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Detection of Synthetic Anti-Obesity Drugs, Designer Analogues and Weight-Loss Ingredients as Adulterants in Slimming Foods from 2015 to 2017

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Abstract

Obesity is a chronic disease associated with serious health problem such as metabolic syndrome, diabetes, hypertension, and cardiovascular disease. Recently, anti-obesity drugs, designer analogues and natural weight-loss ingredients have been found in dietary supplements for rapid weight loss or maintenance. In addition, structurally modified designer analogues are being continuously synthesized to avoid governmental inspections. 25 illegal compounds were assayed using a liquid chromatography coupled with photodiode array detector (LC-PDA) and tandem mass spectrometry (UPLC-MS/MS) analyses. A simultaneous determination method was established and fully validated. In 76 of 370 samples, nine different adulterants were detected including yohimbine, followed by β-phenylethylamine (β-PEA), sibutramine, sennoside A and B, β-methyl phenylethylamine (BMPEA), fluoxetine, ephedrine, phenolphthalein, and icariin. And 12 adulterated products contained a mixture of two or more adulterants. Adequate use of the existing regulation and the development of alternative methods for detecting adulterants are necessary consumers from consuming dietary supplements adulterated with illegal compounds.

Keywords: Adulterant; Sibutramine; Anti-obesity drug; Dietary supplement; Prohibited ingredients; LC-MS/MS

Introduction

Obesity, defined as abnormal or excessive fat accumulation and a body mass index (BMI) above 30 kg/m, is a serious chronic disease and risk factor of metabolic syndrome (MS), type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD). At least 2.8 million obese people die globally each year due to obesity or obesity-related diseases [1]. The prevalence of adult obesity in the Republic of Korea increased from 26.0% in 1998 to 31.7% in 2007 and was 34.8% in 2016 [2,3]. Many studies have reported that only modest weight losses of 5-10% of one's initial body weight was associated with improvements in CVD risk factors, preventions or delays of T2DM, and decreases in other adverse MS risk factors [4-6].

The prevalence of the availability and consumption of dietary supplements is in response to the health problems linked to obesity. However, some dietary supplement result in serious health risks to consumers due to adulteration with prohibited ingredients, dangerous chemicals, and prescription pharmaceuticals. Recently, anti-obesity drugs, their analogues, and natural weight-loss ingredients were found in weight-loss foods for weight-loss and maintenance. In addition, botanical dietary supplements or natural health products were believed as safe because they are "natural". However, illegal compounds, such as anti-obesity drugs, designer analogues, and natural weight-loss ingredients have been detected in these supplements. In 1997, sibutramine was approved to treat obesity in the United States, where it was reported to be effectual for overweight or obese patient populations with a BMI above 30 kg/m or below 27 kg/m in the presence of other cardiovascular risk factors. In 2010, however, the use of sibutramine was banned because of an increase in the relative risk for major adverse cardiac events in elderly overweight and obese patients. To date, the reported designer analogues are mainly sibutramine analogues, including desmethylsibutramine, didesmethylsibutramine, chlorosibutramine, benzylsibutramine, and homosibutramine. Phenolphthalein had been used as an over-the-counter laxative and has often been found together with sibutramine in adulterated weight-loss supplements products. After identifying the potential carcinogenicity of phenolphthalein, it was reclassified in 1997 as unsafe and ineffective [7]. The rapid weight-loss agent 2,4-dinitorphenol (2,4-DNP), which inhibits oxidative phosphorylation, was removed from the market by the FDA in 1938 due to a significant number of side effects such as hyperthermia, tachycardia, diaphoresis, and tachypnea with associated cardiovascular collapse, cardiac arrest and death [8]. Likewise, amphetamine and its derivatives had been used to treat obesity since 1937, though their addictive potential soon became obvious and they were removed from the market for this purpose. Amphetamine-like substances derived from the β-phenylethylamine core structure have been detected in dietary supplements [9]. However, dietary supplements containing these unsafe weight-loss drugs and prohibited ingredients are still available over the internet.

