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Evaluation of Anti-ulcer Activity of *Echinops Persicus* on Experimental Gastric Ulcer Models in Rats

Ali Asadi Rad [1*]
Hossein Najafzadeh-Varzi [2]
Ahmad Farajzadeh-Sheikh [3]

[1]*Educated from Faculty of Veterinary Medicine, Shahid Chamran University, Ahvaz, Iran*
[2]*Department of Pharmacology, Faculty of Veterinary Medicine, Shahid Chamran University, Ahvaz, Iran*
[3]*Department of Medical Microbiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*

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Abstract

Extract of *Echinops persicus* is traditionally used for a long time in Iran for treatment of cough and constipation. This extract is produced by activity of bug (*Situphilus* spp.) on the plant. We documented its anti-tussive effect in rats in our previous study.
The aim of this study was to assess the anti-ulcer effect of *Echinops persicus* in an animal model. In this study we evaluated anti-ulcer effect of *Echinops persicus* by Shay's method in rats. In 3 groups of rats, pylorus was ligatured under anesthesia. The rats were euthanized after 19 hours later and number and level of ulcer in stomach was measured. In group 2 the extract was orally administered 45 minutes before pyloric ligature, and in group 3, it was administered intraperitoneally 20 minutes before pyloric ligature. The number of ulcers in stomach was significantly low in group 2 ($P = 0.01$) and 3 ($P = 0.037$) in comparison with group 1. The level of ulcer was significantly decreased in group 2 ($P = 0.047$) with comparison to group 1. We conclude that, *Echinops* extract can exhibit potentially cytoprotective and anti-ulcer activity.
Key words: *Echinops persicus,* Anti- ulcer, Pyloric ligature, *Helicobacter pylori*

[*]**Corresponding author:**
Ali Asadi Rad, DVM
Educated from Faculty of Veterinary Medicine, Shahid Chamran University, Ahvaz, Iran
E-mail address: ali.asadirad@gmail.com

Introduction

Peptic ulcer is one of the major gastro-intestinal disorders occurring due to an imbalance between offensive and defensive factors. Major offensive factors are acid, pepsin, *Helicobacter pylori (H. pylori)* and bile salts. The defensive factors mainly involve mucus-bicarbonate secretion and prostaglandins,[1] so the reduction of gastric acid production as well as reinforcement of gastric mucosal protection have been the major approaches for therapy of peptic ulcer disease. Nowadays it is accepted that *H. pylori* plays an important role in the peptic ulcers.[2] In addition, stress, diet, smoking, drinking and other factors can cause ulcers by triggering excess acid secretion in the stomach. This evidence has led to the use of drugs to suppress stomach acid secretion in the treatment of peptic ulcer.

These drugs have been tremendously successful. The H2 blockers and anti-acids are used to treat up to 90 % of all ulcers and are the top-selling drugs in the USA. Yet these drugs are not very effective. The relapse rate for ulcers with H2 blockers and antacids is about 50 % over 6 months and as high as 95 % over 2 years.[3-5]

Therefore, there is a need for more effective, less toxic anti-ulcer agents. In recent years, a widespread search has been launched to identify new anti-ulcer drugs from natural sources.[6] Medicinal herbs are considered as potential bioactive agents that can interfere positively or negatively with different cellular processes. They have antioxidant, antispasmodic, carminative, anti-inflammatory and other property.[6]

Treating illnesses with plants dates back to thousands years ago. One of these popular medicinal plants is is *Echinops* spp. The history of *Echinops* displays that it has been used since 6000 BC in Iran. Its scientific name is *Echinops persicus*.

This plant have been growth in Europe and Western Asia especially in Iran and can growth in dry and poor soil .Situphilus is a bug that made sugary latex of *Echinops* while reproduction activity and we use of this latex. This latex made of 24 % terehalose, 13 % cellulose, tannin, fat, 5.7 % albominoide and 18 % starch.[7, 8]

The *Echinops* has been used in ancient world for anti tussive, laxative effect and anti-fever. We couldn't find predictable text for anti-ulcer effect and start this experiment. In this study we use of latex of this plant as anti peptic ulcer agent and done this experiment on the rats.

Materials and Methods

Plant material and preparation of extract. Latex of *Echinops persicus* were purchased from local herb shops in Ahvaz and identified by an expert taxonomist. The latex was ground to very fine powder and made suspension with water and then made the watery extract of *Echinops persicus*.

Dose selection and route of administration. The doses (500 mg kg^{-1}, body weight) selected for the experiments were based on the maximum tolerable dose value and the preliminary experiments conducted on the pharmacological activity of *Echinops*.[9]

This dose was administered intraperitoneally and orally through gastric intubation.

Animals in experiment. Wister albino rats of female sex, approximately at the same age, weighing 200-250 g were obtained from Animal Care Center, College of Veterinary Medicine (Shahid Chamran University Ahvaz, Iran). The Animals were kept under standard conditions of temperature, humidity and light (12 h dark, 12 h light) with free access to food and water. Before testing, the animals were fasted for 48 h, only with access to water.

