Arrhythmogenicity of weight-loss supplements marketed on the Internet

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BACKGROUND We examined nonprescription weight-loss supplements marketed on the Internet for ingredients with potential arrhythmogenic and life-threatening cardiac adverse effects.

OBJECTIVE We aimed to define the risks of life-threatening cardiac adverse effects that are associated with weight-loss supplements marketed on the Internet.

METHODS We entered the key words "weight-loss supplements" and "diet pills" into three popular Internet search engines. The top four nonoverlapping hits from each search engine were purchased. After receipt, the products and their ingredient lists were inspected, and Medline and the Natural Medicines Comprehensive Database were searched for reports of significant associations between each ingredient and various key words for life-threatening cardiac adverse effects.

RESULTS All supplements had the list of ingredients on the label. We identified 60 different ingredients (7.25 ± 4.66 per supplement; range 1–21). Eleven ingredients representing eight different substances (because multiple names were used for some substances) were each associated with two or more reports of life-threatening cardiac complications or death. Eight of the 12 products contained one or more such ingredients, but none of these eight products had warnings about life-threatening cardiac adverse effects on the Web pages, on the labels, or in the package inserts. One product contained *ma huang* (Chinese ephedra), even though the marketing of ephedra-containing products is banned in the United States.

CONCLUSIONS The Internet provides easy access to weight-loss supplements, several of which contain ingredients with potentially life-threatening adverse effects. There is a need for increased public education and awareness regarding such weight-loss products.

KEYWORDS Weight loss; Tachyarrhythmias; Cardiac side effects; Supplements; Obesity; Death

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Introduction

Obesity is rapidly becoming a health problem of epidemic proportions. Since the mid-1970s, the prevalence of overweight and obesity has increased sharply in both adults and children. Data from two National Health and Nutrition Examination Surveys show that among adults aged 20–74 the prevalence of obesity increased from 15% in 1976–1980 to 33% in 2003–2004.[1]

Use of over-the-counter weight-loss supplements has become more common in the United States.[2,3] Retail sales of weight-loss supplements were estimated to be more than $1.3 billion in 2001. Possible reasons for the popularity of these supplements include the social stigma of obesity, desire for a "magic bullet" for weight loss, the supplements' rapid availability without prescription or consultation with a health care professional, the perception that "natural equals safe," and inflated advertising claims.[4]

The Internet is a growing resource for finding health information and purchasing health products, including weight-loss supplements.[5] To our knowledge, the U.S. Food and Drug Administration (FDA) does not strictly regulate the sale and marketing of these supplements on the Internet; unlike prescription drugs, dietary supplements are not required to pass safety studies before being sold to consumers, and the companies that make these supplements are not required to obtain FDA approval to sell them. Furthermore, as Jordan et al[6] have shown, Internet Web sites selling weight-loss supplements do not accurately describe (or do not describe at all) the potential health hazards these products may pose.

The cardiovascular adverse effects of various herbal supplements have been reported previously. With this background, we aimed to define the risks of arrhythmogenic and life-threatening cardiac adverse effects that are associated with weight-loss supplements readily found and purchased on the Internet.

Methods

During the winter of 2007, we used three search engines—www.yahoo.com (Yahoo), www.google.com (Google), and

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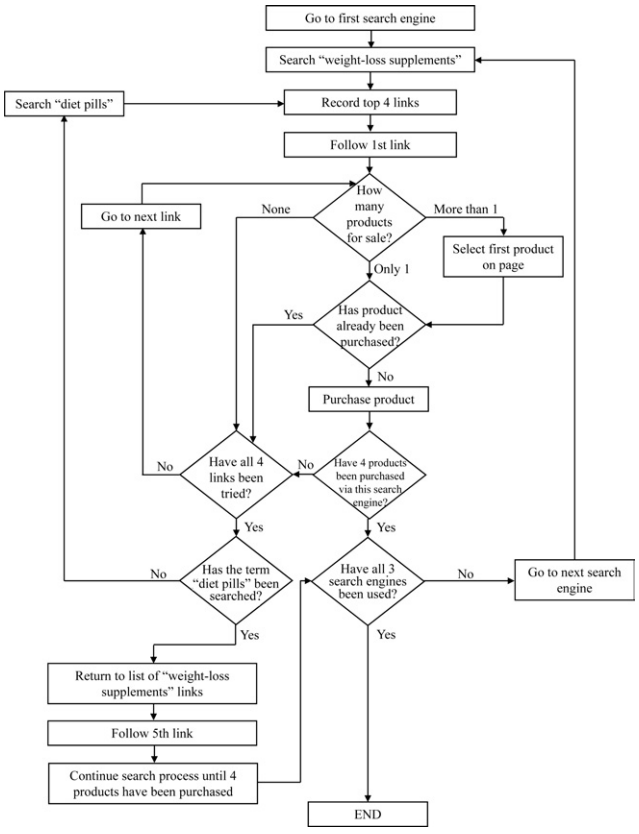

