SDI Review Form 1.6

Journal Name:	**British Journal of Medicine and Medical Research**
Manuscript Number:	**2014_BJMMR_13820**
Title of the Manuscript:	**Dose-dependent Modulation of Lipid Parameters and Inflammatory Biomarkers by δ-Tocotrienol in Hypercholesterolemic Subjects**
Type of the Article	**Original Research Article**

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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PART 1: Review Comments

	Reviewer's comment	Author's comment *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Compulsory REVISION comments	This study evaluated the effect of a composition of 90% δ-tocotrienol/10% γ-tocotrienol (DeltaGold) on plasma lipids, inflammatory biomarkers (at transcripcional and protein levels) and some miRNAs related to cardiovascular diseases in a cohort of hypercholesterolemic patients. Effects of these compound on lipid composition have been previously described, therefore the main contribution of this study regards on the evaluation of inflammatory markers and miRNAs. However, I have several concerns about the data presented in the present work: 1.- As mentioned above, authors should focus mainly in results regarding the effects of DeltaGold on inflammation and miRNA. Great part of the work was focused on lipid parameters. 2.- Description of the study group is not clear. Authors described that only patients with total cholesterol > 5.5 mmol/L (line 118) were included, however the mean value of cholesterol levels seems to be lower than 5.5, as observed in figure 3. If only patients with total cholesterol higher than 5.5 mmol/L were included, it is expected a mean value much higher than the minimum 5.5. 3.- In my opinion, data presented in Tables 3, 4 and 5 represent the main results in this work (effects on inflammatory protein levels, mRNA levels and circulating miRNA). However, the results showed in these tables are not supported by statistical analyses. No dispersion values are presented and there are no p-values for statistical tests. 4.- It is not clear when miRNA are significantly modulated by the DeltaGold treatment. In results section it is described that all the miRNAs evaluated were upregulated, then in discussion is described that miRs-29a, miR-20a and miR-206 were up-regulated. Were all studied miRNAs significantly modulated by the treatment? 5.-Authors stated that all miRNAs evaluated were downregulated in hypercholesterolemic population. Is it supported by any statistical analysis? I think the expression level of miRNAs should be compared to a control group to conclude a higher expression in hypercholesterolemics. 6. Results are poorly discussed for the main results presented in the work. Is the upregulation angiogenic factors beneficial or deleterious for	

	hypercholesterolemics? It seem to be that upregulation of angiogenic the factor FGF-b is beneficial, whereas the upregulation of the anti-angiogenic miR20a is also beneficial. Moreover, there is no discussion about potential limitations of the study, as for example the limited sample size. 7.- Was RNA isolated from plasma? There is no description.	
Minor REVISION comments	1.- Figure 1 at introduction is not necessary. 2.- Description of study design is confuse and extensive. Sub-items 2.1, 2.2 and 2.3 are not justified by the information presented in those items. 3.- It is not clear if LDL cholesterol level was determined by laboratory assay or estimated by Friedwald`s formula. 4.- Why microarray is cited at item 2.5? 5. Authors stated that similar symbols at different columns in figures represent that there was no significant difference. It must be revised for fugures 3-5. For example, was there any difference between phase III and phase VI at figure 3? Or between phase V and VI at figure 4? 6.- I think it could be better to merge figures 3, 4, 5, and 6. 7.- No dispersion measures are presented in table 2. 8.- Please, provide a range for the age of participants. 9.- Results section should be simplified. It is not necessary to include texts describing the analyzed parameters or their implication in cardiovascular disease. 10. There is several paragraph including repetitive information along the manuscript, in the introduction, discussion and even the results section.	
Optional/General comments	The manuscript needs important revision in order to achieve a clear and simpler redaction to improve readability. If there any ethical issue, please clarify.	

Reviewer Details:

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