Green plants of Life

Giyahan Sabz Zendegi

گیاهان سبز زندگی

Clinical Trials and Research of Saffron

Effects of Saffron Extract and its Constituents Crocin on Mood

Depression Clinical Trials					
No	**Date**	**Saffron Compared with**	**Duration**	**Selected**	**Tested**
1	2005	Placebo	8 Week		20
2	2006	Placebo	9 Week		20
3	2004	Imipramine	6 Week		15
4	2004	Fluoxetine	6 Week		20
5	2007	Fluoxetine	10 week		20
6	2013	Fluoxetine	6 Week	75	44
7	2016	Citalopram	6 Week	95	66
8	2016	Fluoxetine	6 Week	94	58

Contents

1. Saffron in Phytotherapy: Pharmacology and clinical uses

Wiener Medizinische Wochenschrift (WMW) 2007; 157: 315-319

Mathias Schmidt, Georges Betti & Andreas Hensel

Themenschwerpunkt

Published: July 2007

Wien Med Wochenschr **157,** 315 (2007). https://doi.org/10.1007/s10354-007-0428-4

Summary:

Saffron (stigmates of Crocus sativus L.) has been used for medicinal purposes for millenaries. Throughout history, uses against cancer and depressive mood can regularly be identified. These applications have also been in the focus of modern research. Promising and selective anti-cancer effects have been observed in vitro and in vivo, but not yet in clinical trials. Antidepressant effects were found in vivo and in clinical pilot studies. Saffron extracts thus have the potential to make a major contribution to rational phytotherapy.

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2. Comparison of Crocus sativus L. and imipramine in the treatment of lid to moderate depression: A pilot double-blind randomized trial;

BMC Complementary and Alternative Medicine 2004; 4

Leelavinothan Pari and Muniappan Latha*

- ***Received: 04 June 2004***
- ***Accepted: 02 November 2004***
- ***Published: 02 November 2004***

BMC Complementary and Alternative Medicine ***volume 4, Article number: 16 (2004)***

Abstract:

Background: The aim of the study was to investigate the effect of aqueous extract of Scoparia dulcis on the occurrence of oxidative stress in the brain of rats during diabetes by measuring the
extent of oxidative damage as well as the status of the antioxidant defense system.
Methods: Aqueous extract of Scoparia dulcis plant was administered orally (200 mg/kg body weight) and the effect of extract on blood glucose, plasma insulin and the levels of thiobarbituric
acid reactive substances (TBARS), hydroperoxides, superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione-S-transferase (GST) and reduced glutathione (GSH) were estimated in streptozotocin (STZ) induced diabetic rats. Glibenclamide was used as standard
reference drug.

Results: A significant increase in the activities of plasma insulin, superoxide dismutase, catalase, glutathione peroxidase, glutathione-S-transferase and reduced glutathione was observed in brain
on treatment with 200 mg/kg body weight of Scoparia dulcis plant extract (SPEt) and glibenclamide
for 6 weeks. Both the treated groups showed significant decrease in TBARS and hydroperoxides formation in brain, suggesting its role in protection against lipidperoxidation induced membrane
damage.
Conclusions: Since the study of induction of the antioxidant enzymes is considered to be a reliable
marker for evaluating the antiperoxidative efficacy of the medicinal plant, these findings suggest a
possible antiperoxidative role for Scoparia dulcis plant extract. Hence, in addition to antidiabetic
effect, Scoparia dulcis possess antioxidant potential that may be used for therapeutic purposes

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3. Crocus sativus L. (petal) in the treatment of mild-to-moderate depression: A double-blind, randomized and placebo-controlled trial.

Phytomedicine 2006; 13: 607-611.

EsmailMoshiri, aAfshin Akhondzadeh, BastibAhamad-AliNoorbalac, Amir-HosseinJamshidid, SeyedHesameddin Abbasie, ShahinAkhondzadeh

Phytomedicine - Volume 13, Issues 9–10, 24 November 2006, Pages 607-611

Abstract:

Depression is a major worldwide health problem. Indeed, by 2020, depressive disorders are estimated to represent the second largest disease burden worldwide. Although a variety of pharmaceutical agents are available for the treatment of depression, psychiatrists find that many patients cannot tolerate the side effects, do not respond adequately, or finally lose their response. Our objective was to assess the efficacy of petal of Crocus sativus in the treatment of mild-to-moderate depression in a 6-week double-blind, placebo-controlled and randomized trial. Forty adult outpatients who met the Diagnostic and Statistical Manual of Mental Disorders, fourth edition for major depression based on the structured clinical interview for DSM IV participated in the trial. In this double-blind, placebo-controlled and randomized trial, patients were randomly assigned to receive capsule of petal of C. sativus 30 mg/day (BD) (Group 1) and capsule of placebo (BD) (Group 2) for a 6-week study. At 6 weeks, petal of C.

sativus produced a significantly better outcome on Hamilton Depression Rating Scale than placebo (d.f.=1, F=16.87, p<0.001). There were no significant differences in the two groups in terms of observed side effects. The results of this study indicate the efficacy of petal of C. sativus in the treatment of mild-to-moderate depression. A large-scale trial is justified.

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4. Comparison of petal of Crocus sativus L. and fluoxetine in the treatment of depressed outpatients:

A pilot double-blind randomized trial Progress in Neuro-Psychopharmacy & Biological Psychiatry 2007; 31: 439-442.

AfshinAkhondzadeh BastiaEsmailMoshiribAhamad-AliNoorbalacAmir-HosseinJamshididSeyed HesameddinAbbasieShahinAkhondzadeh

- ***Received 1 September 2006,***
- ***Revised 7 November 2006,***
- ***Accepted 8 November 2006,***
- ***Available online 15 December 2006.***

Abstract:

Depression is one of the most common neuropsychiatric conditions, with a lifetime prevalence approaching 17%. Although a variety of pharmaceutical agents is available for the treatment of depression, psychiatrists find that many patients cannot tolerate the side effects, do not respond adequately, or finally lose their response. On the other hand, many herbs with psychotropic effects have far fewer side effects. They can provide an alternative treatment or be used to enhance the effect of conventional antidepressants. A number of recent preclinical and clinical studies indicate that stigma and petal of Crocus sativus have antidepressant effect. Our objective was to compare the efficacy of petal of C. sativus with fluoxetine in the treatment of depressed outpatients in an 8-week pilot double-blind randomized trial. Forty adult outpatients who met the DSM- IV criteria for major depression based on the structured clinical interview for DSM- IV participated in the trial. Patients have a baseline Hamilton Rating Scale for Depression score of at least 18. In this double-blind and randomized trial, patients were randomly assigned to receive capsule of petal of C. sativus 15 mg bid (morning and evening) (Group 1) and fluoxetine 10 mg bid (morning and evening) (Group 2) for a 8-week study. At the end of trial, petal of C. sativus was found to be effective similar to fluoxetine in the treatment of mild to moderate depression (F = 0.03, d.f. = 1, P = 0.84). In addition, in the both treatments,

the remission rate was 25%. There were no significant differences in the two groups in terms of observed side effects. The present study is supportive of other studies which show antidepressant effect of C. sativus.

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5. Saffron, and anti-depression herb

by Subhuti Dhamandana, Ph.D, Director, Institute for Traditional Medicine, Portland, Oregon.

Online Published

Summary :

SAFFRON AS A MEDICINAL HERB The medicinal properties attributed to saffron are extensive. Topically, it is applied to improve the skin condition overall and specifically to treat acne. Internally, it is used to improve blood circulation, regulate menstruation, treat digestive disturbance, ease cough and asthmatic breathing, reduce fever and inflammation, calm nervousness, and alleviate depression. In Tibet, saffron is often an ingredient in medicinal incenses; it is considered a tonic for the heart and the nervous system. The active ingredients may be of benefit in inhibiting growth of cancer cells (7–10).

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6. A randomized, double-blind, clinical trial comparing the efficacy and safety of Crocus sativus L. with Fluoxetine for improving mild to moderate depression in post percutaneous coronary

intervention patients Journal of Affective Disorders 155 (2014) 216 – 222

NazilaShahmansouria, MehdiFarokhniab ,Seyed-HesammeddinAbbasia, Seyed EbrahimKassaianaAhmad-AliNoorbala TaftibAmirhosseinGougolb HabibehYekehtazb SaeedehForghanid MehranMahmoodi ana SepidehSaroukhania AkramArjmandi-Beglara, ShahinAkhondzadeh

Journal of Affective Disorders

Volume 155, February 2014, Pages 216-222

- *Received 8 September 2013,*
- *Revised 7 November 2013,*
- *Accepted 8 November 2013,*
- *Available online 16 November 2013.*

Abstract:

Objective

A significant correlation exists between coronary artery diseases and depression. The aim of this trial was to compare the efficacy and safety of saffron versus fluoxetine in improving

depressive symptoms of patients who were suffering from depression after performing percutaneous coronary intervention (PCI).