The animals were divided in three groups of 5. In group 1 (control group) we ligatured pylorus without administration any extract. In group 2 extract with a dose 500 mg kg^{-1}, body weight was orally

administered 45 minutes before pyloric ligature, and in group 3, it was intraperitoneally administered 20 minutes before pyloric ligature with same dose.

In all groups, pylorus was ligatured under general anesthesia.

Pylorus-ligature rats. Ulcer study was performed by pyloric ligation process in rats as described by Shay *et al*.[10] The rats were fasted for 48 h with access to water before the pylorus was ligatured under anesthesia and care was taken to avoid bleeding and occlusion of blood vessels. Under ketamine anesthesia, the abdomen was opened by midline incision below the xiphoid process. The pyloric portion of the stomach was slightly lifted out and ligatured, avoiding damage to its blood bringing. The stomach was located cautiously in its position, and the abdominal muscular and skin layers were closed with sutures. Animals were euthanized 19 h after pylorus ligation (thiopental sodium 50 mg kg^{-1} i.p.). The stomach was detached and opened along the greater curvature and then washed with normal saline (0.9 % w/v of NaCl). The number of ulcer and level of ulcer in stomach was measured. Mean of number and area of ulcer in each group was compared with others, by usage of SPSS software and analysis with ANOVA and with help of LSD test. All tests were two tailed. *P* values of less than 0.05 were regarded as significant.

Results

The number of ulcer in stomach was significantly decreased in group 2 (P = 0.01) and in group 3 (P = 0.037) in comparison with group 1 (Fig. 1). The level of ulcer was significantly decreased in group 2 (Fig. 2), in contrast to group 1 (P = 0.047).

Oral administration of *Echinops* extract at dose 500 mg kg^{-1} and intraperitoneally administration with same dose significantly inhibited the development of gastric lesions in all experiments. The extract also caused significantly decreased of the pyloric-ligation induced basal gastric mucosal injury.

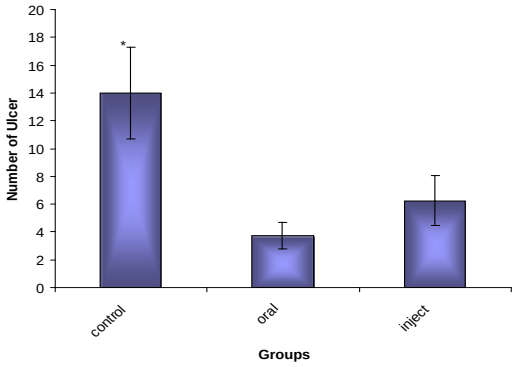

Fig 1. Number of ulcer in each group

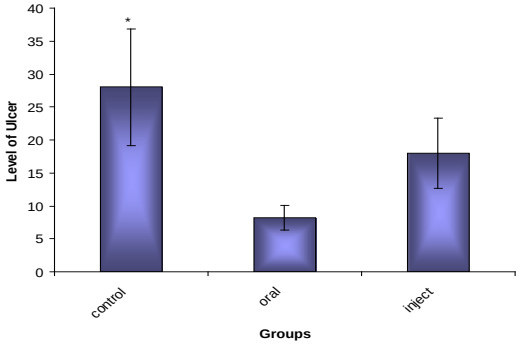

Fig 2. Level of ulcer in each group

Discussion

This study provided a substantial evidence for anti-ulcer and anti-secretary property of an aqueous suspension of *Echinops* extract.

It is still controversial relationship between the acid output and the genesis of acute gastric mucosal lesions (AGML). Our results support this relationship as *Echinops* extract significantly reduced basal gastric secretion and prevented the occurrence of AGML in pylorus-ligatured rats and thus, supporting the hypothesis of "no acid no ulcer".[11] It has been postulated that histamine may be involved in the formation of pylorus-ligature ulcers and play a mediating role in the gastric

secretion stimulated by gastrin, vagal stimulation, and cholinergic agents.[12] It is probably that our extract inhibits histamine secretion and other factors that induce the gastric ulcer in rat. Gastric wall mucus is thought to play an important role as a defensive factor against gastric mucosal damage.[13-14] *Echinops* extract may strengthen gastric mucosa defense mechanisms in experimented rats**.**

The chemical constituents of *Echinops* responsible for its anti-ulcer activity are not known.[8] However, chemical studies demonstrated that *Echinops* contains of 24 % of terehalose, 13 % cellulose, tannin, fat, albominoide 5.7 % and starch 18 %, among others as the major compounds. *Echinops* and its compounds may be having scavenging activity for free radicals or active oxygen which are capable of causing the injury in mucosal stomach.[8, 9]

We conclude that, *Echinops* extract exhibits potentially cytoprotective and anti-ulcer activity through at least one or more possible mechanisms including inhibition of basal gastric secretion, and possible antioxidative activity.

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