Author's response to reviews

Title: Effects of Acai (Euterpe oleracea Mart.) berry preparation on metabolic parameters in a healthy overweight population: A pilot study

Authors:

Jay K Udani (jay.udani@medicusresearch.com)
Betsy B Singh (betsy.singh@medicusresearch.com)
Vijay J Singh (vijay.singh@medicusresearch.com)
Marilyn L Barrett (marilyn@pharmacognosy.com)

Version: 2 Date: 26 November 2010

Author's response to reviews: see over
Effects of Acai (Euterpe oleracea Mart.) berry preparation on metabolic parameters in a healthy overweight population: A pilot study
Jay K Udani, Betsy B Singh, Vijay J Singh and Marilyn L Barrett

Dear Editors for the Nutrition Journal,
We thank you for the reviewer’s comments on our manuscript. We have responded to each comment below and have made the requested changes in the manuscript. We hope that our revised manuscript is now acceptable for publication in your journal. Thank you for your consideration of our revised manuscript.

Reviewer Susanne U Mertens-Talcot
Request: How much acai did the smoothie pack indeed contain? More specific information regarding study treatment is needed. A polyphenolic profile of the extract needs to be added to this manuscript.

Response: Information on the smoothie pack is provided in the MATERIALS AND METHODS section: Investigational product. Each smoothie pack contained 11% dry acai solids (11g). While the anthrocyanin profile was performed and this information is included in the manuscript, a complete polyphenolic profile has not been performed on this product.

Request: Std error or Std dev need to be added to Figure 1.

Response: Figure 1 has been changed in content according to requests by second reviewer. Please see our response to that reviewer below.

Request: The investigators do not distinguish between CRP and hs-CRP - what was investigated?

Response: hs-CRP was measured as stated in the Methods and Results sections.

Request: P16: “Experiments with mice have found that doses of 3.3 to 16.7 g pulp per body weight, given i.p. once or daily for 14 consecutive days, did not cause any genotoxic effects.[19]” - please insert unit for weight – per what bodyweight?

Response: Thanks. Per Kg body weight. The information has been added.

Request: The change in fasting glucose from 98 to 93 may be significant, yet 1-2 subjects easily could make or break this kind of minimal significant differences – what is the clinical significance of the findings?

Response: The reduction in fasting glucose represents a 5.3% reduction from baseline. This is clinically significant as well as statistically significant (p=0.018). As with any pilot study, a few outliers could potentially skew the data; however the outliers would increase the standard deviation and cause the study to lose statistical power. In this particular study, the change from baseline was statistically significant. This was an uncontrolled pilot study. Clearly additional study is necessary in order to further validate these findings.
Request: What about effects size – specifically in a pilot trial, significance does not always mean clinical relevance. This should be carefully discussed for each assay.

Response: we have added information in the Discussion section in this regard.

Request: As is, some of the conclusions are presented in a somewhat overstated manner – this may certainly mislead lay-readers and half-educated acai-enthusiasts. Adjustments should be made throughout.

Response: Done

Reviewer Diana L McKay

Major Compulsory Revisions:

Request: The expression of the post prandial glucose data in Figure 1, and throughout the manuscript is incorrect. Since data was collected over several time points, it should be expressed as area under the curve (AUC). To determine if the peak glucose concentration, or time to peak, was different after acai consumption, the data should first be expressed as % of baseline glucose levels (adjusted) rather than unadjusted individual points. Also, the statistical comparison between post prandial glucose responses at 0 vs. 30 d should use the AUC and adjusted data. It is essential that the presentation of this outcome parameter be revised. Only then can you determine whether the acai had a potential effect on the post prandial glucose response.

Response: Thank you for your comment. Figure 1 has been changed. The data are now expressed as % of baseline glucose levels. The AUC has been calculated and presented in the Results section.

