People's Democratic Republic of Algeria
Ministry of Higher Education and Scientific Research
University of El Oued
Faculty of Nature and Life Sciences
Department of Cellular and Molecular Biology

MASTER THESIS

In partial fulfilment of the requirements for the degree of Master

Major: Biological Sciences

Speciality: Toxicology

THEME

Impact of Dietary Supplements on Kidney Function
A Field Study in the Wilaya of El Oued

Presented by:

- **Aggab Aya**
- **Bekakra Chaima**
- **Ghemam ali Safa**
- **Kerrouche Khadidja**

Jury Members:

• **Dr.**	**Borkhari dalal**	**……**	**President**
• **Dr.**	**Zaime sihem**	**……**	**Examiner**
• **Dr.**	**Aouimeur Meriem**	**……**	**Supervisor**

Academic Year: 2025 – 2026


بِسْمِ ٱللَّهِ ٱلرَّحْمَٰنِ ٱلرَّحِيمِ

Dedication

First and foremost, all praise and gratitude be to Allah…

For He was our support when the days let us down, our light when the roads grew dark, and the strength that carried our hearts whenever they were burdened by exhaustion. Praise be to Allah for always being with us in every moment when we thought we could no longer continue. We thank Him for His hidden kindness, His mercy that always preceded our steps, and for the hardships that exhausted us only to shape us into stronger and more faithful individuals. This achievement is nothing but a blessing from Allah and the result of long patience and countless prayers.

To ourselves…

To the souls that endured these years with all their challenges, pressure, and silent struggles. To the hearts that were weary from the journey but never stopped trying. To the days when success seemed impossible, yet Allah's mercy was always closer than our fears and greater than our hardships.

To our families…

Our true support and the hearts that believed in us even during our weakest moments. Thank you for being our source of comfort, for your endless prayers, and for the love that illuminated our path through the most difficult times.

And to our friendship, the four of us…

To a rare bond that was far more than a simple friendship; it was a home throughout this demanding journey. To the loyalty that united us for years, to the laughter that eased the weight of difficult days, and to the hands that never let go of one another regardless of the circumstances. We grew together, struggled together, stumbled at times together, and rose again together until we reached this moment, carrying the fruit of years of patience and perseverance. This work is not merely a graduation thesis; it is the story of a long journey of effort, strong faith, and hearts that remained united despite every challenge. All praise be to Allah for this achievement, for the blessing of sincere friendship, and for every difficult path that ultimately shaped us into stronger versions of ourselves.

To us, the four of us…

For we were never just a study group, but a story of resilience woven through determination and hope. We walked this path not as individuals, but as one heart with four beats, supporting one another whenever the road became heavy. To us, because we proved that faith, patience, and true friendship can transform the impossible into achievement, hardship into success, and difficult years into memories that will always be remembered with pride.

Acknowledgements

First and foremost, we would like to express our sincere gratitude to Allah Almighty for granting us the courage, strength, and perseverance to accomplish this work.

We would also like to extend our heartfelt thanks to all our professors at the University of El Oued who contributed to our education and training throughout our academic journey.

Our special thanks go to Dr. Azzoux Allaa Eddine, nephrology specialist, who generously shared his knowledge and valuable guidance with us, welcomed us with kindness and openness. We are deeply grateful for his precious time, insightful advice, and generous cooperation, which greatly contributed to the successful completion of this project.

Finally, we would like to thank everyone who contributed, directly or indirectly, to the realization of this graduation project.

Aya & Chaima & Safa & Khadidja

Abstract

This study aims to highlight the effects of excessive and uncontrolled consumption of dietary supplements on kidney health and renal function. The theoretical part focused on the definition and types of dietary supplements, as well as the major kidney diseases associated with the excessive use of supplements such as proteins, creatine, and high-dose vitamins, in addition to the risks related to heavy metal-contaminated products. The practical part was based on a field survey conducted in El Oued involving 200 participants, including 164 healthy individuals and 36 patients, in order to assess supplement consumption habits and awareness of their health risks. The results revealed widespread use of dietary supplements along with insufficient awareness regarding their side effects, especially on kidney health. The study concluded that the irrational use of dietary supplements may pose a serious risk to renal function, highlighting the importance of health awareness and rational consumption of these products.

Keywords: Dietary supplements – Kidney function – Nephrotoxicity – Questionnaire

Résumé

Cette étude vise à mettre en évidence les effets de la consommation excessive et non contrôlée des compléments alimentaires sur la santé rénale. La partie théorique a abordé la définition des compléments alimentaires, leurs types ainsi que les principales maladies rénales liées à l'usage excessif de certains produits comme les protéines, la créatine et les vitamines à fortes doses, sans oublier les risques des compléments contaminés par des métaux lourds. La partie pratique repose sur une enquête réalisée dans la wilaya d'El Oued auprès de 200 personnes, dont 164 personnes saines et 36 personnes malades, afin d'évaluer les habitudes de consommation et le niveau de sensibilisation aux risques sanitaires des compléments alimentaires. Les résultats ont montré une large utilisation de ces produits ainsi qu'un manque de connaissances concernant leurs effets secondaires, notamment sur les reins. L'étude conclut que l'utilisation abusive des compléments alimentaires peut représenter un danger pour la fonction rénale, d'où l'importance de renforcer la sensibilisation et l'utilisation rationnelle de ces produits.

Mots-clés : Compléments alimentaires – Fonction rénale – Néphrotoxicité – Questionnaire

الملخص

تهدف هذه الدراسة إلى إبراز تأثير الاستهلاك المفرط وغير المنظم للمكملات الغذائية على صحة الكلى ووظيفتها، خاصة مع الانتشار الكبير لهذه المنتجات بين الشباب والرياضيين. تناول الجانب النظري تعريف المكملات الغذائية وأنواعها، إضافة إلى دراسة أهم الأمراض الكلوية المرتبطة بالإفراط في استعمال بعض المكملات مثل البروتينات، الكرياتين، والفيتامينات بجرعات مرتفعة، إلى جانب أخطار المكملات الملوثة بالمعادن الثقيلة. أما الجانب التطبيقي فاعتمد على استبيان ميداني أُنجز بولاية الوادي وشمل 200 شخص، من بينهم 164 شخصًا سليمًا و36 شخصًا مريضًا، بهدف دراسة عادات استهلاك المكملات الغذائية ومستوى الوعي بمخاطرها الصحية. وقد أظهرت النتائج انتشار استعمال هذه المنتجات مع وجود نقص واضح في الوعي الصحي حول تأثيراتها الجانبية، خاصة على الكلى. وخلصت الدراسة إلى أن الاستعمال العشوائي للمكملات الغذائية قد يشكل خطرًا حقيقيًا على النشاط الكلوي، مما يستدعي تعزيز التوعية الصحية وتشجيع الاستعمال العقلاني لهذه المنتجات.

الكلمات المفتاحية: المكملات الغذائية - وظائف الكلى - السمية الكلوية - استبيان

List of figures

List of Tables

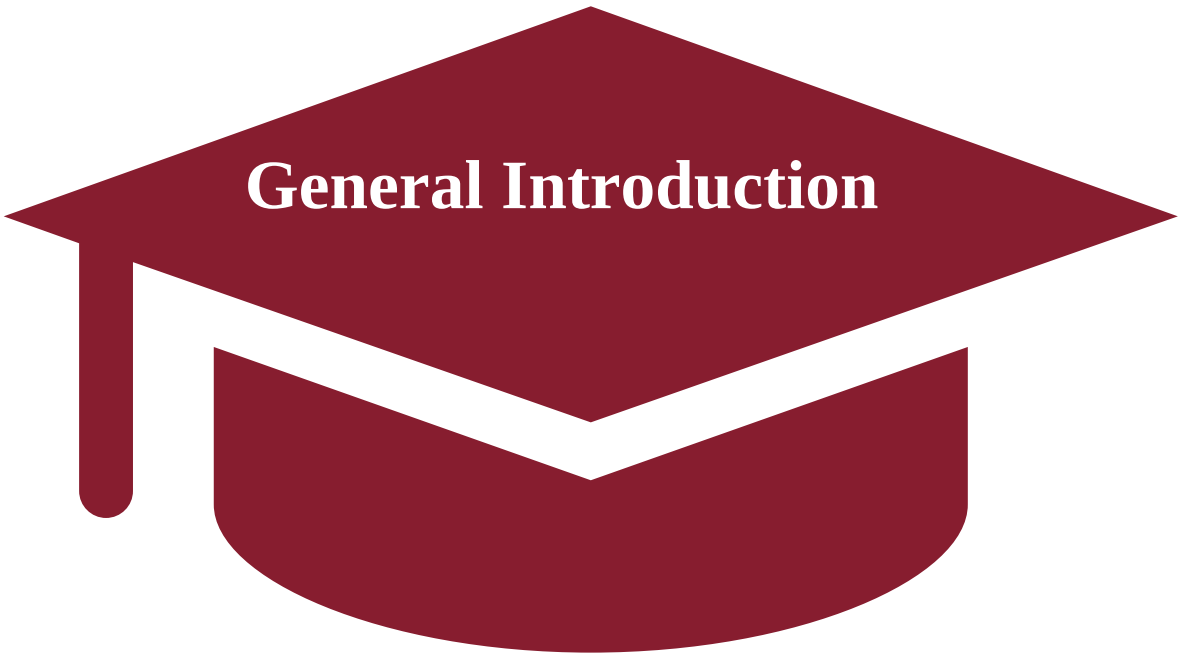
List of Abbreviations

Abbreviation	Full Meaning
ACE	Angiotensin-Converting Enzyme
ADH	Antidiuretic Hormone (Vasopressin)
AIN	Acute Interstitial Nephritis
AKI	Acute Kidney Injury
ANA	Antinuclear Antibody
As	Arsenic
BCAA	Branched-Chain Amino Acids
BUN	Blood Urea Nitrogen
CAERS	CFSAN Adverse Event Reporting System
Cd	Cadmium
CFSAN	Center for Food Safety and Applied Nutrition
CI	Confidence Interval
CKD	Chronic Kidney Disease
CLA	Conjugated Linoleic Acid
CoQ10	Coenzyme Q10
Cr	Chromium
CT	Computed Tomography
CYP24A1	Cytochrome P450 24A1
CYP27B1	25-Hydroxyvitamin D-1alpha-hydroxylase
DCT	Distal Convoluted Tubule
DHA	Docosahexaenoic Acid
DHEA	Dehydroepiandrosterone
DMAA	1,3-Dimethylamylamine
DSHEA	Dietary Supplement Health and Education Act of 1994
DSAERS	Dietary Supplement Adverse Event Reporting System
EFSA	European Food Safety Authority
EPA	Eicosapentaenoic Acid
EPO	Erythropoietin
ESRD	End-Stage Renal Disease
FDA	Food and Drug Administration
FGF-23	Fibroblast Growth Factor-23
GBM	Glomerular Basement Membrane
GFR	Glomerular Filtration Rate
GN	Glomerulonephritis
Hg	Mercury
HPFS	Health Professionals Follow-up Study
IL-18	Interleukin-18
IU	International Unit
KDIGO	Kidney Disease: Improving Global Outcomes
KIM-1	Kidney Injury Molecule-1
Na-K-2Cl	Sodium-Potassium-Chloride Cotransporter
NGAL	Neutrophil Gelatinase-Associated Lipocalin

NHANES	National Health and Nutrition Examination Survey
NKCC2	Na-K-2Cl Cotransporter 2
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
OAT1	Organic Anion Transporter 1
OAT3	Organic Anion Transporter 3
1-Oct	Organic Cation Transporter 1
2-Oct	Organic Cation Transporter 2
OTC	Over-the-Counter
Pb	Lead
PCBs	Polychlorinated Biphenyls
PCT	Proximal Convoluted Tubule
PGE2	Prostaglandin E2
PGI2	Prostacyclin (Prostaglandin I2)
PTH	Parathyroid Hormone
PUFA	Polyunsaturated Fatty Acids
RAAS	Renin-Angiotensin-Aldosterone System
RDA	Recommended Daily Allowance
rHuEPO	Recombinant Human Erythropoietin
ROS	Reactive Oxygen Species
RTA	Renal Tubular Acidosis
SAM	S-Adenosylmethionine
SARMs	Selective Androgen Receptor Modulators
TAL	Thick Ascending Limb
TCM	Traditional Chinese Medicine
TGF	Tubuloglomerular Feedback
UL	Tolerable Upper Intake Level
WHO	World Health Organisation
WPC	Whey Protein Concentrate

Table of contents

Table of contents



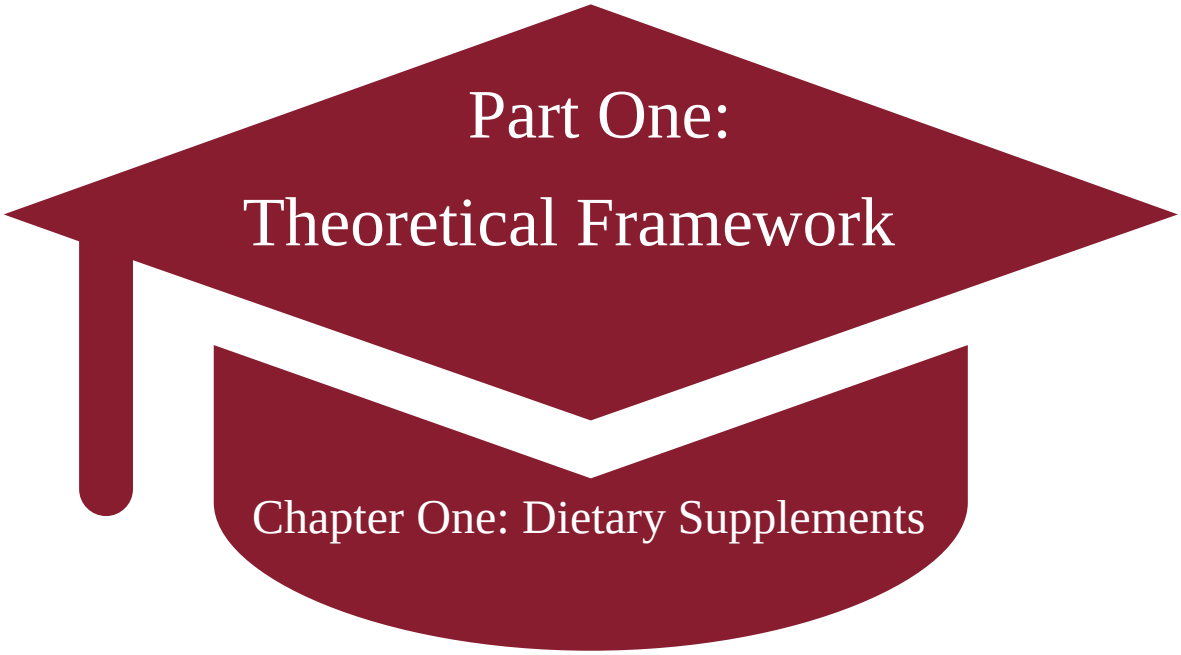
General Introduction

The global market for dietary supplements has undergone exponential growth over the past two decades, evolving from a niche sector serving elite athletes into a mainstream consumer phenomenon with profound public health implications (Smith & Doe, 2021). According to the Global Wellness Institute (2023), the dietary supplement industry was valued at approximately USD 177 billion in 2022 and is projected to exceed USD 280 billion by 2030. This extraordinary expansion is primarily driven by an ageing global population, increased health consciousness, and the rapid proliferation of digital health information (Global Wellness Institute, 2023). However, this rapid commercial growth has occurred largely without commensurate advances in regulatory oversight, creating a significant gap between the consumer perception of inherent product safety and the established toxicological evidence base (Ronzo et al., 2022).

