

Efficacy of hydroalcoholic extract of *Rheum ribes* L. in treatment of Obsessive compulsive disorder: A double blind clinical trial

¹Mehdi Sayyah*, ¹Hatam Boostani, ²Alireza Malayeri , ³Amir Siahpoosh

¹Psychiatrist, Joondi shapoor University of Medical Sciences, Ahwaz, Iran

²Pharmacist, Joondi shapoor University of Medical Sciences, Ahwaz, Iran

³Faculty member of herbal medicine research center, Joondi shapoor university of Medical Sciences, Ahwaz, Iran

ABSTRACT:

Traditionally *Rheum ribes* L. has been used in Iran as sedative and mood enhancer. This study investigated the efficacy and safety of a hydroalcoholic extract of *R. ribes* in treatment of Obsessive Compulsive disorder. Fifty six patients were randomly assigned to receive either fluoxetine (20 mg per day) plus *Rheum ribes* hydroalcoholic extract (1200 mg/day) or fluoxetine (20 mg per day) plus placebo in an 8-week, double blind and parallel-group trial. Patients were assessed before the study and during days 0, 14, 28, 42 and 56 by the Yale-Brown scale and a score sheet on adverse effects. In days 14 and 28, the extract showed a significant superiority over placebo in reducing Obsession and compulsions symptoms. There was no significant difference between the two groups in terms of adverse effects. *Rheum ribes* hydroalcoholic extract has some anti Obsession and Compulsion effects. However, further studies are needed to confirm these findings.

Key words: *Rheum ribes*, Obsessive Compulsive, clinical trial.

INTRODUCTION

Rheum ribes belongs to Polygonaceae family (Zargari, 1997). It grows in Iran and Turkey (Tuzlac, 1991). *R.ribes* L. (Polygonaceae) is a hardy perennial, cultivated in some temperate countries for its edible red leaf stalks (Zargari,1997 and Dehkardy, 2002). Its Persian name is “Rivas” (Zargari, 1997). Stem leaf and stem form of flowers of this plant are edible raw and cooked (Sharifi, 2005 and Bowen, 1995). Traditional herbal medicine stem and root dry plant for the treatment of anemia, anorexia, weakness, anxiety, depression and diabetes (Moemen , 1967). These plant vitamins A, B, C are seen in abundance (Heshmat, 2008). Content of this plant is: Chrysophanol, Physcion, Rhein, Aloe-emodin, Physcion- 8-O-glucoside, Aloe-emodin-8-O-glucoside, Sennoside A and Rhaponticin, Flavonoids (Zargari, 1997 and Octay, 2007). In first clinical trial, Sayyah *et al* reported that

R. Ribes had good effect for treatment of Major depressive disorder (Sayyah, 2009).

Obsessive Compulsive Disorder (OCD) is a heterogeneous disorder of unknown etiology, characterized by the presence of upsetting, persistent worries, images or impulses, which are experienced as intrusive and senseless (obsessions) and/or excessive repetitive behaviors (compulsions) performed in response to these obsessions, or according to rigid rules (American Psychiatric Association, 2000).

The problems in the treatment of psychiatric diseases in developing countries, price is high and complications of this medicine (Sayyah, 2006). In recent years, interest in complementary and alternative medicine has grown rapidly in the world of medicine (Sayyah, 2010). Some of the reasons for this increased interest is related to dissatisfaction with conventional allopathic therapies, desire of patients to be involved more actively in their own health care, and also due to the fact that patients find these alternatives to be more

*Corresponding author: Mehdi Sayyah, Imam General Hospital, Azadegan Avenue, Ahwaz, Iran. Tel.: +98-611-2222114; fax: +98-611-3367571 E-mail: sayah_bargard@Hotmail.com.

congruent with their own philosophical orientations (Astin, 1998 and Boon, 2000). The Center for Diseases Control and Prevention has recently published data indicating that 62% of the adult population in the United States has used complementary and alternative medicine within the preceding 12 months, and almost

19% have used an herbal remedy (Barnes, 2002). Considering the fact that *R. ribes* has anti anxiety effect (Moemen, 1967 and Sayyah, 2009) and increase interest to herbal medicine, we decided to review the effect of *R. ribes* on OCD treatment.

