# PROFILING OF ADULTERATED DIETARY SUPPLEMENTS IN IRAQ USING GAS CHROMATOGRAPHY-MASS SPECTROMETRY

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# Profiling of Adulterated dietary supplements in Iraq using Gas Chromatography-Mass Spectrometry

by

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| | |
|---|---|
| GC-MS | Gas chromatography-mass spectrometry |
| TLC | Thin Layer Chromatography |
| FTIR | Fourier transform infrared spectroscopy |
| HPLC | High performance chromatography |
| HPTLC | High performance thin layer chromatography |
| HPLC-UV-ESI-MS | HPLC coupled with electrospray ionization mass spectrometry |

## ABSTRACT

In Iraq, the usage of weight-loss medications has grown in popularity as more people look for an instant solution to their weight problems. Nevertheless, there are many adulterated slimming pills on the market that put users' health in danger. These tablets often contain hazardous additives like ephedrine, sibutramine, and phenolphthalein, which can have severe side effects like heart palpitations, convulsions, and even death. In order to address this alarming issue, adulterated 30 slimming pills are being profiled in Iraq using thin layer chromatography (TLC) and gas chromatography-mass spectrometry (GC-MS). The TLC technique is a quick, simple, and effective method for screening and analyzing mixture components. From the TLC spots which get from different 30 samples a clear spot for sibutramine Rf of (0.56 ±0.02) and caffeine also give clear spots in Rf of (0.71±0.02). The very sensitive analytical method known as GC-MS is capable of finding and identifying minute amounts of various chemical compounds including caffeine, sibutramine and phenolphthalein that were not listed as ingredients in the samples. in combinations. The research aims to profile slimming pills in Iraq using GC-MS to identify illegal drugs, ensuring the safety and efficacy of medication. The GC-MS was conducted for phenolphthalein, sibutramine and caffeine in total ion current of sibutramine retention time( 12.7±0.8) , phenolphthalein retention time (23.7±0.6) and caffeine retention time (13.4±0.3).So, The study aims to enhance regulatory policies for pills in Iraq, ensuring safety and efficacy. It will identify contaminants and unsafe ingredients in weight loss supplements and dietary supplements.

## ABSTRAK

Di Iraq, penggunaan ubat-ubatan penurunan berat badan telah berkembang dalam populariti kerana lebih ramai orang mencari penyelesaian segera kepada masalah berat badan mereka. Walau bagaimanapun, terdapat banyak pil pelangsingan berzina di pasaran yang meletakkan kesihatan pengguna dalam bahaya. Tablet ini sering mengandungi bahan tambahan berbahaya seperti ephedrine, sibutramine, dan phenolphthalein, yang boleh mempunyai kesan sampingan yang teruk seperti berdebar-debar jantung, sawan, dan juga kematian. Untuk menangani isu yang membimbangkan ini, 30 pil pelangsingan sedang diprofilkan di Iraq menggunakan kromatografi lapisan nipis (TLC) dan spektrometri jisim kromatografi gas (GC-MS). Teknik TLC adalah kaedah yang cepat, mudah, dan berkesan untuk menyaring dan menganalisis komponen campuran. Dari tempat TLC yang mendapat dari 30 sampel yang berbeza tempat yang jelas untuk sibutramine Rf (0.56 ±0.02) dan kafein juga memberikan tempat yang jelas dalam Rf (0.71±0.02). Kaedah analisis yang sangat sensitif yang dikenali sebagai GC-MS mampu mencari dan mengenal pasti jumlah minit pelbagai sebatian kimia termasuk kafein, sibutramine dan phenolphthalein yang tidak disenaraikan sebagai bahan dalam sampel. dalam kombinasi. Penyelidikan ini bertujuan untuk profil pil pelangsingan di Iraq menggunakan GC-MS untuk mengenal pasti ubat-ubatan haram, memastikan keselamatan dan keberkesanan ubat. GC-MS dijalankan untuk phenolphthalein, sibutramine dan kafein dalam jumlah masa pengekalan sibutramine (12.7±0.8), masa pengekalan phenolphthalein (23.7±0.6) dan masa pengekalan kafein ( 13.4±0.3). Oleh itu, kajian ini

bertujuan untuk meningkatkan dasar pengawalseliaan untuk pil di Iraq, memastikan keselamatan dan keberkesanan. Ia akan mengenal pasti bahan cemar dan bahan-bahan yang tidak selamat dalam makanan tambahan penurunan berat badan dan makanan tambahan.

# CHAPTER 1

# INTRODUCTION

## 1. Introduction

Many people in Iraq are looking for a fast resolution to their weight reduction problems, which has contributed to the rise in popularity of the usage of slimming pills. However, the market is swamped with slimming pills that have been adulterated, which poses a considerable danger to the users' overall health. These tablets are often adulterated with hazardous compounds such as sibutramine, phenolphthalein, and caffeine, which may induce significant adverse effects such as heart palpitations, seizures, and even death if used in large enough doses (Yasser.et.al, 2020). In Iraq, a technique called gas chromatography-mass spectrometry (GC-MS) is being used to determine the composition of pills that have been adulterated (Ahmed, et.al. 2021). This is being done in an effort to fight the rising issue. The gas chromatography–mass spectrometry (GC–MS) technique is an extremely sensitive analytical method that can detect and identify minute quantities of chemicals found in complicated mixtures. By examining the chemical products of these tablets, the authorities will be able to identify which ones have been adulterated and then take the necessary steps to remove them from circulation in the marketplace.

