Research Article

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An HPLC–HRMS profiling of dietary supplements declaring andarine (S-4)

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Abstract: Selective androgen receptor modulators (SARMs), including andarine (S-4), have gained significant attention in the dietary supplement market despite their known health risks and prohibition in competitive sports. Although andarine remains widely available, data on its actual presence in dietary supplements are limited. To address this gap, this study assessed the quality of dietary supplements marketed as containing andarine. An HPLC–HRMS method was developed, validated, and applied to analyze three commercially available dietary supplements. HRMS (QTOF) detection, in MS as well as MS/MS regimes, was essential for confirming the presence of andarine and unexpectedly identifying other biologically active substances, specifically the metabolic modulators SR9009 and GW501516, based on precise molecular weights of precursor and product ions relative to reference standards. The analysis revealed discrepancies between the labeled and actual contents of the analyzed dietary supplements. These findings underscore the potential health risks posed by mislabeled and adulterated dietary supplements and highlight the urgent need for stricter quality control and regulatory oversight in the dietary supplement industry.

Keywords: HPLC–HRMS; dietary supplements; SARMs; andarine; SR9009; GW501516

1 Introduction

Andarine (Figure 1), also known as S-4, belongs to the class of selective androgen receptor modulators (SARMs), a group of substances known for their anabolic effects [1]. In recent years, SARMs have gained considerable attention among athletes and individuals seeking performance enhancement, raising significant public health concerns [2]. Although these substances have been explored for potential therapeutic applications, their pharmacological profiles remain insufficiently characterized, and clinical data on their safety and efficacy are limited. Notably, clinical trials on andarine were discontinued due to adverse effects, underscoring the substantial risks associated with its use [3]. Furthermore, since 2008, andarine and other SARMs have been prohibited in competitive sports due to their performance enhancing properties and potential health risks [4]. Despite this, dietary supplements claiming to contain andarine remain widely available, with growing public interest in these products [5].

The quality and safety of such dietary supplements are a major concern. Studies have repeatedly identified serious quality deficiencies, including discrepancies between labeled and actual content (Table 1). Some dietary supplements contain incorrect dosages of andarine, while others include undeclared biologically active substances [6–11]. Given the potentially severe adverse effects of andarine alone [12–15], its presence alongside other unlisted substances further increases the health risks for consumers.

Despite these concerns, research on the actual composition of dietary supplements claiming to contain andarine remains limited. To address this gap, this study aimed to conduct a comprehensive quality control analysis of dietary supplements labeled as containing andarine. For this purpose, we optimized and validated an HPLC–HRMS method, which was subsequently applied to the analysis of three commercially available dietary supplements.

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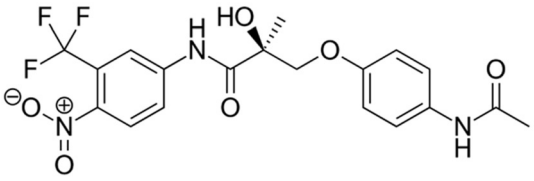
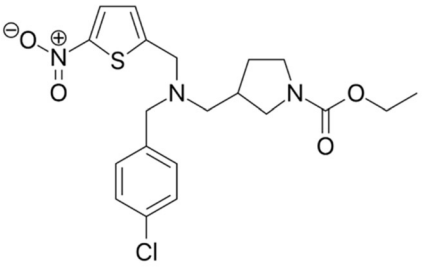
A



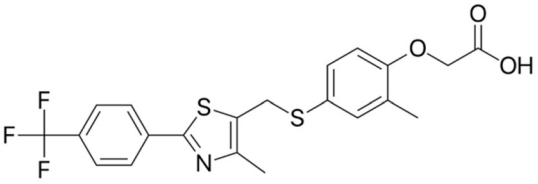
Andarine
CAS Number: 401900-40-1
Molecular Weight: 441.36
Molecular Formula: $C_{19}H_{18}F_3N_3O_6$

B



SR9009
CAS Number: 1379686-30-2
Molecular Weight: 437.94
Molecular Formula: $C_{19}H_{18}F_3N_3O_6$

C



GW501516
CAS Number: 317318-70-0
Molecular Weight: 453.50
Molecular Formula: $C_{21}H_{18}F_3NO_3S_2$

Figure 1: Structure and technical information: (A) Andarine; (B) SR9009; (C) GW501516.

2 Materials and methods

2.1 Chemicals and reagents

All chemicals and reagents used were of LC–MS grade. Reference standards for andarine, clenbuterol (used as an internal standard [IS]), SR9009, and GW501516 were obtained from Sigma-Aldrich (St. Louis, MO, USA). Methanol (MeOH), acetonitrile (ACN), and acetic acid (AA) were sourced from VWR International (Radnor, PA, USA). Ammonium hydroxide (NH_4OH, 25 %) was purchased from Honeywell (Seelze, Germany), while ammonium acetate (Ac) and ammonium bicarbonate (Bc) were obtained from Sigma-Aldrich. Deionized water was prepared using a Millipore Direct Q water purification system from Merck (Darmstadt, Germany).

2.2 Dietary supplements

Three dietary supplements claiming to contain andarine (S-4) were sourced from online retailers identified through a targeted Google search. The search utilized keywords such as “buy andarine” and “buy S-4”, which consistently directed us to three specific websites (www.fitnessbody.sk; www.kamenik.sk; www.musclebody.eu) from which the dietary supplements were purchased.

