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Prescription drugs and dietary supplements for weight loss

Abstract

Despite much advertising to the contrary, there are no dietary supplements that safely and effectively cause weight loss. Moreover, some of them are adulterated with banned prescription drugs as well as narcotics, stimulants, antidepressants, anorectics, laxatives and diuretics. There are several analytical methods, including LC-MS/MS and NMR that can be used to analyze dietary supplements for adulterants. Such methods can be used to detect and quantify them at physiologically relevant concentrations of >1%. Even though many supplements don't contain any of these potentially deadly adulterants, many do contain caffeine and/or green tea extract at such high concentrations that they can also be quite toxic. On the other hand, there are five prescription drugs that are FDA-approved as an adjunct to counseling, diet and exercise for maintaining weight loss. They are orlistat (Xenical® or Alli when sold over-the-counter), lorcaserin (BELVIQ®), phentermine plus extended-release topiramate (Qsymia®), naltrexone plus bupropion (Contrave®) and liraglutide (Saxenda®). Unlike dietary supplements, they were all developed in research programs that were conducted through good laboratory practices (GLP) and manufactured by current good manufacturing practices (cGMP). So, they have been shown to be safe and effective. Moreover, every step in the manufacturing process is monitored and documented to ensure the purity of the drugs. Finally, post-market monitoring of potential adverse side effects is done on these drugs.

Keywords: Orlistat, phentermine, topiramate, lorcaserin, liraglutide, dietary supplements, green tea extract, 1,3-dimethylamylamine, DMAA, 3,4-methylenedioxy-methamphetamine (MDMA)

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Kevin Tran, Kristy Richards, Robert E Smith
Total Diet Research Center, USA

Correspondence: Robert E Smith, Total Diet Research Center, FDA, USA, Tel 9137522473, Fax 9137522122, Email Robert.smith@fda.hhs.gov

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Abbreviations: 5-HT, 5-hydroxytryptamine; BMI, body mass index; DMAA, 1,3-dimethylamylamine; DMBA, 1,3-dimethylbutylamine; DNA, deoxyribonucleic acid; DPP-4, dipeptidyl peptidase-4; EGCG, epigallocatechin-3-gallate; FDA, food and drug administration; MDMA, 3,4-methylenedioxy-methamphetamine; ESI, electrospray ionization; ESI-MS/MS, electrospray ionization coupled to mass spectrometry in which one acquires the mass spectrum of a mass spectrum; LC, liquid chromatography; LC-MS, liquid chromatography coupled to mass spectrometry; MS, mass spectrometry; NMR, nuclear magnetic resonance; PCP, 1-(1-*phenyl cyclohexyl) piperidine*; rDNA, recombinant DNA; SERS, surface-enhanced raman scattering; TLC, thin layer chromatography; UV, ultraviolet; GLP, good laboratory practices; cGMP, current good manufacturing practices; HPLC, high performance liquid chromatography

Introduction

Metabolic syndrome is a serious condition that can cause smoldering inflammation and lead to diabetes, cardiovascular diseases, cancer and neurodegenerative diseases.[1,2] It was described by Reaven.[3,4] Obesity, or excessive weight, is one of the early symptoms.[1] Moreover, obesity can cause social stigma and low self-esteem, which can lead to many health problems, including depression. So, there is a long history of botanicals, drugs and dietary supplements being used to suppress the appetite and/or cause weight loss.[1] However, biology and genetics can work against any attempt to lose much weight. That is, our ancient ancestors were far more likely to suffer from malnutrition than obesity. So, human metabolism will slow down when a person goes on a diet and loses just a few kg. This can be very frustrating and make some people give up. After depriving themselves of the food that they love, they may be tempted to over eat and consume foods that may be tasty, but high in calories and unhealthy simple carbohydrates and fats.[1] As a result, many people desperately look for a single pill that can cause them to lose weight while consuming anything they want, regardless of its sugar or caloric content. This makes them quite vulnerable to vendors of adulterated dietary supplements.

