

## ***Beyond The Label: Autopsy and Case Report of Specific Organ Damage Induced by Sports Supplements***

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### **Introduction**

Individuals who exercise and athletes have frequently used sports supplements to improve their performance and physical appearance. This has become a widespread and accepted practice today (Koncic & Tomczyk, 2013). Globally, it is estimated that between 40% and 88% of athletes use supplements (Silver, 2001). A study conducted by the United States Olympic Committee in 2004 found that approximately 90% of athletes used various supplements. Such high demand has produced countless products specifically designed for individuals who exercise or play sports. However, these products are not scientifically substantiated for use in sports. They are often advertised as containing certain illegal substances added intentionally or unintentionally to enhance the product's effectiveness, despite manufacturers' inadequate controls and storage conditions. Given this, there is growing evidence that the use of these products may not be reliable (Koncic & Tomczyk, 2013). The general belief is that sports supplements consisting minerals, vitamins, and herbal products are natural and safe. However, these products have a wide range of adverse effects, including headaches, muscle cramps and digestive problems, as well as short- and long-term cardiovascular complications, gout, kidney stones and even kidney failure (Jairoun et al., 2020). As these supplements have been found to contain substances such as heavy metals, potent stimulants, or various banned ingredients, concerns regarding their safety extend far beyond simply reviewing the list of ingredients stated on the supplement label (Harty et al., 2018). Cohen (2009) emphasised in his study that the dosage of substances found in supplements can vary widely, from low/therapeutic/detectable doses to potentially toxic doses. Ultimately, the supplement industry has produced numerous products whose efficacy, quality, and contents are questionable (Koncic & Tomczyk, 2013; Deldicque & Francaux, 2016). The benefits provided by sports supplements remain controversial (Suzic Lazic et al., 2011), and their inappropriate use can lead to various organ damage (Thorsteinsdottir et al., 2006; Dara et al., 2008; Whitt et al., 2008) and even death (Fong et al., 2010). Therefore,

this systematic review has been prepared to support awareness and knowledge on the subject by examining in detail the serious side effects caused by sports supplements used by individuals who exercise or play sports to enhance athletic performance, and the sports supplements held responsible for these side effects. When nutritional supplements used in sporting activities may contain toxic or illegal components, discrepancies may exist between the ingredients listed on the labels and the actual contents. Adverse health outcomes are inevitable when combined with a lack of awareness regarding the use of sports supplements (Liu, 2021). Although the use of sports supplements is common among athletes, information regarding their toxicity and mortality tends to be limited to case reports. Whether the scientifically unjustified use of sports supplements stems from a fad or a lack of studies revealing their actual mechanisms and magnitude of effect (Alonso & Fernandez-Garcia, 2020). This systematic review aimed to elaborate on the severe side effects of sports supplements and the details of these supplements.

**This study was from the master's thesis entitled Time to Understand the Side Effects of Supplements Used in Sports: Micro Analysis of Case Reports.**

## Method

### Research Model

This research is a systematic review study conducted to support the awareness and understanding of sports supplement users by extensively examining the serious side effects caused by sports supplements used by individuals who exercise or play sports to enhance athletic performance. A systematic review is a specific methodology that identifies, selects, evaluates, analyses, synthesises, and reports existing studies in a way that allows for reasonably clear conclusions about what is known and what is not known. A systematic review is not considered a traditional literature search, but rather an independent research project that investigates a clearly defined question derived from a policy or practice problem using existing studies (Denyer & Tranfield, 2009).

### Search Strategy

Between June 2011 and July 2021, a search was conducted using the Cochrane Library, PubMed, and Google Scholar databases to access studies in English. The search terms used were 'failure in sports supplements,' 'sports supplements case reports,' 'sports supplements case studies,' and 'side effects of sports supplements case report,' and case reports were filtered. During the search, results from 2011 to 2021 were marked. Study selection was based on the Population, Interventions, Comparisons, Outcomes, and Study Designs (PICOS) approach, with the criteria for each category listed below:

**Population (P):** It is limited to healthy individuals who engage in sports or regular exercise and do not take medication. There is no age restriction.

**Intervention (I):** The data were obtained from published case reports and series concerning various side effects observed due to sports supplements intended to enhance athletic

performance, which did not directly involve using prohibited substances. Therefore, there was no intervention, the intervention criterion was not used in this study.

**Comparisons (C):** As numerical values relating to risks were to be presented, no comparison criterion was used, and priority was given to interpretations.

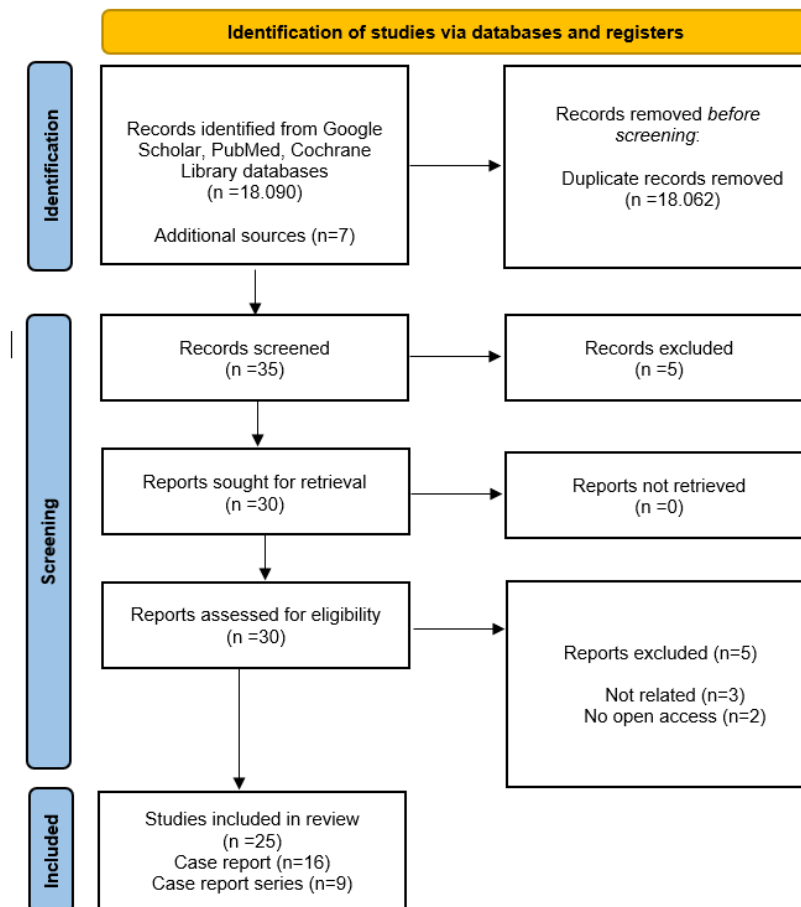
**Outcomes (O):** The contents of side effects caused by sports supplements, their distribution, symptoms observed in relation to their use, the names of sports supplements responsible for side effects, the potential active ingredients they contain, and the percentages exceeding the recommended daily intake of potential active ingredients have been reported.

**Study Types (S):** Case reports and case series indicating that the serious side effects observed were related to the use of sports supplements, detailing the individual's symptoms and clearly discussing vital signs, were included in the review.

The complete search strategy for all database is detailed in Figure 1.

