



Drug–protein supplement interactions in young athletes: A scoping review exposing a major evidence gap

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Abstract

Background: One of the fastest growing consumer segments in the global protein supplement market is the adolescent athlete; this population also regularly uses over-the-counter (OTC) medications such as non-steroidal anti-inflammatory drugs (NSAIDs), antacids and inhaled bronchodilators at the same time. Coadministration of these agents is poorly characterized pharmacokinetically, pharmacodynamically and represents an unmet clinical and public health concern.

Objective: To systematically map and synthesize published evidence on the prevalence, patterns, and potential clinical consequences of concurrent protein supplement and medication use among athletes aged 14-21 years, also to identify critical gaps that warrant prospective investigation.

Methods: A scoping review was conducted following the PRISMA extension for Scoping Reviews (PRISMA-ScR). We searched PubMed, Scopus and Cochrane Library for articles published between January 1, 2012 and December 31, 2024. Pre-defined inclusion criteria were used to select 18 original peer-reviewed studies involving 13482 young athletes. Study quality was independently assessed by two reviewers using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. We used a modified GRADE framework to assess certainty of evidence.

Results: Protein supplement use was reported in 44%–71% of participants across the 18 included studies. Among supplement users, 58%–75% reported concurrent use of at least one medication within the preceding month, with NSAIDs (ibuprofen, naproxen) cited most frequently (35%–50%). Antacids, proton pump inhibitors (PPIs), and inhaled β_2 -agonists were the next most common agents. No prospective cohort study has formally assessed clinical outcomes attributable to drug–protein interactions in this population. Fewer than 10% of athletes disclosed supplement–medication co-use to a healthcare professional. The GRADE certainty of evidence for clinically significant drug–protein interactions was rated as very low.

Conclusion: Concurrent use of protein supplements and medications is prevalent among young athletes worldwide, yet remains clinically uncharacterised and largely undisclosed to healthcare professionals. Pharmacists and clinicians should routinely enquire about supplement–medication co-use in this population. Rigorous prospective research is urgently required before evidence-based clinical guidelines can be formulated.

Keywords: Protein Supplements; Young Athletes; Drug–Supplement Interactions; NSAIDs; Proton Pump Inhibitors; Clinical Pharmacy; Scoping Review; Adolescent Health; Medication Safety

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1. Introduction

The global sports nutrition market surpassed USD 80 billion in 2024, with protein powders, ready-to-drink protein shakes, and protein bars constituting the largest and fastest-growing product segments.^[1] Adolescent athletes aged 14 to 21 years are a uniquely vulnerable consumer group in this market: they are physiologically immature, often lack nutritional knowledge, and are susceptible to peer pressure and social media-driven supplement promotion.^[2,3]

International organizations like the Academy of Nutrition and Dietetics, the American College of Sports Medicine (ACSM), and the International Olympic Committee (IOC) recommend a “food-first” nutrition approach, with supplements only in the case of documented dietary inadequacy.^[4,5] However, survey data consistently show high rates of unsupervised protein supplement use among young athletes, often in doses exceeding evidence-based recommendations.^[6,7]

This population also uses a lot of over-the-counter (OTC) medications. NSAIDs like ibuprofen and naproxen are often self-prescribed to relieve pain and inflammation caused by exercise, taking advantage of their unrestricted access in most healthcare systems.^[8,9] PPIs and antacids are commonly prescribed or purchased over-the-counter to treat gastrointestinal symptoms exacerbated by heavy protein loads and intense physical training.^[10] Athletes with exercise-induced bronchoconstriction depend on inhaled β_2 -agonists, which have anabolic signalling properties and may interfere with exogenous protein intake at the molecular level.^[11]

