Journal of Nutrition and Health Sciences
Volume 4 | Issue 1
ISSN: 2393-9060

Research Article Open Access

Detection of Illicit Substances in Slimming Products Available in UAE

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Citation: Ebtisam AR Alabdooli, Preetha J Shetty, Victor RM Chandrasekaran, Anoop KA (2017) Detection of Illicit Substances in Slimming Products Available in UAE. J Nutr Health Sci 4(1): 103. doi: 10.15744/2393-9060.4.103

Received Date: December 29, 2016 **Accepted Date:** April 22, 2017 **Published Date:** May 18, 2017

Abstract

Slimming products have gained popularity due to its easy availability and quick source to curb obesity. Studies suggest that they often contain banned compounds which produce adverse effects on repeated use. The objective of the present study was to estimate the concentration of illicit substances, sibutramine and phenolphthalein, in the slimming products of different origin which are commonly marketed in UAE using Gas Chromatography-Mass Spectroscopy (GC-MS).

The study revealed that 60% samples contained sibutramine and /or phenolphthalein. The slimming products from Germany and France contained only phenolphthalein, whereas products from USA, Thailand, Italy and England showed the presence of both and the highest concentrations were found in samples from China (2846±455 µg/g; 27 ± 4.2 ng/g). The slimming products from Iran, Lebanon and Morocco were not only free from these adulterants but also less expensive indicating that the high cost does not guarantee the safety of these products.

Keywords: Slimming products, Sibutramine, Phenolphthalein

Introduction

In seeking easier options for weight control, obese people are increasingly resorting to 'quick-fix' slimming agents available over the counter. These products are often advertised to contain purely natural ingredients, hence assumed to be harmless. However, many such products have been reported to contain various illicit agents, including sibutramine, diethylpropion, phenolphthalein, fenfluramine, N-nitroso-fenfluramine, phentermine phenytoin, and even animal thyroid tissue posing a health risk on prolonged usage [1-6]. One study reported that the presence sibutramine and phenolphthalein resulted in high mortality and morbidity in Hong Kong population [4]. Several products have been withdrawn following detection of these adulterants, but many escape as structural analogues are difficult to detect.

Sibutramine, a 'serotonin-noradrenaline re-uptake inhibitor' gives a satiety feeling after a small meal, reducing their food intake [7,8]. Despite several central and peripheral side effects it is used alongside diet and exercise by obese patients resulting in life threatening complications [9-12]. Phenolphthalein on repeated use damages the intestinal mucosa and liver, causes serious psychiatric problems and also produces carcinogenic effect due to estrogenic and clastogenic properties, hence banned [13-15].

The study intended to estimate the concentration of two banned compounds, phenolphthalein and sibutramine, in slimming products from different countries available locally using Gas chromatography (Thermo Scientific, USA) coupled with mass spectrometry (TRACE DSQ) being one of the sensitive techniques that can detect these compounds even at very low concentrations.

Moreover, it compares the cost and quality of various slimming products based on the presence of adulterants detected in various samples. To the best of our knowledge, this is the first study undertaken in UAE for estimation of adulterants and cost comparison.

Materials and Methods

Sample

Slimming products from 10 different countries (three brands from two different batches) were obtained (n=60) from the local market and analyzed in duplicate using GC-MS. The samples from each country were also classified as herbal (22) and non-herbal

(38) depending on their origin.

Chemicals and reagents

Sibutramine stock (1mg/ml) and phenolphthalein powder (HPLC grade) and Codeine-d3 were purchased from Sigma-Aldrich (St. Louis, MO). N-methyl-N-trimethylsilyl-trifluoroacetamide (MSTFA), trimethylchlorosilane (TMCS) were purchased from Fluka (Buchs, Switzerland).

Sample preparation

Samples (0.3g) were extracted using Toxi tube A & B (Agilent technologies, Santa Clara, CA). 50 µL of internal standard codeine-d3 was added and centrifuged at 3800 rpm for 3 min. The supernatant was transferred to glass tube for drying under nitrogen system. 500 µL of ethyl acetate solvent was added for dilution and 100 µL was mixed with 50 µL of MSTFA in GC/MS vial and 2 µL was used for analysis.