Upon receipt, each dietary supplement was inspected to ensure the integrity of the packaging. All samples arrived intact, sealed, and were stored at room temperature prior to analysis. Supplement A (Patriot Lab Andarine S-4) claimed to contain 15 mg of andarine per capsule (cps), Supplement B (QRP Nutrition Andarine S-4) claimed 20 mg per cps, and Supplement C (Biogenic Pharma Andarine S-4) claimed 25 mg per cps. Notably, none of the labels indicated the presence of additional biologically active substances.

2.3 Preparation of solutions and samples

2.3.1 Stock and working solutions

Stock solutions were prepared by dissolving 10 mg of reference standards in 10 mL of MeOH. These stock solutions were then diluted with deionized water to achieve the desired concentrations for working solutions. Both the stock and working solutions were stored at −20 °C until required.

2.3.2 Calibration samples

Calibration samples were prepared by spiking deionized water with working solutions of andarine to achieve final concentrations of 0.25, 0.5, 1, 2, 10, and 50 ng/mL. An IS was added to each sample at a final concentration of 10 ng/mL.

2.3.3 Quality control (QC) samples

Quality control (QC) samples were prepared by adding andarine working solutions to deionized water, resulting in final concentrations of 0.25, 2.5, and 25 ng/mL. The IS

Table 1: Summary of quality control assessments for dietary supplements with declared andarine content.

No.	Form	Label	Identified	Not identified	Dosage match[a]	MS/MS, LOD (ng/mL)[b]	Ref.
1	sol	Andarine	Andarine		No (Low)	LTQ-Orbitrap, Unkn.	[6]
2	cps	Andarine	Andarine		Yes	QqQ/Q-Orbitrap, Unkn.	[7]
3	sol	Andarine	Andarine, Tamoxifen		Yes	QqQ/Q-Orbitrap, Unkn.	[7]
4	sol	Andarine	Andarine		No (Low)	QqQ/Q-Orbitrap, Unkn.	[7]
5	sol	Andarine	Andarine		Yes	Q-Orbitrap, 0.025	[8]
6	sol	Andarine	Andarine		Yes	Q-Orbitrap, 0.025	[8]
7	sol	Andarine	Andarine		Yes	Q-Orbitrap, 0.025	[8]
8	sol	Andarine	Andarine		Yes	Q-Orbitrap, 0.025	[8]
9	sol	Andarine	Andarine		Yes	Q-Orbitrap, 0.025	[8]
10	sol	Andarine	Andarine		No (Low)	Q-Orbitrap, 0.025	[8]
11	sol	Andarine	Andarine		No (Low)	Q-Orbitrap, 0.025	[8]
12	sol	Andarine	Andarine		No (Low)	Q-Orbitrap, 0.025	[8]
13	sol	Andarine	Andarine		No (Low)	Q-Orbitrap, 0.025	[8]
14	sol	Andarine	LGD-4033	Andarine	No	Q-Orbitrap, 0.025	[8]
15	cps	Andarine, LGD-4033, Ibutamoren, Arimistane	Andarine, LGD-4033, Ibutamoren	Arimistane	Unkn.	Q-Orbitrap, Unkn.	[9]
16	cps	Andarine, Ostarine, GW501516		Andarine, Ostarine, GW501516	No	Q-Orbitrap, Unkn.	[9]
17	cps	Andarine, SR9009, GW501516	Andarine, GW501516, Ostarine, Ibutamoren, 1,3-DMAA, 1,4-DMAA, 1-methylhexylamine	SR9009	Unkn.	Q-Orbitrap, Unkn.	[9]
18	cps	Andarine	Andarine, Ostarine		Unkn.	Q-Orbitrap, Unkn.	[9]
19	cps	Andarine, SR9009, GW501516	Andarine, SR9009, GW501516		Unkn.	Q-Orbitrap, Unkn.	[9]
20	cps	Andarine	Andarine, GW501516		Yes	QTOF, Unkn.	[10]
21	cps	Andarine	GW501516, Testosterone	Andarine	No	QTOF, Unkn.	[10]
22	cps	Andarine, Ostarine, RAD140	Ostarine, RAD140	Andarine	No	QqQ, Unkn.	[11]
23	cps	Andarine	Andarine, SR9009, GW501516		No (Low)	QTOF, 0.0125	This study
24	cps	Andarine		Andarine	No	QTOF, 0.0125	This study
25	cps	Andarine		Andarine	No	QTOF, 0.0125	This study

[a]Applicable to the dosage of andarine as declared in cited references. [b]LOD for andarine.

concentration was consistently maintained at 10 ng/mL across all QC samples.

2.3.4 Samples of dietary supplements

Samples of dietary supplements were prepared by first homogenizing the contents of six capsules to ensure uniform distribution. From the homogenized mixture, an amount equivalent to the contents of five capsules was accurately weighed and dissolved in 5 mL of MeOH, followed by centrifugation at 12,500 g for 10 min. The supernatant was then filtered through a 0.22 µm nylon syringe filter (AZ Chrom, Bratislava, Slovakia) and diluted with deionized water to achieve intended concentrations within the linear range of the analytical method.

2.4 Instrumentation

Measurements were performed using an Agilent Infinity 1260 HPLC coupled with an Agilent 6520 MS/MS (QTOF) from Agilent Technologies (Palo Alto, CA, USA). Data acquisition and processing were carried out using MassHunter software, version B.08.00, from Agilent Technologies.

The rationale for selecting the HPLC–HRMS method lies in its ability to provide high specificity and sensitivity, which are crucial for detecting low concentrations of andarine and other biologically active substances in dietary supplements.