To understand the potential risks associated with these unregulated nutritional interventions, it is essential to examine their primary physiological target: the kidneys (Hall & Hall, 2020). As the body's principal organs of filtration, detoxification, and metabolic homeostasis, the kidneys rely on a highly complex anatomical architecture and sophisticated physiological operations to sustain life (Koeppen & Stanton, 2018). Their essential functions include the continuous filtration of circulating blood, the efficient excretion of metabolic waste products, and the precise regulation of electrolyte and acid-base equilibrium (Hall & Hall, 2020). Because they receive a disproportionately high volume of resting cardiac output and actively concentrate systemic solutes, renal structures are continuously exposed to elevated levels of circulating exogenous compounds, rendering them inherently sensitive to chemical disruption (De Broe et al., 2021).

Consequently, the kidneys occupy a position of extreme vulnerability to the adverse effects of excessive or unsupervised dietary supplement consumption (Gabardi et al., 2012). The nexus between dietary supplement use and renal function is increasingly characterized by nephrotoxicity, where specific compounds disrupt renal physiology, induce disease causation, and alter clinical biomarker signatures (Ponnusamy et al., 2014).

This thesis systematically examines this intersection by synthesizing contemporary toxicological evidence and elucidating the biological mechanisms underlying supplement-induced renal injury. Now we will address the following sections: Chapter one, entitled dietary supplements; Chapter Two, entitled renal function; and Chapter Three, entitled effects of dietary supplements on renal activity.



Part One:
Theoretical Framework

Chapter One: Dietary Supplements

1.1 Definition of Dietary Supplements

The term dietary supplement, while appearing self-explanatory, encompasses a legally, scientifically, and commercially heterogeneous category of products that has defied uniform international definition. In the United States, the Dietary Supplement Health and Education Act of 1994 (DSHEA) defines a dietary supplement as a product intended to supplement the diet that contains one or more of the following dietary ingredients: vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, and metabolites. Critically, DSHEA classifies dietary supplements as a subset of foods rather than drugs, thereby exempting manufacturers from the pre-market safety and efficacy evaluations required for pharmaceutical agents (U.S. Food and Drug Administration, 2022).

The European Food Safety Authority (EFSA) adopts a functionally similar but terminologically distinct framework, defining food supplements as concentrated sources of nutrients or other substances with a nutritional or physiological effect, marketed in dose form (European Commission, 2002/46/EC). The World Health Organisation uses the broader concept of nutraceuticals and functional foods, acknowledging that regulatory definitions diverge substantially between jurisdictions. This definitional heterogeneity is not merely semantic; it has direct consequences for consumer safety, as products classified as supplements in one country may require pharmaceutical registration in another, resulting in international regulatory arbitrage and variable product safety standards (WHO, 2021).

For the purposes of this thesis, we adopt a comprehensive working definition: a dietary supplement is any orally consumed product, in concentrated or dose-form, that contains one or more nutrients, bioactive compounds, or herbal constituents intended to supplement the normal diet, and that is not classified or regulated as a conventional food or pharmaceutical drug in the jurisdiction of marketing. This definition encompasses vitamins, minerals, amino acids, proteins, fatty acids, botanical extracts, probiotics, and combination products.

1.2 History of Dietary Supplements

The historical trajectory of dietary supplementation is traceable to antiquity, though its modern institutionalised form is a product of the twentieth century. Ancient Egyptian papyri dating to approximately 1550 BCE document the use of liver extracts to treat night blindness — a condition now attributable to vitamin A deficiency (Semba, 2012). Similarly, mediaeval European physicians prescribed citrus fruits for the prevention of scurvy among sailors, an empirical observation that would not be biochemically rationalised until the identification of ascorbic acid by Albert Szent-Gyorgyi and Charles Glen King in 1932 (Carpenter, 2012).

The isolation and commercial synthesis of vitamins between 1910 and 1940 constituted the first major turning point in the history of supplementation. Casimir Funk's formulation of the vitamine hypothesis in 1912, subsequently refined to 'vitamin', established the theoretical framework for deficiency diseases and their nutritional correction (Funk, 1912, as cited in Bender, 2014). The discovery of vitamin D's role in rickets prevention, followed by the commercial production of synthetic vitamins during the 1930s, transformed supplementation from a medical curiosity into a commercial enterprise (McCollum et al., 1922, as cited in Wolf, 2004),.

The post-World War II era witnessed a second wave of growth, as the United States and European governments, concerned with nutritional deficiencies in recovering populations, promoted vitamin fortification of staple foods and individual supplementation. By the 1970s, the popularisation of 'megadose' vitamin therapy by Linus Pauling — who controversially advocated multi-gram daily doses of vitamin C for the prevention of cancer and infectious disease catalysed a cultural shift towards self-prescribed, high-dose supplementation that persists to the present (Pauling, 1970, as cited in Gorton & Jarvis, 1999).

The enactment of DSHEA in 1994 is widely regarded as the pivotal regulatory moment in the modern history of supplements, fundamentally reshaping the market by reducing barriers to entry and shifting the burden of proof regarding safety from manufacturer to regulator. Between 1994 and 2012, the number of dietary supplement products available in the United States increased from approximately 4,000 to over 55,000, with annual consumer spending exceeding USD 32 billion by 2012. Globally, the twenty-first century has been characterised by the convergence of supplement use with fitness culture, anti-ageing medicine, and digital wellness, producing a market characterised by extraordinary product diversity and, in many cases, inadequate scientific substantiation of claims (Bailey et al., 2013).

1.3 Classification of Dietary Supplements

Given the extraordinary diversity of products encompassed under the dietary supplement rubric, a systematic taxonomic framework is essential for both scientific analysis and regulatory management. We propose a multidimensional classification scheme organised along four principal axes: origin, form, composition, and intended function.

1.3.1 Classification by Origin

Plant-derived or phytogenic supplements constitute the largest and most commercially significant category by product number. This group encompasses single-herb preparations such as Echinacea purpurea (immune function), Silybum marianum (hepatoprotection), Ginkgo biloba (cognitive support), and Panax ginseng (adaptogenic), as well as complex botanical formulas derived from traditional medicinal systems including Ayurveda, Traditional Chinese Medicine (TCM), and African ethnopharmacology (Bent, 2008). Algal-derived products, notably spirulina (Arthrospira platensis) and chlorella, have gained substantial market share in recent years as plant-based protein sources and detoxification agents (Watanabe et al., 2014).

Animal-derived supplements include marine omega-3 fatty acid concentrates (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA] from fish oil), bovine or porcine collagen hydrolysates, glucosamine and chondroitin sulphate derived from crustacean exoskeletons or bovine cartilage, and various glandular preparations. The safety profile of animal-derived products is complicated by the potential for bioaccumulation of environmental contaminants — including heavy metals, polychlorinated biphenyls (PCBs), and organochlorine pesticides — in fatty tissues, a concern of direct relevance to the thesis of renal toxicity (Domingo et al., 2015).

Synthetic or semi-synthetic supplements are manufactured through industrial chemical synthesis or biotransformation of precursor molecules and include the majority of commercial vitamin and mineral preparations. While synthetic vitamins are chemically identical to their naturally occurring counterparts (e.g., ascorbic acid vs. naturally derived vitamin C), differences in bioavailability, accompanying phytochemicals, and dose concentration may affect their physiological and toxicological profiles (Carr & Vissers, 2013).

1.3.2 Classification by Physical Form

Dietary supplements are produced and marketed in a wide variety of physical forms, each with distinct pharmacokinetic implications. Solid oral dosage forms — including compressed tablets, hard and soft gelatin capsules, caplets, and lozenges — represent the most prevalent delivery system, offering manufacturing economy, dose precision, and consumer convenience. Powdered supplements, including protein concentrates, creatine monohydrate, and electrolyte mixes, are typically dissolved or suspended in water or milk prior to consumption and are particularly prevalent in sports nutrition. Liquid formulations, encompassing tinctures, drops, suspensions, and ready-to-drink products, offer potential advantages in absorption kinetics for certain compounds. Novel delivery formats, including transdermal patches, sublingual sprays, and liposomal encapsulates, have expanded the market further, though clinical evidence supporting their superiority is often limited (Bauer et al., 2013).

1.3.3 Classification by Composition

Vitamins represent the most historically significant and commercially dominant compositional category. Fourteen recognised vitamins are divided into water-soluble compounds (the B-vitamin complex and ascorbic acid/vitamin C) and fat-soluble compounds (vitamins A, D, E, and K). The fat-soluble vitamins, by virtue of their hepatic and adipose storage and limited excretion capacity, carry significantly greater toxicity risk at supraphysiological doses than their water-soluble counterparts, a distinction with direct relevance to renal pathology in the case of vitamins A, C, and D (Hathcock et al., 2007).

Minerals are inorganic elements essential to enzymatic function, structural integrity, and electrochemical homeostasis. Macrominerals — calcium, phosphorus, magnesium, sodium, potassium, chloride, and sulphur — are required in gram quantities daily, while microminerals or trace elements — including iron, zinc, copper, manganese, iodine, selenium, chromium, and molybdenum — are required in milligram or microgram amounts. The nephrotoxic potential of minerals, particularly at supraphysiological intake levels, is well established for calcium (hypercalciuria and nephrolithiasis), chromium (interstitial nephritis), and several heavy metals that contaminate low-quality supplement preparations (Jager et al., 2014).

Proteins and amino acids constitute a major segment of the sports nutrition market. Whey protein concentrate and isolate, casein, soy protein, and pea protein are widely consumed for muscle protein synthesis support. Individual amino acids — notably creatine, glutamine, arginine, branched-chain amino acids (leucine, isoleucine, and valine), and beta-alanine — are marketed for performance enhancement, immune function, and recovery. The metabolic load imposed by high-protein supplementation on the kidneys, particularly in individuals with pre-existing renal insufficiency, is a central concern of Chapter Three.

Botanical and herbal extracts encompass an enormous diversity of phytochemicals including alkaloids, terpenoids, flavonoids, stilbenes, and polyphenols. While many exert demonstrably beneficial physiological effects at appropriate doses, a subset — including aristolochic acids found in Aristolochia species, pyrrolizidine alkaloids in comfrey, and safrole in sassafras root — possess well-characterised nephrotoxic and carcinogenic properties. Fatty acid supplements, including omega-3, omega-6, and conjugated linoleic acid (CLA) preparations, complete the principal compositional categories (Gokmen et al., 2013).

To facilitate and clarify the presentation of the above information, the most important classifications of dietary supplements have been summarized in the following table.

Table 1. Classification of Dietary Supplements by Origin, Form, and Composition

Criterion	Category	Examples	Common Products
Origin	Plant-based	Herbs, algae, fungi	Echinacea, spirulina, reishi
	Animal-based	Fish, collagen, beeswax	Omega-3, collagen peptides
	Synthetic / semisynthetic	Lab-synthesised molecules	Ascorbic acid, folic acid
Form	Solid	Tablet, capsule, powder	Multivitamins, protein powder
	Liquid	Tincture, drop, drink	Liquid iron, herbal extracts
Composition	Vitamins	Fat- and water-soluble	Vitamins A, C, D, E, B12
	Minerals	Macro- and micro-minerals	Calcium, magnesium, zinc
	Amino acids / proteins	Essential amino acids, WPC	Creatine, BCAA, whey
	Botanicals / herbals	Phytocompounds, adaptogens	Turmeric, ashwagandha, ginseng
	Fatty acids	PUFA, MUFA, conjugated	Fish oil, CLA, flaxseed oil

Note. BCAA = Branched-Chain Amino Acids; CLA = Conjugated Linoleic Acid; WPC = Whey Protein Concentrate. Adapted from Maughan et al. (2018) and Biesalski et al. (2017). © Thesis author, 2025.