To determine the presence of weight-loss compounds, high-performance liquid chromatography coupled with a photodiode array detector (HPLC-PDA) and tandem mass spectrometry (UPLC-MS/MS) are regarded as powerful and convenient methods. Recently, LC-quadrupole-time-of-flight mass spectrometry (LC-Q-TOF/MS) has been used to detect illegal adulterants in slimming formulas [10,11].

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Some manufactures have even synthesized modified sibutramine analogues to avoid government regulations. Notably these analogues have a similar UV spectrum to that of sibutramine in HPLC-PDA analysis, but they possess a different retention time. Therefore, HPLC-PDA can be a useful method to detect structurally modified analogues during the simultaneous analysis of multiple samples for routine quality control to address the problem of adulterated slimming foods containing drugs. In this study, HPLC-PDA and UPLC-MS/MS were used to develop a rapid and simultaneous method to detect and monitor a total of 25 illegal weight-loss compounds, such as synthetic anti-obesity drugs, designer analogues, and natural weight-loss ingredients, in botanical and dietary supplement products.

Materials and Methods

Chemicals

Sibutramine and orlistat were obtained from Hanmi Pharmaceutical (Hwaseong, South Korea) and Roche Korea (Seoul, South Korea), respectively. Amphetamine, fenfluramine, N-nitroso fenfluramine, and the sibutramine analogues, including desmethylsibutramine, didesmethylsibutramine, chlorosibutramine, and benzylsibutramine were synthesized by the Korean Ministry of Food and Drug Safety (MFDS). β-Phenylethylamine (β-PEA), β-methyl phenylethylamine (BMPEA), 2,4-dinitrophenol (2,4-DNP), glibenclamide, gliclazide, glipizide, glimepiride, liothyronine (T3), levothyroxine (T4), ephedrine, fluoxetine, icariin, yohimbine, and phenolphthalein were purchased from Sigma-Aldrich (St. Louis, MO, USA). Sennoside A and B were purchased from Wako Pure Chemical Industries (Osaka, Japan). All standards were dissolved in methanol at 1 mg/mL as stock solutions and stored at -4°C prior to analysis. LC-grade methanol and acetonitrile were obtained from Merck (Darmstadt, Germany). Formic acid and phosphoric acid were purchased from Sigma-Aldrich and Wako Pure Chemical Industries, respectively. Purified water was prepared using a Thermo Scientific Barnstead Nanopure water purification system (Marietta, OH, USA).

Sample collection and preparation

A total of 370 slimming foods, including dietary, herbal, and nutritional supplements, health functional foods, teas, and beverages advertised for weight-loss or fat-burning were purchased from local markets and on the internet websites from 2015 through 2017. Sample preparation depended on whether the sample was in tablet, capsule, scoop, or teabag form. For the capsuled samples, the contents were mixed after opening at least five, but preferably ten, capsules. The capsule contents and shells were analyzed separately. The five or ten tablets were ground using a mortar and pestle and mixed. For the powder and teabag samples, five units were mixed. Each sample was prepared as follows: Approximately 1.0 g of the pulverized sample was weighed in a 50 mL conical centrifuge tube. Then, analytes were extracted by mixing the sample with 50 mL of 70% methanol for 30 s on a Vortex Maximix II (Thermo Scientific, Waltham, MA, USA) followed by sonication for 20 min. The extract was centrifuged at 4,000 rpm for 5 min at 5°C by a Gyrozen 1736R centrifuge (Daejeon, Korea). A 1 mL aliquot of the extract was filtered through a 0.2 μm pore polytetrafluoroethylene (PTFE) membrane syringe filter (Teknokroma, Barcelona, Spain) before HPLC-PDA or LC-MS/MS analysis.

HPLC-PDA analysis

All samples were analyzed using a Nanospace SI-2 HPLC system with a photo diode array (PDA) detector from Shiseido (Tokyo, Japan). Liquid chromatography analysis was carried out on a Shiseido Capcell Pak C18 MG II column (4.6 × 250 mm, 5.0 μm) with 0.5 mM sodium-1-hexane sulfonate containing 0.1% phosphoric acid and 95% acetonitrile as mobile phases A and B, respectively. The gradient condition was as follows: 0-6 min, 15% B; 6-15 min, 30% B; 15-30 min, 40% B; 30-32 min, 40% B; 32-40 min 100% B; 40-50 min, 100% B; 50-52 min, 15% B; 52-60 min, 100% B. The oven temperature of the column was maintained at 40°C. The HPLC was operated in gradient mode at a flow rate of 1.2 mL/min and an injection volume of 10 μL. The absorption spectra were recorded between 200 and 400 nm and the eluate were monitored by the PDA detector at 210 nm.