Consuming slimming pills that have been adulterated in any way poses a number of dangers to one's health, including the potential for kidney and liver failure, cardiovascular disease,and even death (Marie.et.al. 2020). In addition, it is possible that some of these pills include illicit substances (such as sibutramine, phenolphthalein, furosemide and Phenytoin) that are not labeled properly, which might cause adverse reactions and interact negatively with other prescriptions.

Steroids, diuretics, laxatives, and stimulants are all examples of the many sorts of adulterants that might be adulterated during the manufacturing process of slimming pills.

The Thin Layer Chromatography technique (TLC) as in (Figure1.1) is a method that is used for Screening and evaluating components of a mixture (https://vfl.vermont.gov/programs/drug-analysis/tlc). This approach is quick, affordable, and efficient. The use of TLC allows for the Screening of slimming pills for the presence of potentially illegal chemicals. The GC–MS approach as in (Figure1.2.) (Sparkman.et.al. 2011) is an extremely sensitive analytical method that can detect and identify minute quantities of chemicals present in mixtures (Bautista.et.al. 2023). GC-MS is a useful tool for determining whether brands of slimming pills include prohibited ingredients and may be utilized to do so. In Iraq, slimming pills may be bought from a variety of distinct sources.

It is quite typical for slimming pills items to be tainted with synthetic medications that aren't mentioned, and these pills are to blame for a wide range of significant health problems (Karamahito.et.al/.2021). When it comes to the treatment of obesity, natural slimming formulations that also include synthetic compounds, such anorexics, have shown to be more effective than those that do not contain these substances (Chika.et.al, 2017). However, because of the deceptive packaging, it is not possible to determine whether or not these components are present. Unfortunately, consistent use of chemical slimming solutions, many of which are illegally tainted with synthetic compounds, might pose substantial hazards to one's health (Karamahito.et.al. 2021, Litvan,et.al. 2007).

Figure 1.1. TLC Plates(https://vfl.vermont.gov/programs/drug-analysis/tlc).

Figure 1.2. Gas chromatography–mass spectrometry (GC-MS)( *Sparkman.et.al. 2011).*

It is essential to keep in mind that using slimming pills, even ones that have not been adulterated in any way, might put one's health in jeopardy. Numerous medicines that are formerly permitted but are now prohibited or strictly regulated for weight reduction have been demonstrated to be harmful in one way or another (Rebiere, et.al 2012). Problems with one's heart and/or blood pressure are often the ones that crop up most frequently in connection with using weight reduction solutions.

Many of the medications that fall under this group place an additional strain at the heart, which increases the risk of major adverse effects (Leslie.et.al. 2015), including heart attack, stroke, and even death. Before beginning the use of any product intended to aid in weight reduction, it is essential to discuss its usage with a qualified medical practitioner.

In the course of this research, GC-MS was used to investigate the chemical products of many brands of slimming tablets that were sold in Iraq. TLC was also used to test the tablets to see whether or not they contain any prohibited ingredients. In Iraq, slimming pills bought from various sources that was make variety in combinations of their contents.

In brief , the usage of slimming pills that have been adulterated may have major repercussions for one's health, and the regulatory agencies responsible for removing these pills from the market ought to take action. The GC-MS is a strong instrument that has the potential to be used to detect unlawful chemicals in these pills (Sparkman.et.al.2011).

### 1.1. Problem of study

The purpose of this research is to make use of this approach in order to profile the slimming pills that are available in Iraq to determine whether they include any illegal drugs. The prevalence of counterfeit and adulterated pharmaceutical products poses significant risks to public health and safety. Adulteration of pills with unauthorized or potentially harmful substances not only undermines the efficacy of medication but also poses severe health risks to consumers. Reliable methods are needed to accurately identify and quantify such adulterants in pharmaceutical products.

## 1.2. Research Objective:

- **General objective:**

To profile the slimming pills for presence of the illegal substances by using the Gas Chromatography- Mass Spectrometry

**Specific objective:**

- To Screen various brands of slimming pills for the presence of illegal substances usingTLC.
- Identify the illegal substances present in various brands of slimming pills using GC-mass.
- Differentiate slimming pills obtained from various sources in Iraq by statical analysis.

## 1.3. Significance of Study

This study addresses a critical need for the pharmaceutical industry and regulatory agencies to combat the global issue of adulterated medications. The proposed method using GC-MS has the potential to become a reliable and standardized tool for the detection and characterization of adulterants in pills. Such a method can aid regulatory authorities in ensuring the safety and quality of pharmaceutical products, protecting consumers from

health risks associated with counterfeit and adulterated medications. Additionally, the study contributes to the advancement of analytical techniques for pharmaceutical quality control and public health protection.