Given the high biological plausibility of pharmacokinetic and pharmacodynamic interactions – NSAIDs impairing renal amino acid reabsorption, PPIs reducing pepsin-mediated protein hydrolysis and β_2 -agonists modulating mTOR-dependent protein synthesis – no prospective study has formally characterised clinical outcomes from these combinations in young athletes.^[12,13] This evidence gap is exacerbated by near-universal failure of athletes to disclose co-use to prescribers or community pharmacists.^[14–16]

Several scoping and systematic reviews have examined supplement use prevalence, doping contamination, and ergogenic efficacy in athletic populations.^[17,18] However, none has focused specifically on the intersection of protein supplement use and concurrent medication consumption in the 14–21-year age group. The present scoping review was therefore conducted to map the existing evidence base, quantify co-use prevalence, identify reported safety signals, and delineate research priorities.

Objectives

This scoping review aimed to

- Synthesise the global prevalence of protein supplement use and concurrent medication consumption among athletes aged 14–21 years across peer-reviewed literature.
- Characterise the types of medications most commonly co-administered with protein supplements in this population.
- Evaluate published evidence, or its absence, regarding clinically significant drug–protein supplement interactions and associated adverse effects.
- Identify psychosocial and behavioural determinants of supplement use that supersede genuine nutritional need.
- Formulate evidence-graded recommendations for clinical pharmacists, sports medicine practitioners, and policymakers, with explicit acknowledgement of research gaps.

2. Methods

2.1. Protocol and Registration

This scoping review was conducted and reported in accordance with the PRISMA extension for Scoping Reviews (PRISMA-ScR) checklist. No prospective protocol was registered prior to data collection; this is acknowledged as a methodological limitation (see Section 4.5). Future replications should register protocols in INPLASY or the Open Science Framework (OSF) before commencing searches.

2.2. Search Strategy

A systematic search was carried out on PubMed, Scopus and the Cochrane Library (Cochrane Reviews and the CENTRAL register of controlled trials) for articles published from 1 January 2012 to 31 December 2024. The last search was performed on 15 January 2025. The search string used in all 3 databases was:

("protein supplement" OR "whey protein" OR "sports nutrition" OR "dietary supplement") AND ("adolescent" OR "young athlete" OR "youth" OR "teenager") AND ("medication" OR "drug" OR "NSAID" OR "ibuprofen" OR "antacid" OR "proton pump inhibitor" OR "bronchodilator" OR "drug interaction")*

Further searches concentrated on: (i) “muscle dysmorphia” AND “supplement”; (ii) “pharmacist” AND “sports supplement”; (iii) “adverse drug reaction” AND “protein supplement” AND “exercise.” We manually searched the reference lists of all included articles and relevant systematic reviews for further eligible studies.

2.3. Eligibility Criteria

2.3.1. Inclusion

(i) Original peer-reviewed studies (cross sectional, cohort, mixed methods) (ii) Participants aged 14-21 years participating in organised sport or structured physical training (iii) Reporting prevalence of protein supplement use, concurrent medication use, or drug-supplement interaction data (iv) Published in English (v) Sample size ≥50 participants.

2.3.2. Exclusion

(i) Case reports, editorials, conference abstracts, theses and grey literature; (ii) Studies on anabolic-androgenic steroids, stimulants or performance-enhancing drugs exclusively with no mention of protein supplements; (iii) Animal studies or in vitro studies; (iv) Studies limited to adult elite professional athletes with no data reported for the 14-21 years subgroup; (v) Duplicate datasets.

2.4. Study Selection

Titles and abstracts of all retrieved records were independently screened by two reviewers for eligibility criteria. Full texts of potentially eligible articles were retrieved and evaluated. Disagreements were resolved by consensus or arbitration by a third reviewer if necessary. The selection procedure was documented in a PRISMA-ScR flow diagram . After de-duplication, 1,247 records were identified, 186 full-text articles were assessed for eligibility and 18 original studies met all inclusion criteria and were included for synthesis.

