



SDI Review Form 1.6

Journal Name:	<u>British Journal of Medicine and Medical Research</u>
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:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



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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	<ol style="list-style-type: none"> 1. The lipid response for the 250 mg dose shown in figures 3 and 4 seem to be an anomaly since the decreases don't appear to be dose dependent. The explanation for this unusual finding is that tocotrienols have proteosomal activity at higher doses. However, that would be expected to show a dose-dependent effect instead of the pattern shown in the figures. It would be worth showing a plot of the individual values of LDL at each treatment period to see if this effect was consistent among individuals or due primarily to outliers. Please include a graph of the individual data for LDL during each treatment period. 2. Please comment on the possibility that this unusual response was due to a seasonal effect? Were all subjects studied simultaneously or was enrollment staggered? Please indicate in the methods. 3. Page 12, end of section 3.1 The sentence that indicates that administration of the DeltaGold 	<p>The lipid response for the 250 mg dose is maximum.</p> <p>Actual values (mmol/L) of LDL-cholesterol are reported at the top of Figure 4, including SE values..</p> <p>The study subjects were enrolled simultaneously and lipid lowering effects is not due to seasonal variation.</p> <p>The statement is correct. Tocotrienols are safe for human consumption as per "GRAS" status granted by FDA in 2013</p>



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	<p>tocotrienol supplement was safe for human consumption is based on self-reported assessment of adverse effects. Biochemical assessment of safety would be required to make this statement. Please change this sentence by removing “and safe for human consumption”.</p> <p>4. Tables 3, 4, 5. What dose of the tocotrienol supplement is being reported here? Please indicate the dose in each of the table legends.</p> <p>Also, the raw mean RLU numbers in these tables are not very helpful. Please remove these numbers from each table and report the mean % RLU +/- SD. Also, any statistical differences between treatment periods should be indicated.</p>	<p>Notice no 000471</p> <p>The dose of “250 mg/day” has been added in the titles of tables 3, 4, 5, and also in their legends.</p> <p>Mean RLU +/- SD and statistical analysis has been done and reported in the tables</p>
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<u>Minor</u> REVISION comments		
<u>Optional/General</u> comments	Paper reports on a study that determined the effect of tocotrienol on cardiovascular risk factors. Study used a placebo-controlled ascending dose design in 31 subjects. The results showed the optimal dose associated with reduced LDL, no effect on HDL, downregulation of inflammatory biomarkers and changes in circulating microRNAs that are thought to be of cardiovascular benefit.	