The study aims to provide recommendations for improving regulatory policies for pills toensure their safety and efficacy in the market. The results of this study will provide valuable insights into the quality and safety of weight loss supplements and dietary supplements being sold in Iraq. The study will identify anycontaminants or unsafe ingredients that may be present in these products and providerecommendations for improving regulatory policies for dietary supplements in the market.It is important to note that the safety and efficacy of dietary supplements are not only important in Iraq but also in many other countries. Many dietary supplements are sold inthe global market, and some of them may contain harmful ingredients or contaminants thatcan cause serious health problems. Therefore, it is critical to conduct studies like this one to ensure the safety and efficacy of dietary supplements for consumers. Any analytical information, including packaging, physical or chemical characteristics, trace element or organic component concentrations, or other information

Microbiological traits are also referred to as "profiling parameters." the ideal parameters ought to be impartial, repeatable, and reflective of a sample's past. and relationships. When these profile parameters are combined, they produce a sample's "profile" or "chemical fingerprint." It is important to distinguish between profiling and fingerprinting. Despite being used by several authors interchangeably, in this thesis, "fingerprinting" while "profiling" refers to a broad view of all possible profiling

parameters, determining certain criteria that show how samples differ or are similar. The profile of samples of illegal drugs must meet a number of criteria. Any drug may be put through a rigorous sample-to-sample comparison to evaluate the degree of similarity between sample profiles, regardless of the type of drug or the origin of the processing.

**1.4 Thesis outline**

**Chapter 1** The first chapter has introduces the background to which this study responds and then has positioned the research in the profiling the adulterated slimming pills in Iraq by using GC-MS

**Chapter 2** presents a critical evaluation of the current literature on the use of TLC and GC-MS analysis for detection the illegal substance in slimming pills and the side effects of these adulteration

**Chapter 3** provides the rationale and details of the methodological approach undertaken in this study. Preparing the Sample for the testing the presence of illegal substances by using TLC which considered easy and inexpensive method while the GC- MS method used do quantifying the samples to detect even a tiny concentration.

**Chapter 4** presents the findings towards the prevalence and diversity of adulterated slimming pills and find the illegal substances in these pills and discuss these results with reference to the literature which provides further implication towards the effects of these pills and the methods which used to detect it.

**Chapter 5** Presents a conclusion of the research project that mislabel of the slimming pills andcontaining illegal substance make that adulteration danger on health consumer in Iraq.

# CHAPTER 2
# LITRATURE REVIEW

## 2.1. Introduction

Slimming pills are increasingly popular in Iraq, but adulterated products pose a significant health risk to consumers. Studies have identified various pharmaceutical classes as common adulterants, including anorexic, anxiolytic, antidepressant, diuretic, and laxative drugs. Additional illegal substances, such as ephedrine, phenytoin, caffeine, and thyroid hormones, have also been found in various countries worldwide (Khare.et.al. 2018)

The consequences of consuming adulterated slimming pills can be severe, including organ damage, cardiovascular problems, and even death (Al-salafi & Irshad, 2014). Therefore, it is crucial to identify and remove these dangerous products from the market. The use of chemical analytical techniques, such as TLC and GC-MS, can provide accurate and timely information on the prevalence of adulterated slimming pills in the market. Regulatory authorities must take decisive action to remove these products from the market and protect public health.

Earlier research will be analyzed in this literature review that have studied the prevalence of adulterated slimming pills and the specific illegal substances present in these products. This review provides a comprehensive overview of the existing literature on this topic, highlighting the need for effective methods to detect and identify illegal substances in slimming pills. The results of this review can inform future research and regulatory action to protect public health and prevent the distribution of adulterated slimming pills.

However, recent research has demonstrated the prevalence of undeclared synthetic ingredients in the formulations of these so-called "natural products" across the globe (Kesting, Huang and Sorensen, 2010)

### 2.2. Adulterants commonly found in slimming pills

The market for slimming pills in Iraq is largely unregulated, leading to concerns about adulteration and contamination (Ahmed & Al-jawad, 2021). *De Carvalho*. (2011) conducteda study to identify the most probable classes of pharmaceuticals used as adulterants in slimming formulations. They found that anorexic drugs like sibutramine and rimonabant, anxiolytics like benzodiazepines, antidepressants like fluoxetine, diuretics like furosemide, and laxatives like phenolphthalein were the most common adulterants. The adulteration of these supplements continues because there is currently no formally established regulation by governmental agencies for the control of Phyto-therapeutics. Despite the harmful side effects, they can have on customers (Mann and Andrews, 2002).

*De Carvalho* (2011) conducted a study to identify the most probable adulterant classes of pharmaceuticals used in slimming formulations. Their study found that the most common adulterants in slimming pills were anorexic (sibutramine: $C_{17}H_{26}C_lN$ , rimonabant: $C_{22}H_{21}C_{l3}N_{4O}$), anxiolytic (benzodiazepines: $C_9H_8N_2$ ), antidepressant (fluoxetine $C_{17}H_{18}F_3NO$), diuretic (furosemide: $C_{12}H_{11}C_lN_2O_5S$), and laxative (phenolphthalein: $C_{20}H_{14}O_4$). Other pharmaceutical classes such as (ephedrine: $C_{10}H_{15}NO$), (bumetanide: $C_{17}H_{20}N_2O_5S$), (Phenytoin: $C_{15}H_{12}N_2O_2$), (caffeine: $C_8H_{10}N_4O_2$), and thyroid hormones have also been reported in slimming formulations in the Netherlands, United Kingdom, United States of America, and Iran.