**Figure 1**

*Flow Chart of The Procedure Used to Collect Case Reports Included in the Systematic Review (Liberati et al., 2009)*



**Eligibility Criteria****Inclusion Criteria**

Studies were included if they met all of the following criteria: (a) case report or case report series; (b) studies involving sports supplements related to athletic performance; (c) studies that do not use prohibited substances and open access; (d) Studies that have determined the relationship between the serious side effect observed and the use of sports supplements, and that clearly discuss the symptoms and vital signs; (e) healthy individuals who exercise regularly or athletes.

**Exclusion Criteria**

Studies were excluded if they met all of the following criteria: (a) Articles that directly use prohibited substances and no open access; (b) studies involving sports supplements unrelated to athletic performance; (c) Studies that did not indicate a relationship between the serious side effect observed and the use of sports supplements; (d) studies in which symptoms and vital signs are not clearly discussed; (e) non healthy individuals who exercise regularly or non-athletes; (f): non human studies; (g) case reports and case series involving individuals with any chronic illness or taking medication were excluded from the study, as they could lead to misleading results regarding the effects of sports supplements due to the possibility of interaction between a substance in the supplement and the medication.

**Data Synthesis**

Five studies were found concerning changes in blood plasma caused by the side effects of sports supplements used to enhance athletic performance, 16 studies concerning organ damage, and four studies linking their use to death. The numerical distributions of the contents of these studies included in the research were calculated, and the data were recorded in the SPSS 23 software package, utilising descriptive statistics consisting of frequencies and percentages.

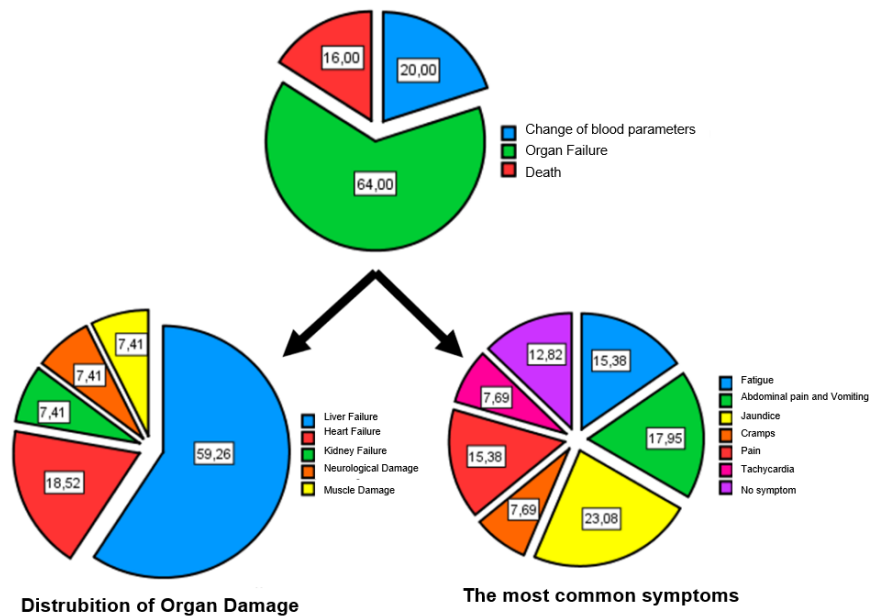
All 25 studies identified through systematic screening were examined in detail and reported within the scope of the thesis. However, in line with this book chapter's aim to provide a more focused and concise presentation, 20 studies are presented in tabular form. The selection was made by prioritising the studies that best represented the topic and provided the most up-to-date evidence. Readers can refer to the original thesis for comprehensive methodological details and a list of all studies.

**Results****Classification of Case Reports and Series**

The findings obtained in relation to the study are explained in detail below.

**Figure 2**

*Classification of Case Reports and Series*



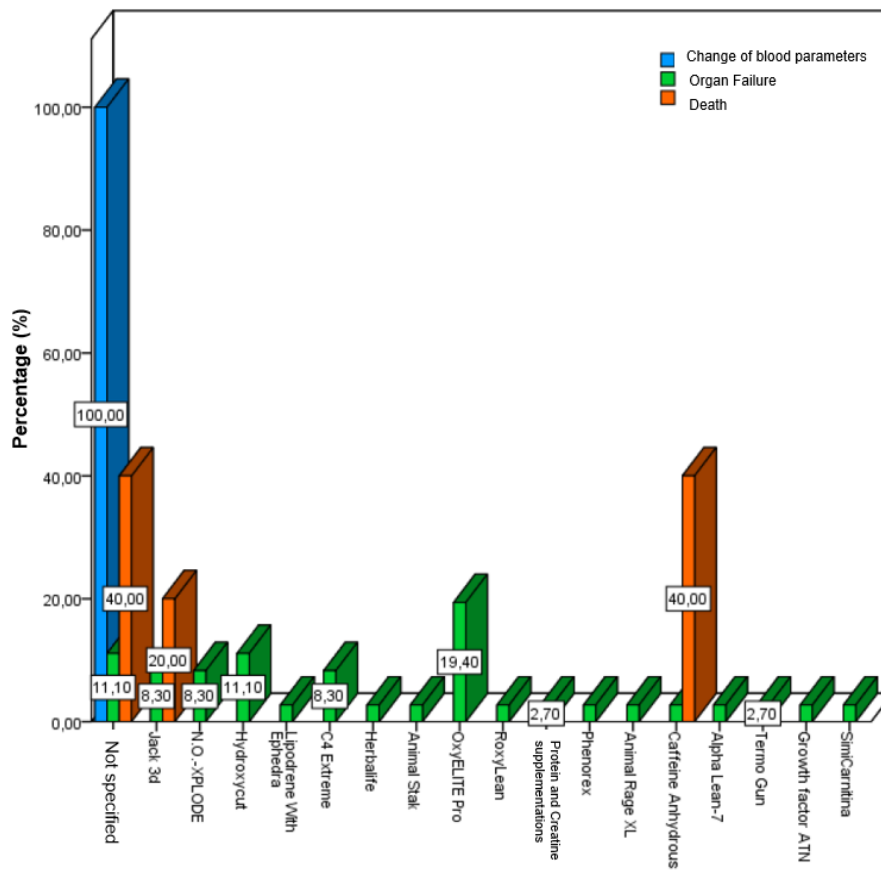
Serious adverse effects in case reports and case series accounted for 64% of organ damage, 20% of changes in blood plasma, and 16% of deaths. Among these, organ damage had the highest rate (64%), with 27 individuals involved in these cases. When examining the details regarding the sample sizes of case reports and series, it was determined that 59.3% were liver damage, 18.5% were heart damage, and 7.4% were kidney, muscle, and neurological damage.

Additionally, the number of individuals who underwent liver transplantation as a result of sports supplement use accounted for 18.75% of all liver damage cases. Looking at the predominant symptoms associated with supplement use, 23.08% of symptoms were related to jaundice, 17.95% to abdominal pain and vomiting, 15.38% to fatigue and pain, and 7.69% to tachycardia and cramps. Although multiple symptoms accompanied all cases, no symptoms were observed in 12.82%.