UPLC-MS/MS analysis

For qualitative analysis, UPLC-MS/MS analysis was carried out on a Waters Xevo TQ-S Tandem MS with an ACQUITY UPLC (Milford, MA, USA). LC separations were performed on an ACQUITY UPLC BEH C18 column (2.1 mm × 100 mm, 1.7 μm) with the column temperature set at 30°C. The mobile phases consisted of 0.1% formic acid in water (A) and 0.1% formic acid in acetonitrile (B) at a flow rate of 0.3 mL/min. The injection volume was 2 μL. The gradient profile was as follows: 0-3 min, 5% B; 3-7 min, 10% B; 7-14 min, 80% B; 14-16 min, 80% B; 16-16.1 min 5% B; 16.1-18 min, 5% B. The conditions of the MS operating parameters were as follows: capillary voltage, ± 3 kV; cone voltage, 25 V; source temperature, 150°C; desolvation temperature, 500°C; desolvation gas flow, 800 L/h.

Determination of linearity, limits of detection, limits of quantification, accuracy, and precision

A simultaneous determination method for illegal weight loss compounds was established and validated for linearity, limits of detection (LOD), limits of quantification (LOQ), accuracy, and precision. Method selectivity was established by comparing the chromatograms of a blank solution (mobile phase B), blank sample, and blank samples spiked with the target analytes. LC chromatograms were checked for interfering peaks and sufficient separation of the analyzed compounds. The linearity of each analyte was examined within the concentration range of 0.5-100 μg/mL using a linear regression model. From the calibration curve, calibration equations, and coefficients of determination (r) were calculated. The LOD and LOQ were calculated as three and ten times the standard deviation (SD) of the concentration acquired from five replicate analyses of spiked samples, respectively. The accuracy of the method was evaluated as the recovery. Five recovery experiments were performed using the spiked samples at a concentration of 5 μg/mL for each standard using matrix-matched calibration. The procedure was repeated the following day to determine the inter-assay effects. From the repeated experimentation, percentages of relative standard deviation (%RSD) were calculated as mean values with standard deviations. Inter-laboratory validation was performed by three laboratories to evaluate the bias and precision of the developed method. Recovery experiments were performed five times using the spiked samples at concentrations of 5 and 25 μg/mL for each standard using matrix-matched calibration. From the results of the recovery experiments, the accuracy and precision of the analytical method were calculated.

Results and Discussion

The continual detection of illegal compounds in dietary supplements has highlighted their serious threat to public health. A total of 24 such illegal adulterants were analyzed using HPLC-PDA and LC-MS/MS in this study. As shown Table 1, the presence of illegally added anti-obesity drugs such as sibutramine, orlistat, sibutramine analogues, other drugs, and natural ingredients were monitored in slimming formulas. These

compounds belong to different pharmacological categories: anorectics (sibutramine, orlistat, and fenfluramine) used to reduce appetite; laxatives (sennosides and phenolphthalein) used to increase intestinal passage; stimulants (amphetamine, BMPEA, ephedrine, β-PEA, and yohimbine) used to induce temporary improvements in either mental or physical function; and anti-depressants (fluoxetine) used to alleviate anxiety disorders.

