Reviewer's report

Title: A Forced Titration Study of the Antioxidant and Immunomodulatory Effects of Ambrotose AO Supplement

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Reviewer: Kevin Croft

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The manuscript by Myers et.al. describes a forced titration study of an antioxidant supplement. The primary end point is serum ORAC.

The supplement used Ambrotose AO is a complex mixture including vitamin E, quercetin and several plant or fruit extracts. While a potentially interesting and useful study, there are several major limitations.

This study does not have a parallel placebo control group.

Group size is small, particularly when subgroup analysis is carried out (based on gender or smoking status) such that we end up with group sizes ranging from n=3 to n=8. It may also not be valid to remove the male smokers from the data.

The ORAC assay is a rather indirect global ex-vivo assay of total antioxidant capacity. It is best applied to plant extracts etc as a measure of antioxidant capacity. It becomes very difficult to interpret when this assay is applied to biological fluids (see Nature Medicine, 14(8), 795, 2008). The variation in the baseline measures of ORAC done 1 week apart indicate some of this difficulty.

While some of the study limitations are stated by the authors (for example in the abstract conclusions) it remains inconclusive that the supplement led to any significant improvement in antioxidant activity.