Methods

In this randomized double-blind parallel-group study, 40 patients with a diagnosis of mild to moderate depression who had undergone PCI in the last six months were randomized to receive either fluoexetine (40 mg/day) or saffron (30 mg/day) capsule for six weeks. Participants were evaluated by Hamilton depression rating scale (HDRS) at weeks 3 and 6 and the adverse events were systemically recorded.

Results

By the study endpoint, no significant difference was detected between two groups in reduction of HDRS scores (P=0.62). Remission and response rates were not significantly different as well (P=1.00 and P=0.67; respectively). There was no significant difference between two groups in the frequency of adverse events during this trial.

Limitations

Relatively small sample size and short observational period were the major limitations of this study.

Conclusion

Short-term therapy with saffron capsules showed the same antidepressant efficacy compared with fluoxetine in patients with a prior history of PCI who were suffering from depression.

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7. Saffron treatment of Fluoxetine-induced sexual dysfunction in women: randomized double-blind placebo-controlled

Study Wiley Online Library. Human Psychopharmacology 2013: 28: 54-60

Ladan Kashani, Firoozeh Raisi, Sepideh Saroukhani, Hamid Sohrabi, Amirhossein Modabbernia, Abbas-Ali NasehiAmirhossein Jamshidi, Mandana Ashrafi, Parisa Mansouri, Padideh Ghaeli and Shahin Akhondzadeh

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human psychopharmacology

Hum. Psychopharmacol Clin Exp 2013; 28: 54–60.

Published online 20 December 2012 in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/hup.2282

Objective:

Saffron (Crocus sativus L.) has shown beneficial aphrodisiac effects in some animal and human studies. The aim of the present

study was to assess the safety and efficacy of saffron on selective serotonin reuptake inhibitor-induced sexual dysfunction in women.

Methods:

This was a randomized double-blind placebo-controlled study. Thirty-eight women with major depression who were stabilized on
fluoxetine 40 mg/day for a minimum of 6 weeks and had experienced subjective feeling of sexual dysfunction entered the study. The patients
were randomly assigned to saffron (30 mg/daily) or placebo for 4 weeks. Measurement was performed at baseline, week 2, and week 4 using
the Female Sexual Function Index (FSFI). Side effects were systematically recorded.

Results :

Thirty-four women had at least one post-baseline measurement and completed the study. Two-factor repeated measure analysis of
variance showed significant effect of time treatment interaction [Greenhouse–Geisser's corrected: F(1.580, 50.567) = 5.366, p = 0.012] and
treatment for FSFI total score [F(1, 32) = 4.243, p = 0.048]. At the end of the fourth week, patients in the saffron group had experienced significantly more improvement in total FSFI (p < 0.001), arousal (p = 0.028), lubrication (p = 0.035), and pain (p = 0.016) domains of FSFI but not in
desire (p = 0.196), satisfaction (p = 0.206), and orgasm (p = 0.354) domains. Frequency of side effects was similar between the two groups.

Conclusions It seems saffron may safely and effectively improve some of the fluoxetine-induced sexual problems including arousal,
lubrication, and pain.

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8. Effect of Saffron on Fluoxetine-induced sexual impairment in men: randomized double-blind placebo-controlled trial.

Original Investigation Psychopharmacology DOI 10.10071s00213-012-2729-6

Amirhossein Modabbernia, Hamid Sohrabi, Abbas-Ali Nasehi, Firoozeh Raisi, Sepideh Saroukhani, Amirhossein Jamshidi, Mina Tabrizi, Mandana Ashrafi & Shahin Akhondzadeh

Psychopharmacology **volume 223**, pages381–388 (2012)

- ***Published: 03 May 2012***

Abstract

Rationale:

Saffron (Crocus sativus L.) has shown aphrodisiac effects in some animal and human studies.

Objectives:

To assess the efficacy and tolerability of saffron in fluoxetine-related sexual dysfunction.

Methods:
This was a 4-week randomized double-blind placebo-controlled study. Thirty-six married male patients with major depressive disorder whose depressive symptoms had been stabilized on fluoxetine and had subjective complaints of sexual impairment entered the study. The patients were randomly assigned to saffron (15 mg twice per day) or placebo for 4 weeks. International Index of Erectile Function scale was used to assess sexual function at baseline and weeks 2 and 4.

