Reviewer's report

Title: Effects of a preparation of Phellodendron and Citrus extracts on the joint and cardiovascular health of osteoarthritis patients: a pilot, double-blind, placebo-controlled study

Version: 1 Date: 4 December 2007

Reviewer: Ezra Bejar

Reviewer's report:

General

1. Is the question posed by the authors new and well defined?
The question is well defined. The findings are also very clear, and NP 06-1 appears to be a promising treatment. A few minor revisions and slight expansion to the discussion and conclusions will truly capture the convincing scientific findings of the researchers.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
Protocol is complete and well defined, however, a few details of the methods for gathering the following data are not described: blood pressure, height, and weight. In addition, the chemistry of the extract is not fully disclosed. While we understand that this is proprietary information, it would be helpful to know the ratio of the 2 plant extracts used.

3. Are the data sound and well controlled?
Should include information on adherence to treatment protocol.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

5. Are the discussion and conclusions well balanced and adequately supported by the data?
The discussion and conclusions are supported by the data, and would be further strengthened with addition of the following:
- Inclusion of normal and osteoarthritic ranges for the LAI
- What the observed changes in LAI scores mean, the validity and reliability of the LAI, and comparison to a positive reference compound, such as naproxen, indomethacin, aspirin, etc.
- A statement addressing the high attrition rate in the normal weight/placebo group
- Proposed reasons to address the following observations:
  + Why a significant weight loss was observed in all groups by time 8
  + What was responsible for the observed changes in lipid profiles
+ Whether diet or activity levels changed during the course of the study.

It would also be helpful to understand adherence to the prescribed treatment dosing & fasting instructions.

6. Do the title and abstract accurately convey what has been found?

As currently written, this article focuses on the cardiovascular health benefits provided by NP 06-1, which appear to be very promising, rather than the positive impact on knee/joint pain flexibility as assessed using the LAI. A discussion on reference score ranges for the LAI, and what the findings in the study reveal according to knee/joint pain flexibility, would really strengthen the osteoarthritic efficacy conclusion for NP 06-1. It would be helpful to know if activity increased over the duration of the study, and whether that may have contributed to the observed weight changes. In addition, safety was identified as a primary point of investigation, and it would be helpful to understand how this was assessed, such as the absence of reports of side effects in subjects receiving active treatment.

7. Is the writing acceptable?

The writing is acceptable, with only a few minor typographical corrections and rewording needed. To reduce the length of the manuscript, and simplify distinctions between the four subject groups, the authors may want to adopt a more descriptive abbreviation for differentiation, such as OA = Overweight/Active Treatment, OP = Overweight Placebo, NA = Normal weight/Active Treatment, NP = Normal Weight Placebo. “Group 1” and “Group 2” are less obvious and the descriptions were subsequently repeated several times throughout the document, which would not be necessary with more descriptive abbreviations. In addition, the statement regarding no BMI changes in any group should be revised to match the results and discussion section on this topic.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

- Brief discussion of safety investigation and outcome measures
- Brief discussion of LAI results and implications, including knee/joint pain & flexibility, whether activity level was impacted, and a summary of treatment impact for the different groups
- Brief discussion addressing observed weight changes, including activity level during the study
- Statistical analysis of attrition rates between different groups, and proposed explanation of any observed differences
- Brief discussion of plant chemistry potentially or likely responsible for observed benefits

Minor Essential Revisions (such as missing labels on figures, or the wrong use of
a term, which the author can be trusted to correct)

- Typographical & grammatical errors (marked up on attached pdf)
- New abbreviations to describe the four groups for clarity and less repetition

Discretionary Revisions (which the author can choose to ignore)

Please provide email to submit pdf attachment separately

**What next?**: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest**: An article of importance in its field

**Quality of written English**: Needs some language corrections before being published

**Statistical review**: Yes, but I do not feel adequately qualified to assess the statistics.