For example, sweetened beverages that are high in fructose, glucose or sucrose have no nutrients and rapidly increase blood glucose concentrations to dangerously high levels.[1] The excess glucose is converted to fat and is stored in adipose cells. Adipose tissue is an active endocrine and immune organ. It secretes lipid hormones (adipokines). So, adipocytes are not just storage cells for triglycerides, but complex cells that must be properly regulated. When caloric intake exceeds energy consumed, adipocytes proliferate. If there is sufficient adipogenesis, metabolic syndrome can be avoided. When adipogenesis is impaired, adipocytes can become dysfunctional and help cause diseases related to metabolic syndrome. This is often called adiposopathy, or sick fat. This fat is especially dangerous when it accumulates in the abdomen. Adipose tissue also produces aromatases which catalyze reactions that are in the biosynthetic pathway for estrogen. That is important because estrogens have important roles in bone homeostasis. In post-menopausal women, circulating estrogen levels decrease, which leads to an increase in the number of adipocytes and decrease in osteoblasts, which can lead to osteoporosis. Adipocytes, osteoblasts and myoblasts originate from a common progenitor, pluripotent mesenchymal stem cells, or MSCs. So, there is a bone-adipose axis, with bones and adipose tissue acting as endocrine organs.[1] So, there is a real need for safe and effective prescription drugs that can help one to lose weight and keep it off.

So, it is unfortunate that many people become frustrated when they lose just a few kg, because even a modest weight loss through counseling, diet and exercise can reduce the incidence of disease by 40-60% over 3-4years.[5] It is even more unfortunate for those people who are not satisfied with a modest loss of weight when they decide to take dietary supplements that may contain narcotics or prescription drugs that were once approved by the FDA and other countries' regulatory agencies, but were pulled from the market due to harmful and sometimes deadly side effects.[6–14] Moreover, deadly narcotics such as cocaine, codeine, ketamine, 3,4-methylenedioxy-methamphetamine (MDMA), methaqualone and 1-(1-*phenyl cyclohexyl) piperidine* (PCP) have been found in some supplements.[11,15] Even those supplements that contain only natural ingredients like the bark of the yohimbe plant (*Pausinystalia johimbe*)[16] or the dried, immature fruits of bitter orange (*Citrus aurantium* L.)[17] can be toxic. So, it is important for the public to be well educated about the value of losing just a few kg and avoiding potentially toxic dietary supplements.

Even the usually quite healthy ingredients in green tea can be toxic when consumed at too high of a dose as green tea extracts,[18–23] even though it may be quite healthy at moderate doses.[24] Caffeine can also be toxic at high doses,[25] so some green tea extracts are decaffeinated.[26] It is usually safe when consumed in moderation (500mg or less daily), and may even protect against some diseases, including Parkinson's disease.[27] However, it can be toxic at doses over 10grams per day for adults. Even though energy drinks contain much less than this, they can still be quite harmful – especially to children and adolescents.[28] In addition, caffeine is an adenosine receptor antagonist. This is important because there are several drugs in clinical trials that target adenosine receptors. That is, all four types of adenosine receptors are elevated in autoimmune diseases and cancer, so they are being investigated as therapeutic targets. So, it will be important in these studies to determine the effects of caffeine consumption on the efficacy of these drugs.[29]

The phenolic compounds (especially epigallocatechin-3-gallate, EGCG) in green tea may help prevent cancer when consumed in moderation.[26,30] The US FDA has approved a topical ointment (sinecatechins 15%, Verege®) for the treatment of external genital and perianal warts caused by the human papillomavirus. The active ingredients are catechins that are extracted from green tea. They are immunomodulators that inhibit major viral functions. Also, meta-analyses of previous publications found that a relatively high consumption of green tea was associated with a 20% and 18% reduction of the risks of breast cancer and colorectal cancers, respectively. In a prospective cohort study of >40000 Japanese adults found that green tea was inversely associated with cardiovascular mortality. Moreover, participants who consumed more than five cups (about 237mL) per day had a significantly reduced incidence of stroke.[31]