Given the structural similarity of some standards, 15 of 25 standards were chosen to determine the linearity, LOD, LOQ, accuracy, and precision of the method across a concentration range of 0.5-100 μg/mL spiked into matrix-blank samples. The obtained regression equations for calibration, coefficients of determination (*r* values), LODs, and LOQs, accuracy, and precision are shown in Table 2. The developed method is capable of separating all analytes under the given gradient conditions. The coefficients of determination (*r*) were in the range of 0.9910-1.0000, and the LODs and LOQs were in the ranges of 1.0-7.5 and 3.0-25.0 μg/mL, respectively. Most of the pharmaceutical adulterants were present at high concentrations in the dietary supplements close to their therapeutic dose. In general, sample dilution was performed in dietary supplements containing sibutramine, designer analogues, and other drugs; the LOD and LOQ are consequently increased. The intra- and inter-day accuracies were evaluated as 89.7-98.22% and 93.0-97.3%, respectively, with precision values were of 1.2-4.9 and 1.1-5.1, respectively. These accuracy and precision values are consistent with the guidelines established by the AOAC [12]. To evaluate the bias and precision of the developed method, three laboratories performed inter-laboratory validation. Overall, the results demonstrate that the HPLC-PDA method presented herein enables an easy and rapid quantification of illegal substances (Table 3).

A total of 370 samples were collected from local markets in the Republic of Korea and over the internet between 2015 and 2017. Due to the straightforward sample preparation, a large number of samples can be analyzed at the same. In the present study, the simultaneous sample determination using HPLC-PDA proved to be a useful method for routine quality control to investigate drug-containing adulterated slimming foods. A total of 9 different illegal compounds were detected (Figures 1 and 2; Table 4). Yohimbine was detected most frequently at levels of 0.1-17.5 mg/g in 45 samples, followed by β-PEA at levels of 4.5-110.5 mg/g in 12 samples, sibutramine at levels of 9.9-135.3 mg/g in 10 samples, sennosides at levels of 1.1-5.6 mg/g in 7 samples, BMPEA at levels of 2.2-40.0 mg/g in 6 samples, fluoxetine at levels of 30.7-52.7 mg/g in 3 samples, ephedrine at levels of 7.3-15.3 mg/g in 2 samples, and phenolphthalein and icariin at levels of 22.0 and 1.8 mg/g, respectively. In addition, 12 of 76 adulterated products contained a mixture of two or more adulterants. Yohimbine and sibutramine were detected every year from 2015 to 2017.

Many types of slimming foods are advertised as being effective for appetite depression or weight loss. Some manufacturers claim that herbal dietary supplements are safe because they are natural. Although some products included in this study were advertised as natural formulas, they also contained the anti-obesity drug sibutramine, fluoxetine, phenolphthalein, and prohibited compounds. Illegally synthesized ingredients are sometimes added to dietary or herbal supplements in amounts exceeding the therapeutic dose, which may pose a serious threat to public health. In this study, some samples contained of sibutramine at levels more than 2-3-fold higher than the therapeutic dose (10-15 mg/day).

Combining drug to maximize weight-loss is common in dietary supplements. For example, both fluoxetine and sibutramine were detected in samples in this study. This combination and a mixture of ephedrine and caffeine were used in the past for the treatment of obesity improve and maintain weight-loss and preserve fat-free mass [13]. Although we did not analyze the level of caffeine in the slimming formulas, natural caffeine, which contain kola nut, guarana, cacao, and green coffee bean and synthetic caffeine were listed in ingredients on the packaging.

In the Republic of Korea, yohimbine, icariin, and sennosides are prohibited ingredients. Yohimbe bark extract has traditionally been used as an aphrodisiac in Africa, and its inclusion in dietary supplements is solely for this purpose. Yohimbine is a natural indole alkaloid that is extracted from the West African tree *Corynanthe yohimbe* bark; it acts as a selective and reversible α_2-adrenergic receptor antagonist and a receptor antagonist for serotonin [14]. The administration of yohimbine prior to exercise was found to enhance the efficacy of exercise training by boosting lipolysis and releasing serum free fatty acids [15]. After consumption of yohimbe bark extract or yohimbine, some people suffered various adverse events such as gastrointestinal distress, tachycardia, anxiety, depression, posttraumatic stress disorder, agitation, hypertension, heart and kidney failure, and hepatitis [14]. Clearly, dietary supplements containing yohimbine should be used with caution in patients with hypertension, kidney failure, and psychiatric conditions [14,15].