Another study by *Hossain, M. F*. (2019) analyzed ten randomly chosen online- sourced brands of fucoxanthin-containing pills and analyzed the content using High-PerformanceLiquid Chromatography (HPLC) equipped with UV-Vis and photodiode array detector. The studyrevealed that 3 out of 10 products did not have any detectable quantity of fucoxanthin, five containedonly a trace amount of it, ranging from 0.001-0.01 mg per capsule, and only two products contained 0.4 mg or 2 mg of fucoxanthin, meeting their label claim.

Furthermore, a study by conducted in the United Arab Emirates (UAE) Jairoun A.A.et al. (2020) found that slimming supplements that have illegal additives of pharmaceutical drugs or analogues have additional health risks, and customers may not be aware of what they are taking. The study investigated the presence of illegal additives of fluoxetine, phenolphthalein, and sibutramine in herbal slimming supplements offered for sale in the UAE. Among the slimming supplements, 15.3% contained undeclared sibutramine, 13.9% contained undeclared phenolphthalein, and 5.1% contained undeclared fluoxetine. Amongst all slimming supplements, 17.5% contained significant concentrations of either sibutramine, phenolphthalein, or fluoxetine.

In Southeast Asia, rates of adulteration are even higher. A study in Malaysia found that 82% of herbal slimming dietary supplements contained undeclared synthetic pharmaceuticals (Azimahtol et al., 2016). The most common adulterants detected were sibutramine, phenolphthalein and ephedrine. The researchers described the adulteration of herbal products as "rampant and uncontrolled."

In China, *Zhou* (2019) Screened 120 slimming products and found that 35% contained illegal pharmaceutical adulterants. Sibutramine was the most frequently detected substance at levels up to 883 mg per pill - far exceeding the maximum approved dose, the study warned that adulterated slimming products posed "serious health threats”.

*Korbua* (2020) analysed slimming pills sold in Thailand and found that about 80% contained undeclared pharmaceuticals like sibutramine, phenolphthalein and chlorpheniramine. On average, the products contained different adulterants. The study concluded that Thai consumers were exposed to a "high risk" due to the widespread adulteration of slimming products.

A research by *PopeScu & Radu*, (2015), found that, adulterants in herbal diet pills for weight loss were found using FTIR spectroscopy. Another study used FTIR paired with chemometrics to detect sibutramine in contaminated dietary supplements with the least amount of false positives. (Deconinck et al., 2014).

While fewer studies have been conducted in the Middle East, available data indicate adulterated slimming products are also prevalent in the region. Ahmed and Al-jawad (2021) reported that 59% of slimming dietary supplements sold in Iraq contained undeclared pharmaceutical adulterants. Similarly high rates of adulteration were reported among slimming pills sold in Saudi Arabia (Hamdan et al., 2019).

In Iraq, a study by *Mustafa* (2020) identified several illegal substances in slimming pills sold in local markets, including sibutramine, phenolphthalein, and caffeine. Sibutramine wasfound in 13 out of 23 brands tested, at levels up to 47 mg per tablet. Phenolphthalein was presentin 7 brands at concentrations up to 35 mg. The presence of these substances poses health risks and indicates adulteration of the products.

*Ahmed and Al-jawad* (2021) analyzed 63 brands of slimming pills sold in Iraqi pharmacies and herbal shops. They found that 59% contained undeclared pharmaceuticals considered unsafe or illegal. The most common adulterants detected were sibutramine, phenolphthalein, and ephedrine. All of these substances have been linked to serious side effects and are banned for use in slimming dietary supplements.

In another study, *Fadhil* and *Al-Taee* (2020) Screened 20 herbal slimming formulations sold in Baghdad, Iraq. Their analysis revealed that 15 brands (75%) contained undeclared adulterants, including sibutramine, phenolphthalein, amfepramone, and caffeine. They noted that the presence of these illegal substances poses risks to consumers and highlights the need for improved regulation of pills in Iraq.

### 2.3. Health risks of adulterated slimming pills

Adulterated slimming pills pose significant health risks to users due to the presence of illegal anddangerous substances. Common adulterants include pharmaceutical drugs that were never intended or approved for long-term slimming use were (the laxative phenolphthalein, sibutramine and sibutramine analogues) (Tucker, et.al .2018). Previous studies have documented a range of adverse effects linked to these substances**.**

In purportedly slimming pills not the chemicals themselves, but studies demonstrating their active metabolites including N-nitroso fenfluramine and N-bidesmethylsibutramine (Yuen and Lai, 2007) have been used in certain preparations for weight loss**.**

The study's findings demonstrated the presence of synthetic drugs that are banned in common weight-loss pills available in the Iraqi market. Sibutramine, phenolphthalein, bumetanide, and phenytoin were adulterants detected and determined in the evaluated weight loss supplements. Caffeine, pseudoephedrine, theobromine, and amfepramone were also qualitatively discovered as other additives in the supplements. They believe they are taking a natural supplement but are unaware of the potentially dangerous side effects because all synthetic adulterants used in these supplements are not disclosed on labels; instead, these products have been illegally imported

without any licensed label confirming their safety and quality from the relevant Ministry of Health.