However, EGCG is like fresh air, fresh water or any other substance. All substances are toxic if given at a high enough dose to the most vulnerable part of the body.[32] That is, the dose is the poison.[33] Still, physiologically tolerable doses of EGCG activate antioxidant signaling pathways that has neuroprotective and anticancer effects.[34,35] However, at higher doses, EGCG suppresses not only the major antioxidant enzymes (superoxide dismutase, catalase, and glutathione peroxidase) but also the antioxidant rescue pathway that it activates at lower doses.[19] So, if one is not careful, attempts to "cure" obesity with weight loss supplements can be dangerous. They can not only cause illness and death, but also can cause consumers of such products to lose their jobs when they fail a urine test because they consumed a supplement that contained an illegal amphetamine, even though its presence was not indicated on the label of the supplement.[36] Moreover, even though the FDA recalled many dietary supplements because they contained banned ingredients, many of them still contained those toxic ingredients in supplements that were purchased at least six months after they were recalled.[37] Perhaps the most concerning weight loss supplements are those that are sold over the black market by calling a friend or a cell phone number provided on internet message boards.[38] Such products are not available in stores or even on freely accessible websites. They are sold as capsules with no imprint on them and no list of ingredients on the label.[38] So, the FDA has issued a warning about weight loss dietary supplements.[6]

On the other hand, counseling, diet and exercise are essential parts of successful weight loss programs.[39] However, it can be quite difficult to keep the weight off after it is lost.[40] So, there are now prescription drugs that can be used to maintain the weight loss.[40–44] Some of them have additional health benefits. The current review will list drugs that have been pulled off the market but are still used in dietary supplements. Also, analytical methods that can be used to see if adulterants and toxins are present will be described. Finally, the prescription drugs that are now available, orlistat, phentermine plus extended-release topiramate (Qsymia®), lorcaserin (BELVIQ®), naltrexone plus bupropion (Contrave®) and liraglutide (Saxenda®), will be reviewed.

Methods

This review is based on information that has been reported in the scientific literature and FDA websites. The articles described were found by using search engines such as Google Scholar, PubMed and Science Direct, as well as references cited in published articles. Searching terms included "weight loss supplements", "toxicity", "green tea extract", "orlistan", "locaserin", "naltrexone", "bupropion" and "liraglutide". The titles and abstracts were screened for possible inclusion in this review. The full texts and lists of references were screened as well to obtain more information.

Results and discussion

Drugs pulled off the market

Treatments for obesity in the past have had limited success. Thyroid hormones were used as early as 1893, but excess use caused several toxicities.[45] Amphetamines became popular in the 1930s, because they suppress the appetite and increase energy expenditure, but they are addictive and toxic.[1] They increase CNS dopamine, norepinephrine and serotonin activities. In fact, Japanese and German soldiers in World War II were given amphetamines, which kept them awake, made them aggressive and kept them from getting hungry. The Germans remembered their experience in World War I when a lack of food at the home front led to widespread protests, riots and eventual defeat. By the late 1930s, it was found that amphetamines could be made and transported much easier than food and they suppress the appetite. Also, Adolf Hitler was given intravenous doses of methamphetamine. It is one of the most deadly and addictive drugs known.[1] However, drugs similar to amphetamines (phentermine and diethylpropion) were approved for short term use.[46] They stimulate the release of dopamine and norepinephrine, but can have serious side effects.

Drugs other than amphetamines can also be problematic.[1] A supposedly "natural" remedy, ephedrine, has caused deaths due to

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heart attacks. It was removed from the market for a while, but is now widely available. Sibutramine is an inhibitor of noradrenaline, serotonin and dopamine reuptake that was once available, but was withdrawn, due to cardiotoxicity and an increased incidence of stroke. Similarly, rimonabant blocks the cannabinoid-1 receptor, but was withdrawn due to excess toxicity.[1]

Two effective and widely used drugs, fenfluramine and dexfenfluramine, were withdrawn from the market because of cardiotoxicity.[1,40,47] They are nonselective serotonergic agonists that help to mediate satiety.[42] Other once promising weight-loss drugs that were withdrawn due to toxic side effects include aminorex and Phenylpropanolamine.[43] So, analytical methods have been developed to analyze dietary supplements for the presence of these banned drugs, as well as laxatives, narcotics, caffeine, anabolic steroids, statins and even legal, FDA-approved weight loss drugs in supplements whose labels don't include them in their lists of ingredients. The drugs that were pulled off the market are summarized in Table 1.

