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Sibutramine identification in weight loss products marketed as natural

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Obesity is a complex and multifactorial disease with a global prevalence that has increased in recent decades. Simultaneously, the media exerts a strong influence by imposing an ideal body standard, which intensifies the search for weight loss methods, often adopted without proper guidance. This study aimed to identify sibutramine in four weight loss products marketed as natural. For this purpose, each sample underwent liquid-liquid extraction with methanol, followed by analysis of the organic extract using gas chromatography-mass spectrometry (GC-MS). Sibutramine was detected in three of the four capsule form weight loss products analyzed. The undeclared presence of sibutramine constitutes adulteration and represents a health risk to consumers, particularly because it is a substance under special regulatory control. The findings reinforce the need for more rigorous and effective regulatory oversight to curb illegal practices in the marketing of weight loss products and protect the health of the population.

Keywords: natural weight loss products; adulteration; sibutramine.

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Introduction

The World Health Organization (WHO) defines obesity as a complex, chronic, and multifactorial disease, characterized by excessive accumulation of body fat. Its occurrence is influenced by genetic, epigenetic, and environmental factors, including inadequate dietary patterns and a sedentary lifestyle (1).
Body mass index (BMI) is the most widely used tool to assess the degree of overweight or obesity, calculated as the ratio between weight (in kilograms) and the square of height (in meters) (Table 1). Additional measures, such as waist circumference, have also been employed to assist in the diagnosis of obesity (1,2).

Table 1. Classification of nutritional status of an adult according to body mass index.

Body Mass Index (BMI)	Classification
< 18,5	Underweight or low weight
≥ 18,5 to 24,9	Normal or eutrophic
≥ 25,0 to 29,9	Overweight or pre-obese
≥ 30,0 to 34,9	Obesity
≥ 35,0 to 39,9	Obesity
≥ 40	Severe obesity

On January 14, 2025, the journal The Lancet Diabetes & Endocrinology published an update on the criteria for evaluation and diagnosis of obesity. Given the limitations of body mass index (BMI), other anthropometric measures were incorporated, such as waist circumference, waist-to-hip ratio, or waist-to-height ratio, as complementary criteria for the diagnosis of obesity (3).
It is estimated that, by 2025, the number of obese individuals will exceed 2.3 billion worldwide. In Brazil, in 2023, the prevalence of overweight was 61.4%, while obesity reached 24.3%, according to data from the Surveillance of Risk and Protective Factors for Chronic Diseases by Telephone Survey (Vigitel)(4).
In a survey conducted by the Brazilian Society of Endocrinology and Metabolism (SBEM) and the Brazilian Association for the Study of Obesity and Metabolic Syndrome (Abeso) on obesity and weight bias, 85.3% of interviewed individuals reported having experienced some form of embarrassment due to excess weight. Additionally, 93.6% of respondents stated they had already attempted to lose weight, with approximately 69% seeking specialized help and 31% trying on their own. Among those who attempted to lose weight without professional guidance, at least 10.3% reported having used medications without a medical prescription (5).
Currently, it is common to observe a relentless struggle with the mirror, a search for the "perfect body," which has been further intensified by the use of social media over the past decade (6). Not only are thin and toned bodies valued, but the image of thinness has also become an ideal associated with health, success, youth, and attractiveness. In this context, the idealized body standard constitutes a risk factor for adopting extreme weight loss measures, such as restrictive diets, medication use, and other methods harmful to health (7).
Although safety is not guaranteed, a significant portion of the population considers the use of "natural weight loss products" an attractive option for weight loss, partly due to their easy accessibility (8). However, inadequate regulatory oversight may lead to adulteration of these

products with anorexigenic substances, antidepressants, and anxiolytics, among others, which represents significant health risks (9, 10).

Sibutramine is the appetite suppressant with the oldest registration still in effect in Brazil, granted by the National Health Surveillance Agency (ANVISA) in 1998 (11, 12).

Sibutramine is an inhibitor of norepinephrine and serotonin reuptake, which promotes satiety by reducing food intake and increasing energy expenditure (13). It is indicated as adjunctive therapy in the treatment of patients with a BMI equal to or greater than 30 kg/m². The treatment must have a maximum duration of two years and must be accompanied by a dietary re-education plan and physical activity compatible with the patient's clinical conditions. The prescription of sibutramine must be made through a type "B2" Prescription Notification, accompanied by the Prescriber's Term of Responsibility (14).