## Changes in Blood Plasma, Organ Damage and Death Caused by Sports Supplements

**Figure 3**

*Changes in Blood Plasma, Organ Damage and Death Caused by Sports Supplements*



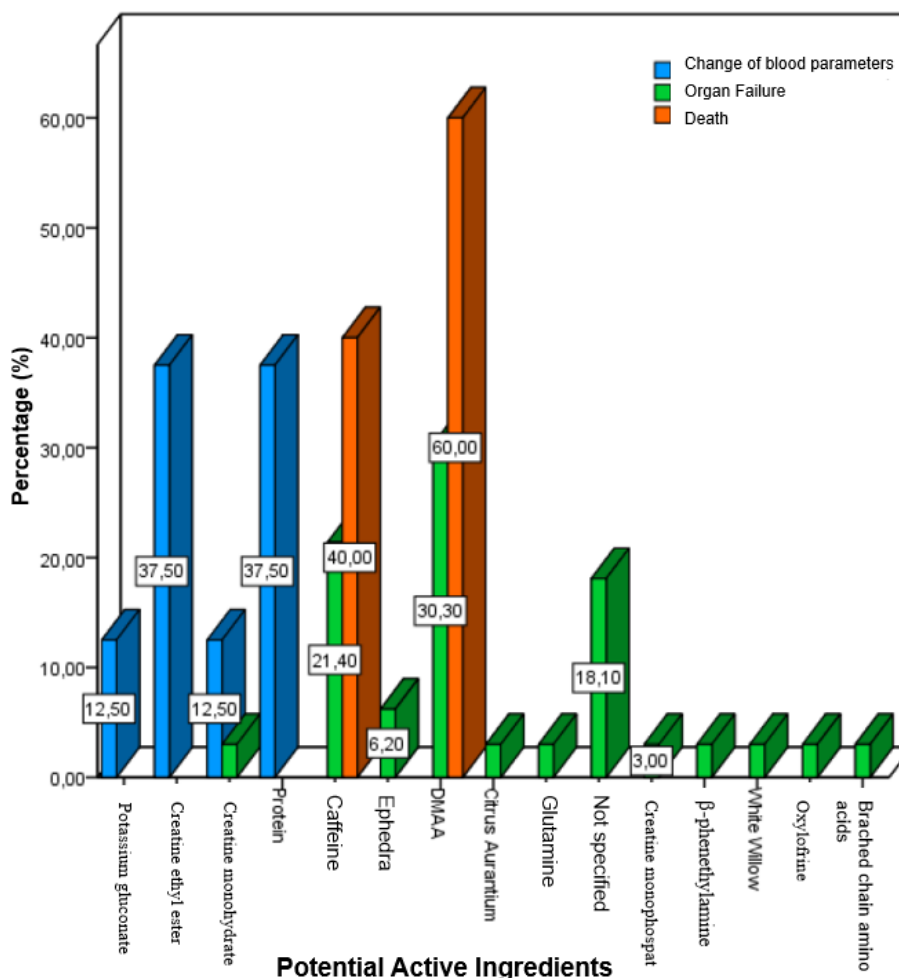
The names of the supplements causing changes in blood plasma have not been specified, and the supplements causing organ damage are, in order, OxyELIT Pro (USP Labs) at 19.4%, Hydroxycut (MuscleTech) at 11.1%, C4 Extreme (Cellucor) at 8.3%, N.O.-Xplode (BSN), Jack 3d (USP Labs), 2.7% with Growth Factor ATN (American Team Nutrition), SimiCarnitina (Farmacia Similares), Lipodrene With Ephedra (Hi-Tech Pharmaceuticals), Herbalife (Herbalife Nutrition), Animal Stak RoxyLean (Animal), Phenorex (Gaspari Nutrition), Animal Rage XL (Universal Nutrition), Caffeine Anhydrous, Alpha Lean-7 (Hard Rock Supplements) and Thermo Gun (Sheer Strength).

The number of supplements causing organ damage is higher than the number of supplements causing changes in blood plasma and death. The supplements causing deaths are Caffeine Anhydrous (40%) and Jack 3d (USP Labs) (20%). The names of the sports supplements responsible for 40% of deaths were not specified in the studies.

## Potential Active Ingredients in Sports Supplements That Cause Changes in Blood Plasma, Organ Damage and Death

Figure 4

*Potential Active Ingredients in Sports Supplements*

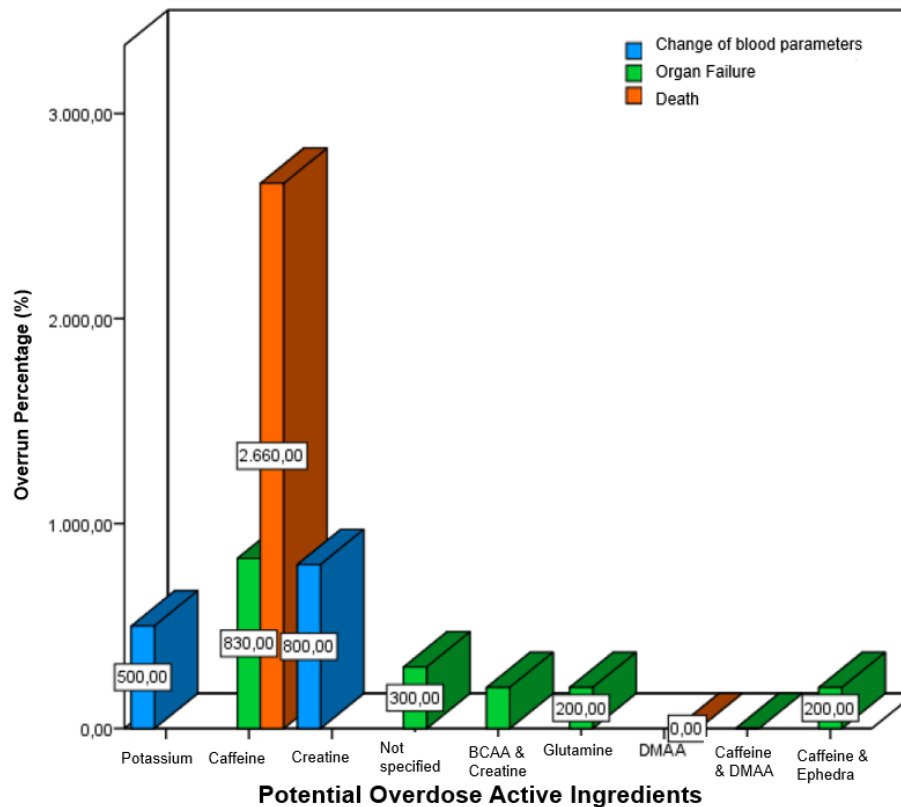


Protein and creatine ethyl ester account for 37.5% of the changes in blood plasma, while potassium gluconate and creatine monohydrate account for 12.5%. Potassium gluconate, creatine ethyl ester, and protein did not cause death or organ damage. The factor most responsible for organ damage (30.3%) is the potential substance DMAA. This is followed by caffeine (21.4%), ephedrine (6.2%), creatine monophosphate (3%), citrus aurantium, glutamine, b-phenethylamine, white willow, oxilofrine, and branched-chain amino acids. None of these substances, except for DMAA and caffeine, caused death. The two potential active ingredients responsible for all deaths are DMAA (60 per cent) and caffeine (40 per cent).

## Percentage of Recommended Daily Intake Exceeded for Sports Supplements Used and Potential Active Ingredients Exceeding the Recommended Daily Intake

### Figure 5

#### *Potential Active Ingredients Exceeding the Recommended Daily Intake*



The supplements causing changes in blood plasma contained five times the recommended amount of potassium (500% excess) and eight times the recommended amount of creatine (800% excess). The caffeine content in supplements causing organ damage was 8.3 times higher than recommended (830% excess), while glutamine, BCAA+creatine and caffeine+ephedrine combinations were taken at twice the recommended amount (200% excess). Sports supplements containing caffeine + DMAA combinations were taken at the recommended amount. Potential active ingredients taken at three times the recommended amount could not be clearly identified. The caffeine contained in the supplements that caused deaths was taken at an average of 26.6 times the recommended amount (2660% excess). Supplements containing DMAA were taken at an average of the recommended amount. As the case series and reports did not provide sufficient information about the supplements used in each case and their quantities, the necessary assessment was made only based on reports containing this information. Accordingly, caffeine is the potential active ingredient most frequently exceeded in the recommended amount. While the average caffeine overdose rate in death reports is 2660%, this rate is 830% in cases of organ damage.