1.4 Uses of Dietary Supplements

The motivations for dietary supplement consumption are multifarious and span the continuum from evidence-based medical necessity to psychologically driven self-medication. Population-level survey data from multiple high-income countries reveals consistent patterns of use stratified by age, sex, health status, and socioeconomic factors. The National Health and Nutrition Examination Survey (NHANES) 2017-2018 data indicate that approximately 57.6% of United States adults report using at least one dietary supplement, with multivitamins, vitamin D, and omega-3 fatty acids constituting the three most commonly used products (Mishra et al., 2021).

Clinically indicated supplementation — prescribed or recommended by healthcare professionals to address documented nutritional deficiencies — represents the most rigorously supported use category. Folic acid supplementation during the periconceptional period is universally recommended for the prevention of neural tube defects (De-Regil et al., 2015). Vitamin D and calcium supplementation is indicated for osteoporosis prevention in post-menopausal women and elderly populations with documented deficiency (Ross et al., 2011). Vitamin B12 supplementation is essential for individuals following strict plant-based diets, as this vitamin is absent from plant foods. Iron supplementation is indicated for iron-deficiency anaemia, and iodine supplementation remains a critical public health intervention in iodine-deficient regions including parts of Africa, the Middle East, and South Asia (Watanabe et al., 2014).

Performance-enhancement supplementation constitutes a rapidly growing use category dominated by athletic and fitness-oriented populations. Global market research indicates that the sports nutrition segment alone exceeded USD 45 billion in 2022 (Grand View Research, 2023). In this context, protein supplements, creatine, caffeine, beta-alanine, and ergogenic herb combinations are consumed with the aim of augmenting muscle hypertrophy, delaying fatigue, accelerating recovery, and enhancing competitive performance. The prevalence of supplement use among competitive athletes ranges from 40% to 100% across studies, depending on sport, level of competition, and geographic region (Diehl et al., 2012).

Self-directed supplementation for disease prevention or treatment without medical supervision represents the use category of greatest concern from a toxicological perspective. Survey evidence suggests that a substantial proportion of supplement users do not disclose their supplement use to treating physicians, creating risks of nutrient-drug interactions, cumulative toxicity from multiple supplement products, and delayed diagnosis of underlying pathology attributed to supplement use (Bailey et al., 2013).

Table 2. Principal Uses of Dietary Supplements Across Population Groups

Population Group	Primary Use	Most Commonly Used Supplements
General adult population	Prevention of deficiency, general health maintenance	Multivitamins, vitamin D, omega-3
Athletes and bodybuilders	Performance enhancement, muscle hypertrophy, recovery	Whey protein, creatine, BCAA, caffeine
Older adults (≥65 years)	Bone health, cognitive support, immune function	Calcium, vitamin D, B12, CoQ10
Pregnant women	Neural tube defect prevention, iron sufficiency	Folic acid, prenatal multivitamin, iron
Vegetarians / vegans	Replacement of nutrients absent in plant diets	B12, iron, zinc, iodine, omega-3 (algal)
Individuals with chronic illness	Adjunct therapy, symptom management	Magnesium, CoQ10, probiotics, herbal extracts

Note. CoQ10 = Coenzyme Q10. Data synthesised from Bailey et al. (2013); Mishra et al. (2021); Diehl et al. (2012); De-Regil et al. (2015). © Thesis author, 2025.

1.5 Motives for Excessive Consumption

The phenomenon of excessive dietary supplement consumption — broadly defined as intake substantially above established tolerable upper intake levels (ULs) or recommended daily allowances (RDAs), sustained over extended periods — is a multifactorial behavioural outcome shaped by individual, social, commercial, and regulatory determinants. Understanding these drivers is essential for the design of effective public health interventions and for contextualising the toxicological consequences examined in subsequent chapters.

1.5.1 Sports and Fitness Culture

The global proliferation of fitness culture, anchored in gym-going, competitive athletics, and the pursuit of idealised body aesthetics, has created a powerful normative environment conducive to supplement overuse. Within this culture, supplement consumption — particularly protein powders, creatine, pre-workout stimulants, and fat burners — has become constitutively associated with athletic identity and efficacy (Knapik et al., 2016). Qualitative research indicates that social norms within gym environments actively encourage supplement use, with peer influence frequently identified as a primary factor in initiation and escalation of consumption (Whitaker et al., 2018).

The concept of 'more is better', deeply embedded in performance culture, leads a substantial proportion of athletes to consume supplements at doses significantly exceeding manufacturer recommendations, under the assumption that supraphysiological dosing will produce commensurately superior results. A survey of competitive bodybuilders by Bianco et al. (2014) found that 54% consumed protein at levels exceeding 2.0 g/kg body weight per day, and 18% exceeded 3.0 g/kg per day — levels associated with increased glomerular filtration pressure and elevated renal metabolic burden. The use of anabolic supplements, including dehydroepiandrosterone (DHEA), testosterone precursors, and selective androgen receptor modulators (SARMs) — often marketed as 'legal steroids' — adds further toxicological complexity, as these compounds exert direct effects on renal haemodynamics and tubular function.

1.5.2 Social Media and Digital Health Influencers

Social media platforms have emerged as the dominant information environment for supplement marketing and health advice among younger demographics, fundamentally altering the landscape of supplement consumption behaviour. Instagram, YouTube, TikTok, and emerging short-video platforms host an ecosystem of health and fitness influencers who routinely promote specific supplement products to audiences numbering in the millions, often in exchange for financial compensation (sponsorship, affiliate marketing, or free product supply) that is inadequately disclosed (Coates et al., 2019).

Content analyses of supplement-related social media posts reveal pervasive misrepresentation: exaggerated efficacy claims, omission of adverse effects, false implication of scientific consensus, and the presentation of anecdotal testimonials as equivalent to clinical evidence (Hendricks et al., 2020). A systematic review by Lentferink et al. (2017) found that the quality of health-related content on social media is consistently poor, with accuracy rates below 50% for fitness and nutrition advice. This misinformation environment is particularly consequential for adolescents and young adults — the demographic groups most susceptible to influencer marketing — in whom supplement-induced renal injury, though rare, has been documented in connection with protein overloading and herbal nephrotoxin exposure (Mena et al., 2018).

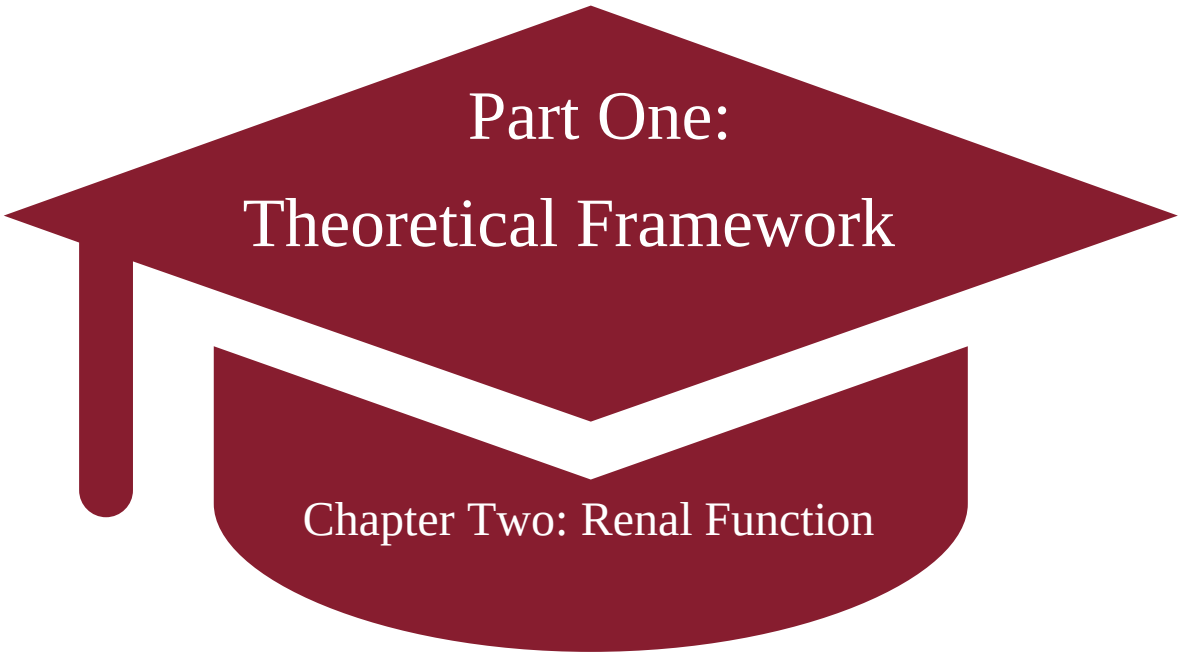
The direct-to-consumer marketing model enabled by social media effectively bypasses the traditional mediating role of healthcare professionals in supplement selection, removing a critical safety filter. A 2021 survey of university-aged supplement users in the United Kingdom found that 68% identified social media as their primary information source for supplement selection, while only 9% consulted a medical professional before initiating use (Smith et al., 2021). The downstream consequence is a high prevalence of dosing errors, polysupplement combinations with unknown interaction profiles, and prolonged use of products with documented hepatotoxic or nephrotoxic potential.

1.5.3 Regulatory Gaps and Inadequate Oversight

The regulatory framework governing dietary supplements in most jurisdictions is characterised by a fundamental asymmetry: the burden of demonstrating safety rests with regulators after a product has entered the market, rather than with manufacturers prior to commercialisation. This post-market surveillance model, entrenched by DSHEA in the United States and maintained in varying degrees across the European Union, Australia, and many developing countries, creates a permissive environment in which dangerous products may remain on the market until adverse event accumulation triggers regulatory action — a process that may take years or decades (Cohen, 2016).

Quality control failures are a pervasive documented problem in the supplement industry. A comprehensive analysis of 246 supplement products by Mathews et al. (2018) found that 32% did not contain the ingredients listed on the label in the declared amounts, while 23% contained undeclared substances including pharmaceutical drug analogues, heavy metals, and undisclosed botanical materials. Particular concern attaches to the contamination of sports nutrition and weight-loss supplements with stimulant drug analogues (e.g., 1,3-dimethylamylamine [DMAA], ephedrine derivatives, and anabolic steroids) and the presence of heavy metals — including lead, cadmium, arsenic, and mercury — at levels exceeding acceptable daily intake thresholds in substandard herbal products (Navarro et al., 2017).

The absence of mandatory adverse event reporting in many jurisdictions, combined with the low rate of supplement-related illness attribution by clinicians and the tendency of consumers to not associate health events with supplement use, results in a systematic under-surveillance of supplement toxicity. The United States Dietary Supplement Adverse Event Reporting System (DSAERS) and the FDA's CFSAN Adverse Event Reporting System (CAERS) are voluntary, population-based reporting systems with known limitations in sensitivity and specificity. Despite these limitations, these systems have documented over 50,000 supplement-related adverse events since 2004, with renal and urinary disorders constituting approximately 8–12% of serious events (FDA CFSAN, 2023).



Part One:
Theoretical Framework

Chapter Two: Renal Function

2.1 Anatomy of the Kidneys

The kidneys are paired retroperitoneal organs located on the posterior abdominal wall on either side of the vertebral column, typically between the T12 and L3 vertebral levels, with the right kidney positioned approximately 2–3 cm lower than the left due to displacement by the right hepatic lobe (Moore et al., 2019). Each adult kidney measures approximately 10–12 cm in length, 5–6 cm in width, and 3–4 cm in anteroposterior depth, and weighs between 125 and 170 grams, with modest sex-based differences. The combined renal parenchyma constitutes less than 0.5% of total body weight yet receives approximately 20–25% of resting cardiac output — a disproportionate perfusion reflecting the metabolic intensity of renal filtration and transport functions (Hall, 2021).

Macroscopically, the kidney is invested by three concentric layers: the fibrous renal capsule (innermost), the perirenal (perinephric) fat within Gerota's fascia, and the pararenal fat (outermost). On coronal section, the parenchyma is organised into two distinct zones: the outer cortex, which is reddish-brown and granular in texture, and the inner medulla, which is striated and pale. The medulla is subdivided into 8–18 conical renal pyramids, each with its apex (papilla) directed toward the renal pelvis and its base abutting the cortex. Cortical tissue between the pyramids forms the renal columns of Bertin, which anatomically separate adjacent pyramids. Each papilla drains into a minor calyx; several minor calyces converge into 2–3 major calyces, which unite to form the renal pelvis — a funnel-shaped expansion of the ureter that exits the kidney at the renal hilum (Standring, 2020).

The hilum also transmits the renal artery, renal vein, lymphatics, and autonomic nerve fibres. The renal artery (a direct branch of the abdominal aorta) divides into anterior and posterior divisions, then into segmental arteries — end arteries that supply discrete vascular territories without anastomosis, rendering infarction of individual segments irreversible. Successive branching produces interlobar, arcuate, and interlobular (cortical radiate) arteries, the last of which give rise to the afferent arterioles supplying individual glomeruli.

At the microscopic level, each kidney contains approximately 800,000 to 1,200,000 nephrons — the fundamental structural and functional units of renal physiology. Each nephron consists of a vascular component (the glomerulus within Bowman's capsule) and a tubular component comprising the proximal convoluted tubule (PCT), the loop of Henle (descending and ascending limbs), the distal convoluted tubule (DCT), and the collecting duct. Nephrons are classified as cortical (approximately 85%), in which the loop of Henle extends only into the outer medulla, and juxtamedullary (approximately 15%), in which the loop of Henle descends deep into the inner medulla — a structural distinction with critical implications for urinary concentration capacity (Bertram et al., 2011).

The glomerulus is a specialised capillary tuft supplied by an afferent arteriole and drained by an efferent arteriole, both of which are under tight hormonal and myogenic regulatory control. The filtration barrier is formed by three layers: the fenestrated glomerular endothelium (pore size 70–100 nm), the glomerular basement membrane (GBM; thickness 320–380 nm), and the podocytes with their interdigitating foot processes forming slit diaphragms (filtration width 30–40 nm). This composite barrier restricts the passage of macromolecules by both size and charge, allowing the free filtration of water, electrolytes, glucose, amino acids, and small molecular weight toxins while retaining albumin and larger proteins in the circulation (Haraldsson et al., 2008).

