Advances of GC-MS in the determination of adulterants in dietary supplements

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Abstract. In recent period of time, mankind has been giving more and more effort towards dietary supplements because now people are more concerned about their health. So, the availability and uses are also increased. For enhancing the frequency and effect of the dietary supplements, synthetic products like Phosphodiesterase Type 5 (PDE-5) Inhibitor, Cocaine, Fluoxetine, or some unwanted steroids are added to the supplements to enhance their market value. The consumption of these adulterated supplements has been linked to health problems and has had a negative impact on the quality and safety of dietary supplements as well as public health. To stop such dishonest practises, analytical techniques that enable quick and accurate testing of dietary supplements for the presence of synthetic drugs are required. For the determination of adulterated products in dietary supplements there are so many hyphenated techniques are available among all Gas Chromatography and Mass Spectrometry (GC-MS) is more specific and delicate because of its unique combination of Mass Spectrometry and Gas chromatography which helps in the field of Separation and structural identification of the adulterant. The role of GC-MS in the detection, quantification, conformation analysis of adulterants in dietary supplements is evaluated critically in the current review.

Keywords: Adulterants, Dietary Supplements, Food products, GC-MS, Hyphenated techniques, Quantification.

1 Introduction

Now a days, people are more conscious about their health hence they are mostly prone to take Dietary Supplements(DS) more and more(dietary-supplements n.d.; J. W. Kim et al. 2013). As per the Food Drug Administration(FDA) Dietary Supplement Health and Education Act of 1994, “A dietary supplement is a product intended for ingestion that, among other requirements, contains a “Dietary ingredient” meant to supplement the diet”(Questions and Answers on Dietary Supplements n.d.). As per the European Commission’s Food Supplements (EUFS), “ Foodstuff that is meant to supplement the usual diet and contains saturated nutrients”(EUFS n.d.). DS are also called Food Supplements (FS) or Nutritional Supplements (NS) which contain vitamins, minerals, etc(Sato, Kodama, and Sengoku 2023). DS are normally dispensed in the form of pills, tablets, capsules, powder, or liquid oral dosage forms in market(DS n.d.). And which is also

easily available online/offline stores and from the black market(MARKET-REPORTS n.d.). To get more profit, pharmaceutical companies are doing adulteration. More than one billion adulterants are reported all over the world(Dastjerdi et al. 2018).

However, sometimes it enhances the effects of the DS, but excessive consumption shows various toxic effects(MARKET-REPORTS n.d.). Which is a more desiccating chapter for public health and legal regulation, so there is an urgent need for determination and identification of adulterants in DS(Dietary supplements sefety n.d.).

The supply chain of dietary supplements now increases globally(Chiba et al. 2020), so the need for techniques to identify a variety of adulterants with a variety of potential has increased significantly. Methods being developed must be adaptable and useful in order to accommodate brand-new issues and new ingredients(Vaclavik, Krynitsky, and Rader 2014). The hyphenated technique that is GC-MS is a selective and sensitive method of determination of adulterants from DS. In recent research records, so many spectroscopy techniques like Ultraviolet-visible Spectroscopy (UV)(Farag et al. 2022),

Raman Spectroscopy(Jiao et al. 2019), Near-Infrared (NIR) Spectroscopy(Bodor et al. 2023; Lukacs et al. 2018), Fourier-transform Infrared Spectroscopy (FT-IR)(Ozen, Banu, Weiss, and Mauer 2003; Popescu and Radu 2015a; Walkowiak et al. 2019), Nuclear Magnetic Resonance Spectroscopy (NMR)(Fadzillah et al. 2017; Hu et al. 2017; H. M. Lee et al. 2011; Yu, Myoung, and Ahn 2021), & Chromatography techniques like Thin-Layer Chromatography (TLC)(Fang et al. 2016; Minh et al. 2019), High Performance Thin Layer Chromatography (HPTLC)(Poplawska et al. 2013),