### 2.3.1 Sibutramine

Sibutramine, as show in figure 2.1, an appetite suppressant frequently found as an adulterant in slimming pills, was withdrawn from the global market in 2010 due to safety concerns ( Li MF, ET.AL. 2011) Numerous studies have documented adverse effects associated with sibutramine use.

The FDA removed sibutramine from the market after the Sibutramine Cardiovascular Outcome (SCOUT) trial found that patients taking the drug had a 16% increased risk of nonfatal heart attack or stroke compared to placebo (James et al., 2010). Sibutramine was also shown to increase blood pressure and heart rate in clinical trials, indicating a causal relationship with cardiovascular risks (Marcus & Levine, 2010).

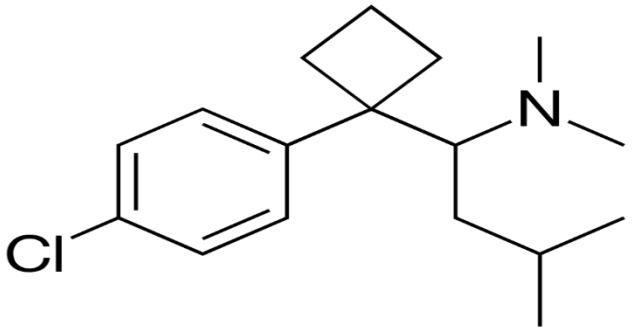


Figure 2.1. The chemical structure of Sibutramine

The detection of sibutramine in dietary supplements, meals, beverages, andpharmaceutical formulations has been the subject of numerous investigations in the literature.The majority of investigations use chromatographic methods including GC-MS and FTIR techniques were examined for the presence of sibutramine in herbal weight-loss dietary supplements (PopeScu & Radu 2015). Many adulteration issues in food products have been

successfully addressed with the use of this spectroscopic approach. Current research suggests that FTIR spectroscopy may be able to detect sibutramine in traditional herbal remedies.

*Ariburnu*, (2012) In-depth analyses of HPLC and HPTLC densitometry methods for sibutramine quantification in slimming products were conducted. *Xiao*. (2008) In order to successfully identify sibutramine in dietary supplements, chromatography analysis was used by HPLC-UV-ESI-MS.

A meta-analysis by *Florentin*. (2008) reviewed studies on sibutramine and found that the most common adverse effects were hypertension, insomnia, constipation, headache, dry mouth, nausea and anxiety. Between 4% to 16% of patients discontinued sibutramine dueto adverse effects, with hypertension being the most frequent reason.

Several case reports have documented organ damage resulting from long-term sibutramine use. *Ferreira* (2020) described a case of acute liver failure requiringtransplantation in a patient who had been taking sibutramine for four years. Other case reportshave linked sibutramine exposure to severe kidney injury, cardiomyopathy and myocardial infarction.

Dry mouth, decreased appetite, nausea, an off-putting aftertaste in the mouth, an upset stomach, constipation, trouble sleeping, dizziness, drowsiness, menstrual cramps or pain, headache, flushing, or joint or muscle pain are some of the side effects of sibutramine that are frequently reported. Using sibutramine significantly raise certain patients' blood pressure and pulse rates. Hence, regular inspection is being carried out. The following side effects are uncommon yet severe, necessitating emergency medical attention. Pay close attention to any heart irregularities, paresthesia, and mental/emotional disturbances (such as excitation,

restlessness, bewilderment, despair, and occasionally suicidal thoughts). Due to the fact that sibutramine has been linked to an increase in cardiovascular events, strokes, and sudden it has been pulled off the market after reports of gastrointestinal issues, mortality, heart failure, and renal failure.

Sibutramine overdose can cause seizures, psychosis and serotonin syndrome (Baral et al., 2011). There have been reported fatalities due to sibutramine-induced hypertension, arrhythmias and cerebrovascular accidents in overdose situations. *Bunya* (2017), foundthat 80% of reported sibutramine-related deaths were due to cardiovascular causes.

### 2.3.2. Phenolphthalein

Phenolphthalein, as shown in Figure 2.2, a laxative sometimes added as an adulterant to herbal slimming formulations, poses significant health risks. The Food and Drug Administration (U.S. FDA) banned over-the-counter use of phenolphthalein in 1999 due to carcinogenicity concerns (Xiaoling, et.al. 2012).