## Case Reports on Organ Damage Associated with the Use of Sports Supplements

The characteristics of case reports concerning organ damage caused by sports supplements used to enhance athletic performance are shown in Table 1.

**Table 1**

*Case Reports on Organ Damage Associated with the Use of Sports Supplements*

| Study ID                      | Samples                                            | Supplement                                        | Potential Active Ingredient | Symptoms                                                                   | Vital Signs                                                                                                                   | Diagnosis            | Final Process                                                                        |
|-------------------------------|----------------------------------------------------|---------------------------------------------------|-----------------------------|----------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|----------------------|--------------------------------------------------------------------------------------|
| Rhidian (2011)                | 36-year-old male marathon runner                   | Unspecified                                       | Caffeine & Ephedra          | Tachycardia<br>Agitation<br>Hypoxia<br>Metabolic acidosis<br>Hypoglycaemia | Body temp: 39°C, K: 6.2 mmol /l, Creatinine: 188 µmol / l, CK: 130.098 U/l, Lactate: 14.7 mmol /                              | Rhabdomyolysis       | The necessary treatments have been administered and the patient has been discharged. |
| Avelar-Escobar et al., (2012) | 17-year-old male bodybuilder                       | N.O.-XPLODE<br>Growth factor ATN<br>SimiCarnitina | Unspecified                 | Vomiting<br>Epigastric pain<br>Jaundice<br>Dark-coloured urine             | AST: 489 U/L, ALT: 640 U/L, ALP: 850 U/L                                                                                      | Acute Hepatotoxicity | The necessary treatments have been administered and the patient has been discharged. |
| Young et al., (2012)          | 26-year-old male soldier (who exercises regularly) | Jack3d                                            | DMAA & Caffeine             | Severe headache<br>Blurred vision in the left eye                          | ALT/AST: 408/223 U, thalamic haemorrhage measuring 2 × 1.8 cm was detected in the head CT scan.                               | Haemorrhagic stroke  | The necessary treatments have been administered and the patient has been discharged. |
| Carol (2013)                  | 25-year-old male soldier (who exercises regularly) | Hydroxycut                                        | Caffeine                    | Severe pain and weakness in the arm and elbow                              | AST: 624 IU/L, ALT:171 IU/L, LDH: 2,865 IU/L, CK: 33.600 IU/L, Myoglobin is positive in urine, BUN and creatinine are normal. | Rhabdomyolysis       | The necessary treatments have been administered and the patient has been discharged. |
|                               | 20-year-old male soldier (who exercises regularly) | Hydroxycut Hardcore                               |                             | Severe cramps<br>Vomiting                                                  | AST: 70 IU/L, ALT: 73 IU/L, CK: 1.040 IU/L, Myoglobin is positive in urine, BUN: 48 mg / dL, Creatinine: 4,0 mg / dL.         |                      |                                                                                      |
| Peterson et al., (2013)       | 28-year-old male soldier (who exercises regularly) | NO Xplode<br>Hydroxycut                           | Unspecified                 | Jaundice<br>Dark-coloured urine<br>Itching<br>Myalgia<br>Fever             | TB: 22,1 mg/dL, AST: 262 IU/L, ALT: 402 IU/L, ALP: 455 IU/L.                                                                  | Liver damage         | Liver enzyme levels have returned to normal.                                         |
|                               | 31-year-old male soldier (who exercises regularly) | Lipodrene With Ephedra                            | Ephedra                     |                                                                            | TB: 30,4 mg/dL, AST: 80 IU/L, ALT: 65 IU/L, ALP: 464 IU/L.                                                                    |                      |                                                                                      |

|                      |                                                      |                                                                |                         |                                                  |                                                                                                          |                               |                                              |
|----------------------|------------------------------------------------------|----------------------------------------------------------------|-------------------------|--------------------------------------------------|----------------------------------------------------------------------------------------------------------|-------------------------------|----------------------------------------------|
|                      | 23-year-old male soldier (who exercises regularly)   | C4 Extreme                                                     | Unspecified             |                                                  | TB: 12,9mg/dL, AST: 423 IU/L, ALT: 301 IU/L, ALP: 582 IU/L.                                              | Liver damage                  | Liver enzyme levels have returned to normal  |
|                      | 46-year-old male soldier (who exercises regularly)   | Herbalife                                                      | Bacterial contamination |                                                  | TB: 12,1 mg/dL, AST: 496 IU/L, ALT: 1191 IU/L, ALP: 301 IU/L.                                            |                               |                                              |
|                      | 31-year-old male soldier (who exercises regularly)   | Animal Stak                                                    | Unspecified             |                                                  | TB: 10,5 mg/dL, AST: 195 IU/L, ALT: 592 IU/L, ALP: 67 IU/L.                                              |                               |                                              |
| Foley et al., (2014) | 45 year-old female soldier (who exercises regularly) | OxyELITE Pro                                                   | DMAA                    | Jaundice<br>Exercise intolerance<br>Steatorrhoea | TB: 26,4 mg/dL, AST: 2514 U/L, ALT: 1980 U/L, ALP: 136 U/L, Creatinine: 0,8 mg / dL.                     | Acute liver failure           | Liver Transplant                             |
|                      | 28 year-old male soldier (who exercises regularly)   | OxyELITE Pro                                                   |                         | Fatigue<br>Drowsiness<br>Jaundice                | TB: 32,0 mg/dL, AST: 1497 U/L, ALT: 2379 U/L ve Creatinine: 0,7 mg/dL.                                   | Acute liver failure           | Liver Transplant                             |
|                      | 19 year-old male soldier (who exercises regularly)   | OxyELITE Pro<br>C4 Extreme<br>Jack 3d                          |                         | Şevere headache<br>Abdominal pain<br>Vomiting    | TB: 1,2 mg / dL, AST: 1155 U / L<br>ALT: >2000 U/L, Creatinine: 0.8 mg/dL and tachycardia were detected. | Chemical-induced liver damage | Liver enzyme levels have returned to normal. |
|                      | 28 year-old female soldier (who exercises regularly) | OxyELITE Pro<br>C4 Extreme                                     |                         | Nausea<br>Abdominal pain                         | TB: 6,7 mg / dL AST: 1285 U/L<br>ALT:1162 U/L, Creatinine: 0,7 mg/dL.                                    | Chemical-induced liver damage | Liver enzyme levels have returned to normal. |
|                      | 23 year-old male soldier (who exercises regularly)   | OxyELITE Pro<br>RoxyLean<br>Protein ve Kreatin<br>suplemanları |                         | Discomfort in the abdominal area<br>Jaundice     | TB: 17,5 mg/dL, ALT: 194 U/L, Creatinine: 1 mg/dL.                                                       | Acute liver failure           | Liver enzyme levels have returned to normal. |
|                      | 23 year-old male soldier (who exercises regularly)   | OxyELITE Pro                                                   |                         | Jaundice<br>Itching                              | TB: 2,8 mg/dL, ALT: 176 U/L, Creatinine: 1 mg/dL.                                                        | Acute liver failure           | Liver enzyme levels have returned to normal. |

