Supporting Information

The Efficacy of Saffron in the Treatment of Mild to Moderate Depression: A Meta-analysis

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Fig. 1S Risk of bias summary: review of authors’ judgement on each risk of bias item for each included study.
**Fig. 2S** Risk of bias graph: review of authors’ judgement on each risk of bias item, presented as percentages across all included studies.
Table 1S List of excluded studies and reason for exclusion.

<table>
<thead>
<tr>
<th>Primary reason for exclusion</th>
<th>Reference number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-human clinical study using saffron</td>
<td>[1-136]</td>
</tr>
<tr>
<td>Efficacy in depression is not evaluated</td>
<td>[137-149]</td>
</tr>
<tr>
<td>Full text article not available</td>
<td>[150-154]</td>
</tr>
</tbody>
</table>

References for supporting information

7. Aritake K, Masaki M, Shoyama Y, Urade Y. Crocin, a carotenoid pigment of saffron, promotes non-rapid eye movement sleep. FEBS J 2013; 280 (Suppl. 1): 521
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17. Bonsall JL, Turnbull GJ. Extrapolation from safety data to management of poisoning with reference to amitraz (a formamidine pesticide) and xylene. Hum Toxicol 1983; 2: 587–592


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74. Lopresti AL, Drummond PD. Saffron (Crocus sativus) for depression: A systematic review of clinical studies and examination of underlying antidepressant mechanisms of action. Hum Psychopharmacol 2014; 29: 517–527


95. Pourpak Z, Majd A, Sobhani S. Comparison of the allergenicity of Crocus sativus L. Pollen grains in the three ecological zones in Iran. Allergy 2012; 67 (Suppl. 96): 377
109. Schrag JD, O’Grady SM, DeVries AL. Relationship of amino acid composition and molecular weight of antifreeze glycopeptides to non-colligative freezing point depression. BBA 1982; 717: 322–326
111. Shahi T, Assadpour E, Jafari SM. Main chemical compounds and pharmacological activities of stigmas and tepals of ‘red gold’; saffron. Trends Food Sci Technol 2016; 58: 69e78


117. Stevinson C. Potential value of Crocus sativus (saffron) extract for treating depression. Focus Altern Complement Ther 2005; 10: 193


# Table 2S Clinical complications and side effects: saffron versus placebo.

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Saffron group (affected/total number of patients)</th>
<th>Placebo (affected/total number of patients)</th>
<th>P</th>
<th>References</th>
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<tbody>
<tr>
<td>dry mouth</td>
<td>3/28</td>
<td>2/28</td>
<td>1.00</td>
<td>Kashani et al., 2018 [27]</td>
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<td>daytime drowsiness, sedation, oversleeping</td>
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<td>7/74</td>
<td>0.36</td>
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<td>headache</td>
<td>8/66</td>
<td>4/61</td>
<td>0.37</td>
<td>Kashani et al., 2018 [27], Moshiri et al., 2006 [35], Akhondzadeh et al., 2005 [25]</td>
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<td>anxiety, nervousness</td>
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<td>3/33</td>
<td>0.32</td>
<td>Moshiri et al., 2006 [35], Akhondzadeh et al., 2005 [25]</td>
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<tr>
<td>lack of sleep, insomnia</td>
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<td>0/30</td>
<td>1.00</td>
<td>Tabeshpour et al., 2017 [29]</td>
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<tr>
<td>tremor</td>
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<td>heart pounding, palpitation</td>
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<td>0.19</td>
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<td>other gastrointestinal complaints</td>
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<td>3/47</td>
<td>0.49</td>
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Table 3S Clinical complications and side effects: saffron versus SSRIs (fluoxetine, citalopram).

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Saffron group (affected/total number of patients)</th>
<th>Placebo (affected/total number of patients)</th>
<th>P</th>
<th>References</th>
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</tbody>
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