MATERIALS AND METHODS

Trial design

The study was a prospective, double-blind, eight-week trial. Two parallel groups of outpatients with OCD in Imam Khomeini Hospital of Ahwaz, Iran participated in the study from September 2009 to March of 2010.

Participants

Eligible participants in the study were 56 patients with OCD with age ranging from 19 to 51 years. All participants were outpatients met DSM-IV-TR criteria for OCD. All patients had normal complete blood counts, hepatic and renal panels and negative toxicological screens. The minimum score 21 or above in the Yale-Brown scale (Y-BOCS) for OCD (Goodman, 1986) was required for entry into the study. The patients did not receive any medicine from two months prior to entering the trial or MAO-inhibitors at least 8 weeks before the study. Patients were excluded from the study if they had a clinically significant organic and neurological disorder, current abuse or dependence on drugs within 6 months, psychotic disorders, and suicide idea. Pregnant or lactating women and those of reproductive age without adequate contraception were also excluded. The trial was performed in accordance with the Declaration of Helsinki and subsequent revisions (World Medical Association, 2000) and approved by ethics committee at Joondi Shapoor University of Medical Sciences. Written informed consents were obtained before entering into the study.

Preparation of medication

The fresh stalks of the plant were collected from Shahrood (Semnan Province, Iran) in June 2008. The plant was identified by the Herbarium of Ferdowsi University; Mashhad, Iran and voucher specimens were deposited. Different parts of plant were cleaned from debris, air-dried and finally grounded to a coarse powder. Stalks were cleaned from debris, washed and

then cut into small pieces before drying. Powdered plant materials (50 g) were extracted with methanol (300 ml) by the aid of a Soxhlet apparatus for 12 h. After filtration, the solvent was removed under reduced pressure using a Rotavapor - RE to give a concentrated extract and the residue was refrigerated until use. In order to preserve the double blind condition, *R. ribes* extract and placebo were dispensed in capsules of identical appearance. *R. ribes* capsules were filled with 400 mg of the extract and talcum powder while placebo capsules were only filled with talcum powder.

Procedures

After obtaining written informed consents from the patients or guardians, participants entered either of the parallel groups using a computer-generated list of random numbers. Patients were randomly assigned to be treated either with Extract of *R. ribes* (1200 mg daily) plus fluoxetine (20 mg) or placebo plus fluoxetine (20 mg), all patients received one oral capsule 3 times a day [one capsule morning (8–9 a.m.) and afternoon (13–14 p.m.) and one capsule nights (22–23 p.m.)] plus fluoxetine (20 mg/day) or placebo. No other psychotropic medication was administered. Participants did not receive any concomitant psychological therapy or support. The participants in this study had not been using any psychiatric medication or therapy from six weeks prior to the beginning of the study. The patients were examined by doctors before the trial and during days 14, 28, 42 and 56. Effectiveness of the treatment was assessed using Y-BOCS. Treatment-induced adverse effects were assessed systematically at each visit by a score sheet designed specifically for the study. The patients were assured that in the case of any severe and uncontrollable side effects, they could withdraw from the study and be treated for the side effects and their OCD will also be treated using standard procedures. The researchers had also agreed upon giving oxazepam 5 mg during the study in the case of experiencing insomnia by the patients.

Statistical analysis

A two-way repeated measures analysis of variance (time–treatment interaction) was used. The two groups as a between subjects factor (group) and the eight weekly measurements during treatment as the within-subjects factor (time) were considered. This was done for Y-BOCS total scores. In addition, a one-way repeated measures analysis of variance with a two-tailed post hoc Tukey mean comparison test was performed in the change from baseline for Y-BOCS scores in each group. To compare the two groups at baseline and the outcome of two groups at the end of

RESULTS

Demographic characteristics and attrition

Fifty six patients enrolled in the study; 29 were assigned to the R.ribes group and 27 to the placebo group. The characteristics of the two study groups are summarized in Table 1. The two groups were well matched and there were no statistically significant differences between the groups regarding demographic factors. The treatment attrition did not differ between the two groups. Two patients used oxazepam 5 mg for one week for treatment of insomnia (one patient in both of the groups).