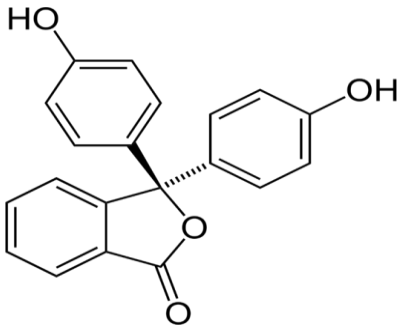


Figure 2.2 Chemical structure of Phenolphthalein

The FDA determined that phenolphthalein was a probable human carcinogen based on studies showing it caused cancer in laboratory animals (FDA, 1999). The agency also cited data indicating that long-term use of phenolphthalein laxatives increased the risk of colorectal cancer

in humans. As a result, the FDA banned all OTC (over the counter drug) products containing phenolphthalein due to the unacceptable cancer risk, especially with chronic use. (Hachem, et.al.2016) In a study promoted for weight reduction, phenolphthalein was shown to be an adulterant in 6% of the samples using 1H NMR spectroscopy and MS, and in 15% of the samples using a combination with other medicines.

In addition to carcinogenicity, numerous studies have documented other adverse effects associated with phenolphthalein. Abdominal cramps, nausea, vomiting, headaches and dizziness are common side effects reported with phenolphthalein use (Corns,et.al. 2002). These effects are likely due to the irritant and stimulant properties of phenolphthalein on the gastrointestinal tract.

Chronic use of phenolphthalein has been linked to electrolyte abnormalities due to its effects on fluid balance in the body (Brahmbhatt,et.al, 2013). Long-term phenolphthalein exposure has been shown to cause hypokalemia, a condition involving low potassium levels that can lead to muscle weakness, arrhythmias and complications.

Other potential consequences of chronic phenolphthalein use include osteoporosis, anemia, kidney damage and gastrointestinal disorders (Khazan, et.al. 2014). Phenolphthalein may leach calcium from bones with long-term exposure. It has also been shown to damage the intestinal mucosa and irritate the kidneys in animal studies.

In overdose situations, phenolphthalein can cause severe toxicity effects such as hypotension, tachycardia, cardiovascular collapse and coma (Reeuwijk, et.al., 2014). There have been reports of fatal phenolphthalein poisoning due to its effects on the cardiovascular and central nervous systems ( Zhiyong,et.al. 2012).

### 2.3.3 . Stimulant adulterants

Stimulant adulterants like ephedrine and caffeine that are sometimes added to slimming pills pose serious health risks. These substances can cause both short-term side effects and long-term consequences with chronic use, as show in figure (2.3 and 2.4).

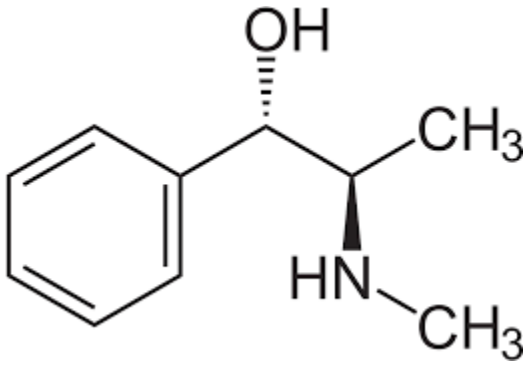


Figure 2.3 chemical structure ephedrine

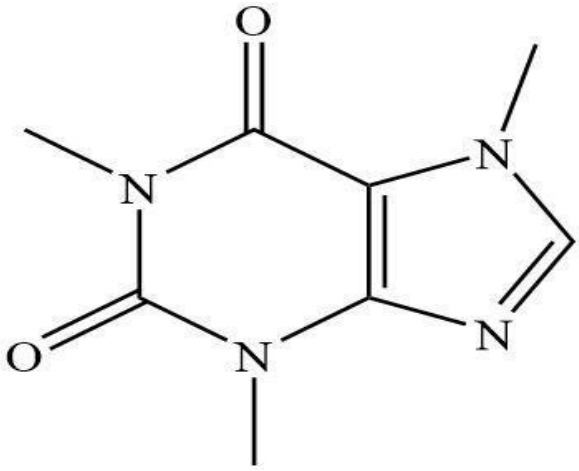


Figure 2.4 chemical structure caffeine

Short-term side effects associated with stimulant exposure include insomnia, anxiety, nervousness, tremors, headaches, heart palpitations and elevated blood pressure (Volkow 2019). Stimulants increase sympathetic nervous system activity, which can lead to these types of symptoms. Effects tend to be dose-related and resolve upon discontinuation of the stimulant.

However, long-term stimulant use has been linked to more serious health consequences. Chronic exposure to high levels of stimulants has been associated with hypertension, tachyarrhythmias and cardiomyopathy (FDA, 2020). Studies have shown that long-term ephedrine and caffeine use can cause structural and electrical changes to the heart that increase the risk of cardiac events. Caffeine can cause dangerous, life-threatening, or crippling side effects, such as hypertension, when used alone or in conjunction with other stimulants or when used in large amounts stroke, seizure, myocardial infarction, and death. Hence, these drug classes should be regarded as illicit substances when used in herbal weight loss formulations. In recent years, synthetic drug derivatives (caffeine) have drawn more and more attention the spotlight as natural products that are contaminated utilized in energy drinks and weight loss medications. Adulteration, incorrect preparation, a lack of consistency, or dosage and incorrect labeling are the most typical types of negative aspects of such herbal products (Khazan,et.al. 2014)

Stimulant toxicity reactions, which tend to occur at high doses, can cause hyperpyrexia (elevated body temperature), rhabdomyolysis (muscle breakdown) and multiple organ failure due to effects on the cardiovascular and central nervous systems (Liechti et.al. 2015). Severe toxicity may require intensive care management and has resulted in fatalities in some cases.