2.4.1 HPLC parameters

Chromatographic separation was performed on a Zorbax Extend C18 column (50 × 2.1 mm, 1.8 µm) from Agilent Technologies at a constant temperature of 40 °C and constant column flow rate of 0.5 mL/min. The mobile phase consisted of 1.0 mM Bc with 0.1 % NH_4OH in deionized water (mobile phase A) and 100 % ACN (mobile phase B). The gradient started at 5 % B, increased to 95 % over 10 min, and was maintained at this level for 5 min. The column was then reconditioned with the initial mobile phase composition for 5 min. The sample injection volume was set to 1 µL.

2.4.2 QTOF parameters

The QTOF mass spectrometer was operated in positive ionization mode with an ESI source and a capillary voltage of 4,000 V. The drying gas temperature was set at 360 °C, with a flow rate of 12 L/min, and the nebulizer gas pressure was maintained at 60 psi. The fragmentor voltage was set to 100 V. The HRMS analysis was performed in Scan mode, monitoring target m/z values of 442.1 for andarine and 277.0 for the IS.

2.5 Method validation

The method was validated according to the ICH Q2(R1) Guideline [16], evaluating characteristics such as linearity, range, LOQ, LOD, accuracy, precision (repeatability and intermediate precision), and specificity.

2.5.1 Linearity and range

The calibration parameters were evaluated based on the analysis of calibration samples prepared at six concentration levels, with each concentration measured on a single day in triplicate. The parameters included the linear range, slope (a), standard deviation of slope (SD_a), intercept (b), standard deviation of intercept (SD_b), and correlation coefficient (r^2). The calculations were performed using linear regression analysis in Microsoft Excel, version 2302, from Microsoft Corporation (Redmond, WA, USA).

2.5.2 LOQ

The LOQ was evaluated using an S/N approach, comparing the measured signals from samples with known low concentrations of andarine reference standard to those from blank samples. LOQ was established as the lowest concentration at which andarine could be reliably quantified with an S/N ratio of 10:1.

2.5.3 LOD

The LOD was evaluated using the same S/N method as the LOQ, focusing on detection rather than quantification of andarine. LOD was established as the lowest concentration at which andarine could be reliably detected, with an S/N ratio of 3:1.

2.5.4 Accuracy and precision

The accuracy and precision were evaluated based on the analysis of QC samples prepared at three concentration levels. Each QC sample was measured five times per day for three consecutive days. Accuracy was determined by calculating the relative error (RE) for intra-day and inter-day measurements. Precision was determined by calculating the relative standard deviation (RSD) for intra-day (repeatability) and inter-day (intermediate precision) measurements.

2.5.5 Specificity

The specificity of the method was evaluated based on the analysis of samples from three dietary supplements. Initial screening revealed that one sample (Supplement B) contained andarine, while the other two samples (Supplements A and C) did not. In samples without andarine, the method's specificity was further assessed by monitoring for potentially interfering components, including substances with the same retention time as andarine.

3 Results and discussion

3.1 Method optimization

3.1.1 HPLC parameters

The initial step in optimizing the HPLC parameters involved the selection of a suitable chromatographic column. Several RP columns were tested, including Accucore aQ (100 × 3.0 mm, 2.6 µm) and Accucore C8 (100 × 2.1 mm, 2.6 µm) from Thermo Fisher Scientific (Waltham, USA); Kinetex Evo C18 (100 × 2.1 mm, 2.6 µm), Kinetex F5 (50 × 2.1 mm, 2.6 µm), Luna Omega Polar C18 (50 × 2.1 mm, 1.6 µm), and Luna Omega PS (50 × 2.1 mm, 1.6 µm) from Phenomenex (Torrance, CA, USA); Sunshell RP-AQUA (100 × 3.0 mm, 2.6 µm) from Chromanik Technologies (Osaka, Japan); and Zorbax Extend C18 (50 × 2.1 mm, 1.8 µm) from Agilent Technologies (Santa Clara, CA, USA). Furthermore, the effects of different organic mobile phase components (MeOH vs. ACN) and the influence of acidic conditions (1.0 mM Ac with 0.1 % AA) versus basic conditions (1.0 mM Bc) on the chromatographic separation of andarine were tested. Optimal chromatographic performance, characterized by optimal peak shape (evaluated through tailing factor), peak height (Figure 2A), peak area, and shortest retention time, was achieved using the Zorbax Extend C18 column, ACN as the organic mobile phase component and basic conditions (1.0 mM Bc).

The next step involved investigating the effect of different mobile phase compositions on the andarine signal intensity. The compositions tested included: (a.) 1.0, 2.5, 5.0, 10.0, 25.0, and 50.0 mM Bc; (b.) 1.0, 2.5, and 5.0 mM Bc with varying concentrations of NH_4OH (0.1, 0.2, 0.4, 0.6, 0.8 or 1.0 %). The results demonstrated that the mobile phase composition had negligible or no effect on andarine retention time. All of the tested compositions produced satisfactory chromatographic peak shapes, as assessed by the tailing factor. Consequently, the height of the peak and the area of the peak (Figure 2B and C) were determined as the main optimization criteria, leading to the selection of 1.0 mM Bc with 0.1 % NH_4OH as the optimal mobile phase composition.

3.1.2 HRMS parameters

In the method optimization phase, various HRMS parameters were systematically tested to achieve the most robust analytical signal for andarine. The factors optimized included capillary voltage (ranging from 1,000 to 5,000 V), drying gas temperature (200–400 °C), drying gas flow (10–15 L/min), and fragmentor voltage (50–150 V). The optimization was guided by the criteria of maximizing the intensity and stability of the analytical signal for andarine. The optimal settings were determined to be a capillary voltage of 5,000 V, a drying gas temperature of 360 °C, a gas flow of 12 L/min, and a fragmentor voltage of 100 V.