Analytical conditions

Fused silica capillary column (30 m X 0.25 mm; Inner Diameter (ID)) bonded with 0.25 µm Dura Bond 5 – Mass Spectrophotometry (DB5-MS; Agilent technologies, Santa Clara, CA) was used as a stationary phase. The analytical conditions were: sample volume 2 µL; injector temperature 280^0 C; septum purge flow 3 mL/min; Purge flow to split vent 50 mL/min; initial oven temperature 70^{0}C and increased to 280^0 C at a rate of 12^0 C/min held for 11 min. Ionization was achieved by a 70 eV electron beam at a current of 2.0 mA. The concentrations of sibutramine and phenolphthalein in the samples were calculated from the masses and retention time. The correlation coefficient for sibutramine and phenolphthalein are 0.997 (Figure 1a and 1b) and 0.996 (Figure 2a and 2b). All estimated values were presented as mean ± Standard Deviation (SD). The concentration of sibutramine and phenolphthalein was compared between herbal and non-herbal products using student's 't' unpaired test ($p<0.05$) and also with cost per gram of sample.

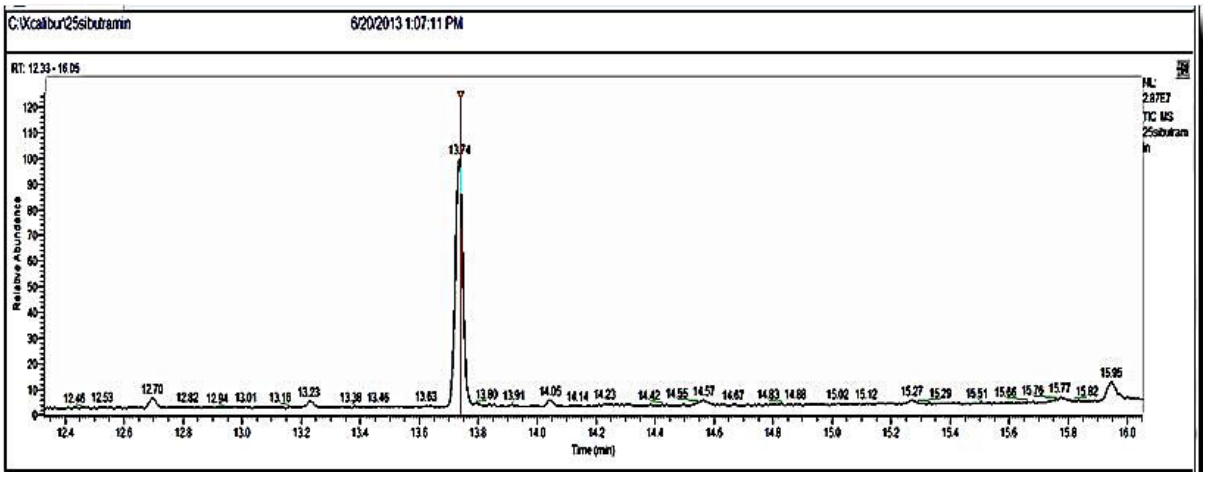

Figure 1a: Spectrum of sibutramine at retention time 13.74 min

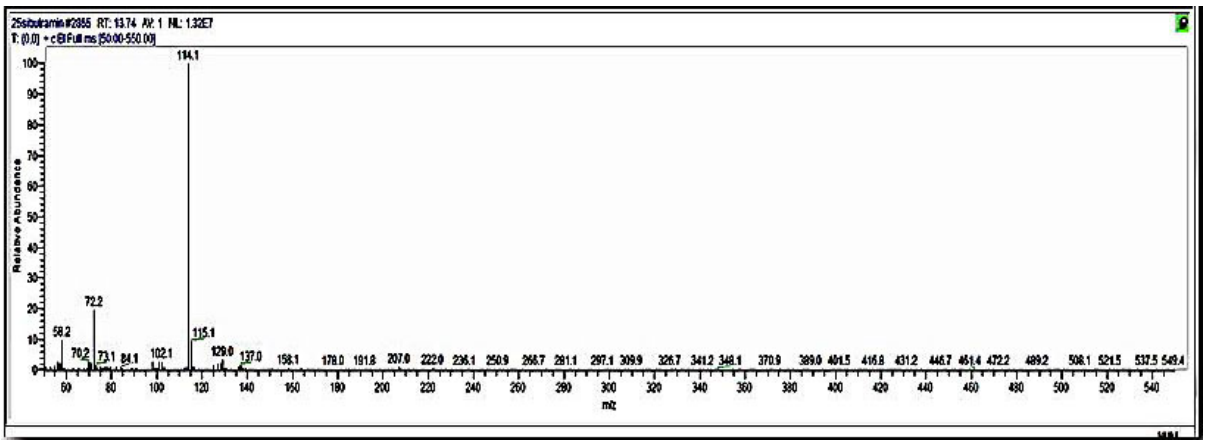

Figure 1b: Fragmented mass of sibutramine 72 m/z and 114 m/z

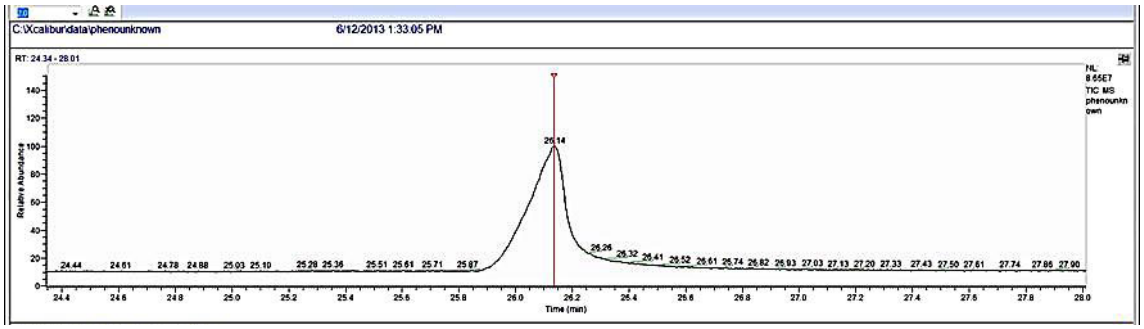

Figure 2a: Spectrum of phenolphthalein at retention time 26.14 min

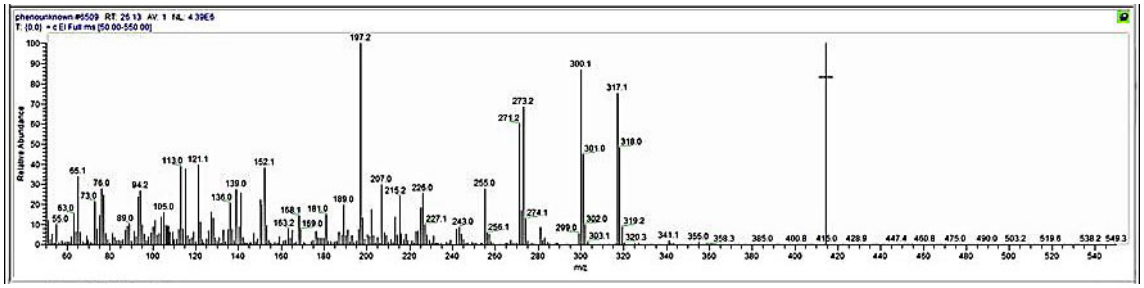

Figure 2b: Fragmented mass of phenolphthalein 225 m/z, 274 m/z and 318 m/z

Results

The results revealed that 60% of the samples contained sibutramine and /or phenolphthalein. 33% of the samples were adulterated with sibutramine and phenolphthalein. Products from China had highest concentration of both sibutramine (2846 ± 455 µg/g) and phenolphthalein (27 ± 4.2 ng/g) as compared to USA, Thailand, Italy and England (Table 1). Products from Germany and France which constituted 27% of the total samples contained only phenolphthalein. There was no significant difference in the concentration of sibutramine and phenolphthalein in herbal (1699 ± 606 µg/g; 15 ± 1.5 ng/g) and non-herbal (1977± 836 µg/g; 16 ± 6.4 ng/g) (Data not shown) slimming products irrespective of the country of origin. All Products from Morocco, Lebanon and Iran were free from these adulterants. The mean costs per gram of sample from different countries versus sibutramine and phenolphthalein concentration were presented in Table 1.

Country	Cost (AED/g)	Sibutramine concentration (µg/g)	Phenolphthalein concentration (ng/g)
USA*	31	1320±439	12.4±4.1
China	15	2846±455	24±4.2
Thailand	15	1928±71	27±1.4
Italy	13	1657±510	16.8±2.8
England	11	2023±994	13.8±1.39
France	7.7	ND	12.9±1.19
Germany	6.5	ND	14.4±2.4
Morocco	6	ND	ND
Lebanon	5	ND	ND
Iran#	2.7	ND	ND

*The most expensive slimming product; # The cheapest slimming product; ND – Nondetectable
The permissible limit for sibutramine by FDA is 15 mg/day and use of phenolphthalein is completely banned.
Table 1: Cost of slimming product and concentration of sibutramine & phenolphthalein in samples from different countries.

Discussion

Slimming products have gained wide popularity in the recent past as obesity has reached epidemic proportions and is a major contributor to the global burden of chronic disease and disability [16-19]. In the present study, 60% slimming products were found to contain with sibutramine and/or phenolphthalein although they have been banned by the Food and Drug Administration (FDA). A study conducted in Hong Kong reported that the presence of these illicit chemicals resulted in high mortality and morbidity [4]. Another study on the slimming products also showed the presence of sibutramine in high concentrations (2400 µg/g) comparable to our study where the highest concentration of sibutramine was also estimated to be 2846 µg/g. Sibutramine