On the basis of these results, the MFDS immediately announced the harmfulness of dietary supplements containing illegal weight-loss compounds to consumers. Further, the MFDS requested that the Korea Communications Commission block internet sites selling such products and informed the Korea Customs Service to prevent their customs clearance. Broadly, this study contributes to food safety through the development of an effective and rapid analytical method for screening illegal compounds.

Conclusions

In this study, 370 weight-loss food samples were collected from 2015 to 2017 and HPLC-PDA and LC-MS/MS were used to analyze for the presence of anti-obesity drugs, designer analogues, and natural weight-loss ingredients. A total of 9 different illegal compounds were detected in 76 of the 370 samples. The most frequently found adulterant was yohimbine, followed by sibutramine, sennoside A and

Classification (Numbers)	Weight-loss compound
Anti-obesity drugs (2)	Sibutramine, orlistat
Sibutramine analogues (5)	Benzylsibutramine, chlorosibutramine, desmethylsibutramine, didesmethylsibutramine, homosibutramine
Hypoglycemic drugs (4)	Glibenclamide, gliclazide, glimepiride, glipizide
Thyroid hormones (2)	Liothyronine (T3), levothyroxine (T4)
Psychotropic drugs (6)	Amphetamine, fenfluramine, fluoxetine, *N*-nitrosofenfluramine, β-methylphenylethylamine (BMPEA), β-phenylethylamine (β-PEA)
Other drugs (3)	Ephedrine, 2,4-dinitrophenol (2,4-DNP), phenolphthalein
Natural ingredients (3)	Icariin, sennosides (sennoside A and B), yohimbine

Table 1: Classification of the 22-weight loss active compounds and 3 natural ingredients investigated in this study.

		Coefficient of determination (r^2)	LOD (µg/mL)	LOQ (µg/mL)	Accuracy (% Recovery)		Precision (%RSD)	
					Intra-day	Inter-day	Intra-day	Inter-day
Single-laboratory validation	**Amphetamine**	0.9999	1	3	92.5	93.9	2.8	2.4
	Benzylsibutramine	0.9999	4.4	14.7	95.1	94.5	1.2	1.1
	BMPEA	0.9987	1	3	92.9	93	3.4	2.7
	2,4-DNP	1	3	10	105.7	107.2	2.1	5.6
	Ephedrine	0.9969	5.5	20	98.2	95.6	3.8	4
	Fenfluramine	0.991	7.5	24.8	93	97	2.6	1.8
	Fluoxetine	0.9991	7	25	98.2	95.3	4.8	5
	Icariin	0.9999	6.7	22.2	93.7	94.7	2.6	4.3
	Glibenclamide	0.994	3.6	12	91.7	96.9	3	2.7
	Liothyronine (T3)	0.9987	5.5	20	97.3	96.1	4	4.8
	Levothyroxine (T4)	0.9991	5.5	20	95.1	93	4.3	4
	Orlistat	0.996	6.1	20	89.7	94.9	2.4	2.5
	β-PEA	1	4	13	96.6	93.5	5	6.6
	Phenolphthalein	0.9941	5.5	20	98	95.3	4.9	5.1
	Sibutramine	0.998	7.5	25	91	97.3	2.5	2.6
	Yohimbine	1	7.5	25	94.5	91.6	2.3	5.7
		Accuracy (%Recovery)				**Precision (%RSD)**		
Multi-laboratory validation		**5 ng/mL**		**25 ng/mL**		**5 ng/mL**		**25 ng/mL**
	Benzylsibutramine	92.2		97.2		1.3		3.1
	Ephedrine	98.2		99.7		3.1		6.8
	Fluoxetine	97.7		99.6		4.1		6.9
	Liothyronine (T3)	96.3		98.9		3.5		6.7
	Levothyroxine (T4)	95.9		101		7		6.3
	Phenolphthalein	94.6		101.2		7.5		5.9

Table 2: Linearity, limits of detection (LOD), limits of quantification (LOQ), accuracy and precision for weight-loss compounds.

