



SDI FINAL EVALUATION FORM 1.1

PART 1:

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

PART 2:

FINAL EVALUATOR'S comments on revised paper (if any)	Authors' response to final evaluator's comments
<p>Optional Comments:</p> <p>1) Lines 134-138 are confusing: would change lines 137-138 to read "...A major factor underlying the failure of OTHER studies to exhibit beneficial effects..."</p> <p>2) Lines 334-336: the data presented are inconsistent with that presented in Figures 3 - 5</p> <p>3) Figure 6: authors have left out the "common symbol" at the top of all bars</p> <p>4) Tables 3 & 5: As all differences are $P < 0.01$, there is no reason to display "$P < 0.05$" at the bottom of the table in the accompanying Legend</p> <p>5) Table 2, Treatment # 4: Do the authors truly have the data to show whether or not the LDL/HDL ratio on treatment was different than baseline ? I question this since their response to my earlier critique of this point has merely been to add "Significant change: to the Table's Legend. What is the P value ? If the data no longer exists to assess this, then say so to the reviewer.</p> <p>6) Line 393: add the words "low dose" before the "gamma and delta tocotrienol"</p> <p>7) There continue to be multiple spelling and spacing errors in the resubmitted manuscript</p> <p>Most importantly, no commentary has been added in the Discussion related to the "Compulsory" revision which I had suggested and feel is necessary with regards to study design and study limitations. I have recopied and printed that immediately below.</p> <p>[The study design is that of a modified Forced Titration with very brief washout periods. The time to development and washout of on target as well as off target drug effects is probably not clearly known. Therefore, this type of study design cannot distinguish response to increased dose from response to increased time on drug or cumulative drug dose effect. This type of study can give a reasonable first approximation of both population average dose response and the distribution of individual dose response relationships. Without a concurrent placebo group, it cannot provide clear evidence of effectiveness. These limitations should be discussed by the authors in their "Discussion" Section.]</p>	<p>These lines have been modified on-Page # 4.</p> <p>Data of all Figures were recalculated and the values are checked and corrected. There were no statistically significant differences among all the groups. Anyway, Table 2 and Figure 6 have been deleted to cut down on the number of Tables and Figures as suggested by one reviewer. $P < 0.05$ deleted in the required Tables.</p> <p>We do have original data of all the Figures and Tables. This Table has been deleted as suggested by other reviewer. It was suggested, the focus should be on cytokines, gene expression and miRNAs rather than on lipid parameters.</p> <p>Added Page # 15. We have tried our best to remove all possible typographical errors and spacing.</p> <p>One paragraph before conclusion section has been added as suggested on Page # 18. The word "preliminary" study has also been added in the Abstract (Page # 2) and also in Discussion section (Page # 18). We hope this will be enough to satisfy the concerns of the reviewer.</p>