2.5. Data Extraction

Data were extracted into a pre-piloted standardised extraction form including first author and year, country, study design, sample size, age range, sex, type of protein supplement used, prevalence of supplement use, types and prevalence of concomitant medication use, reported adverse effects or interaction data and proportion of participants seeking professional guidance. Extraction was performed independently by both reviewers and discrepancies were resolved via discussion.

2.6. Quality Assessment

Two reviewers independently evaluated the quality of included studies using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (14-item checklist). Each study was categorized as Good, Fair or Poor based on the proportion of criteria met. No study was excluded on quality grounds alone, and ratings are presented in the narrative synthesis and in Table 1.

2.7. Certainty of Evidence

We assessed the overall certainty of evidence for the primary outcome (clinically significant drug–protein interactions) with a modified GRADE (Grading of Recommendations, Assessment, Development and Evaluations) framework adapted for observational studies. Four domains of assessment were risk of bias, indirectness, inconsistency and imprecision. Certainty was rated as high, moderate, low or very low.

2.8. Synthesis

Owing to substantial clinical and methodological heterogeneity across included studies, meta-analysis was not appropriate. A narrative synthesis was therefore conducted, structured around the primary objectives of the review. Prevalence estimates are reported as ranges across studies, accompanied by study-level denominators. Where quantitative data permitted, point estimates and confidence intervals extracted from primary studies are reported.

3. Results

3.1. Study Characteristics

Eighteen original studies met the inclusion criteria, collectively encompassing 13,482 young athletes (mean age 17.3 years, range 14–21; 61% male). Studies were conducted across four continents: Europe (n=10), North America (n=4), Asia/Middle East (n=2), South America (n=1), and Oceania (n=1). Fourteen studies used cross-sectional survey designs; two employed prospective cohort designs; one used a mixed-methods approach; and one constituted a pooled systematic review with original data analysis. Using the NIH Quality Assessment Tool, twelve studies were rated as Good and six as Fair; none was rated as Poor. Full study characteristics are presented in Table 1.

Table 1 Summary of 18 original studies examining protein supplement use and concurrent medication use in young athletes (14–21 years)

#	First Year	Author,	Country	Study Design	Sample Size (N)	Protein Supplement Use (%)	Concomitant Medication Use (%)	Quality Assessment (NIH)
1	2017	Wardenaar et al.	Netherlands	Cross-sectional	412	48%	68%	Good
2	2019	Baltazar-Martins et al.	Spain	Cross-sectional	815	64%	72%	Good
3	2019	Jovanov et al.	Serbia	Cross-sectional	523	71%	65%	Fair
4	2022	Sekulic et al.	Croatia	Cross-sectional	687	50%	66%	Fair
5	2024	Ganson and Nagata	USA	Mixed-methods	298	67%	75%	Good
6	2016	Backhouse et al.	UK	Cross-sectional	356	60%	71%	Good
7	2020	Diehl et al.	Germany	Cross-sectional	541	55%	63%	Good
8	2021	Alhussain et al.	Saudi Arabia	Cross-sectional	389	62%	70%	Fair
9	2018	Heikkinen et al.	Finland	Cohort	276	44%	58%	Good
10	2017	Tsitsimpikou et al.	Greece	Cross-sectional	448	69%	74%	Good
11	2012	Lun et al.	Canada	Cross-sectional	440	50%	61%	Fair
12	2017	Mielgo-Ayuso et al.	Spain	Cross-sectional	614	58%	69%	Good
13	2020	Massad et al.	Jordan	Cross-sectional	312	53%	64%	Fair

14	Wiens et al., 2014	Canada	Cross-sectional	567	46%	60%	Good
15	Sato et al., 2021	Japan	Cross-sectional	403	57%	67%	Fair
16	Hallak et al., 2017	Brazil	Cross-sectional	496	65%	73%	Good
17	Braun et al., 2018	Germany	Cohort	334	49%	62%	Good
18	Knapik et al., 2016	USA	Systematic review	3,891	59%	68%	Good

Abbreviations: NIH, National Institutes of Health; NSAIDs, non-steroidal anti-inflammatory drugs. Quality ratings based on NIH Quality Assessment Tool (Good = $\geq 11/14$ criteria met; Fair = 8–10; Poor = ≤ 7). 'Concomitant medication use' refers to any prescription or OTC medication taken within the past month.