being a serotonin reuptake inhibitor increases the level of serotonin in the brain causing early satiety, thus reducing the food intake [20]. Adding phenolphthalein possibly helps to reduce the dose of sibutramine and its associated side effects without altering the weight-loss effects of the product. However, high dose or repeated use leads to cardiovascular adverse effects such as increased blood pressure, tachycardia, palpitations, and seizures [21]. Thus, subjects with a history of hypertension, coronary artery disease, congestive heart failure, arrhythmias, bleeding disorders etc. tend to run a high risk. In the present study, phenolphthalein was found in several slimming products from different countries though it has been withdrawn even as a laxative due to potential carcinogen. Animal studies showed that phenolphthalein induced neoplasia in the ovary, atypical hyperplasia, hematopoietic cell proliferation, toxicity to the kidney and reproductive system in mice [22,23]. However, earlier studies also reported the presence of phenolphthalein as an adulterant in several illicit weight-loss supplements [24,25]. Both these compounds have been regarded unsafe in slimming products as their adverse effects outweigh their desired benefits [26]. The addition of sibutramine and phenolphthalein in the slimming products tend to increase their efficacy, thereby increasing the brand value and price. However, the low priced products analyzed were devoid of these adulterants and pose a lower health risk to the consumers on repeated use (Table 1). It is recommended that all slimming products available in the market should be screened for FDA listed banned substances thus protecting against the ill effects of popular 'quick-fix' remedies to lose weight.

Conclusion

The study revealed that the expensive slimming products from seven different countries contained sibutramine and/or phenolphthalein which have been banned by FDA due to risk of serious heart events. Interestingly, the less expensive products from Iran, Lebanon and Morocco were free from above adulterants. The high cost does not guarantee the safety of these products.

Acknowledgement

We would like to acknowledge Mr. Sagar Thapa for his assistance in the Toxicology Laboratory, GMU, Ajman (UAE).

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