**Abbreviations:** ALP: Alkaline Phosphatase, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, BUN: Blood Urea Nitrogen, Ca: Calcium, CK: Creatine Kinase, DB: Direct Bilirubin, DMAA: 1,3 Dimethyl Amylamine, ECG: Electrocardiography, HDL: High-Density Lipoprotein, IU/L: International Units per litre, K: Potassium, LDH: Lactate Dehydrogenase, LDL: Low-Density Lipoprotein, mEq/L: Milliequivalents per litre, mg/dL: Milligrams per decilitre, mmol/L: Millimoles per litre, mL/min: Millilitres per minute, mm Hg: Millimetres of mercury, ng/L: Nanograms per litre, P: Phosphorus, TB: Total Bilirubin, TC: Total Cholesterol, U/L: Units/litre, °C: degrees Celsius, µmol/L: micromoles/litre.

|                                      |                                                        |                               |                                                              |                                                                     |                                                                                                                                                |                               |                                                                                       |
|--------------------------------------|--------------------------------------------------------|-------------------------------|--------------------------------------------------------------|---------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|---------------------------------------------------------------------------------------|
|                                      | 24 year-old female soldier (who exercises regularly)   | OxyELITE Pro                  |                                                              | Nausea<br>Jaundice<br>Vomiting<br>Itching                           | TB: 6,3 mg/dL, ALT: 3348 U/L, AST: 1725 U/L, Creatinine: 0,8 mg / dL.                                                                          | Chemical-induced liver damage | Liver Transplant                                                                      |
| Smith et al., (2014)                 | A 22-year-old male who exercises regularly             | Phenorex Jack 3d              | Citrus aurantium & DMAA                                      | Chest pain                                                          | Cardiac troponin T: 1.36 ng/mL, CK: 518 U/L, TK: 106 mg/dL, LDL: 52 mg/dL, HDL: 42 mg/dL. Sinus arrhythmia present on ECG.                     | Myocardial infarction         | The necessary treatments have been administered, and the patient has been discharged. |
| Siano (2014)                         | 26 year-old male soldier (who exercises regularly)     | N.O.-Xplode                   | Unspecified                                                  | Abdominal pain<br>Loss of appetite<br>Pink-coloured urine<br>Nausea | Creatinine: 10.64 mg/dL, K: 6.2 mEq/L, BP: 182/94 mmHg, eGFR: 6.8 mL/min, Renal biopsy revealed damage to the renal tubules.                   | Acute tubular necrosis        | When he stopped taking the supplement, his condition returned to normal.              |
| Araujo & Worman (2015)               | 41-year-old male individual who does strength training | Hydroxycut SX-7 Clean Sensory | Unspecified                                                  | Jaundice<br>Nausea<br>Vomiting<br>Fatigue                           | AST: 2360 U/L, ALT: 6218 U/L, ALP: 109 U/L, TB: 8,3 mg/dL, Creatinine: 1.80 mg/dL, Abdominal ultrasound revealed increased liver echogenicity. | Acute liver failure           | The necessary treatments have been administered, and the patient has been discharged. |
| Arshad et al., (2015)                | 41-year-old male individual who does strength training | Unspecified                   | Branched-chain Amino Acids & Creatine (monohydrate)          | Sweating<br>Vomiting<br>Mild shortness of breath                    | Troponin T: 3467 ng/ L, An intracoronary thrombus was detected during angiography.                                                             | Myocardial infarction         | The necessary treatments have been administered, and the patient has been discharged. |
| Kamatovskaia, Leoni & Freeman (2015) | 21 year-old male who exercises regularly               | Unspecified                   | DMAA                                                         | No symptom                                                          | Troponin T: 1.09 ng/mL, CK: 1868 U/L, ST segment elevation detected on ECG.                                                                    | Sudden cardiac arrest         | A cardioverter defibrillator has been implanted.                                      |
| Harris, Winn & Ableman (2017)        | 25 year-old male soldier (who exercises regularly)     | Animal Rage XL                | Caffeine<br>Creatine (monophospat) & $\beta$ -phenethylamine | Severe headache<br>Nausea and vomiting<br>Imbalance                 | Magnetic resonance angiography revealed bilateral cerebellar haemorrhagic stroke.                                                              | Haemorrhagic stroke           | The necessary treatments have been administered, and the patient has been discharged. |

|                            |                                            |                                |                                        |                                                        |                                                                                                                                                             |                     |                                                                                       |
|----------------------------|--------------------------------------------|--------------------------------|----------------------------------------|--------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------------------------------------------------------------------------|
| Andrade et al.,<br>(2018)  | 32 year-old female who exercises regularly | Caffeine Anhydrous (toz formu) | Caffeine                               | Fatigue<br>Anxiety<br>Nausea and vomiting              | Tachycardia (160 bpm), metabolic acidosis (Lactate: 5.3 mmol/L), Glucose: 254 mg/dL, Ca: 2.5 mmol/L, P: 1.8 mg/dL, polymorphic tachycardia detected on ECG. | Cardiac arrhythmia  | The necessary treatments have been administered, and the patient has been discharged. |
| Wang (2019)                | 33 year-old female who exercises regularly | Alpha Lean-7                   | Caffeine                               | Chest tightness<br>Shortness of breath<br>Pre-syncope  | Tremor and tachycardia present, Troponin: 50 ng/L, vital organs, mental status, cardiovascular and respiratory system examinations normal.                  | Cardiac ischaemia   | The necessary treatments have been administered, and the patient has been discharged. |
| Ferreira et al.,<br>(2020) | 36-year-old male MMA fighter               | Thermo Gun                     | Oxilofrine<br>White Willow<br>Caffeine | Lethargy<br>Jaundice                                   | TB: 7 mg/dL, AST: 480 IU/L, ALT: 373 IU/L                                                                                                                   | Acute liver failure | Liver Transplant                                                                      |
| Hatami et al.,<br>(2020)   | 35-year-old female bodybuilder             | Unspecified                    | Glutamine                              | Nausea and vomiting<br>Jaundice<br>Dark-coloured urine | TB: 14,8 mg/dL, AST: 2500 IU/L, ALT: 2400 IU/L, ALP: 492 U/L, A lesion has been detected in the liver using dynamic magnetic resonance imaging.             | Acute liver failure | Liver enzyme levels have returned to normal.                                          |

**Abbreviations:** ALP: Alkaline Phosphatase, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, BUN: Blood Urea Nitrogen, Ca: Calcium, CK: Creatine Kinase, DB: Direct Bilirubin, DMAA: 1,3 Dimethyl Amylamine, ECG: Electrocardiography, HDL: High-Density Lipoprotein, IU/L: International Units per litre, K: Potassium, LDH: Lactate Dehydrogenase, LDL: Low-Density Lipoprotein, mEq/L: Milliequivalents per litre, mg/dL: Milligrams per decilitre, mmol/L: Millimoles per litre, mL/min: Millilitres per minute, mm Hg: Millimetres of mercury, ng/L: Nanograms per litre, P: Phosphorus, TB: Total Bilirubin, TC: Total Cholesterol, U/L: Units/litre, °C: degrees Celsius, µmol/L: micromoles/litre.

## Characteristics of Case Reports Related to Deaths Associated with the Use of Sports Supplements Intended to Enhance Athletic Performance

The characteristics of case reports concerning death caused by sports supplements used to enhance athletic performance are shown in Table 2.