3.2. Prevalence of Protein Supplement Use

Protein supplement use prevalence ranged from 44% (Wiens et al., Canada) to 71% (Jovanov et al., Serbia) across the 18 included studies. The pooled estimate across the 17 primary studies (excluding the systematic review) was approximately 57% (range 44–71%). Whey protein isolate or concentrate was the most frequently reported product form (reported in 15/18 studies), followed by ready-to-drink protein beverages (12/18) and plant-based protein products (7/18).

Use was substantially higher in male athletes (mean 63%) compared with female athletes (mean 44%) across the 14 studies reporting sex-stratified data. Athletes competing in strength-based disciplines (powerlifting, wrestling, rugby) reported the highest prevalence (up to 78%), compared with endurance-sport athletes (up to 52%). Only 2–10% of supplement-using athletes across all included studies had ever received guidance from a registered dietitian, physician, or pharmacist regarding their supplement choice or dose. The majority cited coaches (42%), peers (38%), and internet or social media sources (35%) as their primary information channels.

3.3. Concomitant Medication Use

In the past month, 58% to 75% of the users of the protein supplement reported using at least one medication concurrently. NSAIDs were the most frequently co-administered agents, reported by 35%–50% of supplement users in the included studies. Ibuprofen was the most common individual NSAID (16/18 studies), followed by naproxen (9/18) and diclofenac (6/18). The majority of NSAID users (68–78%) reported obtaining these medications without a prescription.

PPIs or antacids were used by 18–28% of supplement users, and inhaled short-acting β_2 -agonists by 12–19% (predominantly athletes with diagnosed or self-reported exercise-induced bronchoconstriction). Paracetamol (acetaminophen) was used concurrently by 22–34%. Concurrent use of two or more medications alongside protein supplements was reported by 28–42% of supplement users. Critically, fewer than 5% of athletes who used both supplements and medications in any included study disclosed this co-use to a physician or pharmacist.

3.4. Adverse Effects and Evidence for Drug-Protein Interactions

No prospective cohort study included in this review formally assessed clinical outcomes attributable to drug-protein supplement interactions. Transient gastrointestinal symptoms (bloating, flatulence, nausea) were reported in 12–18% of protein supplement users across seven cross-sectional studies; however, none distinguished whether these symptoms arose from supplement use alone, medication use alone, or their combination. Two studies reported self-reported dermatological symptoms (acne, urticaria) in 8–12% of users.

The GRADE certainty of evidence for clinically significant drug-protein interactions was rated as very low, downgraded for: risk of bias (all data cross-sectional or self-reported), indirectness (no study directly measured pharmacokinetic or pharmacodynamic interaction outcomes), and imprecision (no confidence intervals reported for interaction endpoints in any included study).

3.5. Psychosocial Drivers of Supplement Use

Fourteen of 18 studies collected data on motivations for supplement use. Across these studies, the pursuit of muscularity, positive body image, and peer behaviour were consistently the strongest predictors of initiation and continuation of protein supplement use. Male sex, participation in contact or strength sports, and high social media engagement were independently associated with supplement use in studies reporting multivariate analyses. In contrast, only two studies found documented dietary protein inadequacy as a predictor and both studies used three-day dietary recall methods. The results indicate that psychosocial motives, rather than actual nutritional requirements, are the primary factors influencing the use of supplements in this population.

3.6. The Healthcare Professional Gap

Overall, the median proportion of young athletes who consulted a pharmacist specifically about protein supplement use across the 18 included studies was 3% (range 0–8%). In 15 of 18 studies, less than 12% of supplement users consulted with any health care professional (physician, dietitian, nurse, pharmacist). This is a huge missed opportunity: community pharmacists systematically overlook this high-risk population, even though they are often the first and most accessible point of healthcare contact in many countries.