The following image is a diagram illustrating the anatomical and functional structure of the human kidney, highlighting its most important internal parts.

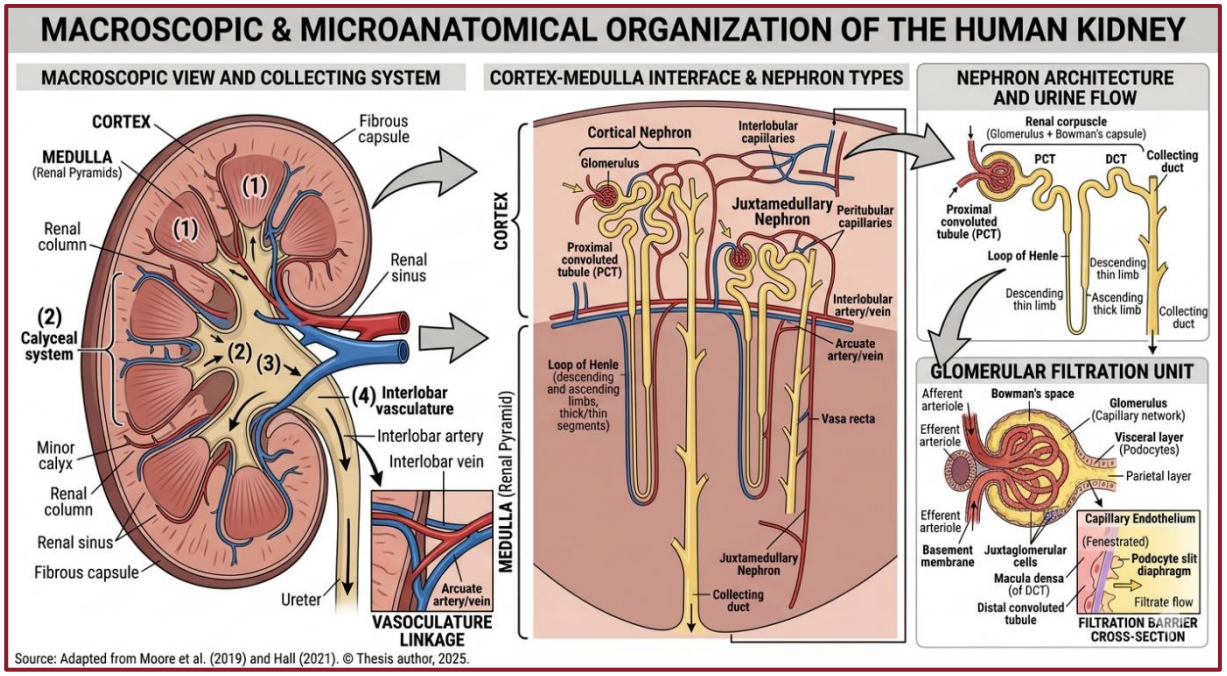


Figure 1. Schematic Diagram of the Macroscopic Anatomy of the Human Kidney © Thesis author, 2025.

2.2 Physiology of the Kidneys

Renal physiology is characterised by the simultaneous execution of multiple complex and interdependent functions, all ultimately directed toward the maintenance of internal homeostasis. We may conceptually organise renal physiology around five primary functional domains: filtration, reabsorption, secretion, excretion, and endocrine activity.

2.2.1 Glomerular Filtration

Glomerular filtration is the initial and rate-limiting step of urine formation. Plasma is ultrafiltered across the glomerular filtration barrier under a net hydrostatic pressure gradient (Starling forces), producing an ultrafiltrate (primary urine) that is compositionally similar to plasma but devoid of cells and large proteins. The glomerular filtration rate (GFR) — the volume of plasma filtered per unit time across all nephrons — is the most widely used clinical index of overall renal function. In healthy adults, GFR ranges from approximately 90–120 mL/min/1.73 m² body surface area, equating to roughly 180 litres of ultrafiltrate produced daily, of which over 99% is subsequently reabsorbed in the tubular segments (Hall, 2021).

GFR is regulated by alterations in afferent and efferent arteriolar resistance, mediated by intrinsic (myogenic reflex, tubuloglomerular feedback [TGF]) and extrinsic (sympathetic nervous system, renin-angiotensin-aldosterone system [RAAS], prostaglandins, natriuretic peptides) mechanisms. Angiotensin II selectively constricts the efferent arteriole, thereby maintaining GFR despite reductions in renal perfusion pressure — a compensatory mechanism exploited pharmacologically by angiotensin-converting enzyme (ACE) inhibitors in the treatment of chronic kidney disease. Prostaglandins (PGE2 and PGI2), synthesised within the renal cortex and medulla, exert vasodilatory effects on the afferent arteriole; their inhibition by non-steroidal anti-inflammatory drugs (NSAIDs) — which are widely used as unscheduled over-the-counter supplements in many regions — can precipitate acute reductions in GFR, particularly in haemodynamically vulnerable patients (Bacchi Modena et al., 2012).

2.2.2 Tubular Reabsorption and Secretion

The proximal convoluted tubule (PCT) reabsorbs approximately 60–65% of filtered sodium, water, glucose, amino acids, bicarbonate, and phosphate through a combination of active carrier-mediated transport, cotransport systems, and secondary active mechanisms. The PCT is also the principal site of transcellular reabsorption and secretion of organic anions and cations, including pharmaceutical drugs, their metabolites, and naturally occurring organic acids — a function mediated by a diverse family of organic anion transporters (OAT1, OAT3) and organic cation transporters (OCT1, OCT2) on the basolateral and apical membranes. These transporters also mediate the cellular accumulation of heavy metals and nephrotoxic herbal compounds, rendering the PCT particularly susceptible to toxin-induced injury (Nigam et al., 2015).

The loop of Henle, particularly its thick ascending limb (TAL), reabsorbs approximately 25–30% of filtered sodium via the Na-K-2Cl cotransporter (NKCC2), generating the hypertonic medullary interstitium essential for urinary concentration. The distal convoluted tubule and collecting duct perform fine regulation of sodium, potassium, acid-base balance, and water reabsorption under the hormonal control of aldosterone (sodium retention and potassium secretion) and antidiuretic hormone (ADH/vasopressin; water reabsorption via aquaporin-2 channels). The capacity for urinary concentration or dilution up to a maximum of approximately 1200 mOsmol/kg and minimum of approximately 50 mOsmol/kg, respectively, provides the kidney with the homeostatic flexibility required to accommodate wide variation in dietary fluid and solute intake (Bankir et al., 2016).

2.2.3 Acid-Base Regulation and Electrolyte Homeostasis

The kidneys are the principal organs of long-term acid-base regulation, buffering the daily endogenous acid load (approximately 40–80 mEq H+ per day produced by metabolic processes) through titration of filtered bicarbonate, generation of new bicarbonate via ammoniagenesis, and excretion of titratable acid in the form of NH4+ and H2PO4-. Disruption of these mechanisms — as occurs in proximal tubular injury from nephrotoxic compounds — may result in proximal renal tubular acidosis (type 2 RTA), characterised by bicarbonate wasting, hypokalaemia, and Fanconi syndrome (Curthoys & Moe, 2014).

Electrolyte homeostasis, particularly the regulation of calcium, phosphorus, and magnesium — elements relevant to dietary supplementation — involves complex interplay between renal tubular reabsorption and hormonal regulators including parathyroid hormone (PTH), calcitriol (1,25-dihydroxyvitamin D3), and fibroblast growth factor-23 (FGF-23). The kidney is the site of the final hydroxylation step in the bioactivation of vitamin D, converting 25-hydroxyvitamin D3 (calcidiol) to the active metabolite 1,25-dihydroxyvitamin D3 (calcitriol) via the mitochondrial enzyme 25-hydroxyvitamin D-1alpha-hydroxylase (CYP27B1). Supraphysiological vitamin D intake from supplementation can overwhelm this regulatory system, resulting in hypercalcaemia, hypercalciuria, and ultimately nephrocalcinosis or nephrolithiasis (Marcinowska-Suchowierska et al., 2018).

2.2.4 Endocrine Functions

Beyond their filtration and homeostatic roles, the kidneys are significant endocrine organs. They synthesise and secrete erythropoietin (EPO) from peritubular interstitial cells in the cortex in response to hypoxia, thereby stimulating red blood cell production in the bone marrow. The recombinant form of erythropoietin (rHuEPO) is classified as a performance-enhancing drug in sports but is also present in certain unregulated supplement preparations. The kidneys also produce renin from juxtaglomerular cells in the afferent arteriole wall, initiating the RAAS cascade that regulates blood pressure and volume homeostasis. Additionally, the kidneys degrade and excrete insulin,

parathyroid hormone, and other peptide hormones, such that renal failure is accompanied by diverse endocrine dysregulation (Gomez et al., 2014).

2.3 Renal Pathology: Selected Kidney Diseases

The structural complexity and physiological intensity of renal function render the kidneys vulnerable to a wide spectrum of pathological processes. We review here the principal categories of renal disease most relevant to the toxicological context of this thesis, with particular attention to those in which dietary supplement exposure has been identified as a causal or contributing factor.

2.3.1 Acute Kidney Injury (AKI)

Acute kidney injury (AKI), previously termed acute renal failure, is defined by the Kidney Disease: Improving Global Outcomes (KDIGO) criteria as an abrupt increase in serum creatinine by 0.3 mg/dL or more within 48 hours, or by 1.5 times baseline within 7 days, or urine output below 0.5 mL/kg/h for 6 or more hours (KDIGO, 2012). AKI affects approximately 13.3 million individuals per year globally and is associated with a short-term mortality of 23.9% in hospitalised patients. The pathophysiological mechanisms of AKI are conventionally classified as prerenal (reduced renal perfusion), intrinsic renal (direct tubular, glomerular, or interstitial injury), and postrenal (obstructive). In the context of dietary supplement nephrotoxicity, intrinsic AKI predominates, typically via acute tubular necrosis (ATN) or acute interstitial nephritis (AIN) induced by herbal nephrotoxins, heavy metals, or protein overload (Mehta et al., 2015).

2.3.2 chronic kidney disease (CKD)

Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for more than 3 months, with implications for health (KDIGO, 2013). CKD is classified into stages G1-G5 based on estimated GFR (eGFR) and into categories A1-A3 based on albuminuria levels. The global prevalence of CKD is estimated at approximately 9.1% of the general population, representing approximately 700 million individuals. Risk factors include diabetes mellitus, hypertension, glomerulonephritis, autoimmune disease, obstructive uropathy, and — increasingly recognised — chronic exposure to nephrotoxic substances including certain dietary supplements and herbal preparations. CKD progression is characterised histopathologically by interstitial fibrosis, tubular atrophy, glomerulosclerosis, and vascular rarefaction, culminating in end-stage renal disease (ESRD) requiring dialysis or transplantation (Bikbov et al., 2020).

2.3.3 Nephrolithiasis (Kidney Stones)

Nephrolithiasis is defined by the formation of crystalline aggregates (calculi) within the renal collecting system. The global lifetime prevalence of nephrolithiasis is approximately 10–15%, with significant geographical and dietary variation (Scales et al., 2012). Calcium oxalate stones, accounting for approximately 70–80% of cases, are most directly relevant to dietary supplement exposure: high-dose vitamin C supplementation (exceeding 1 g/day) is metabolised in part to oxalate, substantially increasing urinary oxalate excretion and stone-formation risk, particularly in individuals with hyperoxaluria, inflammatory bowel disease, or prior nephrolithiasis. Uric acid stones (5–10% of cases) may be potentiated by high-protein supplement consumption increasing purine load. Calcium phosphate stones may arise in the context of chronic vitamin D toxicity producing hypercalciuria (Ferraro et al., 2016).

2.3.4 Aristolochic Acid Nephropathy and Herbal Nephrotoxicity

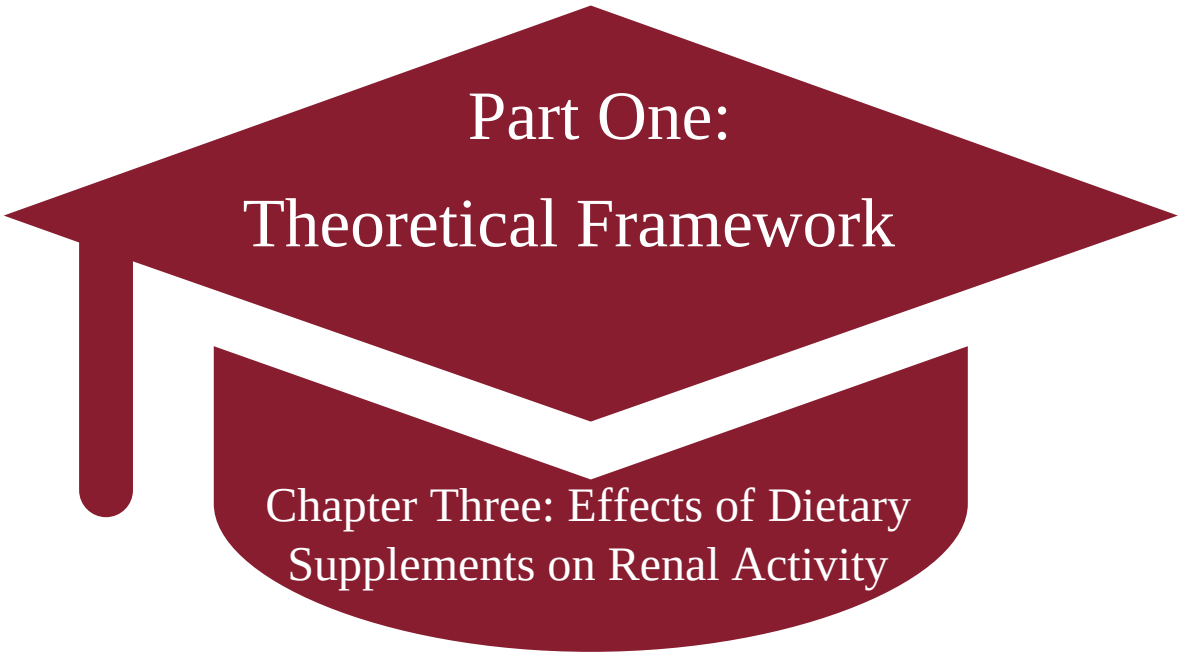
Aristolochic acid nephropathy (AAN), formerly termed Chinese herb nephropathy or Balkan endemic nephropathy in geographically distinct contexts, represents perhaps the most dramatically

documented case of herbal supplement-induced renal disease. First reported in Belgium in the early 1990s among women consuming a weight-loss preparation containing Aristolochia fangchi, AAN is characterised by rapidly progressive interstitial nephritis, tubular atrophy, and a high risk of progression to ESRD (Vanherweghem et al., 1993, as cited in Gokmen et al., 2013). A pivotal finding is the association of AAN with a high incidence of upper urinary tract urothelial carcinoma — reported in up to 50% of ESRD patients with AAN in some series — attributable to the formation of aristolactam-DNA adducts by the aristolochic acid metabolite aristolactam I (Stiborova et al., 2016).