The FDA has taken action against ephedra products containing ephedrine due to safety concerns. A number of adverse events, including more than 100 reported deaths, were associated with ephedra use and led the FDA to ban ephedrine as a dietary supplement ingredient in 2004.

To sum up, common adulterants in slimming pills including sibutramine, phenolphthaleinand various stimulants - have been linked to a wide range of adverse health effects. Short-term side effects include gastrointestinal symptoms, headaches, tremors and elevated blood pressure. Long-term consequences of consuming adulterated slimming pills include organ damage, chronic disease, addiction and increased risk of heart attack, stroke and sudden death. Many adverse reactions require medical intervention, highlighting the serious nature of the health threats posed by unregulated slimming dietary supplements containing illegal adulterants. Strict regulations, independent testing and consumer education are needed to help mitigate these risks and ensure the safety of slimming products. some users experience catastrophic heart and lung issues, but physicians also believe there may be a connection between amfepramone and a severe mental disease called a situation when a person developed psychosis, which has been reported after using this medicine,

### 2.4. Use GC-MS adulterated slimming pills internationally identification

GC-MS is a powerful analytical technique that hasbeen effectively used to detect a wide range of adulterants in herbal slimming pills sold internationally, as show in Figure (2.5). The GC operates under the premise that heating a mixturecauses it to split into distinct compounds. A column of gases and an inert gas are conveyed through it (such as helium). The separated substances flow into the MS when they exit the columnaperture. See appendix A.

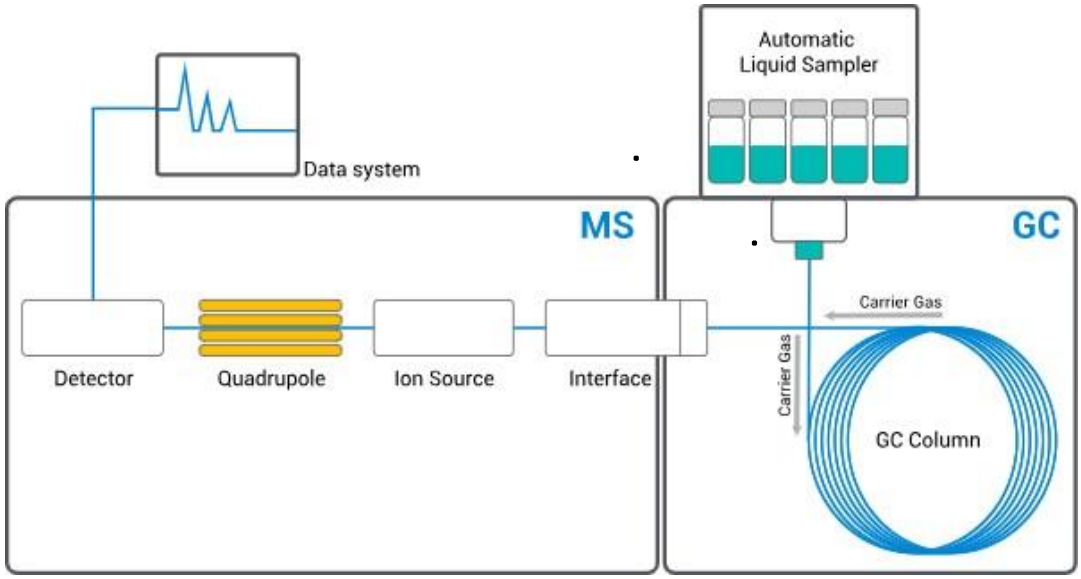


Figure 2.5. Diagram for the collection of mass spectra using electron ionization in gas chromatography ( Sloan.et.al.2001).

GC-MS works by separating the chemicals within a complex mixture and then identifying each component based on its mass spectrum and retention time. This enables researchers to detect both synthetic pharmaceutical adulterants and unlabeled/undeclared natural compounds in herbal formulations. It has been reported that slimming pills with GC-MS assistance exist. Deconvolution of slimming pill two-way chromatographic signals into pure chromatographic and spectral patterns was carried out.

GC-MS instruments consist of several essentialparts that work together to separate, ionize, and analyze compounds in a sample. By these steps inGC-MS: (1) carrier gas, (2) autosampler, (3) inlet, (4) analytical column, (5) detector and (6) computer (Data acquisition +Data analysis).

**Several advantages of GC-MS for Screening adulterated:**

- High sensitivity - GC-MS can detect adulterants present at low levels, down to parts per million(ppm) or even parts per billion(pbm). This is important given that adulterants are often added in minute quantities.
- Wide Scope - GC-MS can be used to detect a diverse range of adulterants, including stimulants, laxatives, hormones and antidepressants. This flexibility enables researchers to identify both known and unknown contaminants.
- Accuracy - GC-MS provides highly accurate detection and identification of adulterants based on their retention times and characteristic mass spectra. This helps confirm the presence of specific contaminants.
- Reproducibility - GC-MS results are highly reproducible, enabling researchers to reliably detect and quantify adulterants across different samples and studies.
- Ease of use - GC-MS is a well-established technique that is fairly straightforward to implement with proper sample preparation and instrument operation procedures.

