Author's response to reviews

Title: Comparative Absorption of Curcumin Formulations

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Our revisions reflect all reviewer’s suggestions and comments. Detailed responses to the reviewer are given below.

Reviewer’s (Dong Liang) report:
Minor comments: (1) it is not clear why ”population pharmacokinetic modeling” was used in this study. What specific results did this modeling provide? (2) The authors may consider add more detailed statistical method description in the Statistical Analysis Section of the Methods, since nonparametric and ANOVA have been described in the Result section under Table 1”

Thank you for your kind suggestions. We have now added more detail to the “Methods - Statistical Analysis” section. The reasons for using population pharmacokinetic modeling are: population pharmacokinetic evaluates the variability among levels including the variability attributed to within-subjects (intra-subject), between subjects (inter-subject), between products (inter-products), and the unexplained variance (error) within the population for which the products are prescribed. The plasma concentrations were auto-correlated within the individual subjects, meaning that a higher extent of bioavailability that one subject showed when taking one product correlated with a higher extent of bioavailability for the other products. The curcuminoid concentrations were also auto-correlated as they are derivatives and a metabolite of curcumin. The only data model that can be used when the data assumption auto-correlation of residuals (independence) is violated is a Linear or Non-Linear Mixed Effects Model which analyzes the data across various levels of subjects, products, curcuminoids, and cross-interactions. The Non-Linear Mixed Effects Model is a population (subject-specific with random effects that can be explained by the subjects) based pharmacokinetic model compared to the population-averaged model which does not analyze the differences of the subjects in levels.