Aristolochic acids are present in numerous species of the Aristolochiaceae family, some of which have been used in traditional medicinal systems of Asia, Europe, and Africa for centuries. Despite regulatory restrictions in many countries, aristolochic acid-containing preparations continue to circulate in herbal supplement markets globally, particularly through online channels, with documented cases of AAN reported from North America, Europe, Asia, and Africa. This example vividly illustrates the intersection of regulatory insufficiency, traditional medicinal practice, and the globalisation of supplement distribution in the generation of serious renal harm (Nortier et al., 2015).

2.3.5 Glomerulonephritis

Glomerulonephritis (GN) encompasses a heterogeneous group of immune-mediated conditions characterised by glomerular inflammation, proteinuria, haematuria, hypertension, and variable reduction in GFR. While the primary causes of GN include autoimmune conditions (IgA nephropathy, lupus nephritis), post-infectious triggers, and systemic vasculitides, dietary supplements have been implicated in GN through several mechanisms: direct complement activation by certain herbal polysaccharides, deposition of drug-induced immune complexes, and the provocation of anti-nuclear antibody (ANA) production by phytoestrogens and other immunologically active botanical compounds. The nephrotoxic potential of supplements containing chromium, gold, and mercury — elements found as contaminants in substandard herbal preparations — includes the induction of membranous GN through heavy metal-antigen complex formation (Gabardi et al., 2007).



Part One:
Theoretical Framework

Chapter Three: Effects of Dietary Supplements on Renal Activity

3.1 Conceptual Framework

The relationship between dietary supplement consumption and renal function disruption is best understood within a multi-level toxicological framework that integrates exposure characteristics (dose, duration, bioavailability), host vulnerability factors (pre-existing renal function, genetic polymorphisms, hydration status, comedications), and compound-specific mechanisms of nephrotoxicity. Figure 2, presented below, schematises the principal pathways through which dietary supplement exposure may culminate in clinically significant renal dysfunction.

This framework draws on the 'dose-response paradigm' of classical toxicology (Paracelsus' principle: the dose makes the poison), recognising that many supplement components that are beneficial or neutral at recommended doses become nephrotoxic at supraphysiological or chronic high-dose levels. It also incorporates the 'threshold model' of toxicant-mediated renal injury, which holds that the kidney possesses considerable functional reserve — typically manifest as glomerular hyperfiltration compensating for nephron loss — that may mask early injury until a critical proportion of nephron function is irreversibly lost. Finally, the framework acknowledges the 'individual susceptibility model', recognising that genetic polymorphisms in drug-metabolising enzymes and renal transporters, co-existing medical conditions, and nephron endowment at birth substantially modify individual risk.

Critically, the framework distinguishes between direct nephrotoxicity (supplement compound or its metabolite directly injures renal cells) and indirect nephrotoxicity (supplement-induced systemic metabolic disturbance secondarily impairs renal function). Examples of direct mechanisms include aristolochic acid intercalation into proximal tubular cell DNA, heavy metal inhibition of mitochondrial respiratory chain enzymes in tubular epithelium, and oxalate crystal deposition in the tubular lumen. Indirect mechanisms include hypercalcaemia from vitamin D toxicity reducing renal perfusion, hyperfiltration from high protein load increasing glomerular capillary pressure, and metabolic acidosis from ketogenic supplement protocols impairing tubular acid secretion.

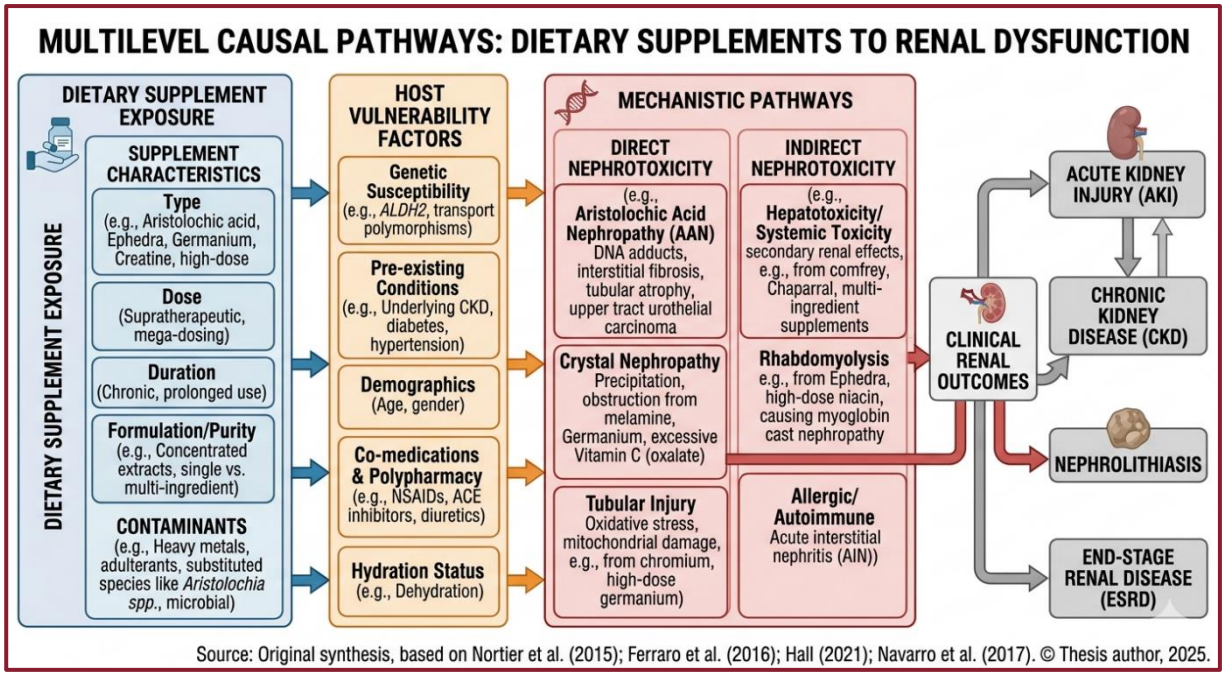


Figure 2. Conceptual Framework: Pathways from Dietary Supplement Consumption to Renal Dysfunction

3.2 Diseases Caused by Dietary Supplement Consumption

The spectrum of renal diseases attributable to or exacerbated by dietary supplement consumption encompasses virtually all major categories of renal pathology, from acute to chronic and from glomerular to tubular and interstitial. We systematically review the principal clinical entities, their associated supplement exposures, and the mechanistic evidence supporting causal attribution.

3.2.1 Protein Supplement-Induced Glomerular Hyperfiltration and CKD Progression

The relationship between dietary protein intake and renal function has been studied for over a century, originating with the observation by Addis and colleagues in the 1920s that protein feeding increases renal blood flow and GFR. Contemporary evidence establishes that habitual protein consumption substantially above physiological requirements induces glomerular hyperfiltration — an increase in GFR above age- and sex-adjusted normal values — through afferent arteriolar vasodilation and increased glomerular capillary hydraulic pressure (Kalantar-Zadeh et al., 2017). While this adaptation is haemodynamically compensated in individuals with intact renal function, it is widely held that sustained hyperfiltration accelerates glomerulosclerosis and CKD progression in individuals with pre-existing nephron loss or reduced renal reserve (Brenner et al., 1982, as cited in Kalantar-Zadeh et al., 2017).

Contemporary sports nutrition practices have introduced a novel population-level experiment in extreme dietary protein consumption. The International Society of Sports Nutrition currently recommends 1.6–2.2 g/kg/day for hypertrophy-oriented athletes, acknowledging that some practitioners consume substantially more (Stokes et al., 2018). A systematic review and meta-analysis by Antonio et al. (2016) found that healthy resistance-trained athletes consuming very high protein diets (3.3 g/kg/day) for 1 year did not exhibit significant changes in standard renal function markers, suggesting that healthy kidneys may tolerate extreme protein loads. However, a critical weakness of existing literature is the nearly universal exclusion of participants with pre-existing renal impairment, subclinical diabetic nephropathy, or reduced nephron number — precisely the subpopulations at greatest risk. A prospective cohort study by Kalantar-Zadeh et al. (2017) demonstrated that in CKD patients, each 10 g/day increment in total protein intake was associated with a 5% higher risk of ESRD, underscoring the clinical importance of distinguishing between healthy and renally compromised populations.

3.2.2 Vitamin C-Induced Nephrolithiasis and Oxalate Nephropathy

Ascorbic acid (vitamin C) is among the most widely consumed dietary supplements globally, with an estimated 40% of United States adults reporting regular use and market retail figures exceeding USD 800 million annually (Mishra et al., 2021). While the role of ascorbic acid in immune function and as an antioxidant is well established, supraphysiological supplementation (exceeding 1 g/day) has been associated with increased urinary oxalate excretion through metabolic conversion of ascorbate to oxalate, a well-characterised but dose-dependent biochemical pathway (Ferraro et al., 2016).

A landmark prospective cohort study by Taylor et al. (2004, as cited in Ferraro et al., 2016) involving 85,557 women in the Nurses' Health Study found that vitamin C supplementation was not associated with nephrolithiasis risk in women. However, an equivalent study in the Health Professionals Follow-up Study (HPFS) involving 45,251 men found that men consuming 1,000 mg/day or more of supplemental vitamin C had a hazard ratio of 1.41 (95% CI: 1.11–1.80) for incident kidney stones compared with non-users (Taylor et al., 2004). More concerning is the well-

documented occurrence of oxalate nephropathy — a severe and potentially irreversible form of AKI characterised by tubular obstruction by calcium oxalate crystals — in individuals with inflammatory bowel disease, prior gastric bypass surgery, or genetic hyperoxaluria who consume high-dose vitamin C supplements, as well as in case reports of otherwise healthy individuals consuming intravenous vitamin C or mega-dose oral preparations exceeding 6 g/day (Nasr et al., 2020).

3.2.3 Vitamin D Toxicity and Hypercalcaemic Nephropathy

Vitamin D supplementation has become virtually ubiquitous in the adult population of many countries, driven by evidence linking vitamin D deficiency to bone disease, cardiovascular risk, immune dysfunction, and cancer. The rapid expansion of vitamin D supplementation, combined with availability of high-potency preparations (10,000–50,000 IU capsules) marketed directly to consumers, has generated a parallel increase in clinical presentations of vitamin D toxicity, or hypervitaminosis D (Holick, 2017).

Vitamin D toxicity occurs predominantly at chronic intakes exceeding 10,000 IU/day, though cases have been reported at lower doses in individuals with granulomatous disease, Williams syndrome, or CYP24A1 mutations impairing vitamin D catabolism (Marcinowska-Suchowierska et al., 2018). The primary toxic mechanism is hypercalcaemia arising from enhanced intestinal calcium absorption and excessive bone resorption driven by supraphysiological calcitriol levels. Hypercalcaemia exerts nephrotoxic effects through multiple pathways: (1) vasoconstriction of the afferent arteriole reducing GFR; (2) calcium-sensing receptor activation in the collecting duct impairing ADH-mediated water reabsorption (nephrogenic diabetes insipidus); (3) precipitation of calcium phosphate crystals in the renal tubules and interstitium (nephrocalcinosis); and (4) hypercalciuria driving nephrolithiasis (Bilezikian et al., 2020). Several case series have documented acute kidney injury, nephrocalcinosis, and irreversible CKD in individuals following excessive vitamin D supplementation, including individuals without pre-existing renal disease (Taylor & Davies, 2016).

3.2.4 Creatine Supplementation and Renal Function

Creatine monohydrate is the most extensively researched and commercially ubiquitous ergogenic supplement, consumed by an estimated 40–60% of competitive athletes in strength and power sports (Lanhers et al., 2017). The safety of creatine supplementation for renal function has been extensively debated, generating a substantial and somewhat contradictory literature. The crux of the interpretive challenge is that creatine supplementation predictably and substantially increases serum creatinine — the most commonly used proxy for GFR in clinical practice — because creatine is non-enzymatically converted to creatinine in muscle at a rate proportional to total body creatine content. This elevation in serum creatinine, which may reach 0.5–1.0 mg/dL above baseline, can falsely suggest a decline in GFR when interpreted without knowledge of creatine supplementation (Pline & Smith, 2005).