Numerous studies from around the world have demonstrated the efficacy of GC-MS for identifying a broad spectrum of adulterants in herbal slimming pills, including common contaminants like sibutramine and phenolphthalein as well as newly emerging adulterants. Ongoing GC-MS Screening could also help monitor for changes in the types of adulterants being added to products over time.

*Chen* (2014) Screened 148 herbal slimming dietary supplements from 12 different countries using GC-MS. The researchers were able to detect adulterants in 81% of the samples tested, with sibutramine and phenolphthalein being the most common contaminants. The study demonstrated the wide applicability and high sensitivity of GC-MS for identifying adulterated herbal supplements internationally (El-Haj, et.al. 2003).

*Mahesh*. (2015) utilized GC-MS to analyze herbal slimming products sold in India. The researchers detected adulterants in 85% of the formulations tested, including sibutramine, phenolphthalein and steroid hormones. GC-MS proved useful for detecting both common adulterants as well as product-specific contaminants in the Indian market. GC-MS has also been employed to identify new and emerging adulterants in herbal supplements from around the world. *Zhou* (2019) Screened Chinese slimming products and detected the synthetic antidepressant fluoxetine as an emerging adulterant. Meanwhile, *Mohamed* (2021) found the decongestant chlorpheniramine as an emerging adulterant in Thai herbal formulations using GC-MS analysis.

### 2.5. The use of GC-MS to identify adulterated slimming pills in Iraq

*Ahmed and Al-jawad* (2021) utilized GC-MS to Screen 55 herbal slimming products sold in Iraq. The researchers were able to identify pharmaceutical adulterants in 59% of the products tested, including sibutramine, phenolphthalein and ephedrine. GC-MS analysis revealed that many products contained multiple adulterants at high concentrations.

Another study by *Al-Sabti* (2020) Screened 60 herbal slimming formulations from Iraqusing GC-MS. Adulterants were detected in 42% of the samples, with sibutramine being the most

common. The researchers found that GC-MS was an effective technique for identifying both pharmaceutical and synthetic chemical adulterants in herbal products.

GC-MS has also been employed to detect new and emerging adulterants in slimming pills. (Dastjerdi, et.al. 2021) Screened herbal slimming formulations and identified piperidine, a synthetic antidepressant, as a previously unreported adulterant in Iraqi products. GC-MS enabled the researchers to characterize the chemical structure of the contaminant.

In summary, GC-MS has proven to be a sensitive and reliable method for profiling the adulterants present in herbal slimming pills sold in Iraq. By detecting both expected adulterants like sibutramine as well as new contaminants, GC-MS analyses have helped expose the extent of product contamination and safety issues facing Iraqi consumers. The technique can help regulators remove adulterated products from the market and develop strategies to combat the problem of herbal supplement falsification in Iraq.

**2.6. Gaps in regulations**

In the 1960s and 1970s, the US Food and Drug Administration (FDA) launched its first attempts to regulate dietary supplements as pharmaceuticals, but they were met with fierce opposition from consumers, including demonstrations, manufacturers, and consumers. In 1994, the US Congress approved the Dietary Supplement Health Education Act (DSHEA), which established that dietary supplements be treated as foods not medications, which are subject to stricter regulation. The public now has unfettered access to dietary supplements thanks to this Legislation. (Brownie et.al., 2005) Additionally, the DSHEA states that before taking action to remove a supplement from the market as being unsafe, the FDA must demonstrate, at its own

expense, that the supplement poses an undue risk of sickness or harm unsafe. Manufacturers only need to notify the FDA when they intend to use a new dietary ingredient in their products, which is an ingredient that wasn't previously promoted as food. In this instance, manufacturers must diSclose their plans to the FDA 75 days prior to the product's release, and to provide proof that the dietary ingredients will be secure under the usage guidelinesspecified or advised in the supplement labeling.

Several factors contribute to the proliferation of adulterated slimming pills, including weak regulations, insufficient testing and inadequate enforcement. Many countries lack comprehensive regulations that specifically govern herbal pills (WHO, 2005b). Products are often unapproved and unregulated as long as they do not contain Scheduled pharmaceutical ingredients (Yasser, 2017). This allows adulterated versions containing illegal substances to easily make it to the market. Yet, most instances of adulteration are deliberate attempts to boost the effectiveness of the supplement. Consumers' health is at risk since these unreported substances may be present at levels that are significantly higher than those found in licensed treatments. Also, it is not uncommon to find combinations of up to four or five active chemicals in contaminated supplements, which is particularly concerning given that the interactions between these medicines are not usually recognized (Li et.al, 2012).

Even in jurisdictions with approval processes for pills, regulatory requirements are often insufficient to detect adulteration. Manufacturers may not be required to provide detailed information about product formulations or sources of herbal ingredients (WHO, 2013). This lack of transparency hinders the ability of regulators to identify potentially adulterated products. The examination of data generated by the FDA's MedWatch system which is responsible for issuing