Peer Review File

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Reviewer A

Comment 1: I suggest a close edit of the entire manuscript for language, grammar and style, ideally by a native English speaker.
Reply 1: Manuscript was revised by native English speaker.

Comment 2: In the introduction, it may also be worthwhile to include some comments about herbal therapies, which are gaining popularity amongst the general public (citation: pubmed.ncbi.nlm.nih.gov/9820257). Herbal therapies are also often a fertile ground for new drug candidates and the development of modern medicines, as in the case of St John's wort and curcumin, which has well-demonstrated antidepressant effects (citation: pubmed.ncbi.nlm.nih.gov/28064110 and pubmed.ncbi.nlm.nih.gov/28236605).
Reply 2: As the reviewer suggested, the clinical trials on cognitive function of *Curcuma longa* extract and its constituent, curcumin were incorporated in the test as the therapeutic model by herbal medicines.

Comment 3: Authors should consider presenting the studies reviewed and referenced in a table format for greater readability and clarity. It may be useful to have a summary table for the key experimental/animal studies referenced.
Reply 3: A new Table 3 which summarize papers including in this review was prepared and incorporated in the test.

Comment 4: "It is easily suggested that crocetin derivatives as shown in Fig. 1 affect to LTP strength because sugar residues are important for the activities of natural products such as cardiac steroids (40), ginsenosides (41) and saikosaponins (42) indicating that much sugar moiety in a molecule is stronger than that of smaller molecule" - I have no idea what this means. Please rephrase.
Reply 4: Since the relation was confirmed by the author's investigation (Sugiura M, Shoyama Y, Saito H et al. Crocin (crocetin di-gentiobiose ester) prevents the inhibitory effect of ethanol on long-term potentiation in the dentate gyrus in vivo. J Pharmacol Exp Ther 1994; 271: 703-707.) the sentence was leaved, but the other references (40, 41, 42) were removed.

Comment 5: 'Learning' and 'saffron' are misspelled in Figure 1.
Reply 5: As reviewer commented two words are mistakes. So that figure 2 was changed correctly.

Comment 6: In terms of the safety of saffron use, authors should add that saffron, crocin, safranal and crocetin showed some embryonic malformation in animal's

models at high doses and there are insufficient clinical trials on the safety of saffron use in pregnancy.
Reply 6: As the reviewer suggested a new section “5. Safety of saffron and its constituents” was added. This section summarize the safety of saffron and its constitutes, crocin, safranal, picrocrocin including pregnancy related problems and their side effects.

Comment 7: Scientific names such as "Crocus sativus" should be italicized throughout the manuscript.
Reply 7: All scientific names were changed to italics.

Reviewer B
Comment 1: English is poor.
Reply 1: Manuscript was revised by native English speaker.

Comment 2: Title is not including the concept of author.
Reply 2: Title was changed to “Cognitive functions of saffron and its major constituent crocin, a narrative review”

Comment 3: You should add a new section that the possibility of sleep quality improvement by saffron and crocin for good memory.
Reply 3: As the reviewer suggested a new section “Sleep quality improvement by saffron and crocin for good memory” was inserted.

Comment 4: You should add Perkinson's disease in P5, line67.
Reply 4: Three references related to Perkinson’s disease were added in the text..

Comment 5: P22, reference 19, compounds is misspelled!
Reply 5: ocmpounds was changed to Compounds.