The weight of evidence from randomised controlled trials and long-term observational studies in healthy individuals suggests that creatine supplementation at recommended doses (3–5 g/day maintenance) does not impair true GFR as measured by cystatin C, inulin clearance, or nuclear medicine methods (Antonio & Ciccone, 2013). However, several case reports and small series have documented AKI in individuals consuming very high-dose creatine (20+ g/day, consistent with the 'loading phase' protocol), in individuals with undiagnosed focal segmental glomerulosclerosis, and in combination with other nephrotoxic supplements or agents. The potential for creatine to mask early CKD by artificially elevating creatinine, thereby delaying clinical recognition of renal function decline, represents an underappreciated public health concern (Taner et al., 2011, as cited in Jabeen & Naeem, 2019).

3.2.5 Herbal Supplement-Associated Nephrotoxicity

Herbal and botanical supplements constitute a heterogeneous category with a disproportionate burden of serious nephrotoxicity relative to their market share. Beyond aristolochic acid nephropathy, reviewed in Chapter Two, several additional herbal substances merit specific attention. Chromium picolinate — widely marketed for weight loss and insulin sensitisation — has been associated with interstitial nephritis and tubular necrosis in case reports, with proposed mechanisms involving chromium-induced oxidative stress and DNA damage in tubular epithelial cells (Martin et al., 2006). Thunder god vine (Tripterygium wilfordii) preparations, used in Traditional Chinese Medicine for autoimmune and inflammatory conditions, have been associated with acute tubular necrosis in multiple case reports. Pennyroyal oil (Mentha pulegium), marketed as an herbal abortifacient and menstrual stimulant, contains the hepatotoxin and nephrotoxin pulegone, with documented cases of acute multi-organ failure including AKI (Gordon et al., 1982, as cited in Stickel et al., 2005).

A systematic review of herbal supplement nephrotoxicity by Gabardi et al. (2007) identified 36 species with documented renal adverse effects, encompassing mechanisms including nephrolith promotion, direct tubular toxicity, immune-mediated GN, and electrolyte disturbance. The review estimated that herbal nephrotoxicity accounts for between 3% and 35% of AKI cases in Asian countries with high rates of traditional medicine use, compared with approximately 2–5% in Western countries — though these figures likely underrepresent true incidence due to ascertainment bias and underreporting.

3.3 Heavy Metal Overload from Contaminated Supplements

Heavy metal contamination of dietary supplements represents a toxicological issue of potentially vast public health significance, given the global scale of supplement consumption, the inadequacy of routine quality control testing, and the insidious nature of heavy metal nephrotoxicity. Heavy metals — defined here as metallic elements with densities exceeding 5 g/cm³ that exert toxic effects at low concentrations — include lead (Pb), cadmium (Cd), mercury (Hg), arsenic (As), and chromium (Cr), all of which have been detected above regulatory thresholds in marketed dietary supplement products.

3.3.1 Sources and Prevalence of Contamination

Heavy metals enter dietary supplement products through multiple pathways. Botanical raw materials accumulate heavy metals from contaminated soil, irrigation water, and industrial atmospheric deposition, a process particularly prevalent in Ayurvedic, Chinese, and African herbal products sourced from regions with high industrial activity or historical smelting contamination. A landmark analysis by Saper et al. (2008) of 193 Ayurvedic herbal medicine products purchased from stores in Boston found that 20% contained detectable levels of lead, mercury, or arsenic, with lead concentrations reaching 37,000 micrograms per gram in some products. A more recent systematic review by Posadzki et al. (2013) reported contamination with at least one heavy metal in 18% of herbal medicines tested across 26 included studies.

Beyond botanical contamination, heavy metals may be introduced as intentional ingredients in some traditional medicinal formulations (notably rasa shastra preparations in Ayurveda, which employ processed metallic compounds including lead sulphide, mercury sulphide, and arsenic sulphide as therapeutic agents), as manufacturing process contaminants (from equipment or packaging), or as adulterants in counterfeit or substandard products. The globalisation of supplement manufacturing and distribution, with supply chains spanning multiple jurisdictions with variable regulatory standards, further complicates quality assurance.

3.3.2 Nephrotoxic Mechanisms of Specific Heavy Metals

Lead nephrotoxicity, documented since antiquity in the form of 'lead nephropathy' among ancient Romans who used lead vessels for food preparation and wine storage, manifests as proximal tubular dysfunction at low-level chronic exposure and as direct tubular necrosis at acute high-dose exposure. Lead is accumulated in proximal tubular epithelial cells via organic anion transporter pathways, where it inhibits mitochondrial oxidative phosphorylation, disrupts calcium signalling, generates reactive oxygen species (ROS), and forms intranuclear inclusion bodies (complexes of lead and protein) that are pathognomonic on renal biopsy (Barbier et al., 2005). Epidemiological evidence from the Third National Health and Nutrition Examination Survey (NHANES III) linked blood lead levels within the so-called normal range (1.2–9.9 µg/dL) to a 7.6% reduction in GFR, suggesting that there is no safe level of lead exposure for the kidneys (Muntner et al., 2003, as cited in Barbier et al., 2005).

Cadmium nephrotoxicity is characterised by preferential damage to the proximal tubule, attributable to the high expression of the metal transporter ZIP8 and subsequent intracellular accumulation once the cadmium-binding protein metallothionein-1 is saturated. The cardinal manifestation is low-molecular-weight proteinuria (beta-2-microglobulinuria, retinol-binding protein) reflecting impaired tubular reabsorption of filtered proteins, accompanied by glucosuria, aminoaciduria, and phosphaturia — the full Fanconi syndrome picture — at higher exposures (Nordberg et al., 2015). The WHO tolerable weekly intake for dietary cadmium is 7 µg/kg body weight; analysis of multiple dietary supplement products — including calcium supplements, protein powders, and certain herbal preparations — has found cadmium concentrations sufficient to contribute materially to weekly cadmium exposure, particularly in heavy supplement users (Maret & Sandstead, 2006).

Arsenic exerts nephrotoxicity through multiple convergent mechanisms, including inhibition of pyruvate dehydrogenase and alpha-ketoglutarate dehydrogenase (impairing mitochondrial energy production), methylation-related depletion of methyl groups from SAM (S-adenosylmethionine), generation of hydroxyl radicals, and direct DNA strand breaks in tubular epithelial cells (Hughes, 2002). Inorganic arsenic (as opposed to organic arsenobetaine found in seafood) is the species of greatest nephrotoxic concern; it undergoes renal concentration and excretion, exposing tubular cells to higher concentrations than most other organs. Mercury, consumed through contaminated fish-containing supplements or certain traditional preparations, is associated with immune-complex membranous glomerulonephritis and proximal tubular necrosis, with mechanisms involving direct thiol group binding and autoimmune induction (Barregard et al., 2010).

Table 3. Changes in Renal Biomarkers Associated with Selected Dietary Supplements

Supplement / Substance	Biomarker Affected	Direction of Change	Clinical Implication
Vitamin C (high dose, >2 g/day)	Urinary oxalate, serum creatinine	↑ Oxalate; ↑ Creatinine	Calcium oxalate nephrolithiasis; AKI risk in susceptible individuals
Vitamin D (>10,000 IU/day chronic)	Serum calcium, GFR	↑ Calcium; ↓ GFR	Hypercalcaemia-induced nephropathy; nephrocalcinosis
Creatine (≥5 g/day long-term)	Serum creatinine, creatinine clearance	↑ Creatinine (spurious)	Apparent renal function decline; may mask true GFR reduction

Protein powders (>2.5 g/kg/day)	Urea, GFR, renal blood flow	↑ Urea; ↑ Glomerular pressure	Glomerular hyperfiltration; progressive CKD in pre-existing renal insufficiency
Aristolochic acid (herbal)	Tubular markers (KIM-1, NGAL)	↑ Tubular injury markers	Aristolochic acid nephropathy; ESRD and urothelial carcinoma
Heavy metals (Pb, Cd, As in contaminated supplements)	Urinary beta-2-microglobulin, GFR	↑ Tubular leak; ↓ GFR	Proximal tubular dysfunction; Fanconi syndrome; chronic nephrotoxicity
Chromium picolinate (excess)	Serum chromium, urinary protein	↑ Chromium; ↑ Proteinuria	Interstitial nephritis; oxidative tubular damage
NSAIDs / analgesics (OTC, chronic)	GFR, renal prostaglandins	↓ GFR; ↓ Prostaglandin synthesis	Analgesic nephropathy; papillary necrosis

Note. AKI = Acute Kidney Injury; CKD = Chronic Kidney Disease; ESRD = End-Stage Renal Disease; GFR = Glomerular Filtration Rate; KIM-1 = Kidney Injury Molecule-1; NGAL = Neutrophil Gelatinase-Associated Lipocalin. Data synthesised from Navarro et al. (2017); Ferraro et al. (2016); Marcinowska-Suchowierska et al. (2018); Gokmen et al. (2013); Barbier et al. (2005). © Thesis author, 2025.

3.4 Symptoms of Supplement-Induced Renal Injury

The clinical presentation of supplement-induced renal injury spans a wide continuum from complete asymptomatic subclinical dysfunction detectable only by sensitive biomarkers, to florid uraemic syndrome requiring emergency renal replacement therapy. The symptomatological profile is determined by the nature of the renal injury (glomerular, tubular, interstitial, or vascular), its severity and acuity, and the presence of underlying vulnerability factors. A staged clinical framework, correlating renal injury pattern with symptomatological and laboratory presentation, is presented in Table 4.

3.4.1 Early and Subclinical Presentations

The earliest detectable manifestation of supplement-induced glomerular injury is glomerular hyperfiltration, paradoxically characterised by an apparently supranormal GFR (>120 mL/min/1.73 m² in adults) reflecting compensatory hyperperfusion of residual nephrons following silent nephron loss. This stage is typically asymptomatic and identifiable only through systematic screening with GFR measurement or sensitive urinary biomarkers. Microalbuminuria — defined as urinary albumin excretion of 30–299 mg/24 h — is the earliest detectable biomarker of glomerular injury, reflecting disruption of the size- and charge-selective filtration barrier before frank proteinuria develops (Remuzzi & Bertani, 1998, as cited in Kalantar-Zadeh et al., 2017). Novel tubular injury biomarkers, including urinary kidney injury molecule-1 (KIM-1), neutrophil gelatinase-associated lipocalin (NGAL), and interleukin-18 (IL-18), are detectable before serum creatinine rises, providing an important early-warning window for intervention (Coca et al., 2012).

Low-molecular-weight proteinuria, characterised by urinary excretion of beta-2-microglobulin, alpha-1-microglobulin, and retinol-binding protein, signals proximal tubular dysfunction and is the hallmark early finding of heavy metal nephrotoxicity, particularly cadmium and mercury exposure. In the context of supplement-related heavy metal ingestion, this finding may precede the development of overt CKD by years or decades, making it a critical target for early detection in exposed populations.

3.4.2 Acute Presentations

Acute kidney injury from supplement exposure may present with the classic triad of oliguria (urine output less than 400 mL/24 h), oedema (periorbital, pedal, ascites), and uraemia (elevated blood urea nitrogen and serum creatinine with associated symptoms of nausea, vomiting, confusion, and hiccups). Flank or costovertebral angle pain is a prominent symptom when AKI is caused by bilateral nephrolithiasis with urinary tract obstruction, or by severe renal parenchymal oedema from acute interstitial nephritis. Visible haematuria (macrohaematuria) may accompany stone passage, glomerulonephritis, or severe papillary necrosis.

Acute interstitial nephritis (AIN), increasingly recognised as a complication of herbal supplement and high-dose OTC analgesic use, typically presents with the triad of fever, rash, and eosinophilia — though this classic presentation is present in fewer than 30% of biopsy-confirmed AIN cases. More commonly, AIN manifests as otherwise unexplained AKI with urinary eosinophiluria, sterile pyuria, and subnephrotic proteinuria, evolving over days to weeks following initiation of the offending supplement. Removal of the causative agent and, where appropriate, corticosteroid therapy may result in partial or complete renal recovery if instituted promptly (Perazella & Markowitz, 2010).

3.4.3 Nephrolithiasis Presentation

Kidney stone disease attributable to supplement consumption presents classically with severe, colicky flank pain radiating to the groin (ureteric colic), gross haematuria, nausea, and vomiting. The onset of symptoms typically follows the movement of a stone from the renal pelvis into the ureter, with pain severity reflecting the degree of ureteric obstruction and hydroureteronephrosis. Diagnosis is confirmed by non-contrast computed tomography (CT) urography, the gold-standard imaging modality for nephrolithiasis, and by stone composition analysis following spontaneous passage or surgical retrieval — with calcium oxalate identification suggesting vitamin C excess and uric acid stones suggesting high-protein or purine supplement consumption.

Recurrent nephrolithiasis, particularly when associated with identified metabolic risk factors amenable to dietary and supplementation modification (hyperoxaluria, hypercalciuria, hyperuricosuria), requires systematic metabolic workup including 24-hour urine collections for calcium, oxalate, uric acid, citrate, and creatinine. The identification of supplement contribution to stone risk is of direct therapeutic relevance, as dose reduction or discontinuation of the offending supplement may substantially reduce recurrence risk without pharmacological intervention (Ferraro et al., 2016).

3.4.4 Chronic and End-Stage Presentations

Chronic kidney disease attributable to supplement exposure may be clinically indistinguishable from CKD of other aetiologies in its advanced stages, presenting with the symptoms of uraemia (fatigue, anorexia, nausea, pruritus, impaired cognition), anaemia (from EPO deficiency), hypertension (from volume overload and RAAS activation), metabolic bone disease (from calcitriol deficiency and hyperphosphataemia), and peripheral neuropathy (from uraemic toxin accumulation). The clinical history of supplement use — particularly herbal preparations, high-dose vitamins, and sports nutrition products — should be specifically and systematically elicited in all CKD patients, as supplement contribution is likely underrecognised in clinical practice.