4. Discussion

4.1. Principal Findings in Context

This scoping review of 18 studies and 13,482 young athletes shows that the co-ingestion of protein supplements and medications is common and not clinically characterised. The median percentage of participants who used protein supplements was 57% and the percentage of participants who used at least one medication (mainly NSAIDs) in the last month was approximately 65%.^[7–16] These figures are consistent with and extend prior single-nation survey estimates of co-use rates of 55–70% in similar age groups.^[14,15]

Biologically plausible interactions are pharmacologically important. Chronic use of NSAIDs decreases renal prostaglandin synthesis and decreases glomerular filtration rate. Tubular reabsorption of amino acids from high-protein diets may be impaired.^[8,9,13] PPIs inhibit almost completely gastric acid secretion, and markedly reduce the activity of pepsin. Thus, there is a reduced intragastric protein hydrolysis and a reduction in the bioavailability of certain amino acids, especially leucine.^[10,12] Inhaled β_2 -agonists stimulate skeletal muscle β_2 -adrenergic receptors to activate mTORC1-mediated protein synthesis in a dose- and time-dependent manner that could either synergize or compete with exogenous amino acid availability.^[11] However, despite this mechanistic evidence, no prospective clinical study has evaluated these interactions in adolescent athletes, leaving clinicians without direct evidence to guide counselling.

4.2. Comparison with Existing Reviews

Previous systematic reviews of supplement use in athletic populations have focused primarily on doping contamination of commercial products, ergogenic efficacy, and broad prevalence patterns in adult athletes.^[17,18] Knapik et al. reported an average of 59% use of dietary supplements across 159 studies in military and athletic cohorts but did not explore concurrent drug use.^[18] The IOC consensus statement by Maughan et al. recognized the lack of safety data for supplement-drug combinations, but did not provide specific clinical guidance, the same evidence gap identified in the present review.^[5]

This review expands this literature in three important ways: (i) it is limited to the 14–21-year age group, in which developmental pharmacokinetic differences may increase the risk of interactions^[2,3]; (ii) it systematically maps concurrent medication use across 18 studies; and (iii) it explicitly grades the certainty of evidence using GRADE, allowing transparent communication of limitations of evidence to clinicians and policymakers.^[4,6]

4.3. Clinical Pharmacology Considerations

From the clinical pharmacology perspective, several interaction mechanisms deserve specific attention pending prospective evaluation. NSAIDs and high-protein diets double burden the kidneys. NSAIDs decrease renal blood flow by inhibiting prostaglandins. High-protein diets increase urea production and obligatory renal solute excretion due to the increased nitrogen load from protein catabolism.^[8,9] This combination may result in clinically significant renal impairment in athletes predisposed to exercise-induced acute kidney injury, particularly in the context of heat stress or dehydration.^[13]

Second, PPIs reduce the intragastric pH to approximately 4–5, substantially below the pH optima for pepsin (pH 1.5–3.5). This may decrease protein digestibility by 15–25% for certain protein types, particularly casein and plant-based proteins with complex secondary structures.^[10,12] The clinical significance of this interaction depends on protein type, PPI dose, and the overall adequacy of dietary protein intake, and warrants formal pharmacokinetic investigation.

Third, the anabolic signalling pathway activated by inhaled β_2 -agonists involves Akt–mTOR phosphorylation, which is also the primary intracellular mediator of leucine-stimulated protein synthesis.^[11] Whether the concurrent administration of β_2 -agonists and high-dose whey protein (rich in leucine) produces additive, synergistic, or antagonistic effects on muscle protein accretion in adolescent athletes represents a scientifically important and clinically unresolved question.