Table 1 Summary of drugs pulled off the market

Drug	Conclusion	Reference
Amphetamines	Addictive and toxic	1
Ephedrine	Caused deaths due to heart attacks	1
Sibutramine	Withdrawn from the market	1
Rimonabant	Withdrawn from the market	1
Fenfluramine	Withdrawn from the market due to cardiotoxicity.	1,40,47
Dexfenfluramine	Withdrawn from the market due to cardiotoxicity.	1,40,47
Aminorex	Withdrawn from the market due to toxic side effects	43
Phenylpropanolamine	Withdrawn from the market due to toxic side effects	43

Analytical methods

For adulterants to be toxic, they must be ingested at physiologically relevant concentrations.[48,49] So, methods based on high performance liquid chromatography (HPLC) with UV detection can be used to screen for their presence in dietary supplements.[48] When more efficient columns with smaller particle sizes are used, the method is called ultra-high performance LC or UPLC.[1] UPLC with diode array UV detection was used to analyze weight loss supplements for anorectics (sibutramine, rimonabant, fenfluramine, amfepramone, phentermine) used to reduce appetite, stimulants (amphetamine, ephedrine, metformin, synephrine, caffeine, yohimbine) used to induce temporary improvements in either mental or physical function, antidepressants (phenobarbital, fluoxetine, penfluridol) used to alleviate anxiety disorders, laxatives (phenolphthalein) used to raise intestinal transit, diuretics (bumetanide, furosemide, spironolactone, triamterene, althiazide) used to increase loss of water, and also vitamins (nicotinamide) and amino acids.[50] Another method used thin layer chromatography (TLC) and surface-enhanced Raman scattering (SERS) to identify adulterants.[49] It had a limit of detection of 1%, which is considered to be the smallest amount of adulterant which can have significant pharmaceutical effects or toxicity.[49] Others used capillary zone electrophoresis with capacitively coupled contactless conductivity detection to detect furosemide, hydrochlorothiazide, chlorthalidone and amiloride (diuretics), phenolphthalein (laxative), amfepramone (anorexic) and fluoxetine and paroxetine (antidepressants).[51]

However, HPLC, UPLC and TLC with UV or SERS detection can only identify known compounds like 1,3-dimethylamylamine (DMAA), which was recently banned by the FDA.[52] A DMMA standard was used in the analyses.[52] It was first approved in 1948 as a nasal decongestant, but was withdrawn from the US market over 40years ago.[52,53] It was reintroduced in 2006 as a dietary supplement ingredient and sold in sports and weight loss supplements with over $100million in sales in 2010 alone.[53] However, concerns about its toxic side effects led regulatory agencies in the USA, the UK, the Netherlands, Brazil, and elsewhere to ban or pressure manufacturers to remove DMAA from supplements.[52] So, unscrupulous vendors have started selling supplements that contain a synthetic analogue, 1,3-dimethylbutylamine (DMBA), which was identified by ultra-high performance liquid chromatography (UHPLC) coupled to mass spectrometry (UPLC-MS).[52]

An LC can also be coupled to an MS.[1] Sibutramine was quantified by LC coupled to a MS that uses electrospray ionization (ESI) in ESI-MS/MS.[54] That is, ESI is a soft ionization technique that can be used to produce ions that can be fragmented to produce the mass spectrum of a mass spectrum, or MS-MS.[1] LC-MS/MS was also used to analyze dietary supplements for 28 specific narcotic adulterants.[55] It was also used to detect bisacodyl, desmethylsibutramine, didesmethylsibutramine, ephedrine, fluoxetine, pseudoephedrine, senoside A, sennoside B and sibutramine.[56] A quadrupole time of flight mass spectrometer (LC/QTOF-MS) was used in the MS/MS mode to detect and quantify the major active ingredient (yohimbine) in yohimbe.[16] Another group used not just LC-MS/MS but also gas chromatography coupled to MS (GC-MS) to identify and quantify sibutramine, phenolphthalein, bumetanide, phenytoin, caffeine pseudoephedrine, theobromine and amfepramone in herbal weight loss supplements.[57] For more rapid screening, a portable ion mobility spectrometer can be used to detect sibutramine.[58] Another approach is to use immunochromatographic assays in commercially available kits.[11] It was used to identify thyroid hormones and the illegal drug PCP (also known as angel dust) in imported herbal weight loss supplements.[11]