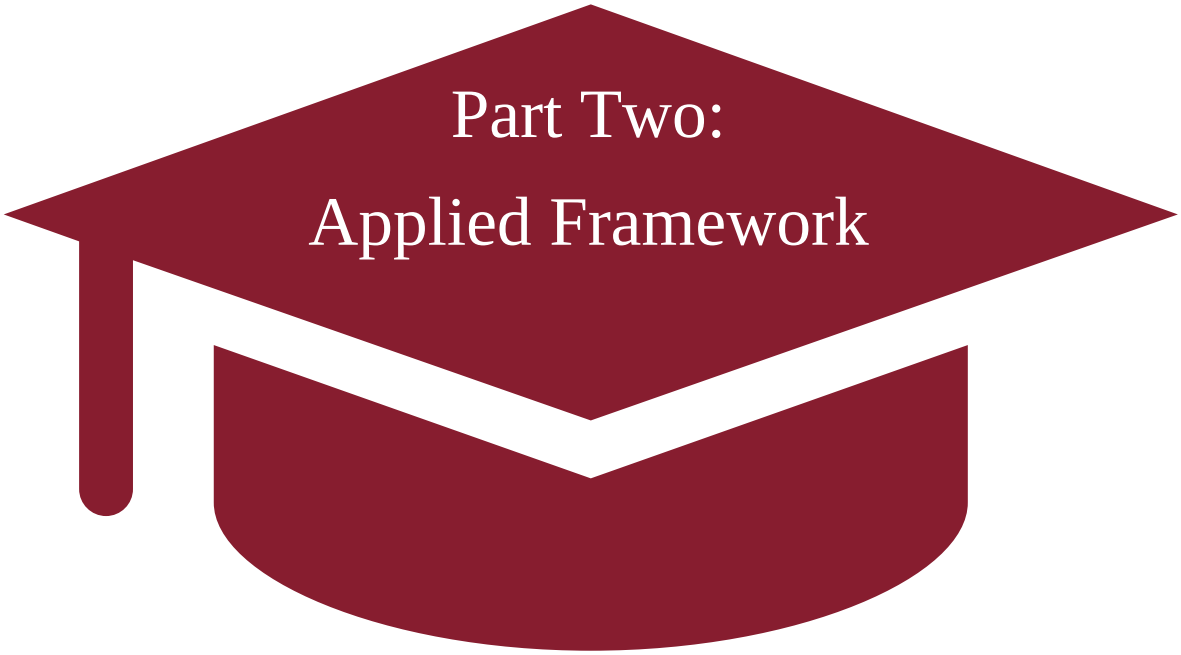
End-stage renal disease (ESRD) resulting from supplement-induced nephrotoxicity, though representing only a fraction of total ESRD incidence, has been documented in the context of AAN, severe analgesic nephropathy, recurrent oxalate nephrolithiasis, and chronic cadmium toxicity from

contaminated herbal preparations. The personal, social, and economic burden of ESRD — encompassing lifelong dialysis dependency or the challenges of transplantation — underscores the critical importance of supplement safety surveillance, patient education, and clinician awareness as preventive measures.

Table 4. Clinical Stages, Symptoms, and Laboratory Findings of Supplement-Induced Renal Injury

Stage	Renal Injury Pattern	Clinical Symptoms	Laboratory Findings
Early / subclinical	Glomerular hyperfiltration	Asymptomatic or mild fatigue; polyuria	Microalbuminuria; ↑ GFR (paradoxical); mild ↑ creatinine
Acute (AKI)	Acute tubular necrosis; oxalate deposition	Oliguria/anuria; flank pain; oedema; nausea	↑↑ Serum creatinine; ↑ BUN; ↓ GFR; haematuria; pyuria
Nephrolithiasis	Calcium oxalate / uric acid stones	Severe colicky pain; haematuria; nausea/vomiting	↑ Urinary oxalate/urate; crystals on urinalysis; stone on imaging
Chronic (CKD progression)	Interstitial fibrosis; tubular atrophy	Persistent fatigue; hypertension; anaemia; weight loss	↓ GFR (<60 mL/min/1.73 m²); proteinuria; anaemia; ↑ phosphate
End-stage (ESRD)	Total nephron loss	Uraemic symptoms: confusion, pericarditis, pruritus, vomiting	GFR <15 mL/min/1.73 m²; hyperphosphataemia; metabolic acidosis

Note. AKI = Acute Kidney Injury; BUN = Blood Urea Nitrogen; CKD = Chronic Kidney Disease; ESRD = End-Stage Renal Disease; GFR = Glomerular Filtration Rate. Data synthesised from KDIGO (2012); Ferraro et al. (2016); Navarro et al. (2017); Marcinowska-Suchowierska et al. (2018); Perazella & Markowitz (2010). © Thesis author, 2025.



Part Two:
Applied Framework

1. Objective of the study

This study aims to highlight the serious renal risks associated with the uncontrolled consumption of dietary supplements, particularly among athletes and elderly individuals. It focuses on revealing the silent consequences of excessive intake of proteins, vitamins, and herbal products without medical supervision, based on direct field observations from dialysis centres.

2. Study area

The study area is located in El Oued Province, one of the main oases of the northern Algerian Sahara. It is situated in southeastern Algeria, 650 km from the capital, in the northeastern part of the northern Sahara. The figure 3. shows an administrative map of El Oued Province in Algeria (Direction hydraulique a El Olued (DRH))

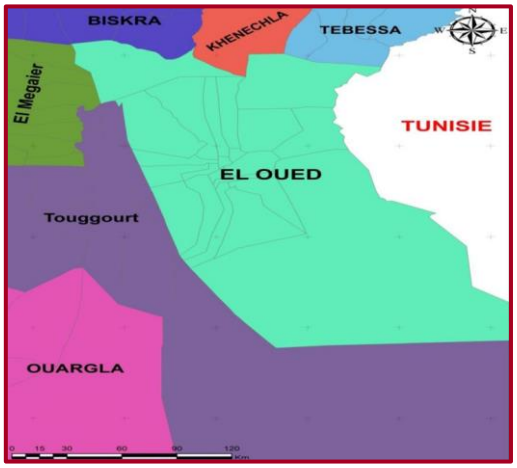


Figure 3. The Administrative Boundaries of the Wilaya of El Oued

3. Materials and Methods:

The study relied on a self designed questionnaire to collect data on dietary supplement use. The survey was distributed both physically and online using smartphones and computers. We used Microsoft Excel to organize and analyze the collected responses, creating statistical graphs and charts. Additionally, internet access was essential for distributing the survey and reaching participants. All tools used were standard digital resources, ensuring a smooth and efficient data collection process

4. Survey and population

Data Collection Tool

The current study relied on the _questionnaire_ as the main tool for data collection, due to its suitability for the nature of the descriptive analytical study and its ease of application to a sample of _200 individuals_. The questionnaire was designed by the researcher based on previous studies and the objectives of the study, and clarity and simplicity of linguistic phrasing were observed to suit all educational levels of the sample members. The questionnaire was distributed in two ways: _electronically_ via social media platforms to reach the general population, and _in paper format by hand_ inside the _Public Hospital "El Shaheed Ben Omar Djilani"_ to reach patients. This questionnaire was distributed from 18/02/2026 to 20/05/2026. The questionnaire consisted of _7 sections_ including _25 questions_ distributed as follows:

1. First Section: Demographic Information - Questions 1 to 4_

It aims to identify the personal characteristics of the sample members, and includes: gender, age group, educational level, and occupation or activity.

2. Second Section: Health History - Questions 5 and 6_

It addresses the health status of the participants, by asking about the presence of chronic diseases such as diabetes, high blood pressure, and kidney diseases, in addition to the presence of a family history of kidney diseases.

3. Third Section: Consumption of Dietary Supplements - Questions 7 to 12_

It focuses on the patterns of dietary supplement consumption among the participants, and includes: the extent of supplement use, their types, duration of use, source of obtaining them, adherence to the recommended dose, and exceeding the dose.

4. Fourth Section: Health Indicators of Kidney Function - Questions 13 to 15_

It aims to assess the preliminary indicators of kidney function among the participants, through conducting laboratory analyses during the past year, noting elevated creatinine or urea, and symptoms associated with supplement intake such as flank pain, swelling, and fatigue.

5. Fifth Section: Risk Awareness - Questions 16 to 21_

It measures the level of participants' awareness of the renal risks associated with supplements, their sources of information about them, their support for imposing medical control, and conducting periodic examinations, with an open question about the greatest risk in their opinion.

6. Sixth Section: Risk Assessment Using Likert Scale - Questions 22 to 23_

It uses a five-point Likert scale from 1 to 5, where 1 = Strongly Disagree and 5 = Strongly Agree, to measure participants' attitudes towards the safety of supplements at low doses, the danger of excessive intake, and the necessity of medical supervision.

7. Seventh Section: Open Question - Question 24_

It allows participants to express their opinions and recommendations to reduce the risks associated with the random use of dietary supplements.

5- The Analysis results of the questionnaire

5.1. Analysis of Questionnaire Data from Healthy Individuals

5.1.1. Distribution of the Questionnaire by Gender

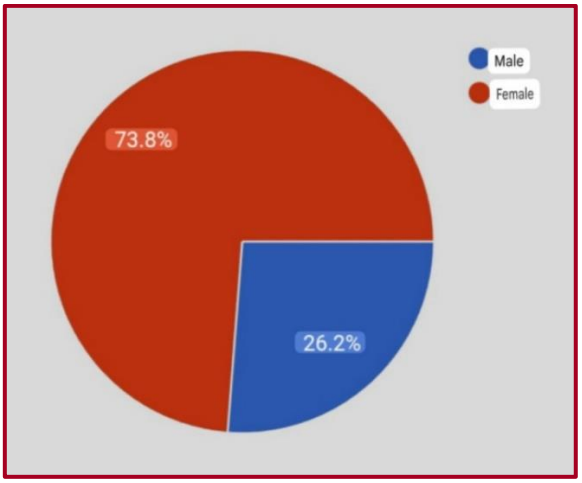


Figure 4: The Proportions of Genders

Question (1): Pie Chart Showing the Gender Distribution of Participants (164 Responses), Where the Percentage of "Female" Responses Was 73.8%, While the Percentage of "Male" Responses Was 26.2%.

5.1.2. Distribution of the Questionnaire by Age

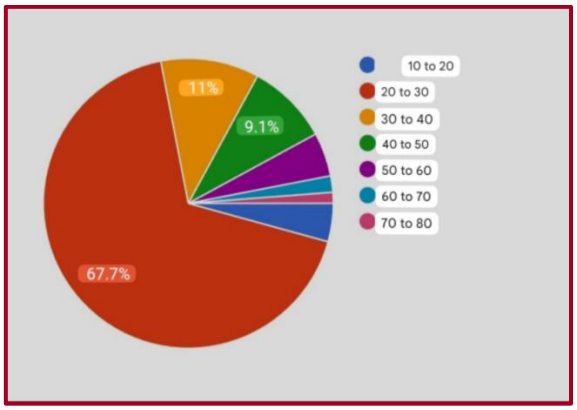


Figure 5: The Proportions of Age Groups

Question (2): Pie Chart Showing the Age Group of Participants (164 Responses), Where the Highest Percentage Was for the "20 to 30" Group at 67.7%, Followed by the "30 to 40" Group at 11%, Then the "40 to 50" Group at 9.1%, While the Remaining Small Percentages Were Distributed Among the Other Age Groups.

5.1.3. Distribution of the Questionnaire by Educational Level

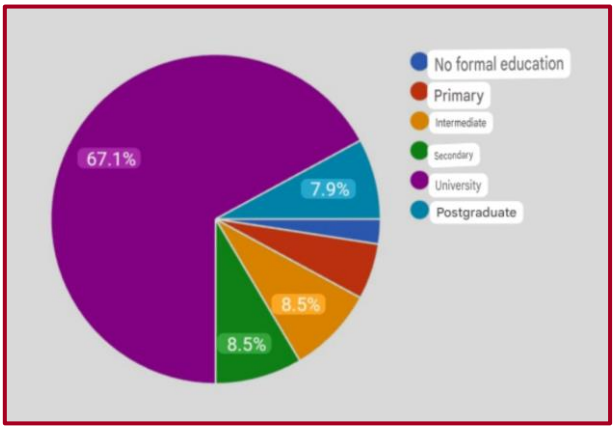


Figure 6: The Proportions of Educational Levels

Question (3): Pie Chart Showing the Educational Level of Participants (164 Responses), Where the Highest Percentage Was for the "University" Level at 67.1%, Followed by the "Intermediate" and "Secondary" Categories with an Equal Percentage of 8.5% for Each, Then the "Postgraduate Studies" Category at 7.9%, While the Remaining Small Percentages Were Distributed Among the "Primary" and "I Do Not Have Formal Education" Categories.

5.1.4. Distribution of the Questionnaire by Occupation or Activity

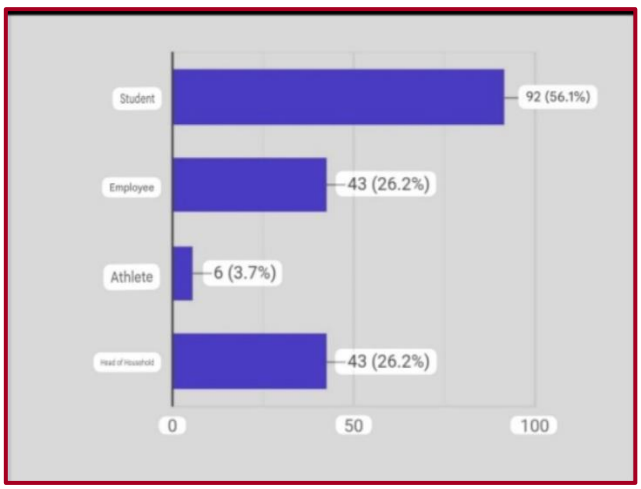


Figure 7: The Proportions of Occupation or Activity

Question (4): Bar Chart Showing the Occupation or Activity of Participants (164 Responses - with the Ability to Select More Than One Answer), Where the Highest Percentage Was for the "Student" Category at 56.1%, Followed by the "Employee" and "Head of Household" Categories with an Equal Percentage of 26.2% for Each, While the Percentage of the "Athlete" Category Was 3.7%.

