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LETTER TO THE EDITOR

Response to Dr Inchiosa

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Our opportunity to respond to the letter by Inchiosa allows us to expand upon and update a number of important points that were not fully addressed in our paper 'Multinutrient supplement containing ephedra and caffeine causes weight loss and improves metabolic risk factors in obese women: a randomized controlled trial'.[1] Inchiosa correctly points out that our study tested the effect of a high-potency mixture of vitamins, minerals, omega-3 fatty acids and botanical extracts including ephedra and caffeine, against a control formula containing 100% of the Daily Value of vitamins and minerals. This is indeed a controlled study design that has been used in numerous other studies assessing ephedra and caffeine, and our title, introduction and conclusions very carefully note the multinutrient formula that was tested, rather than drawing conclusions regarding only the effects of ephedra and caffeine.

We believe that it is unlikely that a *Garcinia cambogia* extract containing (−)-hydroxycitric acid (HCA) could have accounted for approximately 60% of the weight loss noted in our results. While a few studies suggest that HCA can reduce food intake or promote weight loss,[2] a number of other studies have produced negative results.[3–5] One of us (PJH) has recently completed a double-blind, placebo-controlled study in overweight/obese men and women, administering HCA (2700 mg/day) plus chromium polynicotinate (400 μg/day) for 12 weeks. No differences were measured in appetite, energy intake, body weight or body composition (personal communication), suggesting a minimal contribution of HCA, if any, to the body weight and body fat loss reported in the current study.

It is correctly noted that the treatment group had a significantly higher baseline body weight than the control group, although all participants were randomly assigned at the inception of the study in a double-blind manner. We do not think this initial difference accounts for the substantial differences in body weight and body fat loss noted at the end of the study. While differences in the reported daily energy intake at baseline between the two groups are duly noted, one must be skeptical of self-reported diet records, which give at best a rough estimate of a person's true energy intake. Indeed, we note that numerous self reports from our participants showed an unusually low estimation of energy intake (two <2512 kJ/day (<600 kcal/day) and six <4186 kJ/day (<1000 kcal/day)), which raises doubt regarding the accuracy of the baseline energy intake measurements.

The issue of palpitations was considered very carefully by the study physicians and authors. Self-reported symptoms from all participants were noted and graded by one of us (HJS) as mild, moderate or severe. All reports of palpitations were minor, and none of them persisted more than a few days. At no point was any participant removed from the study as a result of these symptoms. Electrocardiograms were obtained regularly on all participants, read (blindly) by one of us (JCR; a board-certified cardiologist) and none of the readings showed any patterns that caused concern. Palpitations are a well-known side effect of ephedra and caffeine, but at the doses used in our study, they seemed to subside and disappear after a brief period. Our observation is consistent with tachyphylaxis of this effect and with other studies on ephedrine/ephedra and caffeine previously published in this journal.[6,7]

Statements about the legal and regulatory status of dietary supplements containing ephedra and caffeine contained in our paper were accurate in March 2006, at the time of its online publication. Subsequent to the online publication, on 17 August 2006, the Tenth US Circuit Court of Appeals upheld the FDA's position that unregulated sale of supplements containing ephedra and caffeine posed a public health risk. Most recently, a petition was filed asking the US Supreme Court to review the Tenth Circuit Court of Appeals ruling on 3 January 2007,[8] thus this is still an evolving issue. Regardless of the next legal decision, it is important to note that the FDA's decision was based on unregulated use that enabled anyone to freely obtain ephedra and caffeine even if its use was contraindicated by existing medical conditions, and to consume these supplements in uncontrolled amounts. A viable alternative to unrestricted use would be the regulated use of ephedra and caffeine by prescription with proper physician monitoring, which in our opinion remains a viable option to debate.

Table 1 Summary of meta-analysis of weight loss drugs

Agent	*Duration (months)*	*Number of studies*	*Mean weight loss (kg) from meta-analysis*	*95% CI range (kg)*
Sibutramine	12	5	−4.45	−3.6 to −5.3
Orlistat	12	22	−2.89	−2.3 to −3.5
Phentermine	6	6	−3.60	−0.6 to −6.0
Bupropion	12	3	−2.77	−1.1 to −4.5

Abbreviation: CI, confidence interval.
Adapted from Li *et al.*[9]

Lastly, we disagree with Inchiosa's assertion that 'it would appear difficult to conclude that this prescription represents a useful option for the treatment of obesity.' Table 1 summarizes a recent meta-analysis of the currently approved medications used for the treatment of obesity and the range of weight loss associated with each.[9] Many of these studies included a low-calorie diet in addition to the medication. In our 9-month study, participants were asked not to alter their normal dietary patterns or to change their physical activity levels. The mean weight loss in the treatment group (7.61 kg; 95% confidence interval: 5.3–9.7 kg) is greater than the means noted for any of the drugs. While it is inappropriate to compare a single study to a larger number of studies investigating the effects of pharmaceutical agents, our results suggest that further studies of dietary supplements containing ephedra and caffeine are warranted. Rather than dismiss a modest level of ephedra and caffeine, combined with vitamins, minerals and omega-3 fatty acids, as not useful for the treatment of obesity, additional studies are needed to determine if such an approach, prescribed and monitored by a physician, can safely and effectively be employed as one aspect of addressing the current obesity epidemic.

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