For those who have a nuclear magnetic resonance (NMR) spectrometer, there is this option for analyzing supplements.[59,60] Unlike UPLC with either UV or MS/MS detection, NMR is capable of qualitative and semi-quantitative analysis without the need for standards.[32,59,60] That is, NMR, UV and MS/MS measure the interactions between electromagnetic energy and matter. In NMR, one

measures the absorption of radio frequencies (RF) by nuclei that are present in a strong magnetic field, while UC measures the absorbance of UV energy and MS/MS measures the ion intensity, or amount of ions that reach a MS detector as fragments of a primary ion. Different compounds have different UV absorptivities and produce different ion intensities in MS, so standards are required for quantification. On the other hand, all the hydrogens in a compound will absorb the same amounts of RF energy in a 1H-NMR spectrum, regardless of the compound. Even though the term absorptivity is not used in NMR spectroscopy, the concept is applicable. If the 1H-NMR spectrum is acquired properly, with sufficient time delays between broadband RF pulses, all of the hydrogens will have the same tendency to absorb the RF energy. So, the signals or peaks that appear in a 1H-NMR spectrum will have integrals (peak areas) that are directly proportional to their abundance.

So, the areas (integrals) of signals due to the four different hydrogens in caffeine will be almost identical and have chemical shifts of 3.30, 3.36, 3.72 and 7.98ppm.[59] On the other hand, the two $–CH_3$ groups (six hydrogens) and one $–CH_2$- group in β-hydroxy-β-methyl butyrate will produce signals whose integrals are in a ratio of 3:1. The chemical shifts will depend on the pH and solvent, with the calcium salt of β-hydroxy-β-methyl butyrate in D2O being different from those of β-hydroxy-β-methyl butyric acid in CDCl3. So, a method was developed in which dietary supplements were first extracted with ethanol and then mixed with water and D_2O in a phosphate buffer at pH 7.4.[59] Since the normal standard for setting 0.00ppm (trimethylsilane, TMS) is not soluble in water, 0.1% 3-(trimethylsilyl)-propionic acid-d4 (TSP) was included in the mixture and it was used to set the chemical shift scale and as an internal standard for semi-quantitative analysis.[59] Chemical shifts that can be used to identify 53 different compounds were reported.[59] Subsequently, the results of quantifying nine of these compounds in dietary supplements were compared for the method that used TSP vs. calibration standards.[60] The results were quite close to each other.[60] Moreover, 1H-NMR is a faster method than LC-MS/MS.[60]

Current prescription drugs

There are five drugs that are FDA approved for weight loss as additions to reduced calorie diets and physical activity. They are orlistat (Xenical® or Alli when sold over-the-counter), lorcaserin (BELVIQ®), phentermine plus extended-release topiramate (Qsymia®), naltrexone plus bupropion (Contrave®) and liraglutide (Saxenda®). Unlike dietary supplements, they were all developed in research programs that were conducted through good laboratory practices (GLP) and manufactured by current good manufacturing practices (cGMP). So, they have been shown to be safe and effective. Moreover, every step in the manufacturing process is monitored and documented to ensure the purity of the drugs. Finally, post-market monitoring of potential adverse side effects is required.

Orlistat is the hydrogenated derivative of lipstatin, a lipase inhibitor that is used to treat dyslipidemia.[37] By inhibiting the hydrolysis of fatty acyls groups in triglycerides, orlistat reduces the amount of free fatty acids taken up by the intestines.[37] The main side effects (diarrhea and flatulence) are due to the increased amount of undigested fat.[37] After sibutramine was removed from the market, orlistat was the only FDA-approved drug for weight loss.[41] By 2012, though, the FDA had approved two more drugs for weight loss: lorcaserin (BELVIQ®) and phentermine plus extended-release topiramate (Qsymia®).[43] Then, in 2014, a combination of bupropion and naltrexone (Contrave®) in extended release capsules was also approved by the FDA.[61] Finally, in December, 2014, the FDA approved liraglutide (Saxenda®).[62]