During the subsequent method application phase that involved investigating the presence of other biologically active substances in supplements claiming to contain only andarine, collision energy (CE) was specifically evaluated across a range of 10–60 eV in MS/MS regime. For biologically active substances such as SR9009 and GW501516, the optimal CE was found to be 30 eV, which provided the highest intensity and stability for the analytical signals of their product ions (Figures 3 and 4).

3.2 Method validation

3.2.1 Linearity, range, LOQ and LOD

The calibration parameters are presented in Table 2. The linear relationship was determined in the range of 0.25–50 ng/mL with a r^2 of 0.9999. The LOQ, representing the first point of the calibration line, was determined to be 0.25 ng/mL. The LOD was determined to be 0.0125 ng/mL, which is the best of the previously published LODs for andarine in dietary supplement matrices (Table 1).

3.2.2 Accuracy and precision

The results of the QC sample analysis are presented in Table 2. Intra-day RE ranged from 0.8 % to 3.7 %, while inter-day RE ranged from 0.9 % to 3.7 %. Repeatability and intermediate precision did not exceed 1.2 % and 3.4 %, respectively.

3.2.3 Specificity

Figure 5 demonstrates the high specificity of the method, indicating that the andarine signal (Supplement B) is not

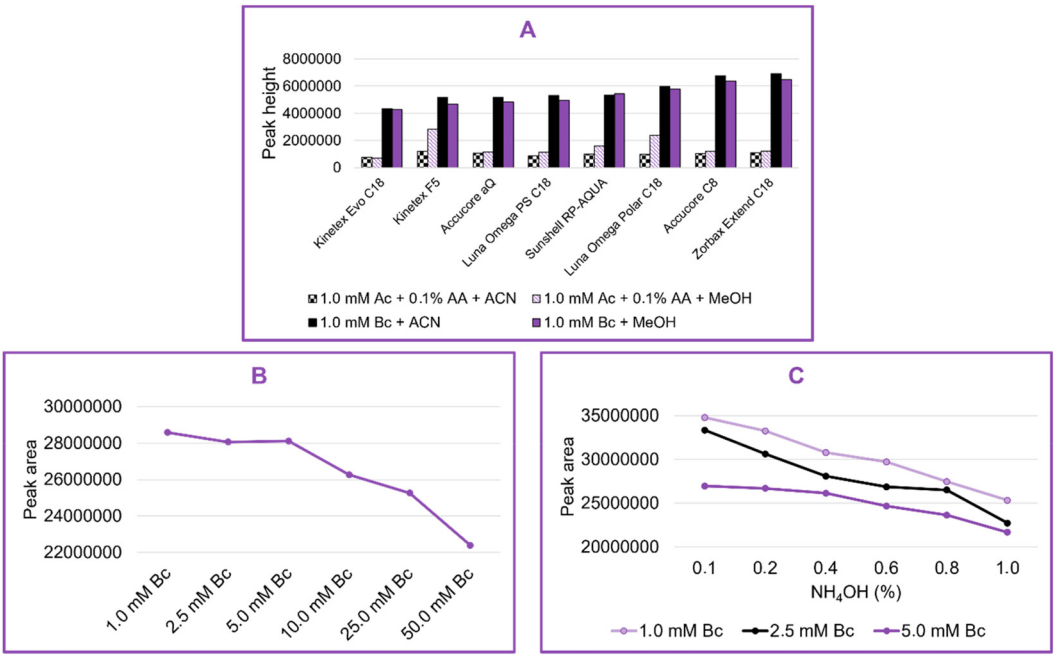


Figure 2: Optimization of HPLC parameters: A = selection of the chromatographic column; B = optimization of the mobile phase via different Bc concentration; C = optimization of the mobile phase via different NH_4OH concentration.

affected by other signals originating from the matrix of dietary supplements (Supplements A and C), such as those from other biologically active substances or excipients.

3.3 Method application

Following the validation process, the proposed method was applied to the analysis of three commercially available dietary supplements (Supplements A, B, and C) with declared andarine content. None of these dietary supplements claimed the presence of other biologically active substances on their labels.

The analysis revealed the presence of andarine only in Supplement B (Figure 2). However, the estimated andarine content of this dietary supplement (3 mg per cps) deviated significantly from the claim on the label (20 mg per cps). Andarine was not detected in Supplements A or C (Figure 5). Furthermore, no other biologically active substances were found in Supplements A and C.

In Supplement B, two additional biologically active substances, metabolic modulators, that were not declared on the label were identified in Scan mode (Figures 6A,B and 7A,B): SR9009 (a REV-Erb-α receptor agonist, Figure 1) and GW501516 (a PPARδ receptor agonist, Figure 1), both of which are not approved for human use [7] and are banned in sports [4].

The presence of these metabolic modulators in Supplement B was confirmed by comparing their mass spectra with reference standards of SR9009 and GW501516 in Product Ion Scan mode in MS/MS regime at a CE of 30 eV (Figures 6C,D and 7C,D).

Based on these findings, the following observations can be made: (a) analyzed dietary supplements exhibit significant qualitative deficiencies, consistent with the observations of other authors in similar products [6–11]; (b) the proposed method could serve as a reliable and highly sensitive tool for identifying and quantifying andarine, as well as for screening other biologically active substances, targeted and untargeted (expected and unexpected), in dietary supplements.