This study aimed to qualitatively identify the presence of sibutramine in weight loss products sold online.

Materials and Methods

Standard and Reagent

Methanol (98.8%, UV/HPLC grade) was purchased from Dinâmica (Indaiatuba, SP, Brazil). The sibutramine standard (sibutramine hydrochloride monohydrate, purity ≥ 98%) was obtained from a compounding pharmacy.

Samples

Four different weight loss products marketed through WhatsApp and Instagram accounts were analyzed, including herbal medicines, a dietary supplement, and a product labeled only as a "dietary regulator." All samples were in capsule form and claimed to be natural products. They were numbered from 1 to 4, as detailed in Table 2.

Table 2. Sample description.

Sample	Identification	Dosage	Composition
1	Dietary supplement	1 capsule daily, after breakfast	Phaseolamin (white kidney bean), morosil, nitric oxide (beetroot), *Crocus sativus*, *Rhodiola rosea*, ashwagandha, horsetail, collagen, L-theanine, cactinea, arginine, glutamine, guar gum, psyllium and spirulina
2	Dietary regulator	1 capsule at 10 a.m.	Caffeine, bamboo shoot, *Garcinia cambogia*, peruvian apple, *Pholia magra*, *Hoodia gordonii*, green coffee and phaseolamin
3	Herbal medicine	1 capsule at 10 a.m.	Flaxseed, artichoke, eggplant, chia, orange, passion fruit, ginger, psyllium, peruvian maca, beetroot, aloe vera, quince, Garcinia and calunga (caralluma)
4	Herbal medicine	1 capsule at 9 a.m.	Seaweed, peruvian maca, garcinia, cascara sagrada, hibiscus, senna, sweet anise, ginger, passion fruit, citrus, flaxseed, artichoke, eggplant, psyllium, mulberry, white tea and safflower

Extraction

For extraction, 0.2 g of each sample was weighed, placed in Falcon tubes, and extracted with 10 mL of methanol under agitation for 1 minute. The samples were then centrifuged at 3,000 rpm for 4 minutes. Aliquots of 10 µL of the supernatant were transferred to glass vials containing 1 mL of HPLC-grade methanol and analyzed by gas chromatography-mass spectrometry (GC-MS). The methodology was adapted from previous studies (8, 10).

Gas Chromatography-Mass Spectrometry (GC-MS)

The obtained extracts were analyzed using an Agilent Technologies GC System 7820A coupled to a 5975 Series MSD mass spectrometer, with an HP-5MS column (30 m × 0.25 mm × 0.25 µm). Helium (He) was used as the carrier gas, with a flow rate of 1 mL·min⁻¹. The injector was set at 250 °C, with an injection volume of 1 µL in splitless mode. The oven temperature program was as follows: 60 °C, maintained for 1 minute, then increased at 50 °C·min⁻¹ to 150 °C, 6 °C·min⁻¹ to 200 °C, and 16 °C·min⁻¹ to 280 °C, which was held for 6 minutes. The mass spectrometer was run in full scan mode, operating over a range of m.z-1 50 to 500.

Results and Discussion

The four weight loss product samples were extracted with methanol and analyzed by GC/MS to investigate potential adulterants. No sibutramine was identified in sample 2, as shown in Figure 1. However, sibutramine was detected in samples 1, 3, and 4. The confirmation of this substance's presence was based on the correspondence between the retention time and the mass spectrum obtained, compared to the analytical standard (Figures 1 and 2). Signals were considered positive when they presented: (i) retention time compatible with the standard; (ii) mass spectrum with similarity equal to or greater than 80% compared to the National Institute of Standards and Technology (NIST) library; and (iii) presence of characteristic ions of sibutramine.

However, it is essential to consider the inherent limitations of GC-MS, particularly regarding the

physicochemical properties of the analytes. For a substance to be analyzed by this technique, it must exhibit volatility and thermal stability, as chromatographic separation occurs in the gas phase and under elevated temperatures. Highly polar or thermolabile compounds require prior chemical derivatization to enable detection. Thus, although GC-MS is a sensitive and selective technique for a wide range of organic compounds, its applicability may be restricted when adulterants do not meet these requirements. In such cases, the use of complementary analytical techniques, such as liquid chromatography coupled to mass spectrometry (LC-MS), is recommended to expand the detection spectrum and ensure a more comprehensive analysis.