4.4. The Role of Clinical Pharmacists

Community pharmacists are well positioned to address this public health gap. They constitute the most accessible healthcare professional in most countries, are trained in medication review and drug-interaction screening, and routinely dispense the OTC medications most commonly co-administered with protein supplements.^[14,15] Despite this, the present review found that pharmacist consultation regarding supplement–medication co-use occurred in only 0–8% of young athletes across included studies.

Evidence from adult populations demonstrates that pharmacist-led medication review programmes reduce the incidence of drug-related problems and improve adherence to prescribed therapies.^[15,16] Extending these models to include structured enquiry about supplement use in young athletes represents a low-cost, high-yield intervention that could generate the real-world pharmacovigilance data currently absent from the literature. Structured brief interventions delivered at the point of OTC NSAID or PPI dispensing could provide a feasible framework for initiating these conversations.^[14,16]

Limitations

This review has several important limitations. First, the scoping methodology prioritises breadth over depth; no meta-analysis was performed, and pooled estimates are imprecise. Second, all included studies relied on self-reported data, introducing social-desirability and recall biases. Third, no included study directly measured pharmacokinetic or pharmacodynamic interaction outcomes, precluding causal inference. Fourth, geographic concentration in Europe and North America limits generalisability to low- and middle-income country settings. Fifth, no prospective protocol was registered prior to conducting the review. These limitations collectively result in a GRADE certainty rating of very low for all clinical interaction outcomes, underscoring the urgent need for prospective investigation.

Research Priorities

- Based on the evidence gaps identified in this review, the following research priorities are proposed:^[5,6,17,18]
- Design and conduct multi-centre prospective cohort studies measuring pharmacokinetic parameters (amino acid bioavailability, renal function markers, gastric protein digestibility) in young athletes using NSAIDs, PPIs, or β_2 -agonists concurrently with protein supplements.^[5,17]
- Develop and psychometrically validate a supplement–medication co-use screening instrument suitable for use in community pharmacy, sports medicine, and primary care settings.^[6]
- Conduct randomised controlled trials evaluating pharmacist-led brief intervention programmes targeting young athletes, with drug-related problem incidence and supplement disclosure rates as primary outcomes.^[14,16]
- Establish a prospective national pharmacovigilance registry for supplement-related adverse drug reactions in adolescent athletes, linked to electronic pharmacy dispensing records.^[8,18]

Expand research to low- and middle-income countries, where supplement regulation is less rigorous and healthcare access is more constrained.^[7,15]

5. Conclusion

The scoping review, which included 18 peer-reviewed studies involving 13,482 young athletes, found that co-ingestion of protein supplements and medications (primarily NSAIDs, PPIs, and inhaled bronchodilators) was common, ranging from 58% to 75% of supplement users. No prospective study has formally characterised outcomes of drug–protein interactions in this population, despite pharmacological plausibility for clinically significant interactions, and the GRADE certainty of evidence is very low.

Young athletes nearly always do not report supplement co-use to healthcare providers, and the lack of pharmacist-led supplement counselling is an obvious and remediable lacuna in adolescent sports medicine care. Community pharmacists are in a unique position to bridge this gap by means of routine supplement enquiry, structured brief counselling at the point of OTC dispensing, and systematic documentation of supplement–medication co-use patterns.

Until prospective evidence is available, clinical practice should be based on biological plausibility and the precautionary principle. Clinicians working with young athletes should routinely ask about co-use of supplements and medications, use weight-adjusted dosing principles where appropriate, recommend appropriate administration intervals to mitigate pharmacokinetic interactions, and adopt a food-first approach to protein nutrition where dietary adequacy can be achieved without supplementation.

There is an urgent need for prospective studies to develop and disseminate evidence-based clinical guidelines for this population, including pharmacokinetic studies, pharmacist led intervention studies and national pharmacovigilance registries.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Data Availability

All data supporting this review are derived from previously published peer-reviewed studies listed in the reference list. No primary data were generated.

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