When compared with other approaches for detecting SARMs, our HPLC–HRMS (QTOF) method provides complementary advantages. LC–MS/MS methods using QqQ instruments are widely applied in the quality control of dietary supplements due to their robustness and high sensitivity; however, they typically target a limited number of analytes, which may miss emerging or unexpected compounds [7, 11, 17]. Orbitrap-based HRMS platforms offer excellent mass accuracy and powerful untargeted screening capabilities, though they often require longer acquisition and data processing times [6–9]. QTOF instruments, as used in our study, have also been successfully employed for SARM analysis [10, 17, 18], providing a balance

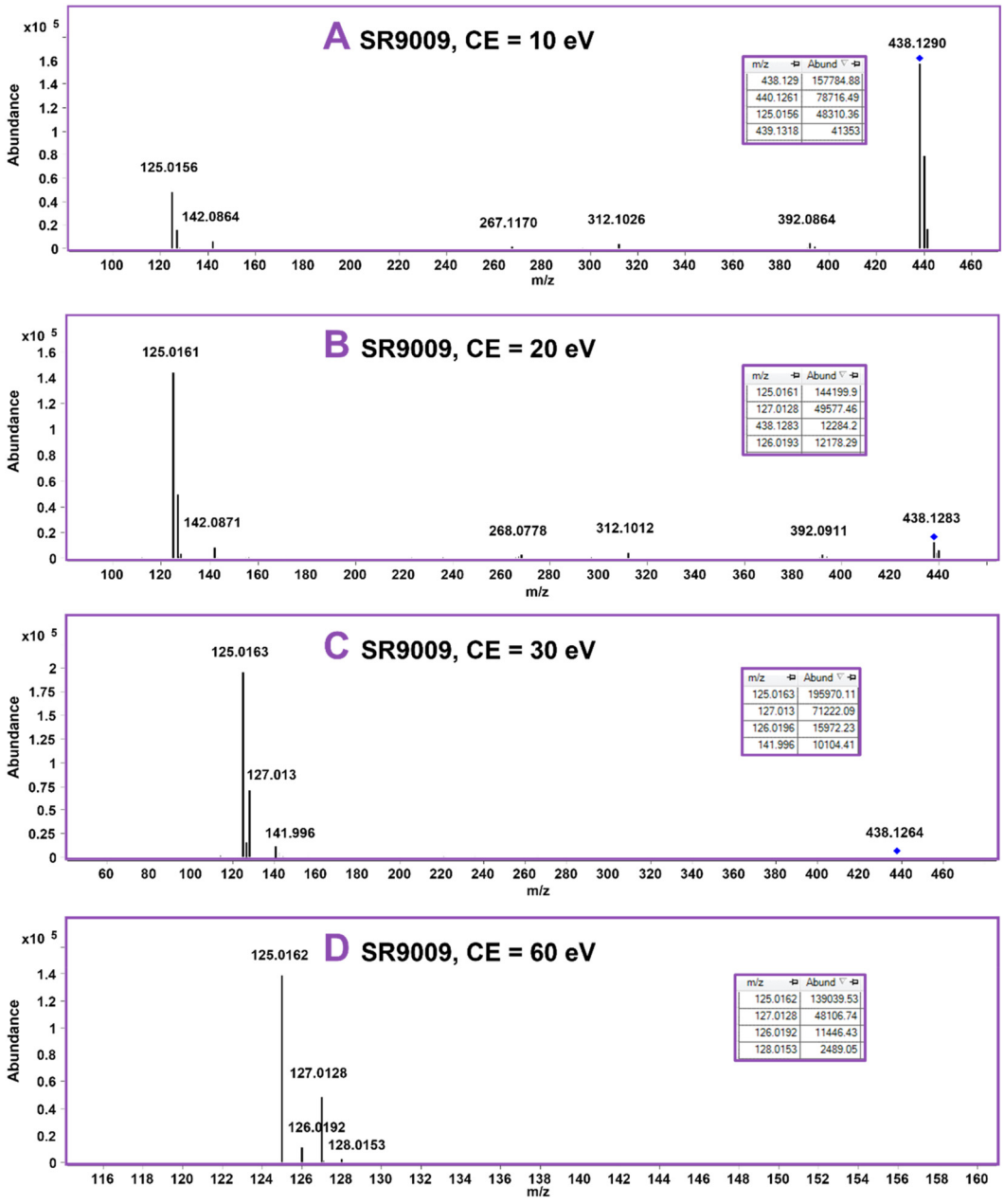


Figure 3: Optimization of collision energy (CE) for SR9009: A (10 eV); B (20 eV); C (30 eV); D (60 eV).

between sensitivity, accuracy, and data acquisition speed. More recently, portable MS devices and ambient ionization techniques have been explored for on-site screening, but their sensitivity and quantification capabilities remain limited compared with laboratory-grade systems [19, 20]. In this context, our method achieves the lowest reported LOD for andarine in dietary supplement matrices, combining high sensitivity with the ability to detect unexpected or emerging compounds, thus complementing both targeted and untargeted approaches.

3.3.1 Mislabeling, adulteration, and health risks of SARM-labeled dietary supplements

Our findings, consistent with similar studies conducted in other regions (Table 1), indicate that the issue of mislabeling and the presence of undeclared, potentially hazardous (e.g. carcinogenic GW501516 [21], potentially carcinogenic SR9009 [22]) biologically active substances in dietary supplements labeled as containing andarine is not unique to Central Europe but represents a broader, global concern.