Request: If collected samples are still available, it would also be of great interest to see if there were any differences in the post prandial insulin response (again expressed as AUC or adjusted for baseline levels) between the 2 standardized meals. Although this additional analysis is optional, it is strongly encouraged to enhance the quality and merit of this manuscript.

Response: Unfortunately the samples are no longer available.

Request: Although the collection of dietary data is mentioned, it does not appear to have been accounted for in the results. How do we know that the effects shown are not due to changes in dietary intake? If subjects’ dietary intake was not assessed at both the beginning and end of the intervention, then these changes could have been due to their background diet, and not to the acai product.

Response: 3-day food recall diaries were recorded at baseline and after 4 weeks. Based on the assessment of macronutrient content (fat, protein, carbohydrates) and total caloric intake, the diet of the subjects did not change over the course of the study. This information has been added to the manuscript.

Request: The methods section should be revised to include adequate detail about each method, and pertinent references, so that the experiment can be reproduced by others.
Response: Information is included in the methods section on the assays used to quantify clinical findings.

Request: References to other studies in the introduction and elsewhere must clearly state whether the significant changes mentioned are compared to baseline values, or a placebo group.

Response: done.

Request: Authors should be clear in all statements that this is an uncontrolled pilot study, and that there are clear limitations to the interpretation of these findings.

Response: done.

Request: Although the changes observed over 30 d are statistically significant, it is unclear whether they are clinically important. Lowering the values from the upper end of the normal range to the mid range is not meaningful.

Response: We have added a reference to an epidemiologic study on the prevention of Diabetes (Tuomilehto et.al., NEJM 2001) that showed that overweight subjects randomized to various lifestyle interventions that caused reductions of less magnitude (fasting glucose reduced by 4mg/dL (3.6%) and reduction in cholesterol of 5mg/dL (2.3%)) which were associated with significant reductions (58%) in the risk of becoming diabetic.

Request: Table 2 is unnecessary, and Figure 1 should be revised.

Response: Table 2 is deleted and Figure 1 is revised.

Request: Overall, the authors have not done an adequate job of justifying the conduct of this study or placing the results in the context of other work in this area of research, i.e., dietary bioactives.

Response: The Results and Discussion sections have been separated and studies on anthocyanins have been added.

Specific comments:

Page 2, last sentence under Methods (in Abstract): Please indicate these measures were assessed acutely following a standardized meal at both baseline and end of the intervention.

Response: phrase added.

Page 2, first sentence under Results: Please change to “Compared to baseline levels, there were reductions... following the 30 d treatment.”

Response: done.

Page 2, sentence 2: Please use the term borderline significant rather than “nearly significant.”
Response: done.

Page 2, sentence 3: Please revise to indicate the change in post prandial glucose was baseline and end of intervention periods.

Response: done.

Page 3, first sentence under Conclusion: Please consider revising as follows – “In this uncontrolled pilot study, consumption of acai pulp reduced levels of selected markers of metabolic disease risk in overweight adults suggesting that further studies are warranted.”

Response: changed.

Page 4, paragraph 2, sentence 3. Please remove the word “natural.” Vitamins C and E are not endogenously produced.

Response: deleted.

Page 5, paragraph 2, sentence 3. Please indicate whether the percentages given are % weight or % of kcal.

Response: by weight, added

Page 5, paragraph 2, sentence 6. Please give some indication why there are apparent discrepancies in the measured anthocyanin contents of acai.

Response: Only one group distinguished the sugar in the glucoside. Total measurements of anthocyanins were per liter for one group and dry weight for the other. Amendments made to the paragraph.

Page 5, paragraph 2, sentence 7. Please indicate the fiber and phytosterol contents as they are the only components mentioned in sentence 1 that lack details in this paragraph.

Response: fiber and phytosterol removed from the first sentence as these constituents are not explored as “active” constituents.

Page 6, paragraph 1, sentence 3. What assay did the authors of ref 11 use to assess antioxidant capacity in vivo? The antioxidant activity of acai differs according to the assay used. Please describe the antioxidant activity of acai assessed in other studies.