Analyte	Molecular formula (molecular weight)	Precursor ion (*m/z*)	Product ion (*m/z*)	Cone voltage (V)	Collision energy (V)
Amphetamine	$C_9H_{13}N$ (135.21)	136.2	91.0, 118.8	15	15, 8
Benzylsibutramine	$C_{20}H_{24}ClN$ (313.87)	314.4	91.1, 125.0, 191.1	62	22, 18, 12
BMPEA	$C_9H_{13}N$ (135.21)	136.2	91.0, 118.8	15	15, 8
Chlorosibutramine,	$C_{17}H_{25}Cl_2N$ (314.30)	314.1	139.0, 153.0, 173.0	20	15, 13, 17
Desmethylsibutramine	$C_{16}H_{24}ClN$ (265.84)	266.2	125.1, 139.1, 153.0	10	24, 14, 6
Didesmethylsibutramine	$C_{15}H_{21}ClN$ (251.80)	252	125.1, 139.1, 153.0	15	22, 11, 10
2,4-DNP	$C_6H_4N_2O_5$ (184.11)	182.95	109.1, 137.0	62	22, 17
Ephedrine	$C_{10}H_{15}NO$ (165.23)	166.2	148.2, 117.2, 91.1	15	12, 19, 26
Fenfluramine	$C_{12}H_{16}F_3N$ (231.26)	232.1	159.1, 109.2, 119.1	65	23, 42, 42
Fluoxetine	$C_{17}H_{18}F_3NO$ (309.33)	310.4	148.0, 43.8, 117.0	15	10, 10, 14
Glibenclamide	$C_{23}H_{28}ClN_3O_5S$ (494.00)	492.1	170.0, 367.0, 377.9	16	31, 20, 26
Gliclazide	$C_{15}H_{21}N_3O_3S$ (323.42)	322.2	169.8, 105.9, 127.0	30	35, 50, 19
Glimepiride	$C_{24}H_{34}N_4O_5S$ (490.63)	489	224.9, 364.0, 350.0	18	36, 22, 18
Glipizide	$C_{21}H_{27}N_5O_4S$ (445.54)	444.1	319.0, 169.9, 103.0	23	30, 40, 39
Homosibutramine	$C_{18}H_{28}ClN$ (293.19)	294.2	125.1, 139.1	20	40, 20
Icariin	$C_{33}H_{40}O_{15}$ (676.66)	677.3	369.1, 531.2, 313.1	26	32, 16, 58
Liothyronine (T3)	$C_{15}H_{12}I_3NO_4$ (650.98)	625.1	606.1, 478.1, 508.0	30	20, 40, 20
Levothyroxine (T4)	$C_{15}H_{11}I_4NO_4$ (776.87)	778.1	732.0, 324.1, 478.8	35	28, 20, 50
N-Nitrosofenfluramine	$C_{12}H_{15}F_3N_2O$ (260.26)	261	159.1, 109.0, 119.0	40	23, 45, 45
Orlistat	$C_{29}H_{53}NO_5$ (495.73)	496.5	160.3, 114.2, 319.3	25	13, 12, 21

Phenolphthalein	$C_{20}H_{14}O_4$ (318.32)	319	225.0, 197.1, 141.1	25	21, 39, 31
β-PEA	$C_8H_{11}N$ (121.18)	122.3	105.0, 77.0	20	20, 20
Sennosides (A and B)	$C_{42}H_{38}O_{20}$ (862.75)	861.2	386.2, 699.2, 224.1	32	36, 28, 40
Sibutramine	$C_{17}H_{26}ClN$ (279.84)	280.2	125.1, 139.1, 202.0	10	28, 16, 28
Yohimbine	$C_{21}H_{26}N_2O_3$ (354.44)	355.2	144.2, 212.2, 117.2	18	32, 20, 40

Table 3: MRM parameters of 25 illegal weight-loss compounds.