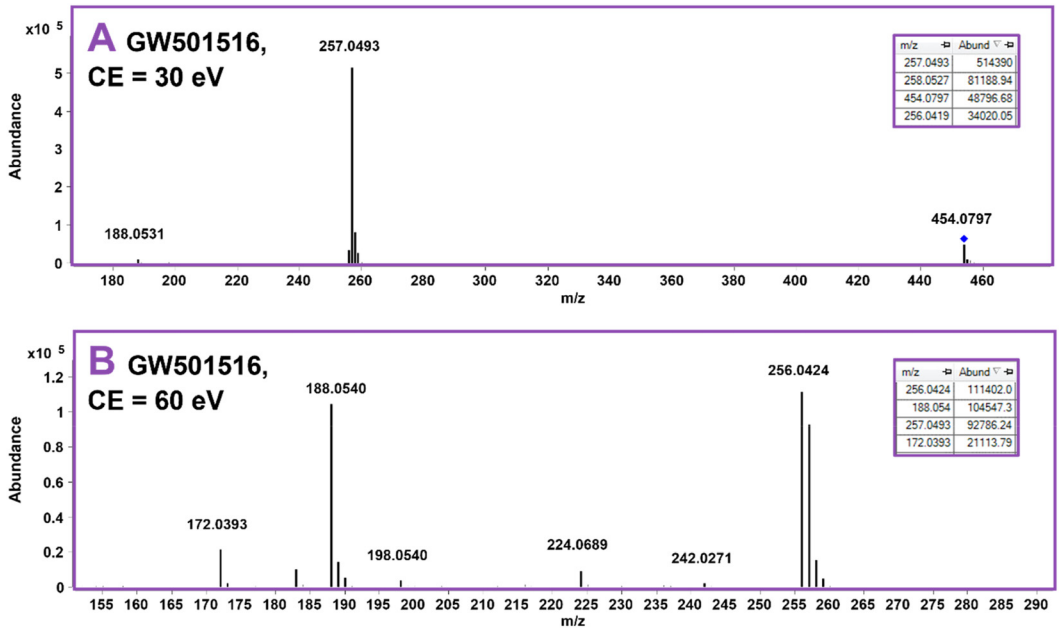


Figure 4: Optimization of collision energy (CE) for GW501516: A (30 eV); B (60 eV).

Table 2: Validation characteristics of the proposed HPLC–HRMS method.

Calibration samples (n = 6)							
Linear range (ng/mL)	***a***	**SD_a (n = 18)**	***b***	**SD_b (n = 18)**	**r^2**	**LOQ (ng/mL)**	**LOD (ng/mL)**
0.25–50	0.3074	0.009	0.0085	0.0062	0.9999	0.25	0.0125

QC samples (n = 3)							
	Intra-day (n = 5)				Inter-day (n = 15)		
Level	**c_N[a]**	**c_F[b]**	**RE (%)**	**RSD (%)**	**c_F[b]**	**RE (%)**	**RSD (%)**
Low	0.5	0.506	3.7	1.2	0.517	3.4	3.4
Medium	2.5	2.496	0.9	0.2	2.517	3.7	1.1
High	25	24.860	0.8	0.6	24.882	0.9	0.5

[a]Nominal concentration. [b]Found concentration.

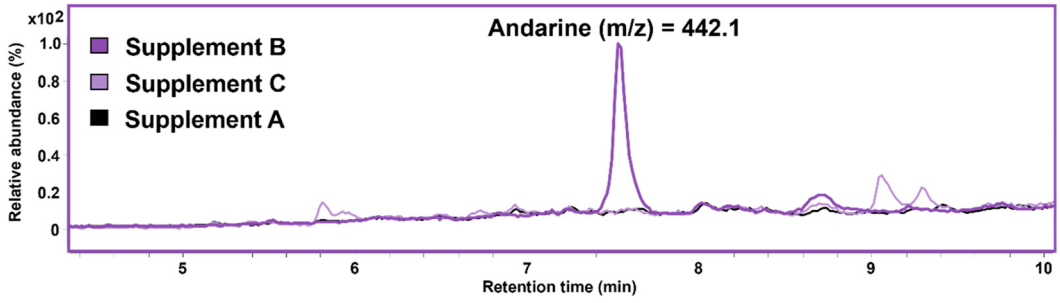


Figure 5: Extracted ion chromatograms (m/z = 442.1) obtained from HPLC-HRMS measurement of three commercially available dietary supplements claiming to contain andarine.