High Performance Liquid Chromatography (HPLC)(Avula et al. 2015; Poplawska et al. 2013), Ultra-Performance Liquid Chromatography (UPLC)(N. S. Kim et al. 2021; Roh et al. 2011), Gas Chromatography (GC)(Laposchan, Kranenburg, and Asten 2022; W. Lee et al. 2020; Muschietti, Redko, and Ulloa 2020). After all, for specific determination, there are so many hyphenated techniques that are Liquid Chromatography-Nuclear Magnetic Resonance Spectroscopy (LC-NMR)(Tokunaga, Akagi, and Okamoto 2017),

Liquid Chromatography-Nuclear Magnetic Resonance Spectroscopy-Mass Spectrometry (LC-NMR-MS)(Sarker and Nahar 2012), Liquid Chromatography-Mass Spectrometry (LC-MS)(Agrawal et al. 2016), Gas Chromatography-Mass Spectrometry (GC-MS)(Pratiwi et al. 2021). Amongallhyphenatedtechniques GC-MS is more specific because generally most of the DS are volatile in nature(Rocha, Amaral, and Oliveira 2016). GC-MS not only has the property of separation for similar structure analogues but provides MS spectra patterns for analytes using ionisation techniques (EI)(Mokhtar et al. 2016). By solving these spectra, we can elucidate the specific structure, which eventually helps to determine the adulterants used in DS in a more specific manner(Patel, Author, and Bhatt 2021).

This review gives an overall idea about the application of Mass Spectrometry (MS) coupled with Gas Chromatography (GC-MS) technique in the detection of adulterants quantitatively and qualitatively present in DS. Gas chromatography (GC) is applied for the specification and separation of adulterants present in DS, & with the help of Mass Spectrometry (MS) structure elucidation of adulterants can be done. This current review was prepared using information from the last few years and included web information and databases. Although not exclusively, the keywords from this paper were among the search terms used.

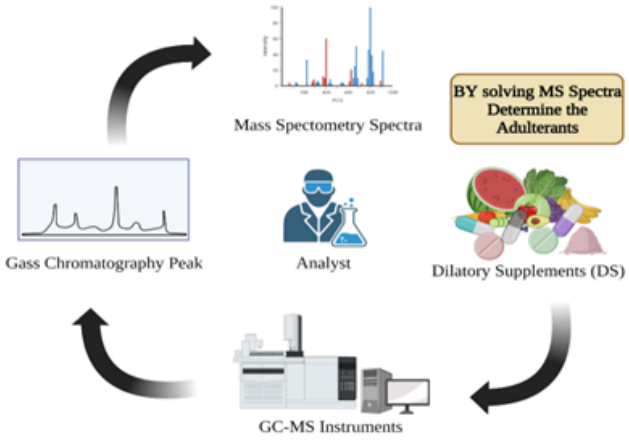


Fig. 1 Detection of pharmaceutical adulterants from dietary supplements

2 Regulation on Adulteration of Dietary Supplements

Globally there is no common document to categorise the products recognized vastly as dietary supplements, complementary medicines, nutraceuticals, or food supplements in various countries(Dwyer, Coates, and Smith 2018). This is the most common difficulty faced in any deliberation for the circulation of dietary supplements(Rashighi and Harris 2017).

In India Food Safety and Standards Authority of India (FSSAI) has provide a guideline for approval of the nutraceutical products in the Indian market(FSSAI n.d.). The enactment contains 21 chapters and in the 4th article (22 of the act) clarify about manufacturing, marketing (sold or distribute) of nutraceutical products, various fortified food and dietary supplements(Dr Swathi Putta 2020).

In the Nutraceutical Regulation act, 2016, under 'General Requirements,' the FSSAI stated that simple combination of vitamins and minerals formulated in tablets, capsules, syrup formats shall not be included in any of the class of these standards unless when vitamins and minerals are imparted(Nutraceutical Regulation act, 2016 n.d.).