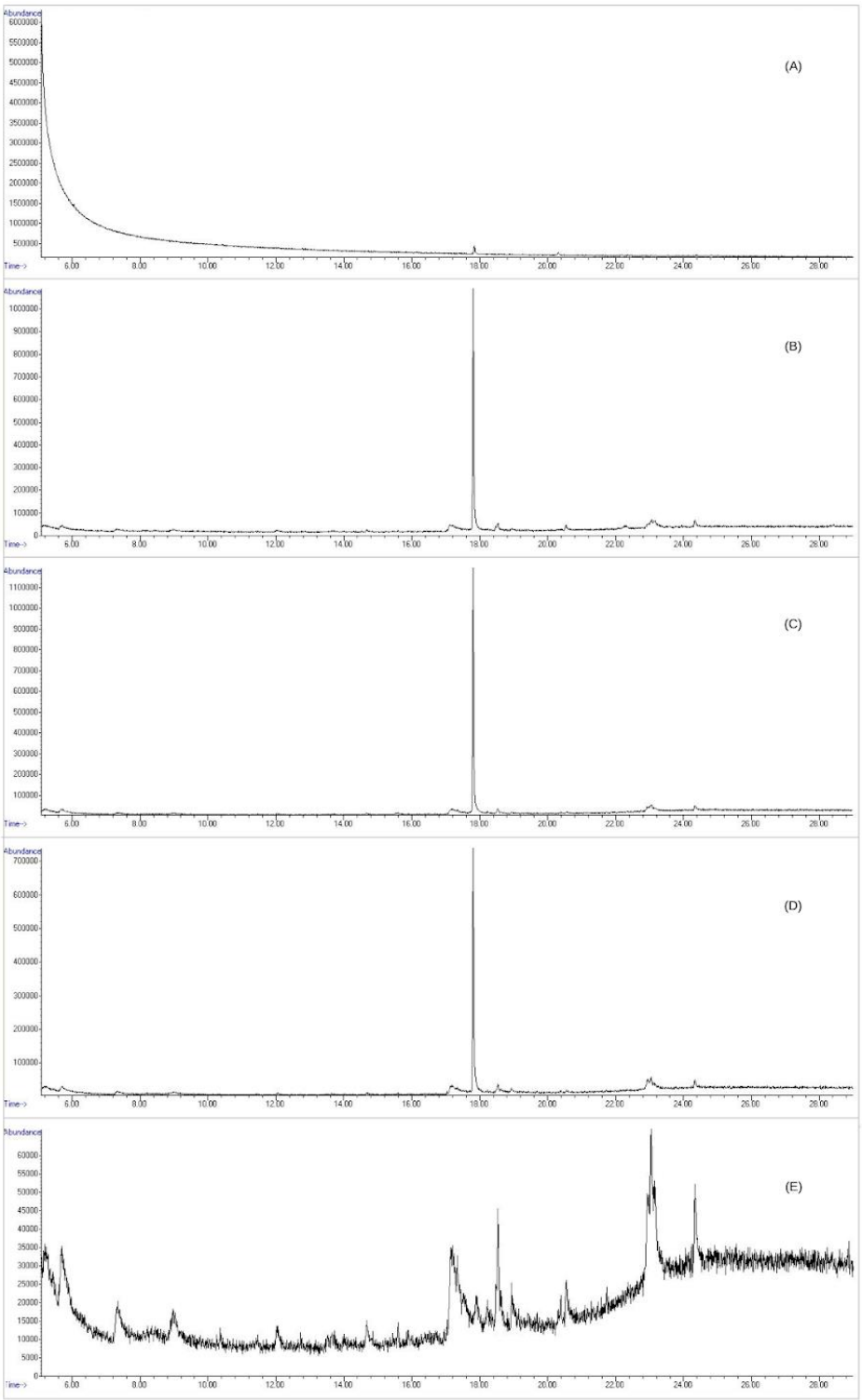

Figure 1 – Comparison between the sibutramine standard chromatogram and the profiles obtained from the samples. (A) Sibutramine standard chromatogram. (B) Chromatographic profile of sample 1. (C) Chromatographic profile of sample 3. (D) Chromatographic profile of sample 4. (E) Chromatographic profile of sample 2.