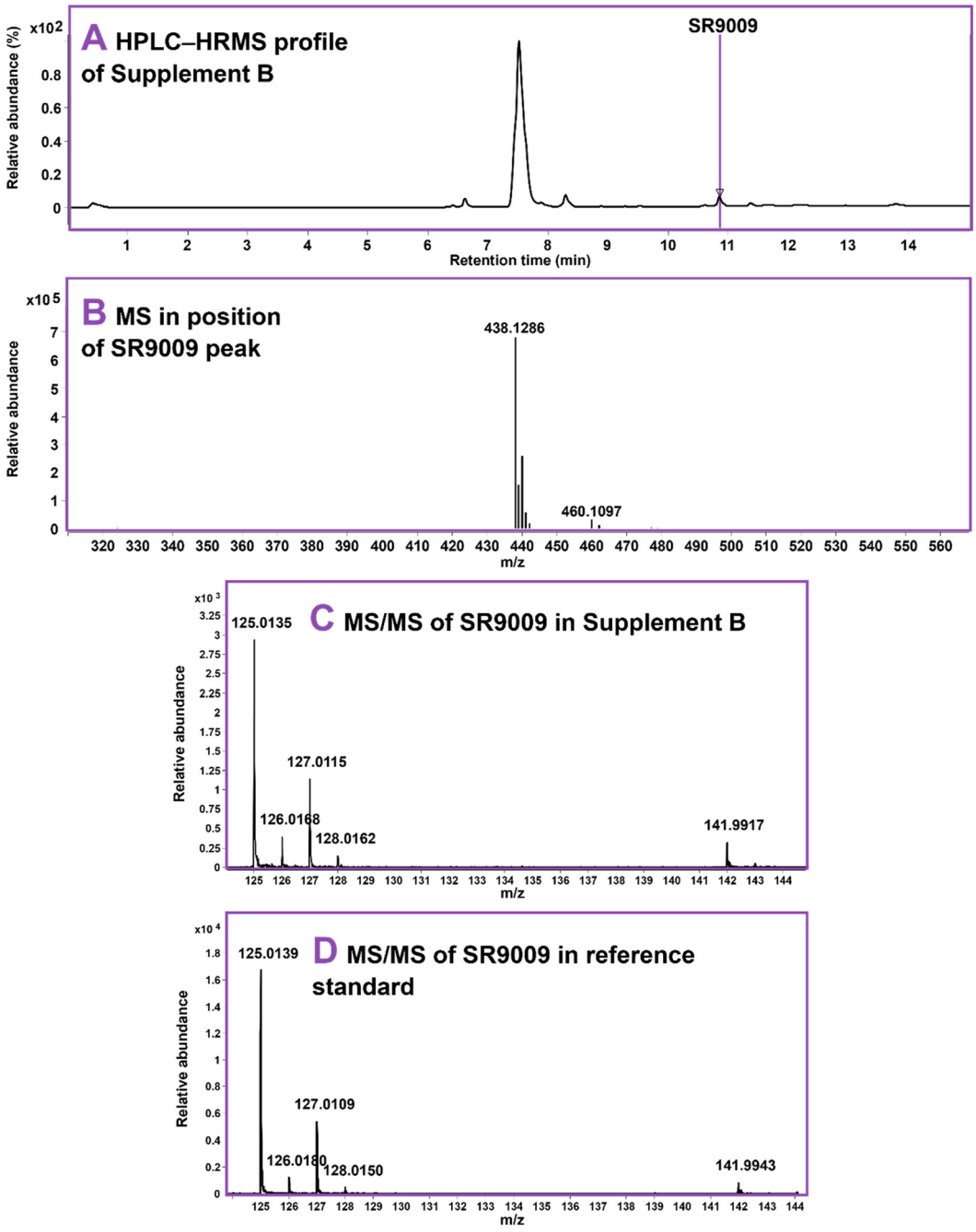


Figure 6: Undeclared metabolic modulator SR9009 in Supplement B: A = chromatogram of Supplement B in Scan mode; B = mass spectrum under the peak of SR9009; C = Supplement B: product ion scan mass spectrum of SR9009 (CE = 30 eV); D = reference standard: product ion scan mass spectrum of SR9009 (CE = 30 eV).

Similar patterns of mislabeling and/or adulteration have also been documented in dietary supplements marketed as containing other SARMs, such as AC-262,536 (also known as accadrine) [8], AC-105 (also known as acadibol) [9], LGD-3303 [9], LGD-4033 (also known as anabolicum, ligandrol, or VK5211) [7–11, 17, 18, 23], ostarine (also known as enobosarm, GTx-024, MK-2866, or S-22) [7–11, 17, 18, 23], RAD140 (also known as testolone) [7–9, 11, 17, 18, 23], S-23 [8–11, 18], and YK-11 (also known as myostine) [8–11, 17, 18]. Furthermore, many dietary supplements are