Figure 1 Search method used to identify supplements for purchase.

www.msn.com (MSN)—with the goal of purchasing four nonoverlapping products from each search engine for a total of 12 products. Our search procedure (see Figure 1) was as follows: We first searched the term "weight-loss supplements" on each search engine—Yahoo first, then Google, then MSN. If any search produced overlapping results (i.e., if one or more of the top four hits from a given search engine matched a hit from a previously used search engine), we then searched for the term "diet pills." If there was still overlap, we returned to the list of hits from the "weight-loss supplements" search, starting with the fifth hit and continuing down the list until four products were purchased via that search engine.

The Web pages and all packages and inserts were inspected for warnings about cardiovascular adverse effects. We identified the ingredients exactly as they were listed on the package labels, and we performed a comprehensive search of Medline and of the Natural Medicines Comprehensive Database for any reported association between each ingredient and cardiac arrhythmias or other life-threatening cardiac adverse effects. The key words "cardiac arrhythmias," "ventricular tachycardia," "ventricular fibrillation," "myocardial infarction," "cardiac arrest," and "death" were used in each database search.

Results

Each of the 12 products was purchased online and delivered to us at a designated U.S. address without any restrictions. All products had a list of ingredients on the label. From these lists, we identified 60 different ingredients (7.25 ± 4.66 per supplement; range 1–21) exactly as they were listed on the labels. Of these ingredients, 42 were herbal extracts, five were synthetic compounds, four were minerals, and nine were vitamins or other organic substances. Eleven of the listed ingredients—which corresponded to eight different substances, because some ingredients were listed by various names—were associated with at least one report of life-threatening cardiac events or death; in fact, all eight ingredients were associated with two or more such reports. Eight of the 12 products included at least one of these ingredients. Warnings about potential adverse effects did not appear on any of the Web pages from which we purchased these eight products or on the labels and other materials shipped with these products. One product's list of ingredients included *ma huang* (Chinese ephedra), even though the marketing of ephedra-containing products is banned in the United States.

The other potentially hazardous ingredients were bitter orange (also listed as *Citrus aurantium* and synephrine HCl), green tea (also listed as *Camellia sinensis*), buckwheat, guarana, ginseng (listed as Korean ginseng), licorice root, caffeine anhydrous, and *ma huang* root. Eight of the 12 products contained one or more of these ingredients (see Table 1).

Discussion

In this study, we examined 12 weight-loss supplements and identified eight ingredients with reported life-threatening cardiac adverse effects. We briefly review these ingredients and discuss the risks that they may pose to consumers.

Ma huang, or Chinese ephedra, is also known as ephedra, *Ephedra distachya*, and *Ephedra vulgaris*. Its principal alkaloid constituents are ephedrine and pseudoephedrine, both of which are nonselective α- and β-receptor agonists. Ephedra is taken orally for weight loss and to enhance athletic performance.[7] In 2001, ephedra accounted for less

Table 1 The distribution of ingredients with reported serious cardiac adverse effects among the 12 weight-loss products

Product	Ingredient(s)
1	Bitter orange[a]
2	None
3	Bitter orange,[b] buckwheat
4	Bitter orange,[a] ginseng
5	Bitter orange, green tea, guarana
6	None
7	Caffeine anhydrous, green tea[c]
8	Green tea
9	None
10	None
11	Bitter orange,[b] caffeine anhydrous, green tea, licorice root
12	*Ma huang* root (ephedra)

[a]Labeled "synephrine HCl."
[b]Labeled "*Citrus aurantium*."
[c]Labeled "*Camellia sinensis*."