Response: paragraph added.

Page 6, paragraph 2, sentence 2. Is 2% acai by wt in diet or is it per kg body wt? At the end of this sentence, indicate whether the change was compared to baseline levels or a placebo group. Same with Sentence 3.

Response: done.
Page 6, paragraph 2, sentence 5. More details about this experiment are required. Subjects? Baseline diet? Placebo-controlled? Time to achieve the reported increase in ORAC?

Response: more information added.

Page 6, paragraph 3, sentence 1. Change “expected to assist...” to “hypothesized.”

Response: done.

Page 6, paragraph 3, sentence 2. How is this proprietary preparation different than other acai products that have already been tested? The ingredient list would be helpful. An analysis of the polyphenols present would also be helpful. Are there any other nutrients present in this prep?

Response: This preparation differs than previously tested products in the manner in which it was sourced, processed, and packaged. Chemically it is not different than other acai preparations.

Page 7, paragraph 2, sentence 5. Please revise this sentence. “This pilot study provides an important indication...” is a conclusive statement, not a hypothesis or study objective.

Response: done.

Page 8, 1st full paragraph. Please justify why you gave overweight subject at risk of metabolic syndrome sugar rather than a non-caloric sweetener.

Response: The study product requires a sweetener for flavor and the sponsor does not have any experience regarding the hedonics (taste/mouth feel/etc) with non-sugar sweeteners. We felt that the use of a non-sugar sweetener would introduce a variable that we could not account for in this small pilot study

Page 8, same paragraph. How do you know if the subjects just took a picture of the same beverage day after day without consuming it?

Response: The pictures were time/date stamped and were different day by day given the background and location of the picture.

Page 9, paragraph 1. Please indicate whether exclusion criteria included the use of any specific medications.

Response: In the Methods section it states that if they “used immunosuppressive drugs” they were excluded and “intake of steroids, anti-inflammatory drugs, multi-vitamins and anti-oxidants were prohibited during the study.”

Page 10, paragraph 1, last sentence. Describe and justify the need for subjects to avoid foods containing nitrates.

Response: Food containing nitrates were excluded from the standardized meal so as not to interfere with the measurement of exhaled (breath) nitric oxide metabolites (eNO).
Page 10, and elsewhere in the Methods section. There needs to be enough detailed information about the specific methods used in this study so that other may reproduce it. Ex., how was eNO measured using the device? Where is the reference for this method?

Response: Further information regarding the eNO measurement has been added, along with a reference.

Page 11, paragraph 1. Why wasn’t postprandial insulin measured along with glucose?

Response: The choice was made to measure postprandial capillary glucose which is considered more accurate in an Oral Glucose Tolerance Test. In addition, obtaining blood samples using finger-pricks is preferable for patient comfort, when compared to serial blood draws. Thus there were no samples that could be used for measuring insulin levels and only postprandial glucose values were available.

Page 12, paragraph 2 and elsewhere. Readers of this journal are well aware of the definition of overweight.

Response: Most definitions have been removed.

Page 12, paragraph 3. Please justify the statement, “It is expected that this nutrients in the pulp were bioavailable.” How does the dose used in this study compare to the dose used in the pharmacokinetic study?

Response: The statement has been removed.

Page 12, paragraph 4. The upper end of the normal range is still normal. How many subjects had levels over 100?

Response: The statement regarding fasting glucose levels has been removed.

Page 13, paragraph 1. Since antioxidant capacity is not measured in this study, you cannot say that the results were attributable to a concomitant increase in this parameter.

Response: The statement has been removed.

Page 13, paragraph 2. The upper end of a normal range is still normal. Are the changes observed clinically relevant?

Response: we have added information in this regard to the Discussion section.

Remainder of manuscript: Unclear where the results end and the discussion begins. Also, need conclusion.

Response: The Results, Discussion sections and Conclusion sections have been separated.