

• Research Article

Effects of rhubarb (*Rheum ribes* L.) syrup on dysenteric diarrhea in children: a randomized, double-blind, placebo-controlled trial

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ABSTRACT

BACKGROUND: *Rheum ribes* L. is a plant native to China, Iran, Turkey, India, and a few other countries. Antidiarrheal activity is considered to be one of its important properties according to various systems of traditional medicine. An increasing rate of bacterial resistance to antibiotics has led to treatment failure in some cases of shigellosis in children, and underlines a need for safe, efficient and valid options.

OBJECTIVE: The purpose of this study is to evaluate the efficacy of *R. ribes* syrup as a complementary medicine for treatment of shigellosis in children.

DESIGN, SETTING, PARTICIPANTS AND INTERVENTIONS: This randomized, double-blind, placebo-controlled trial started with a group of 150 children aged between 12–72 months with suspected *Shigella* dysentery. *R. ribes* syrup or placebo syrup was administered to the intervention and control groups, respectively for 5 days. In addition, the standard antibiotic treatment (ceftriaxone for the first 3 days and cefixime syrup for 2 further days) was administered to both groups.

MAIN OUTCOME MEASURES: Body temperature, abdominal pain, need for antipyretics, defecation frequency, stool volume and consistency and microscopic stool examination were recorded as outcome measures. Any observed adverse effects were also recorded.

RESULTS: Mean duration of fever and diarrhea in the *R. ribes* group was significantly lower than that in the placebo group ($P = 0.016$ and 0.001 , respectively). In addition, patients in the *R. ribes* group showed shorter duration of need for antipyretics and shorter duration of abdominal pain ($P = 0.012$ and 0.001 , respectively). However, there were no significant differences between the two groups regarding the microscopic stool analyses. Furthermore, no adverse effect was reported.

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CONCLUSION: *R. ribes* syrup can be recommended as a complementary treatment for children with *Shigella* dysentery.

TRIAL REGISTRATION: Iranian Registry of Clinical Trial: IRCT2014070518356N1.

Keywords: traditional Persian medicine; herbal medicine; *Rheum ribes* L; rhubarb; dysentery; shigellosis; diarrhea

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1 Introduction

The mortality rate of shigellosis dysentery is still high, especially in children of developing countries.^[1] The main treatment is rehydration and administration of antibiotics, but the increasing rate of bacterial resistance to antibiotics has led to treatment failure in some cases. Thus, other safe, efficient and valid treatment options are required for management of shigellosis in children.^[2]

The plant kingdom is a valuable source for different antimicrobial agents. This is because of secondary metabolites and other chemicals which are produced by plant for defense against microbial attack.^[3]

Rheum ribes L. (Polygonaceae) is a plant native to Western Asia and is grown in Turkey, Iran, India, China and a few other countries.^[4,5] In addition to medicinal applications, it is usually considered as an edible fruit and used for making jam or syrup by locals.^[6,7] *R. ribes* is a popular herb in different traditional medicine systems and its documentation dates back to *Sen Nung Pents'ao Jing* (22–250 A.D.).^[8] In these systems, *R. ribes* is employed for treating a variety of symptoms and diseases, such as emesis, diabetes, hypertension, obesity, and various psychological disorders.^[9,10] Moreover, one of its important uses in different nations' traditional medicines is antidiarrheal activity. It is also used for gastrointestinal hemorrhages.^[11,12]

In Iran, *R. ribes* is called *Rivas*.^[4] According to traditional Persian medicine, this plant is useful for both fever and dysentery.^[13–15] Avicenna (980–1037 A.D.),^[16] in his famous book, *Canon of Medicine*, explained about *R. ribes*: Temperament of *Rivas* is cold and dry; it is refrigerant and acts as an antipyretic agent ... *Rivas* is beneficial in bilious and bloody diarrhea (*Eshal e Damavy*).^[13] Its fruit was also mentioned as an astringent medicine and recommended for treatment of diarrhea by famous Persian physicians, such as *Aghili Shirazi* (1670–1747 A.D.) in *The Storehouse of Medicaments*.^[14,17–19]

It is noticeable that different parts of *R. ribes*, such as root and stem, have shown a significant antioxidant activity in previous research.^[20,21] *R. ribes* is a rich source of different vitamins such as A, B, C and E.

It also possesses several minerals and trace elements including calcium, phosphorus, iron, potassium, sodium, magnesium, zinc, copper and selenium.^[22] Previous investigations had shown that the aerial parts of this medicinal plant comprise a variety of active ingredients, such as chrysophanol, physcion, emodin, quercetin, 5-desoxyquercetin, quercetin 3-*O*-rhamnoside and quercetin 3-*O*-rutinoside.^[23] According to previous studies, *R. ribes* root extract has a significant activity against several Gram-positive and -negative bacteria.^[3,24] Also, its stalk and leaves' significant activity against *Shigella spp.* has been documented.^[5]

To the best of our knowledge, there have been no clinical studies on the efficacy and safety of *R. ribes* in children with shigellosis. Therefore, this study was designed to evaluate the effects of *R. ribes* on duration of fever, diarrhea and abdominal pain in children with shigellosis dysentery. Additionally, we aimed to assess its efficacy on microscopic examination of their stool, stool's consistency and volume, frequency of defecation as well as need for antipyretics. A safety assessment was also done simultaneously with the evaluation of its efficacy.

2 Materials and methods

2.1 Trial design

This study was a randomized, double-blind, placebo-controlled and parallel-group clinical trial.

2.2 Study setting

This study was conducted in the inpatient ward of Ardakan Ziaei Hospital, Yazd, Yazd Province, Iran, from August 2014 to January 2016. The study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences (Code: 17/1/65410). It was registered in the Iranian Registry of Clinical Trials with the registration number of IRCT2014070518356N1. A signed informed consent form was obtained from the parents of each child before enrollment.

2.3 Inclusion and exclusion criteria

Only children aged 12 to 72 months fulfilling the following criteria were enrolled in the study: (1) suffering from diarrhea (loose stool more than 3 times per day) for

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