**Table 2**

*Case Reports on Deaths Associated with the Use of Sports Supplements*

| Study ID               | Samples                            | Supplementation    | Potential Active Ingredient | Symptoms                            | Vital Signs                                                                                                                                                                                          | Diagnosis             | Final Process |
|------------------------|------------------------------------|--------------------|-----------------------------|-------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|---------------|
| Eliason et al., (2012) | 22-year-old male soldier           | Unknown            | DMAA                        | Leg cramps<br>Loss of consciousness | High fever (40.8 °C), K: 7.4 mEq/L, Na: 149 mEq/L, Creatinine: 2.3 mg/dL, Glucose: 188 mg/dL, Metabolic acidosis (Lactate: 38.2 mg/dL), CK: 7.3 U/L, Cardiac Troponin I: 0.069 ng/mL                 | Sudden cardiac arrest | DEATH         |
|                        | 32 years old female soldier        |                    |                             | Shortness of breath<br>Leg cramps   | Shock present, hypotensive (77/36 mmHg), tachycardic (109 bpm), metabolic acidosis (Lactate: 21.5 mmol/dL), K: 5.2 mEq/L, Na: 133 mEq/L, Creatinine: 1.8 mg/dL, Glucose: 261 mg/dL, AST/ALT <5 IU/L. |                       |               |
| Jabbar & Hanly, (2013) | 39 year-old male bodybuilder       | Caffeine Anhydrous | Caffeine                    | Severe vomiting                     | The autopsy revealed 350 mg/L of caffeine in the blood.                                                                                                                                              | Sudden cardiac arrest | DEATH         |
| Poussel et al., (2013) | 44-year-old male bodybuilder       | Caffeine Anhydrous | Caffeine                    | Sweating<br>Tremor<br>Tachypnoea    | K: 2.6 mmol/L, WBC: 14,740 g/L CK: 9040 IU/L, Troponin I: 31.01 µg/L and 190 mg/L caffeine was detected in the blood.                                                                                | Sudden cardiac arrest | DEATH         |
| Archer et al., (2015)  | 30-year-old female marathon runner | Jack 3d            | DMAA                        | Rigidity in the lower extremities   | Bicarbonate: 22.6 mmol/L, Lactate: 18 mmol/L, Glucose: 2.9 mmol/L, K: 9.67 mmol/L, Na: 136.9 mmol/L.                                                                                                 | Acute heart failure   | DEATH         |

**Abbreviations:** ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, CK: Creatine Kinase, DMAA: 1,3 Dimethylamylamine, g/L: gram per litre, IU/L: International Unit per litre, K: Potassium, mEq/L: milliequivalent per litre, mg/dL: milligram per decilitre, mm Hg: millimetre of mercury, mmol/dL: millimole per decilitre, mmol/L: millimole per litre, Na: Sodium, ng/mL: nanogram per millilitre, U/L: Unit per litre, WBC: White Blood Cell, °C: degree Celsius, µg/L: microgram per litre.

**Recent Developments (2022-2025)**

While the main arguments and structure of the thesis have been retained, an additional literature review has been conducted to enhance the currency and depth of this book chapter, given the rapidly evolving nature of scientific knowledge.

Update Method: A search was conducted using the Cochrane Library, PubMed, and Google Scholar databases between 2022 and 2025 using the terms ‘failure in sport supplements,’ ‘sport supplements case reports,’ ‘sport supplements case studies,’ and ‘side effects of sport supplements case report,’ and case reports were filtered. The search was limited to studies published after the thesis defence. During this process, newly emerging case reports on the subject (Erfanifar et al., 2022; Gokdemir & Ulutan, 2022; Khan et al., 2022; Ridha et al., 2023; Altaf et al., 2024; Pallangyo et al., 2024; Kermanshah et al., 2025) were identified and integrated into the relevant sections of the book chapter, enriching the existing discussion.

As a result, seven case reports were obtained. Six of these were related to organ damage and one was a case report related to death. The table below summarises information on current case reports identified during this process that have made significant contributions to the subject.

**Table 3***Case Reports on Organ Damage and Deaths Observed between 2022 and 2025*

| Study ID                | Samples                                  | Supplement                  | Potential Active Ingredient  | Symptoms                                                                    | Vital Signs                                                                                                                                                   | Diagnosis                                      | Final Process                                                                                                        |
|-------------------------|------------------------------------------|-----------------------------|------------------------------|-----------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| Gokdemir & Ulutun, 2022 | 22 years old male bodybuilder            | Jack 3D                     | DMAA                         | Arrhythmia, Tachyarrhythmia                                                 | BP: 130/80 mmHg, Pulse: 126/min<br>RR: 18/min<br>Temperature: 36,5 C°                                                                                         | Atrial Fibrillation (Arrhythmia)               | The bodybuilder converted to normal sinus rhythm after the second line therapy.                                      |
| Pallangyo et al., 2024  | 25 years old male fitness trainer        | Pre-workout (Not specified) | Caffeine or theophylline,    | Crushing mid-sternal chest pain                                             | BP: 114/71mmHg, Pulse: 58 /min<br>LDL: 1.02mmol/L, HDL: 1.53mmol/L, TG: 0.77mmol/L<br>Cholesterol: 2.96 mmol/L<br>troponin I: 5.14ng/mL<br>CK-MB: 78.1 ng/mL. | Myocardial infarction                          | He was released from the hospital with drug therapy. He demonstrated normal function during his four-week follow-up. |
| Altaf et al., 2024      | 36 years old man who exercised regularly | Pre workout (Not specified) | Creatine or caffeine         | Progressive weakness and numbness in both lower limbs, pain and sensitivity | AST: 2168 U/L<br>ALT: 501 U/L<br>Creatinine: 4.9 mg/dl<br>BUN: 50 mg/dl<br>CK: 84983 U/L<br>Na: 131 mEq/L<br>K: 7.3 mEq/L                                     | Severe Rhabdomyolysis, kidney and liver damage | He has been discharged following treatment.                                                                          |
| Ridha et al., 2023      | 35 years old man who exercised regularly | Pre workout (Not specified) | Not specified                | Abdominal pain                                                              | Lipase: 3000 U/L.                                                                                                                                             | Pancreatitis                                   | He has been discharged 2 days later following treatment.                                                             |
| Erfanifar et al., 2022  | 20-year-old male athlete                 | Growth hormone injection    | Growth hormone/ Somatotropin | Hallucinations                                                              | White blood cell: 15800 /L<br>Urea: 33 mg/dl<br>AST: 157 U/L<br>ALT: 359 U/L<br>CKMB: 374 U/L<br>CPK: 2620 U/L                                                | Rhabdomyolysis                                 | Died                                                                                                                 |

|                         |                                        |                                         |                      |                                                                                                |                                                                                                                                                        |                |                                                                                                                 |
|-------------------------|----------------------------------------|-----------------------------------------|----------------------|------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|-----------------------------------------------------------------------------------------------------------------|
| Kermanshah et al., 2025 | 35 years old healthy man who exercised | Pycnogenol (Maritime Pine Bark Extract) | Polyphenolic complex | Myalgia, soreness, and tea-colored urine, mild tenderness and edema in upper extremity muscles | CK: 154000 U/L<br>AST: 2400 U/L<br>ALT: 700 U/L                                                                                                        | Rhabdomyolysis | The supplement was discontinued and intensive fluid therapy was administered. The patient made a full recovery. |
| Khan et al., 2022       | 29 years old male bodybuilder          | SARM supplements                        | SARM                 | Jaundice, fatigue, itching, pale stools and dark urine                                         | Hematocrit: 51.9%,<br>Platelet: 470/ $\mu$ L, total bilirubin: 16.9 mg/dL<br>AST: 79 U/L<br>ALT: 165 U/L,<br>ALP: of 213 U/L.<br>Ferritin: 602.1 ng/ml | Hepatic Injury | Liver function tests returned to completely normal within six months.                                           |

**Abbreviations:** BP: Blood Pressure, RR: Respiratory Rate, DMAA: 1,3 Dimethyl Amilamin LDL: Low Density Lipoprotein HDL: High Density Lipoprotein, TG: Triglyceride, CK-MB: Creatin Kinase -MB, AST: Aspartate Transaminase, ALT: Alanine Aminotransferase, CK: Creatine Kinase, U/L: Units/Liter, mg/dl: milligram per decilitre, Na: Sodium, K: Potassium, mEq/L: milliequivalent per litre, CPK: Creatine Phosphokinase, SARM: Selective Androgen Receptor Modulators, ALP: Alkaline phosphatase.