In Food Safety and Standard (FSS) Regulation act, 2011, provide information and guidelines for permit and enrolment in food occupation; labelling and packaging; Food additives and product standards; forbid and limitation on sales; laboratory and sampling evaluation of contaminants, toxins, and residues(Food Safety and Standard (FSS) Regulation act, 2011 n.d.). FSS also provided a guideline in 2015, for food, nutraceuticals, health supplements and use of food for special diet, food for particular medical use, fortified foods, and novel food(5e31306a72882Direction_FSS_Product_Animal_Feed_29_01_2020.pdf n.d.). On December 31, 2018, the FSSAI issued a notice restricting the use of a number of ingredients in nutraceutical foods(notice n.d.).

USA regulates DS beneath the regulation of Dietary Supplement Health and Education Act of 1994 (DSHEA) where they mention that if any dietary product is adulterated or misbranded it withdraw form market(notice n.d.). That shows all the Firms to be accountable for inspecting the toxicity levels and labelling of their outcome as per the DSHEA Act by Food Drug Administration (FDA) regulation. FDA also has the

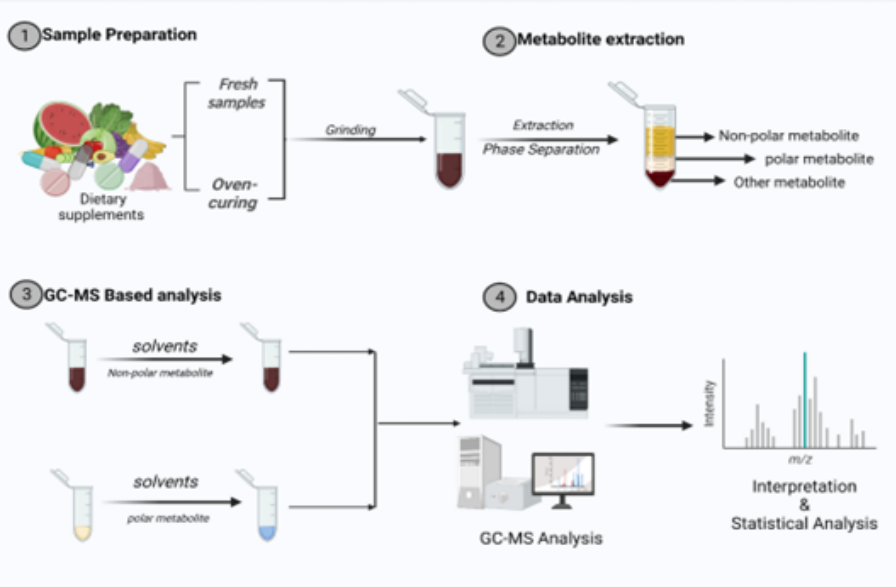
responsibility to take action against spurious dietary supplement after it enters the market(Dietary Supplements USFDA n.d.).

European Food Safety Authority (EFSA) works on the safety of Dietary supplements which is legally considered as foods/ special category of food in Europe(EUROPEAN FOOD SAFETY AUTHORITY n.d.). The vitamins, minerals, and substances used their sources that can used in the production of dietary supplements are governed by harmonised legislation(EUROPEAN FOOD SAFETY AUTHORITY n.d.). The European Commission has established harmonised regulations for ingredients other than vitamins and minerals to protect consumers from potential health risk(EFSA n.d.). The commission also keeps a list of substances whose use is restricted because it is known or suspected that they may have effect the consumer health(European Advisory Services (EAS) 2007). In Dec 2017 EFSA published the summery report on Dietary Reference Values for nutrients(European Advisory Services (EAS) 2007).