Lorcaserin is a 5-HT2C receptor agonist that was discovered after doing a structure-activity relationship (SAR) analysis of a set of compounds that contain a 3-benazepine structural motif.[63] This is bicyclic system that was based on the arylethylamine structure that is in serotonin, also known as 5-hydroxytryptamine (5-HT) and other agonists. The intramolecular Heck reaction was conducted on a series of readily available substituted phenethylamines to synthesize the different compounds.[63] Activated 5-HT2C receptors decrease food intake through the proopiomelanocortin system of neurons.[64] In a clinical trial, 47.5% of the subjects who received 10mg lorcaserin once daily lost 5% or more of their body weight. All of them also went through diet and exercise counseling. Unlike the nonselective 5-HT agonists, fenfluramine and dexfenfluramine, lorcaserin did not cause valvulopathy or any other serious side effects.[64]

Qsymia® is an extended-release capsule that contains a relatively low dose of phentermine and topiramate.[43] It is approved for weight management in people with at least one co-morbidity (such as hypertension) and with a body mass index (BMI)≥27kg/m^2 and weight loss for those with BMI≥30kg/m^2. As mentioned earlier, phentermine is a selective 5-HT2C agonist. That is, it prevents the binding of 5-HT to the 5-HT2C receptor, but does not affect its binding to other 5-HT receptors. Topiramate is an anticonvulsant that was first synthesized in an attempt to discover good inhibitors of an important enzyme in gluconeogenesis, fructose-1,6-diphosphate.[65] It was not a good inhibitor, but its structure includes an O-sulfamate moiety that resembles the sulfonamide in other anticonvulsants that were already known. So, it was tested in an animal model and did so well that it eventually received FDA approval.

A recent article compared lorcaserin, naltrexone plus topiramate and naltrexone.[66] Lorcaserin and naltrexone are classified as Category IV by the U.S. Drug Enforcement Agency because of their potential for abuse, but the combination of naltrexone plus topiramate has not. All three of these are contraindicated in pregnant women. The combination of naltrexone plus topiramate has additional contraindications, including a warning in bold on the box that warns about the risk of suicides, as do all other antidepressants. Lorcaserin is taken twice daily and does not require titration. The combination of naltrexone plus topiramate does require titration and is taken once daily. There is also a long list of drug interactions for all three products.[66] Contraindications for naltrexone and bupropion include uncontrolled hypertension, seizures, anorexia nervosa, bulimia, abrupt discontinuation of consumption of alcohol, benzodiazepines, barbituates and antiepileptic drugs, use of other products containing bupropion, chronic opioid use, during or within 14days of taking monoamine oxidase inhibitors, pregnancy or known allergies to any of the ingredients.[66] Contraindications for phenteramine plus topiramate include pregnancy, glaucoma, hyperthyroidism, during or within 14days of taking monoamine oxidase inhibitors, known hypersensitivity or idiosyncrasy to sympathomimetic amines.[66] Pregnacy is the only contraindication for lorcaserin.[66]

Liraglutide is the most recently FDA-approved drug for weight management.[67] It had already been approved at doses up to 1.8mg for treating type-2 diabetes.[68] A clinical trial showed that doses up to 3.0mg per day were safe and effective when given as an adjunct to diet and exercise to subjects who were obese, but didn't have type-2 diabetes.[68] It not only helped subjects maintain an average weight loss of 7.8kg over two years, but it also caused a decrease in body fat (15.4%). Moreover, the two-year prevalence of prediabetes and metabolic syndrome decreased by 52 and 59% respectively. Blood pressure and dyslipidemia also decreased.[68] This was followed by a Phase III clinical trial that confirmed the safety and efficacy of

liraglutide.[69] More recently, it has been shown that lorcaserin can reduce the severity of sleep apnea as well as body weight in obese adults.[70] It can also improve cardiovascular risk factors.[71]