According to Table 3, a 22-year-old male bodybuilder was admitted to the hospital with a sudden onset of palpitations and shortness of breath. His blood pressure was 130/80 mmHg, pulse was 126/min and arrhythmic, respiratory rate was 18/min, and temperature was 36.5°C. Physical examination revealed tachyarrhythmia. When asked directly about his supplements, he stated that he was using Jack3d, a bodybuilding supplement. It is quite noteworthy that a sports supplement triggered this severe arrhythmia in a healthy young man with no structural heart disease (Gokdemir & Ulutan, 2022).

A healthy 25-year-old guy presented with an immediate feeling of crushing mid-sternal heartburn lasting 4 hours. His health issues began approximately an hour after finishing his 2-hour workout at the fitness centre. He was taking a pre-workout product for eight months as a component of his fitness program. Three days before going to the hospital, he began “dry scooping”. Dry scooping, the dangerous act of taking in pure pre-workout protein powder in the hopes of experiencing a more noticeable energy spike, has grown into a global fitness practice. Coronary enzyme levels were high, with troponin I rising at 5.14 ng/mL and CK-MB at 78.1 ng/mL. The foregoing history and clinical signs led to the diagnosis of anterolateral ST-elevation myocardial infarction (Pallangyo et al., 2024).

A 36-year-old male was transported to the intensive care unit after presenting with increasing weakness and numbness in both lower extremities, as well as discomfort and soreness. The patient reported the leg pain as “electric,” starting in the left anterior hip and spreading to the foot. First lab results showed acute renal failure, raised liver enzymes, high serum creatine kinase (CK), and acid-base abnormalities, involving hyperkalaemia and anion gap acidosis. His condition had severe rhabdomyolysis, a potentially fatal electrolyte and acid-base imbalance, hemoconcentration, dehydration, and kidney and liver damage. He was on a regular exercise regimen and had been taking a pre-workout supplement for the previous two months. He reported taking a workout aid high in creatine monohydrate, a standard, easily accessible, and frequently promoted pre-workout supplement. It was stated that the problem was linked to using pre-workout supplements and exercise (Altaf et al., 2024).

A 35-year-old man who exercised regularly, reported to the hospital’s emergency room with stomach pain, increased enzyme levels in his pancreas, and radiographic abnormalities consistent with acute pancreatitis. The patient’s medical history showed no prior risk factors for pancreatitis. The liver enzymes, lipid composition, and IgG4 serum test were all within normal ranges. Lipase level was detected as 3000 U/L. Further investigation revealed that the patient started using a new exercise supplement about a month ago to improve his workouts and performance. He acknowledged using pre-workout supplements. The male patient gave the investigators the brand name of the pre-workout supplement he was consuming, and the investigators began looking into

specific ingredients of the supplement and their potential link to pancreatitis. The investigators stated that the mix of ingredients in the sports supplement may raise the risk of pancreatitis and other organ harm (Ridha et al., 2023).

A young athlete presented to the hospital emergency room with delusions after using 300 mg subcutaneous growth hormone injections. He was tachycardic with moderate hypertension. Lab results showed hypernatraemia (157 mEq/L), hyperkalaemia (5.3 mEq/L), elevated LDH (1448 U/L), and CPK (2620 U/L), all pointing to rhabdomyolysis. He was said to have taken 30 subcutaneous somatropin injections, each carrying 10 mg/1.5 mL, to improve performance for the upcoming bodybuilding competition. After several episodes of hyperthermia, hypertension, and possibly pulmonary embolism, he died after a somatropin overdose (Erfanifar et al., 2022).

Kermanshah and colleagues described a case in a 2025 study with a 35-year-old male patient who exercised regularly and complained of extensive myalgia, discomfort, and tea-colored urine. A medical exam revealed minor soreness and oedema in the upper extremity muscles. Laboratory testing revealed a baseline CK value of 154,000 U/L, aspartate aminotransferase (AST) of 2,400 U/L, alanine aminotransferase (ALT) of 700 U/L, and normal kidney function (creatinine: 0.7-0.8 mg/dL). CK values greater than 150,000 U/L are unusual and indicate significant skeletal muscle degeneration. Following an in-depth follow-up conversation in the hospital, the patient admitted that he had taken excessive amounts of Pycnogenol, an over-the-counter pine bark extract supplement, for “antioxidant/energy” benefits. The actual product name was unclear. This example implies a link between high Pycnogenol intake and severe rhabdomyolysis caused by low physical exercise. According to the authors, this instance is relevant because it indicates that even ‘natural’ or ‘herbal’ supplements can induce dangerous side effects when used in excessive dosages (Kermanshah et al., 2025).

Khan and colleagues published a case report in 2022 about a 29-year-old bodybuilder who got jaundice, tiredness, and abnormal liver function tests after initiating Selective Androgen Receptor Modulators (SARM) intake. The patient came to the hospital with jaundice, fatigue, itching, pale stools and dark urine. Initial laboratory tests showed haematocrit 51.9%, platelet count 470/ $\mu$ L, total bilirubin 16.9 mg/dL, direct bilirubin 12.1 mg/dL, AST 79 U/L, ALT 165 U/L, and ALP 213 U/L. The total iron-binding capability is 428 mcg/dL, with iron saturate at 41% and ferritin at 602.1 ng/mL. Further research revealed that the patient began taking a SARM supplement for bodybuilding around four weeks prior. Liver damage was diagnosed due to bile stasis and neutrophil accumulation (microabscesses) associated with supplement use. The supplements were discontinued, and supportive treatment was administered. Liver function tests were regular within 6 months (Khan et al., 2022).

## **Discussion and Conclusion**

This study, 25 case reports and series involving serious adverse effects associated with using sports supplements were evaluated in the Cochrane Library, PubMed, and Google Scholar databases between June 2011 and July 2021.

According to the results obtained;

- The case reports and series examined revealed that 64% of serious adverse effects were related to organ damage, 20% to changes in blood plasma, and 16% to death. When examining the details of the case reports and series related to organ damage in terms of sample size, it was determined that 59.3% of these damages were liver damage, 18.5% were heart damage, and 7.4% were kidney, muscle, and neurological damage.

In contrast to these findings, a large-scale field study reporting side effects associated with supplement use found that deaths accounted for 2.2% of all cases; hospitalisations accounted for 25.4%; life-threatening outcomes accounted for 7.9%; and serious adverse outcomes accounted for 35.5% of all cases (Timbo et al., 2018).