	2014 (n= 89)		2015 (n=128)		2016 (n=153)		Total (n=370)	
	Detected number	Concentration (mg/g)	Detected number	Concentration (mg/g)	Detected number	Concentration (mg/g)	Detected number	Concentration (mg/g)
BMPEA			4	3.0-40.0	2	2.2-6.1	6	2.2-40.0
Ephedrine	1	15.3			1	7.3	2	7.3-15.3
Fluoxetine					3	30.7-52.7	3	30.7-52.7
Icariin			1	1.8			1	1.8
PEA			7	4.5-103.2	5	6.0-110.5	12	4.5-110.5
Phenolphthalein					1	22	1	22
Sennosides (A and B)	1	1.1			6	1.3-5.6	7	1.1-5.6
Sibutramine	4	47.4-79.2	4	9.9-135.3	2	27.6-101.2	10	9.9-135.3
Yohimbine	9	1.0-6.9	26	0.2-17.5	10	0.1-13.8	45	0.1-17.5
Combination above two adulterants	0		6		6		12	
Total	15		36		24		75	

Table 4: The number and concentrations of illegal weight-loss compounds detected in herbal and dietary supplements from 2015 to 2017.

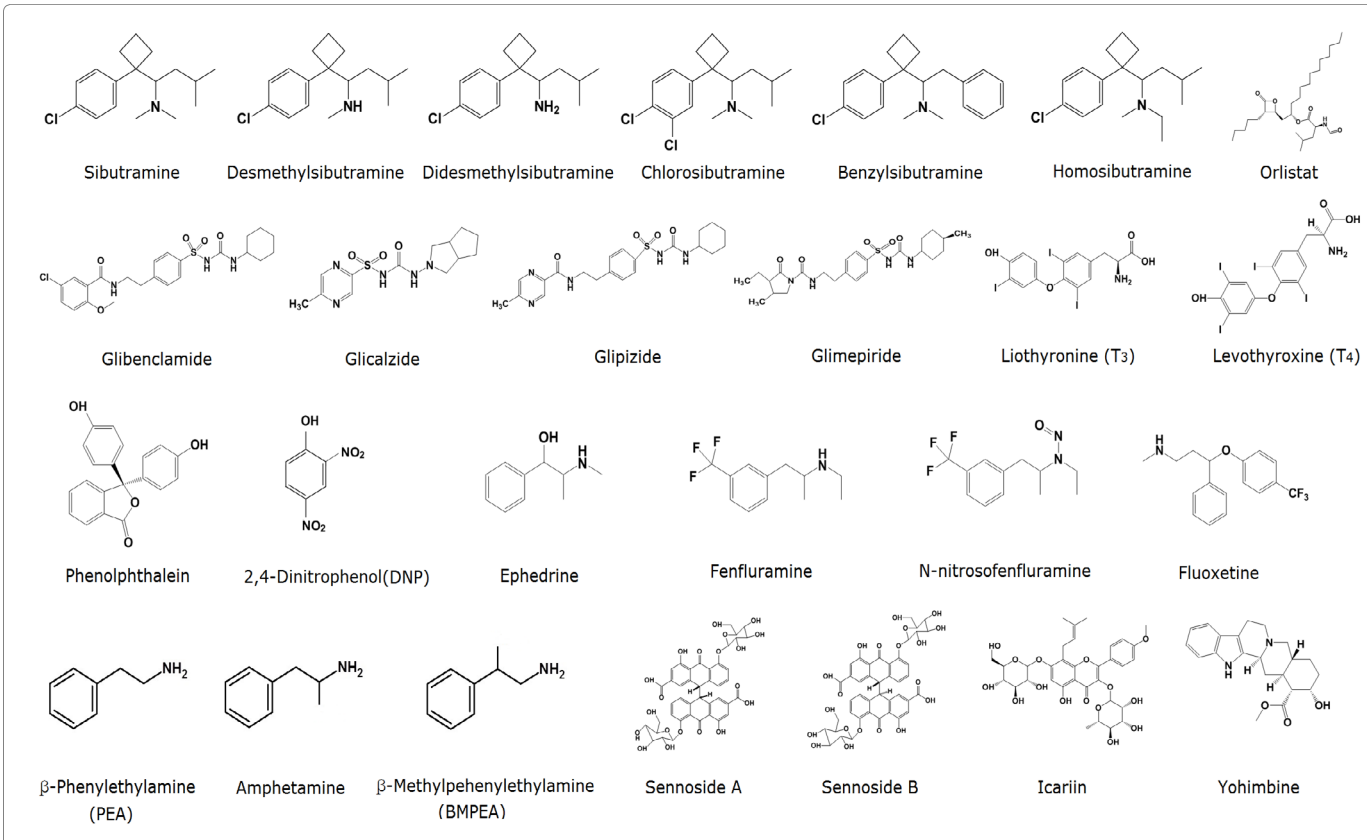

Figure 1: Chemical structures of weight-loss compounds.