Liraglutide is an analogue of glucagon-like peptide 1, or GLP-1.[68,71,72] GLP-1 is a hormone that is secreted by L-cells in the intestines after eating.[71] It stimulates insulin secretion while decreases glucagon production, resulting in less biosynthesis of glucose in the liver. GLP-1 also slows gastrointestinal motility and increases satiety. However, it is rapidly hydrolyzed in a reaction catalyzed by dipeptidyl peptidase-4 (DPP-4). So, recombinant DNA (rDNA) can be used to make analogues of GLP-1 that have different amino acids in them, making them resistant to DPP-4 degradation. So, liraglutide is a GLP-1 agonist in which amino acid 34 is changed from arginine to lysine and a palmitoyl (C-16) group is attached through a glutamyl spacer. This makes liraglutide resistant to DPP-4 degradation and slows its absorption from subcutaneous tissue.[71] Since most obese people have tried losing weight several times, liraglutide is especially useful in weight management.[72] That is, after losing weight, there is a decrease in the concentration in the blood of the appetite-suppressing hormone leptin that is secreted by adipose tissue. However, obese people are resistant to leptin. They have a higher concentration of leptin when fasting without the appetite-suppressing activity. So, leptin can be thought of as an anti-fasting signal. In addition, peptide YY is released by the ileum and colon in response to eating food. It exists in the blood in two forms: the intact peptide YY and amino acids 3-36 of YY, or PYY3-36.[73] In a recent study, it was shown that liraglutide can inhibit the increase in the concentration of free leptin receptor in blood plasma and cause an increase in PYY3-36, thus preventing a gain of the weight that was lost.[72] The prescription drugs for maintaining weight loss are summarized in Table 2.

Table 2 Summary of prescription drugs for maintaining weight loss

Drug	Conclusions	References
Orlistat	Reduces the amount of free fatty acids taken up by the intestines.	37
Lorcaserin	Decrease food intake through the proopiomelanocortin system of neurons.	64
Phentermine	For Weight Management	65
Diethylpropion	For Weight Management	46
Phentermine plus extended-release topiramate	For weight management in people with at least one co-morbidity (such as hypertension) and with a body mass index (BMI)≥27kg/m^2 and weight loss for those with BMI≥30kg/m^2.	43
Naltrexone plus bupropion	Maintain weight loss, but contraindicated in pregnant women.	66
Liraglutide	Maintain an average weight loss of 7.8kg over two years, but it also caused a decrease in body fat.	67–71

Conclusion

In conclusion, there is no dietary supplement or prescription drug that can cause weight loss safely and effectively. Moreover, some dietary supplements have been found to be adulterated with banned prescription drugs as well as narcotics, stimulants, antidepressants, anorectics, laxatives and diuretics. There are several analytical methods, including LC-MS/MS and NMR that can be used to analyze dietary supplements for adulterants. Such methods can be used to detect and quantify them at physiologically relevant concentrations of >1%. Even though many supplements don't contain any of these potentially deadly adulterants, many do contain caffeine and/or green tea extract at such high concentrations that they can also be quite toxic. On the other hand, there are five prescription drugs that are FDA-approved as an adjunct to counseling, diet and exercise for maintaining weight loss. They are orlistat (Xenical® or Alli when sold over-the-counter), lorcaserin (BELVIQ®), phentermine plus extended-release topiramate (Qsymia®), naltrexone plus bupropion (Contrave®) and liraglutide (Saxenda®). Unlike dietary supplements, they were all developed in research programs that were conducted through good laboratory practices (GLP) and manufactured by current good manufacturing practices (cGMP). So, they have been shown to be safe and effective. Moreover, every step in the manufacturing process is monitored and documented to ensure the purity of the drugs and post-market monitoring of potential adverse side effects is required. Finally, physicians should warn their patients about the dangers of taking dietary supplements for weight loss, not just because they may be toxic, but also because they can cause them to flunk drug tests. They should also tell their patients to inform them about any dietary supplement that they take – be it for weight loss or anything else. They should also give their patients positive feedback and congratulations when they lose just a few kg. Finally, they should tell their patients to report any adverse side effects to them immediately when taking prescription drugs, so they can inform the pharmaceutical companies that made the prescription drugs. This article should not be taken as reflecting FDA policy or regulations.

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Conflict of interest

The author declares no conflict of interest.

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