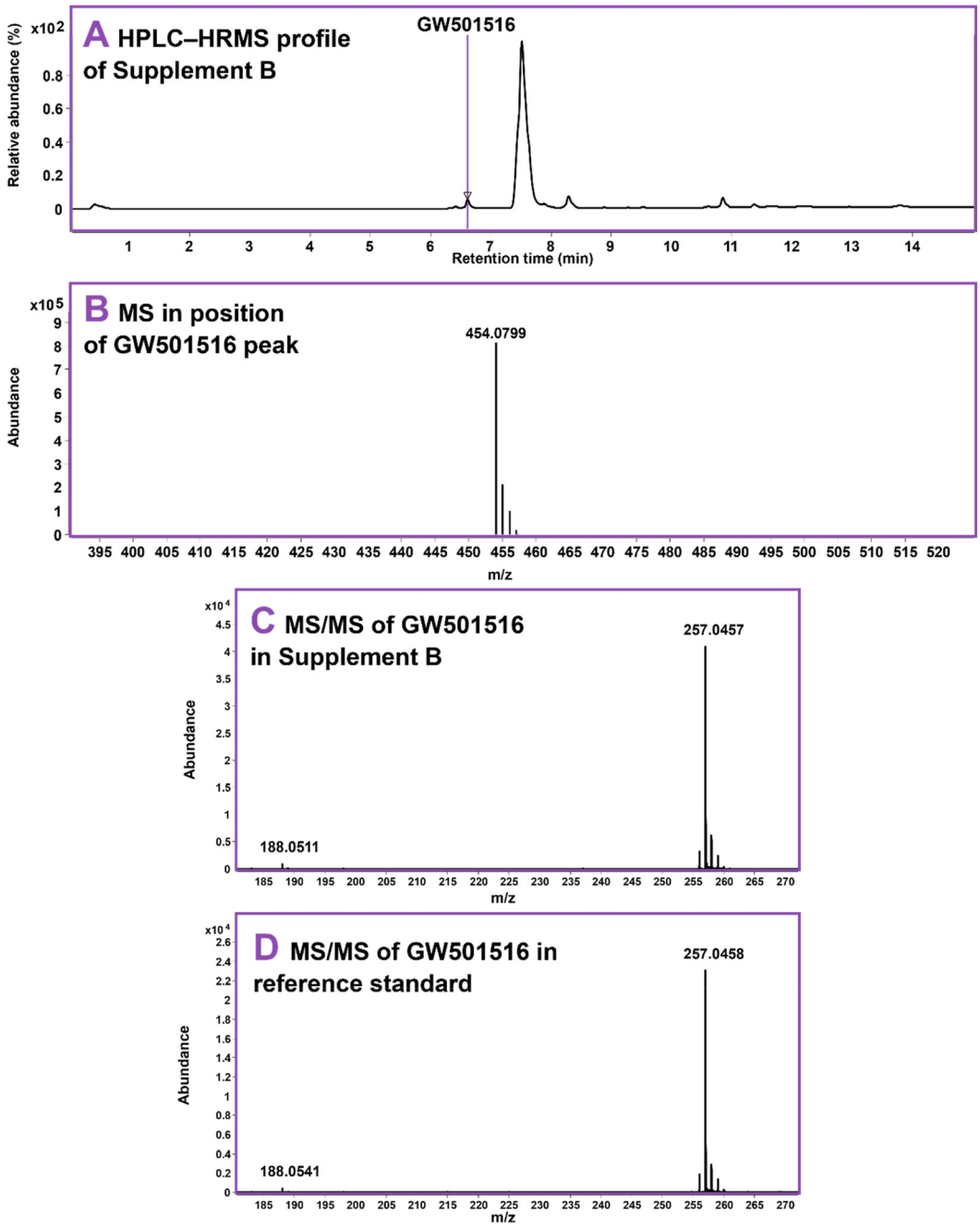


Figure 7: Undeclared metabolic modulator GW501516 in Supplement B: A = chromatogram of Supplement B in scan mode; B = mass spectrum under the peak of GW501516; C = Supplement B: product ion scan mass spectrum of GW501516 (CE = 30 eV); D = reference standard: product ion scan mass spectrum of GW501516 (CE = 30 eV).

labeled as SARMs, despite the fact that the listed ingredients are not SARMs, for example GW501516 (also known as cardarine) [7, 9–11, 17, 18], SR9009 (also known as stenabolic) [7, 9, 11, 17], or the growth hormone secretagogue ibutamoren (also known as MK-677) [7, 9–11, 17, 18].

Beyond issues of labeling and composition, the consumption of SARM-labeled dietary supplements poses serious health risks to consumers. In 2017, the U.S. Food and Drug Administration issued a public warning stating that the use of SARMs was linked to life-threatening adverse events, including drug-induced liver injury (DILI), myocardial infarction, and stroke, while also emphasizing that the long-term effects of SARMs on the human body remain unknown [14]. Although the exact mechanisms of SARM-induced DILI

have not yet been fully elucidated, it is assumed that an idiosyncratic immune-mediated response plays a central role [24]. The most frequently reported clinical manifestation is jaundice, which was present in all published cases [24–42]. Other reported symptoms include abdominal pain, nausea, vomiting, diarrhoea, fatigue, anorexia, malnutrition, weight loss, myalgia, pruritus, dark urine, and acholic stool – symptoms consistent with the diagnosis of bland cholestasis.

In a 2022 survey conducted by researchers at the University of Miami Miller School of Medicine involving 343 users of SARM-labeled dietary supplements, 54.5 % of respondents reported adverse effects. The incidence of adverse effects was significantly higher among users who had taken SARMs for longer than 3 months. The most reported effects included mood swings, testicular atrophy, and acne. Less common effects were hair loss, lethargy, irritability, yellow vision, and elevated blood pressure [12]. Of particular concern is the frequent report of testicular atrophy, which may suggest suppression of spermatogenesis. However, the current understanding of SARM-induced disruption of the hypothalamic–pituitary–gonadal axis is limited [43].

These findings underscore the urgent need for coordinated international regulatory action to establish and enforce stringent standards for the labeling, composition, and safety of dietary supplements containing or marketed as SARMs.

4 Conclusions

This study highlights the critical need for rigorous quality control assessments of dietary supplements claiming to contain prohibited substances. Andarine is a biologically active substance that has not been authorized for use in either medicinal products or dietary supplements. Consequently, any dietary supplement claiming to contain andarine is an illegal and potentially dangerous product.

The analysis of three such dietary supplements revealed discrepancies between the labeled content and the actual composition. Only one of them contained andarine, and even then, at a concentration lower than declared on the label. Furthermore, this product was found to contain undeclared metabolic modulators, SR9009 and GW501516, both of which are associated with potential health risks and are prohibited in competitive sports.

These findings suggest the need for careful consideration of the risks posed by mislabeled or adulterated dietary supplements and highlight the value of advanced analytical methods for accurately identifying and quantifying these biologically active substances. The HPLC–HRMS method, which was optimized and validated in this study, demonstrated specificity, sensitivity, and accuracy, thereby offering a potentially useful tool for regulatory authorities and researchers involved in monitoring the safety of dietary supplements. At present, it represents the most sensitive analytical method for determining andarine in the dietary supplement matrices.

Looking ahead, further developments in analytical workflows may enhance the surveillance of SARM-labeled dietary supplements. Expanding screening libraries will allow simultaneous detection of a broader range of novel agents, while miniaturized or ambient ionization techniques could reduce sample preparation and analysis times. Moreover, AI-supported data processing and predictive fragmentation tools are expected to improve both the speed and reliability of HRMS-based identifications. Such innovations may significantly strengthen regulatory and monitoring efforts.

Given the growing public interest in SARMs and their availability, there is a clear case for enhanced regulatory oversight and comprehensive market surveillance. This study contributes to the discussion on the regulation of dietary supplements claiming to contain SARMs and points to the potential benefits of further research. Future studies might consider expanding the analysis to include a wider range of SARMs, commercial products and regions, thereby contributing to efforts aimed at safeguarding public health.

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