**Reviewer's report**

**Title:** The in vitro antifungal activity of flavonoids against Trichophyton rubrum is due to the inhibition of fatty acid synthase and a reduction in ergosterol content

**Version:** 2  **Date:** 14 January 2013

**Reviewer:** Susana Zacchino

**Reviewer's report:**

**Major Compulsory Revisions**

This revision cannot be published in its present form because some issues are of concern in this paper and must be solved by authors:

1) Authors refer to M38 A CLSI document of 2002. In this document, dermatophytes are not included. If authors take into account M38A2 document (2008), they will realize that the strain of Trichophyton rubrum that they used, appears to be resistant to fluconazole. In fact MIC of fluconazole against MYA3108 strain is 63 µg/mL. However, CLSI M38A2 document recommends that the MIC of fluconazole against a QC strain of Trichophyton rubrum must be between 0.5-4 µg/mL.

2) Authors state that they purchased from SIGMA “natural flavonoids FAS inhibitors”. However, not all these flavonoids were neither FAS inhibitors nor antifungal as they demonstrated in table 2.

3) page 5, within Fungal isolates: Please clarify the voucher number of the clinical isolate of T. rubrum. If it is a clinical isolate, it would not be ATCC.

4) Quercetin should not be considered highly active, because it has a MIC of 125 µg/mL and so, it should be considered inactive. It is known that a pure compound is considered active if it has a MIC not over 20 µg/mL (or lower).

5) An explanation is needed on why 0.5 MIC was used as the sub-inhibitory concentration and not other one.

6) Tables 2-4 must be included within the paper and not as supplementary material.

7) Introduction:

Within Background:

- Lines 3-4: From “Superficial infections" to "also been reported" must be eliminated.

Lines 10 -20: From “Azoles" to "is increasing" must be eliminated because this paragraph refers to antifungals for systemic infections and not superficial ones.

Line 22: Change: “against fungi” to “against dermatophytes”

Page 5: lines 6-7: eliminate the paragraph “More recently” to with “antifungal activity”
Structures of trans-chalcone must be added. Maybe the name should be: non-substituted chalcone.

The conclusion is poor.

Page 11, line 4: eliminate: “Considering the high antifungal activity of quercetin.

Page 11: line 10: You put that quercetin was tested only at MIC and in the abstract it says at MIC and at 0.5 MIC. Clarify.

Page 11: Eliminate lines 14 to 20, from “a branch” to “sterols”. The following phrase: “In fact” … to “yeast” must be shifted to introduction.

Page 12: Lines 5 to 8: From "This difference" to "(data not shown)" must be eliminated because it contains a flaw. If you have a value of MFC, it is fungicide. So, both are fungicidal according to your statement, one more potent than the other.

Revise page 13, from lines 8 to 15.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.