Table 1- Demographic data of the participants

Characteristic	Fluoxetine+ Placebo Group(27)	Fluoxetine+ R.ribes Group(29)	P
Sex	Female: 15	Female: 16	Ns
	Male: 12	Male: 13	
Marital status	Married: 16	Married: 15	Ns
	Single: 11	Single: 14	
Age (Years)	Mean (SD) 29±2.15	Mean (SD) 28±5.46	Ns

Efficacy: fluoxetine plus R.ribes versus fluoxetine plus placebo

As shown in Fig. 1, the mean Y-BOCS scores gradually declined in the both study groups during the trial. ANOVA revealed significant effect of time (F=35.65, p<0.01). The effect of treatment was

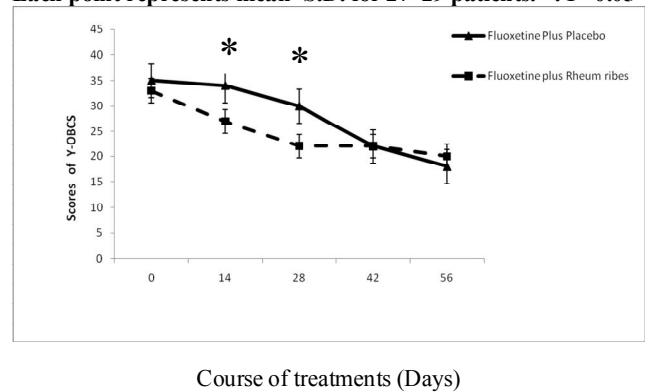
the trial, an unpaired Student's t-test with a two-sided P value was used. Results are presented as mean±SEM and differences were considered significant with P of 0.05 or higher. To compare the demographic data and frequency of side effects between the protocols, Fisher's exact test (two sided) was performed.

Side effects

Side effects were systematically recorded throughout the study and were assessed using a checklist administered by the psychiatrist of the study on days 0, 14, 28, 42, and 56.

significant (F=3.15, p=0.035). Time-by-treatment interaction was significant (F=4.1, p=0.003). The difference between the two treatments was significant after 14 days (t=1.45, P=0.036) and 28 days (t=1.01, P=0.000).

Fig. 1. Effect of R.ribes plus fluoxetine on score of Y-BOCS. Each point represents mean±S.D. for 27–29 patients. *: P<0.05



Clinical complications and side effects

Side effects were observed over the trial. The difference in the frequency of side effects between the fluoxetine plus R.ribes and fluoxetine plus placebo was not significant (see Table 2). Two patient withdrawn from study (two patients from each groups) (P=0.31).

Retention in treatment

52 patients completed the 8-week trial, while 2 patients discontinued treatment for consent withdrawal. The treatment retention did not differ between the 2 groups in Demographic (P=0.31).

Table 2- Reported adverse effects

Side effect	Fluoxetine +Placebo Group(27)	Fluoxetine+ R.ribes Group(29)	P
Somnolence	1	1	Ns
Headache	1	2	Ns
Blurred vision	2	3	Ns
Constipation	2	2	Ns
Decreased appetite	0	1	Ns
Nausea	1	0	Ns
Tremor	0	1	Ns

DISCUSSION

OCD is ranked among the 10 most disabling medical conditions worldwide (Murray ,1996),since obsessions and compulsions can cause manifest functional impairments, preventing sufferers from completing household duties, reducing their occupational performance, interfering with their leisure activities, and negatively affecting family, marital and social relationships (Niederauer ,2007 and Gururaj ,2008 and Mancebo ,2009 and Moritz ,2008). Therefore, there is a compelling demand for new types of antidepressants. The present study was aimed at assessing the putative anti compulsive and obsession effect of the extract of *R. ribes L.* The results of this study show that the

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R.ribes has positive effects on obsession and compulsion and it seems that the positive effects start from the second week. In addition, the results did not show any serious side effects. Effects of *R.ribes* are similar to fluoxetine effects on OCD.

The results of this study and previous studies (Sayyah, 2009) showed *R.ribes* is effective on anxiety and depressive disorder, without any serious side effects.

The findings of this study should be considered with caution. The experimental group was small. In addition, the short term of the study (8 weeks) was another disadvantage of the study and it seems that longer periods of treatment and study would result in more reliable data. Use of outpatients, difficulty entering the trial and ease of withdraw from it, were among other limitations of the trial. In the future trial the authors try to eliminate these limitations as using outpatients will be one of these strategies

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