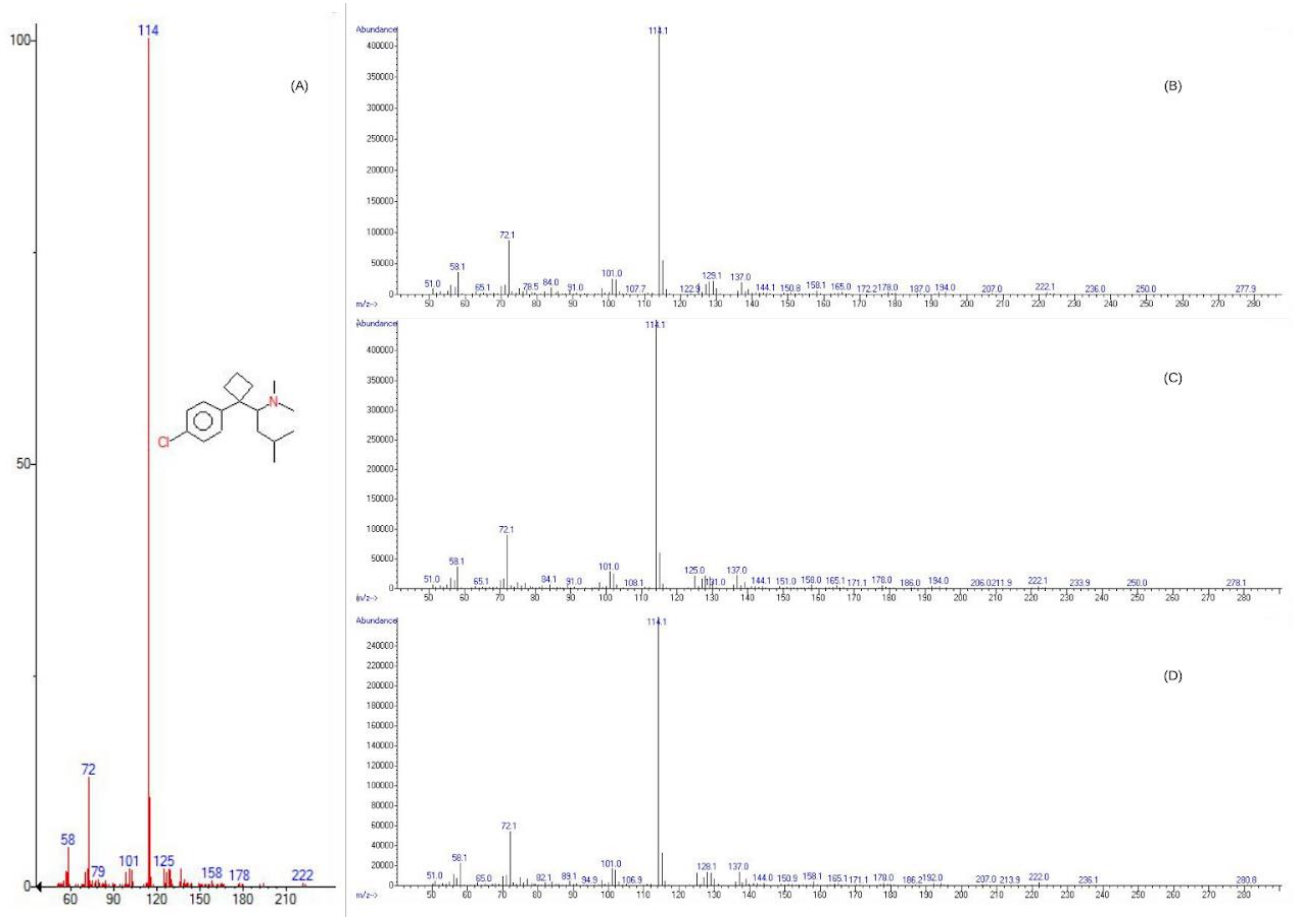

Figure 2. Comparison between the NIST sibutramine mass spectrum and the results obtained from the samples. (A) NIST sibutramine mass spectrum. (B) Mass spectrum of sample 1. (C) Mass spectrum of sample 3. (D) Mass spectrum of sample 4.

The identification of sibutramine in the dietary supplement and herbal medicine samples analyzed in this study reinforces its position as one of the most frequently detected adulterants in weight loss products irregularly marketed, with the aim of enhancing weight loss and reducing costs (15, 16).