- When looking at the predominant symptoms associated with supplement use, 23.08% of symptoms were related to jaundice, 17.95% to abdominal pain and vomiting, 15.38% to fatigue and pain, and 7.69% to tachycardia and cramps. Although multiple symptoms accompanied all cases, no distinct symptoms were observed in 12.82%.

Contrary to these findings, in a study conducted with active individuals who regularly used sports supplements before exercise, when participants were asked about the side effects they experienced, 25.6% reported nausea and 23.4% reported cardiac abnormalities (rapid heartbeat, palpitations) In another study examining side effects associated with supplement use, 51.3% of cases were reported to show no symptoms (Palmer et al., 2003).

- The number of individuals who have undergone liver transplantation as a result of sports supplement use accounts for 18.75% of all liver damage cases. When examining sports supplements that cause organ damage, it was determined that OxyELIT Pro (USP Labs) was specifically responsible for liver damage, while the sports supplements Caffeine Anhydrous and Jack 3d (USP Labs) caused both organ damage and deaths.

Similarly, a systematic review of studies conducted on liver damage associated with supplement use in the Latin American population indicated that 22% of cases with liver damage required a liver transplant (Santos et al., 2020). In a study examining the side effects associated with the use of the sports supplement OxyELITE Pro (USP Labs), liver damage was reported in 55 individuals, with hospitalisation occurring in 60% of these cases and liver transplantation in 5% (de Boer & Sherker, 2017).

In another study evaluating the side effects associated with the use of DMAA-containing products in Texas, it was reported that 80.4% of individuals experiencing side effects used the sports supplements OxyELITE Pro (USP Labs) and 14.3% used Jack 3d (USP Labs) (Forrester, 2013).

- The potential active ingredients most responsible for changes in blood plasma is protein and creatine ethyl ester; the potential active ingredients that cause significant organ damage and deaths are DMAA and caffeine.

In contrast to the findings of this study, a meta-analysis on the side effects of supplements in active individuals who exercise regularly and use supplements showed a moderate correlation between creatine and dry mouth; caffeine showed a moderate correlation with tremors, protein showed a high correlation with constipation and numbness, and casein protein showed a high correlation with heart palpitations and a moderate correlation with nausea. The same study reported that protein supplements containing casein and soy proteins were responsible for many side effects (Gillani et al., 2020).

- When examining the excess amounts of sports supplements, it was observed that supplements causing changes in blood plasma contained up to 8 times (800% excess) creatine, while sports supplements causing organ damage contained up to 2 times (200% excess) BCAA, creatine, glutamine, caffeine and ephedrine.
- The active ingredient most frequently exceeded in excess of the recommended amount is caffeine, with the average caffeine excess rate in death reports being 2660%, while the rate for organ damage is 830%.

In a study involving the chemical analysis of creatine content in 33 creatine supplements available on the Italian market, it was generally determined that 50% of the analysed products exceeded the maximum creatine dosage recommended by the European Food Safety Authority (EFSA) (Moret et al., 2011).

In addition, recent case reports increasingly indicate that supplements used to enhance athletic performance can lead to serious organ damage and even death, even in young and healthy individuals. For example, Gokdemir & Ulutan (2022) reported that a 22-year-old bodybuilder developed serious arrhythmia after using a supplement called Jack3d, while Pallangyo et al. (2024) documented that a pre-workout supplement taken using the ‘dry scooping’ method caused anterolateral myocardial infarction. Altaf et al. (2024) emphasised that a pre-workout product containing creatine monohydrate resulted in severe rhabdomyolysis, kidney and liver damage. In addition, Ridha et al. (2023) revealed the link between a similar supplement and pancreatitis, while Erfanifar et al. (2022) reported a case where excessive growth hormone use led to death. Products thought to be plant-based also carry similar risks; Kermanshah et al. (2025) reported that excessive Pycnogenol intake led to severe rhabdomyolysis, raising CK levels above 150,000 U/L, while Khan et al. (2022) reported that SARM use resulted in biopsy-confirmed cholestatic hepatitis. These cases demonstrate that perceiving these products as ‘natural’ or ‘harmless’ is misleading and that effective pharmacovigilance and increased physician-patient awareness are urgently needed.

In almost all case reports examined between 2022 and 2025, the exact dosage and brand name of the supplements used were not specified. This situation reflects one of the most fundamental problems in the sector: lack of oversight and transparency (Costa et al., 2021). The absence of brand information makes it impossible to determine specific

product responsibility; the lack of dosage information prevents the establishment of a threshold value for toxicity and the establishment of a dose-response relationship (Hayes et al., 2020). Even more worrying is that this uncertainty allows for the masking of much more serious risks, such as the hidden content of supplements or product contamination. Cohen and colleagues found that 66.7 per cent of dietary supplements purchased and analysed at least six months after the FDA recall still contained banned ingredients. This indicates that a significant proportion of recalled supplements remain counterfeit despite the measures taken by the FDA (Cohen et al., 2014). The lack of brand information makes it impossible to identify and recall such specific products from the market (Hayes et al., 2021). Therefore, this methodological shortcoming does not diminish the clinical significance of the findings; instead, it provides strong evidence that these products operate in a grey area where existing regulatory mechanisms are inadequate. (Cohen et al., 2014).

In conclusion, the inappropriate use of sports supplements sold online, which are easily accessible and not approved by regulatory authorities, by individuals who exercise or play sports to enhance athletic performance can produce serious risks such as changes in blood plasma and organ damage, and can lead to death. The data obtained from this study could support consumers' awareness and understanding of the subject and contribute to identifying interventions aimed at reducing the risk of side effects associated with using sports supplements. These current case reports demonstrate that the spectrum of adverse events associated with the use of sports supplements can be more serious than anticipated. This evidence highlights the ongoing relevance of the issue and the critical importance of regulating these products and increasing physician awareness.

### **Take-Home Messages**

- Individuals who exercise or play sports should be supported and informed to purchase sports supplements rigorously tested for toxic or illegal ingredients, subjected to third-party testing, and approved.
- Although the contents of supplements used may be natural or plant-based, they should not be used indiscriminately without consulting an expert due to reasons such as contamination, counterfeit products, hidden ingredients, illicit substances, scepticism about content, quality concerns or misinformation on labels. Professional help should be sought.
- The tendency towards dangerous sports supplements that harm or kill users should not be overlooked. Necessary studies should be conducted and necessary steps taken to design an effective system to prevent even one person from being harmed or killed.
- In addition to the necessary regulations concerning the sale of sports supplements that are released onto the market without undergoing sufficient control procedures and are easily accessible online, conducting toxicological studies and reporting on them could effectively enable users to make appropriate choices.
- It should be remembered that the ingredients listed on the label may not always be present in the bottle. The contents of sports supplements should be identified through

advanced analysis and their compliance with the label should be verified, and/or systems should be developed to ensure this.

- Although there is positive evidence regarding the use of various supplements, it may be advisable for users to use sports supplements after conducting a cost-benefit analysis, considering their individual differences and the requirements of their sport or exercise.
- Finally, athletes or individuals who exercise can be educated on the subject by specialists such as pharmacists, sports dieticians, and doctors; reports on the side effects of sports supplements ([www.safetyreporting.hhs.gov](http://www.safetyreporting.hhs.gov)), safe/approved supplements ([www.consumerlab.com](http://www.consumerlab.com) / <https://sport.wetestyourtrust.com/>), prohibited substances ([www.wada-ama.org](http://www.wada-ama.org)) and general information about supplements ([www.drugfreesport.com](http://www.drugfreesport.com)).

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