicals

Prednisolone powder and hydrocortisone acetate enema were procured from Iran Hormone Pharmaceutical Co. (Tehran, Iran) and Valeant Pharmaceutical Co. (Saint-Laurent, Canada), respectively. All of organic solvents were of analytical grade and provided by Merck (Germany).

2.5 Animal grouping

Six groups of rats (n=6) were included in the study. Normal control group received the drug delivery vehicle (normal saline 2 mL/kg, orally) without induction of colitis. Rats in model control group received the vehicle (normal saline 2 mL/kg, orally) and were subjected to the colitis induction procedure. Volatile oil treatment groups received low, medium or high doses of volatile oil (100, 200, and 400 mg/kg) orally in a volume of 1 mL for 5 consecutive days before ulcer induction. Prednisolone group received prednisolone (4 mg/kg, orally) for 5 consecutive days before ulcer induction.

2.6 Experimental protocol

The test samples including solutions or suspensions of drugs or plant extract were freshly prepared. The plant extraction was prepared as 1% (v/v) Tween-80 in suspension form. Acute colitis was induced by acetic acid using a technique introduced by Mascolo *et al*[19]. Briefly, rats were fasted for 36 h with access to water *ad libitum* and observed to ensure their health before induction of colitis. The rats were lightly anesthetized with ether. A flexible plastic catheter with an outside diameter of 2 mm was inserted 8 cm into the colon via the anus. Diluted 4% acetic acid (2 mL) was injected into the colon and the rats were maintained in a