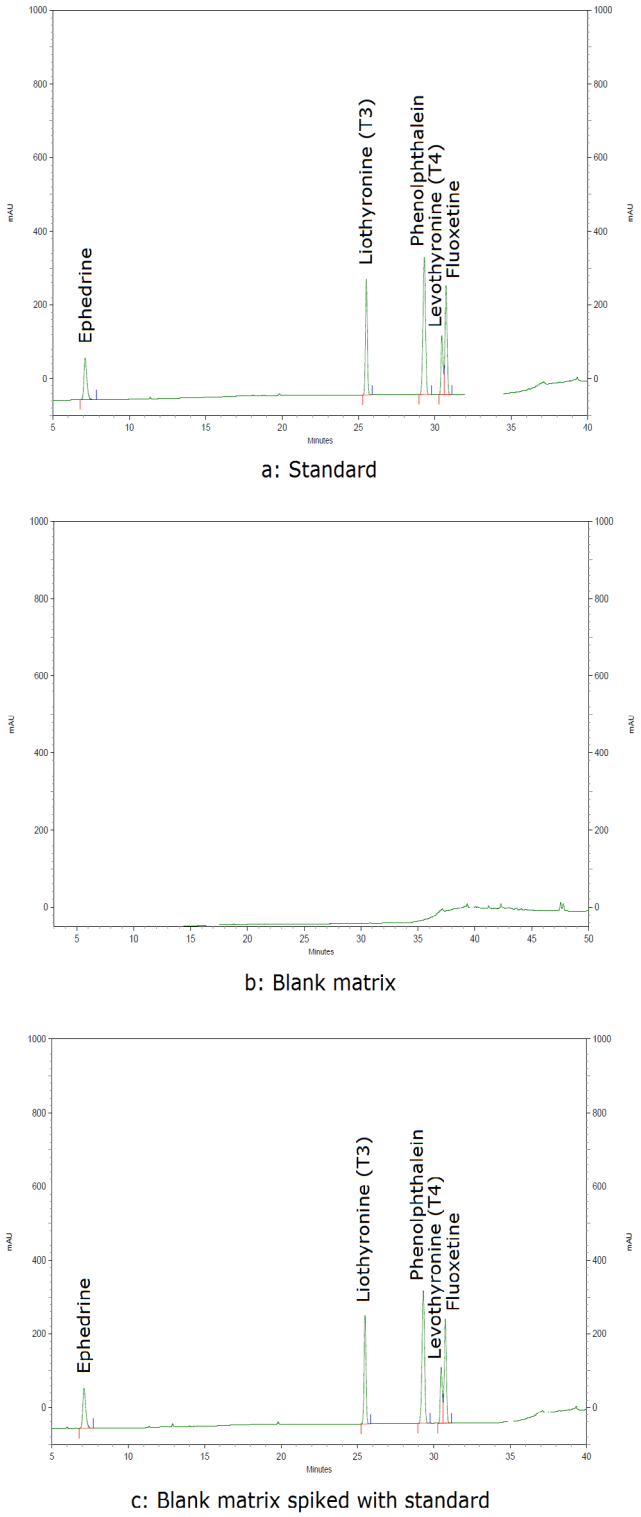

Figure 2: Representative chromatograms of ephedrine, fluoxetine, liothyronine (T3), levothyronine (T4), and phenolphthalein (Accuracy parameter).

B, fluoxetine, ephedrine, phenolphthalein, and icariin. The method developed herein may be useful for screening dietary supplements adulterated with synthetic anti-obesity drugs, designer analogues, and illegal natural weight-loss ingredients. Overall, it is vital that existing regulations are adequately enforced and that alternative methods are developed to detect adulterants in slimming foods in order to protect public safety.

Conflict of Interest

All authors declare no conflicts of interest.

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