3 GC-MS Method for analysis of adulterant

The utilization of GC-MS for the assessment of pharmaceuticals is because of its unique properties for separation and structural elucidation of the compounds(Vaclavik, Krynitsky, and Rader 2014), its limit of detection (LOD) and limit of quantification (LOQ) in nano label(Armbruster, Tillman, and Hubbs 1994), and GC-MS is also popular for its properties in target analytes(Morimoto et al. 2019), in particular volatiles and thermal stability. Apart from that, GC-MS is popular worldwide, has relatively chipper hardware, and provides spectral information,

Fig. 2 General principle of detection of adulterants from dietary supplements



making it an important tool for routine quantitative tests for DS for the presence of syntactic pharmaceuticals(Vaclavik, Krynitsky, and Rader 2014). Table 1 summarises some methods for the detection of syntactic pharmaceutical ingredients in DS. The use of GC-MS can be used in the structural elucidation of designer drugs, whereas other hyphenated

techniques like LC-MS and LC-NMR cannot provide sufficient information(Parr et al. 2004). which was discussed below for new pharmaceutical adulterants in DS. GC-MS was used by Zhang et al.(Zhang et al. 2022)to detect 93 anabolic androgenic steroids found in nutraceuticals. A 17m long capillary column with a width of 0.2mm and a film thickness of 0.11m was employed. The temperature conditions were as follows: 140 °C as the starting temperature, gradually increase 140-180 °C at 40 °C/min, 180-230 °C at 3 °C/min, 230-300 °C, and kept at 300 °C for 4 minutes. This approach was designed and tested to detect anabolic steroids in real time. It demonstrated extraction recovery rates of greater than 50%(Zhang et al. 2022).

Wang et al.(Wang et al. 2022) determined phthalic acid esters from the edible oil by using Shimadzu GC with a Shimadzu 8400 autosampler and 8040 GC-MS system with a separation column of (30 m × 0.25 mm × 0.25 μm) dimensions. The flow rate chosen was 1.2ml/min using helium (99.999% purity) as the carrier gas. The temperature condition was kept at 250 ◦C. the choice of solvent for the extraction was a crucial part so different organic solvents like methanol, acetonitrile, and n-hexane were chosen. The highest intensity esters were obtained from the analysis in which methanol was used as the solvent. Acetonitrile showed somewhat similar results but it has more toxicities related to it than methanol(Wang et al. 2022).

Rutar et al.(Rutar et al. 2022) reported the nutritional quality and safety of a spirulina dietary supplement. Its nutritious amino acid content was determined using GC-MS, which used a 7890B GC and a 5977A series GC/MSD to analyse amino acids. The dimensions of the capillary column were 10 m 0.25 mm 0.15 mm. At a flow rate of 1.5ml/min, helium was used as the carrier gas. Specific amino acids such as alanine (ALA), glutamic acid (GLU), hydroxylysine (HLY), leucine (LEU), phenylalanine (PHE), threonine (THR), valine (VAL), aspartic acid (ASP), glycine (GLY), hydroxyproline (HYP), lysine (LYS), and others were identified by comparing peak retention times with previously identified amino acids in the standard(Rutar et al. 2022).

Parthasarathy et al.(Parthasarathy et al. 2022) analysed different samples of edible oils from different parts of India to detect adulterants using GC-MS. The samples collected were of groundnut, sesame, coconut, mustard, olive, sunflower and soyabean oils. The HP5MS capillary column infused with silica was used and the dimensions of column was (30 m×250 mm×0.25 mm). The carrier was helium gas, flowing at a constant rate of 1.0 ml/min. It gave an outcome that the fatty acids compositions of the oils between the unrefined and commercially available sesame oils varied a lot(Parthasarathy et al. 2022).