Results:
Thirty patients finished the study. Baseline characteristics as well as baseline and final depressive symptoms scores were similar between the two groups. Effect of time × treatment interaction on the total score was significant [Greenhouse–Geisser-corrected, F (1.444, 40.434) = 6.154, P = 0.009]. By week 4, saffron resulted in significantly greater improvement in erectile function (P < 0.001) and intercourse satisfaction domains (P = 0.001), and total scores (P < 0.001) than the placebo group. Effect of saffron did not differ significantly from that of placebo in orgasmic function (P = 0.095), overall satisfaction (P = 0.334), and sexual desire (P = 0.517) domains scores. Nine patients (60%) in the saffron group and one patient (7%) in the placebo group achieved normal erectile function (score > 25 on erectile function domain) at the end of the study (P value of Fisher's exact test = 0.005). Frequency of side effects were similar between the two groups.

Conclusions:
Saffron is a tolerable and efficacious treatment for fluoxetine-related erectile dysfunction.

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9. Pharmacology 2014 Crocus sativus L. in the treatment of mild to moderate depression in post percutaneous coronary intervention patients.

- *Published Web*

10. Comparison of Saffron versus Fluoxetine in Treatment of Mild to Moderate Postpartum Depression: A Double-Blind, Randomized Clinical Trial

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Abstract:

Introduction:

Postpartum depression is a common mental health problem that is associated with maternal suffering. The aim of this double-blind clinical trial was to compare safety and efficacy of saffron and fluoxetine in treatment of mild to moderate postpartum depression.

Methods:

This was a 6-week, double-blind, randomized clinical trial. Subjects were women aged 18–45 years with mild to moderate postpartum depression who had Hamilton Depression Rating Scale (HDRS 17-item) score≤18. Eligible participants were randomized to receive either a capsule of saffron (15 mg capsule) or fluoxetine (20 mg capsule) twice daily for 6 weeks. The primary outcome measure was to evaluate efficacy of saffron compared to fluoxetine in improving depressive symptoms (HDRS score).

Results: There was no significant effect for time×treatment interaction on HDRS score [F (4.90, 292.50)=1.04, p=0.37] between the 2 groups. 13 (40.60%) patients in the saffron group experienced complete response (≥50% reduction in HDRS score) compared with 16 (50%) in the fluoxetine group and the difference between the 2 groups was not significant in this regard (p=0.61). Frequency of adverse events was not significantly different between the treatment groups.

Discussion:

The results of this study may suggest that saffron is a safe alternative medication for improving depressive symptoms of postpartum depression. Nevertheless, it should be mentioned that the trial is not well powered and should be considered a preliminary study. Therefore, large clinical trials with longer treatment periods and comparison with placebo group would be appropriate for future studies.

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11. Crocus sativus L. versus Citalopram in the Treatment of Major Depressive Disorder with Anxious Distress: A Double-Blind, Controlled Clinical Trial

Alireza Ghajar , Seyede Morvarid Neishabouri, Nafiseh Velayati , Leila Jahangard, Nasrin Matinnia, Mohammad Haghighi, Ali Ghaleiha, Mohsen Afarideh, Samrand Salimi, Alipasha Meysamie, Shahin Akhondzadeh

Affiliations:

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- ***received 15.06.2016***
- ***revised 19.08.2016***
- ***accepted 19.08.2016***

Abstract:

Introduction Saffron (Crocus sativus L.) has demonstrated antidepressant effects in clinical studies and extensive anxiolytic effects in experimental animal models.

Methods 66 patients with major depressive disorder accompanied by anxious distress were randomly assigned to receive either saffron (30 mg/day) or citalopram (40 mg/day) for 6 weeks. Hamilton Rating Scale for Depression (HAM-D) and Hamilton Rating Scale for Anxiety (HAM-A) were used to assess treatment effect during the trial.

Results:

60 participants finished the study. Patients who received either saffron or citalopram showed significant improvement in scores of the Hamilton Rating Scale for Depression (P-value < 0.001 in both groups) and Hamilton Rating Scale for Anxiety (P-value < 0.001 in both groups). Comparison of score changes between the 2 trial arms showed no significant difference (P-value = 0.984). Frequency of side effects was not significantly different between the 2 groups.