The presence of sibutramine in both herbal medicines and dietary supplements is inconsistent with Brazilian legislation. The Board of Directors' Resolution (RDC), 26/2014 defines herbal medicine as a product obtained exclusively from plant raw materials, without the addition of isolated or highly purified active substances—whether synthetic, semi-synthetic, or natural—or combinations with extracts of plant or animal origin (17). Dietary supplements, as established by RDC No. 243/2018, are products intended for oral administration in pharmaceutical forms, aimed at complementing the diet of healthy individuals with nutrients, bioactive substances, enzymes, or probiotics, isolated or combined. Brazilian legislation prohibits the inclusion of substances subject to special control in their composition, as regulated by Ordinance No. 344, of May 12, 1998, which includes sibutramine (18, 19).

The results of the present study corroborate previous research in Brazil that also identified undeclared adulterants in natural weight loss products. A 2012 study reported the presence of synthetic substances in herbal weight loss products seized by the Health Surveillance Management for Medicines and Related Products of the Health Surveillance Service of Minas Gerais (GVMC/SVS-MG). Among the 40 samples analyzed, all contained adulterants, including femproporex, fluoxetine, and chlordiazepoxide (9). More recently, a 2023 study evaluated three different natural weight loss products marketed informally in Foz do Iguaçu (PR) and detected sibutramine as an adulterant in all samples (8).

International studies have similarly reported the illegal addition of synthetic substances in weight loss products. A 2021 study analyzing capsules, tablets, and teas from Canada, the USA, China, Malaysia, India, and the United Arab Emirates, as well as products of unknown origin, found adulteration by sibutramine, fluoxetine, or phenolphthalein in 17.5% of 137 samples; 15.3% contained sibutramine (20). In 2014, eight samples acquired in Iran, originating from China and some Southeast Asian countries, were analyzed; all samples, declared as natural herbal mixtures, contained undeclared components, with six containing sibutramine (21).

ANVISA maintains a list of irregular weight loss products to facilitate identification and control of their marketing (22). The agency also provides a public consultation tool on its portal, allowing access to information on weight

loss and other irregular products (23). However, enforcement actions have proven insufficient: of the four samples analyzed, one was listed by ANVISA as irregular yet remains available online (8).

RDC No. 50/2014, along with subsequent amendments, prohibits prescribing or dispensing sibutramine in doses exceeding 15 mg/day (14). The indiscriminate use of adulterated weight loss products poses serious health risks, particularly due to uncertainty regarding the nature and quantity of pharmacologically active substances. Users of herbal weight loss preparations containing undeclared sibutramine may experience adverse effects ranging from mild headaches to severe cardiovascular disorders, depending on the dose (20). These effects are described in the professional package insert for sibutramine monohydrate hydrochloride, listing very common reactions such as constipation, dry mouth, and insomnia, and common reactions including tachycardia, palpitations, hypertension, vasodilation (hot flashes), nausea, aggravation of hemorrhoids, delirium, dizziness, paresthesia, headache, anxiety, sweating, and taste alterations (24, 25).

Sibutramine use is contraindicated in patients taking other centrally acting medications for weight loss or psychiatric disorders, as well as in those with type 2 diabetes associated with other risk factors, coronary artery disease, and other clinical conditions (14, 25).

The 2010 Sibutramine Cardiovascular Outcomes (SCOUT) study—a randomized, double-blind, placebo-controlled clinical trial conducted from January 2003 to March 2009 in 298 centers across 16 countries with 10,744 participants—demonstrated that individuals with pre-existing cardiovascular disease undergoing prolonged treatment with sibutramine had an increased risk of non-fatal myocardial infarction and non-fatal stroke. Based on these findings, sibutramine remains contraindicated for patients with a history of cardiovascular disease (13).

Following the SCOUT study, the U.S. Food and Drug Administration (FDA), which had approved sibutramine in 1997, withdrew its recommendation for use due to cardiovascular risks, requesting the manufacturer to remove the product from the market (26). In Brazil, however, sibutramine continues to be monitored for its safety profile (14).

Conclusion

The identification of sibutramine in three of the four weight loss products labeled as "natural" by GC-MS highlights a recurring and concerning practice of adulteration. The undeclared presence of a substance subject to special control, associated with various adverse effects and contraindications — especially in individuals with pre-existing cardiovascular pathologies — represents a significant risk to public health, aggravated by the easy access to these products through online platforms.

Conflicts of interest

None to declare.

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