Lin et al.(Lin et al. 2018) used hydrogen as a carrier gas to test contaminated medications from traditional Chinese medicine and nutritional supplements. There were 83 TCM samples and 40 diet supplements. The GC-MS analysis was carried out using a 5977A MSD mass spectrometer and an Agilent 7890B GC system with column dimensions of 30 m x 0.25 mm (0.25 m film thickness) with a retention time of 10 g/mL, helium and hydrogen were used as carrier gases. According to the findings of this investigation, utilising hydrogen instead of helium lowered the run time of drug analytes, lowering the cost of analysis(Lin et al. 2018).

Fabresse et al.(Fabresse et al. 2021) recommended employing GC-MS analysis on a Focus GC attached to a Triples Duo autosampler and combined with a DSQ II single quadrupole to evaluate samples of nutritional supplements confiscated from the illegal market among bodybuilders. Separation was carried out using an Uptibond 5 (5% phenyl - 95% dimethylpolysiloxane) column from Interchain (Montlucon, France) with helium as the

carrier gas at a constant flow rate of 1.2 mL/min at 250 °C. A number of doping compounds were discovered by qualitative and quantitative analysis(Fabresse et al. 2021).

Guerrero-Esperanza et al.(Guerrero-Esperanza et al. 2023) took a total of eleven marketed samples of vegetable oils from a vendor in Irapuato and Mexico. There are two soy oils (SO1 and SO2), a canola oil (CO), two sunflower oils (OSF1 and OSF2), grape seed oil (GO), olive oil (OO), avocado oil (AO) and a mixture of three sunflower, soy, canola, and safflower oils mix (OM1, OM2, OM3). All the above-mentioned sample were kept in their native condition at room temperature throughout the testing. The GC-MS test was conducted by a PAL autosampler with a capillary column of dimension (100m x 0.25mm ID, 0.2 μm) and Agilent 6890 N GC and 5975 MS with CTC- and at a flow rate of 1ml/min helium was used as a carrier gas (Guerrero-Esperanza et al. 2023).

Di Donato et al.(Di Donato et al. 2021) examined 30 saffron samples gathered from three distinct locations of Italy. For this evaluation, a Saturn 2000 GC-MS system with a Star GC 3400 CX gas chromatograph coupled to an ion-trap mass detector was employed. The capillaries utilised (Varian Factor Four VF5-MS) have dimensions of 30m x 0.25mm x 0.25m film thickness. Helium IP was employed as the gas, and it was released at a flow rate of 1.0 ml/mi. The gas used was Helium IP, which was expelled at a flow rate of 1.0 ml/min. The initial column temperature was kept at 120 °C for 5 min and gradually increased by 2.5 °C/min to 195 °C and held for 1 min, then ended up at 270 °C at a rate of 15 °C/min and held for 9 min. and the retention times of the aliphatic hydrocarbons (C7-C40) were responsible for determining the retention indices of the obtained compounds. In order to ensure the authenticity and topographical descent of the samples, it was confirmed that the samples were received straight from the reputed syndicates. The results were elicited using the HS-SPME/GC-MS analysis of the Retention Index Standard by diluting it using water-ethanol mixture and administering similar conditions as those utilized by the assessment of bona fide and spurious or adulterated saffron samples(Di Donato et al. 2021)

4 Conclusions

The adulteration of DS frequently increases and it was the big concern for both consumer and regulatory agencies worldwide. Regulatory don't have any specific rules and regulation for the safety assessments of dietary supplements. Which is helps to manufacturer or sellers to intentionally adulterate supplements by including pharmaceutical drugs or analogues substances in order to increase product effectiveness. Consumers are also not that much aware about the drug interaction and consumption the unusual pharmaceuticals adulterants effect. Now available GC-MS methods are enabled select analysis qualitatively and quantitatively target to analysis and adulterated Pharmaceuticals in DS. It is possible that, the range of these methods will broaden to permit the simultaneous analysis of an even greater number of pharmaceuticals for multiple classes that differ significantly in their physicochemical properties. It is hoped that using of GC-MS device to develop authentication methodology further could provide us useful outcomes and make a significant contribution to the identification of adulterants in food products.

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