5.1.5. Distribution of the Questionnaire by Chronic Health Condition

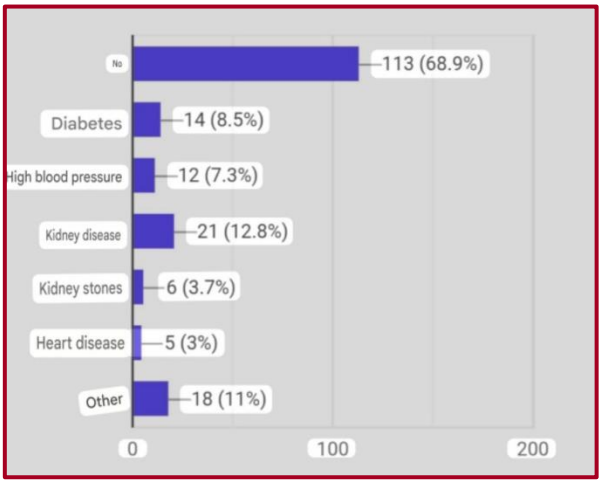


Figure 8: The Proportions of Chronic Health Conditions

Question (5): Bar Chart Showing Diagnosis of Chronic Diseases (164 Responses - Multiple Choices), Where the Percentage of Those Who Do Not Suffer "No" Was 68.9%, Followed by "Kidney Disease" 12.8%, "Other" 11%, "Diabetes Mellitus" 8.5%, "Hypertension" 7.3%, "Kidney Stones" 3.7%, and the Lowest Was "Cardiovascular Diseases" 3%.

5.1.6. Distribution of the Questionnaire by Family History of Kidney Disease

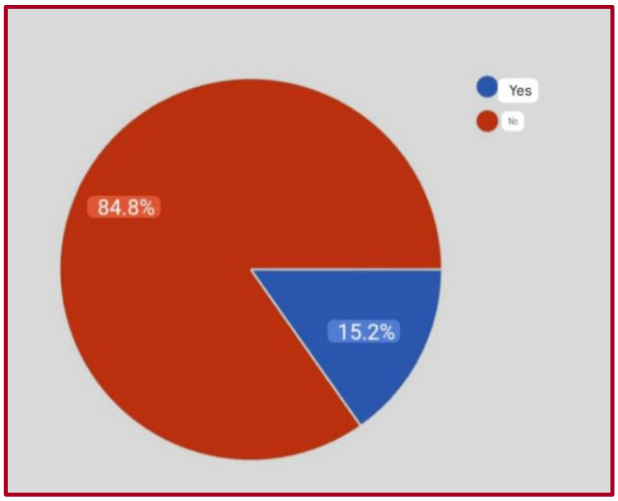


Figure 9: The Proportions of Family History of Kidney Disease

Question (6): Pie Chart Showing the Presence of a Family History of Kidney Diseases (164 Responses), Where the Percentage of "No" Responses Was 84.8%, While the Percentage of "Yes" Responses Was 15.2%.

5.1.7. Distribution of the Questionnaire by Previous Dietary Supplement Intake

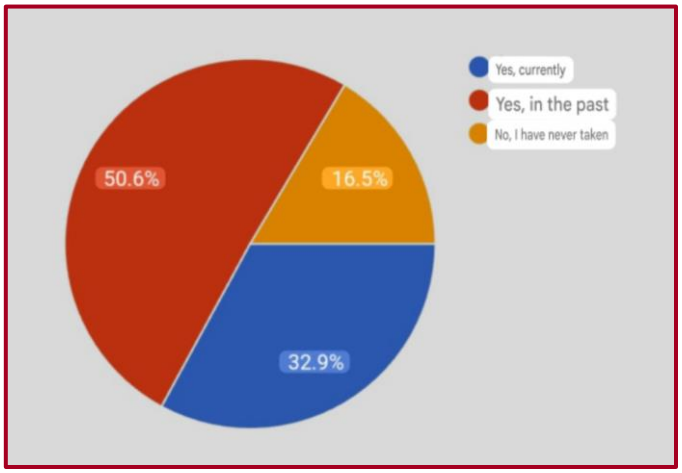


Figure 10: The Proportions of Previous Dietary Supplement Use

Question 7: Among the 164 respondents, 50.6% reported that they had consumed dietary supplements in the past, 32.9% indicated that they are currently consuming them, while 16.5% stated that they have never consumed dietary supplements.

5.1.8. Distribution of the Questionnaire by Dietary Supplement Use

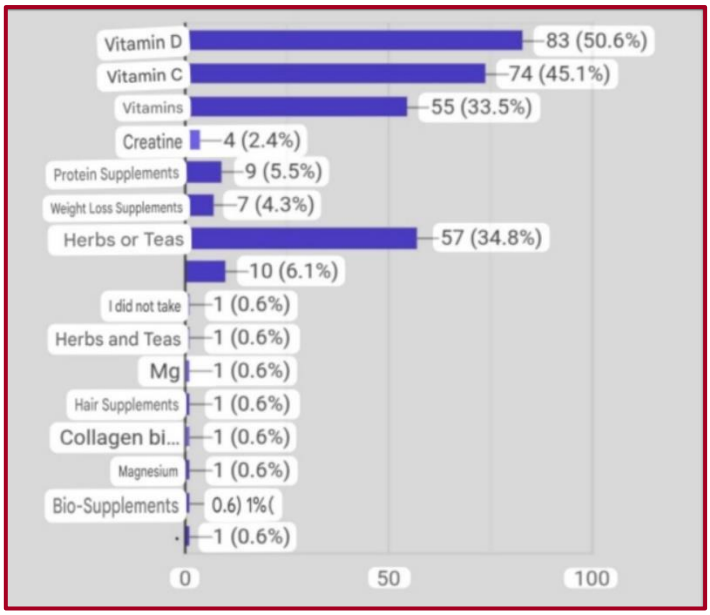


Figure 11: The Proportions of Types of Dietary Supplements Used

Question 8: The most frequently reported supplements were Vitamin D (50.6%), followed by Vitamin C (45.1%).

Multivitamins accounted for 33.5% of responses, while herbal products represented 34.8%. Protein supplements (5.5%), weight-loss supplements (4.3%), and creatine (2.4%) were less commonly reported. Other supplements were mentioned only occasionally.

5.1.9. Distribution of the Questionnaire by Duration of Dietary Supplement Intake

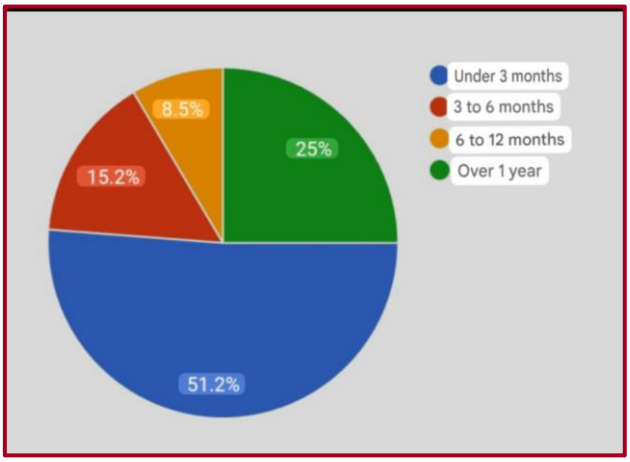


Figure 12: The Proportions of Duration of Dietary Supplement Use

Question 9: Among the respondents, 51.2% reported using dietary supplements for less than 3 months. A quarter of participants (25%) had been using supplements for more than one year, while 15.2% had been taking them for 3 to 6 months and 8.5% for 6 to 12 months.

5.1.10. Distribution of the Questionnaire by Mode of Dietary Supplement Intake

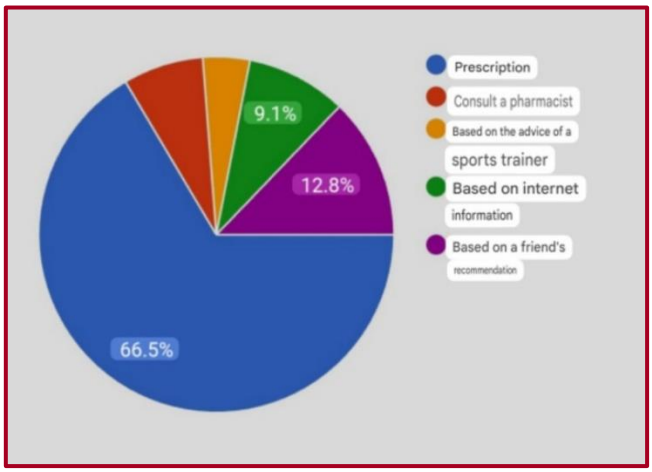


Figure 13: The Proportions of Dietary Supplement Administration Methods

Question 10: Most respondents (66.5%) reported taking dietary supplements based on a medical prescription. In addition, 12.8% used them following recommendations from friends, while 9.1% relied on information obtained from the internet. Smaller proportions reported taking supplements based on advice from a pharmacist or a sports coach.

5.1.11. Distribution of the Questionnaire by Recommended Dosage of Dietary Supplements

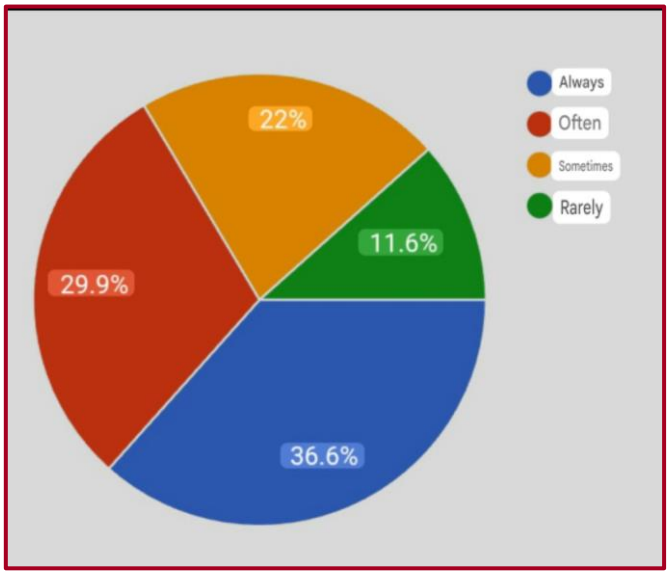


Figure 14: The Proportions of Adherence to Recommended Dietary Supplement Dosages

Question (11): Among the participants, 36.6% reported always following the recommended dosage, while 29.9% stated that they often follow it. Furthermore, 22% indicated that they sometimes respect the recommended dosage, whereas 11.6% reported rarely following it.

5.1.12. Distribution of the Questionnaire by Exceeding the Recommended Dosage

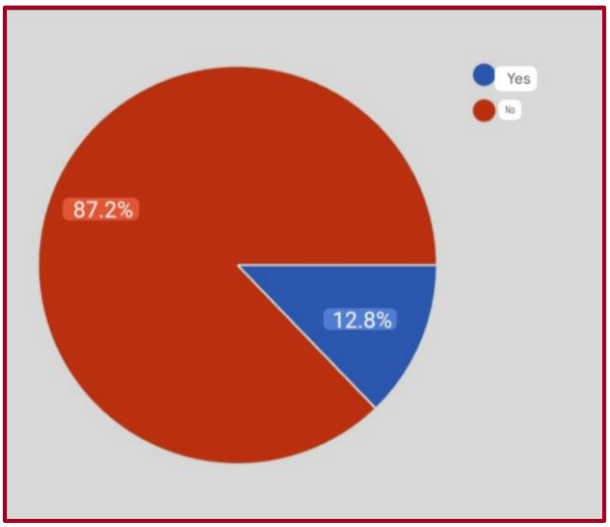


Figure 15: The Proportions of Exceeding the Recommended Dietary Supplement Dosage

Question (12): The majority of respondents (87.2%) stated that they had never exceeded the recommended dosage of dietary supplements. In contrast, 12.8% reported that they had exceeded the recommended dosage at least once.

5.1.13. Distribution of the Questionnaire by Kidney Function Tests

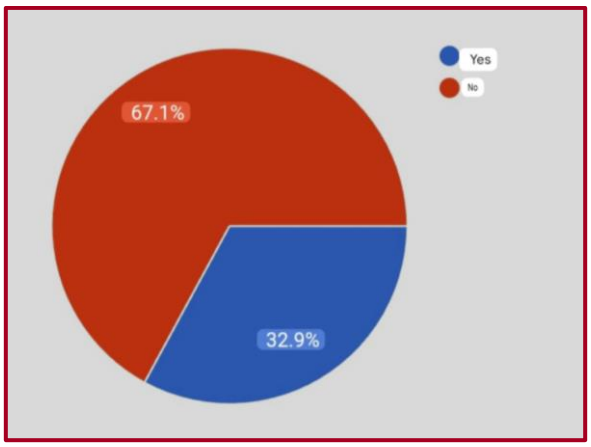


Figure 16: The Proportions of Kidney Function Tests Performed in the Past Year

Question (13): A pie chart showing the extent to which participants (164) underwent kidney function tests during the past year.

1. The majority (in red - "No"): Represents 67.1% of all participants. This means that approximately twothirds of the sample did not undergo any kidney function tests during the past year.

2. The minority (in blue - "Yes"): Represents only 32.9%. This means that less than one-third of the participants adhere to or have undergone this periodic testing.

5.1.14. Distribution of the Questionnaire by Kidney Tests

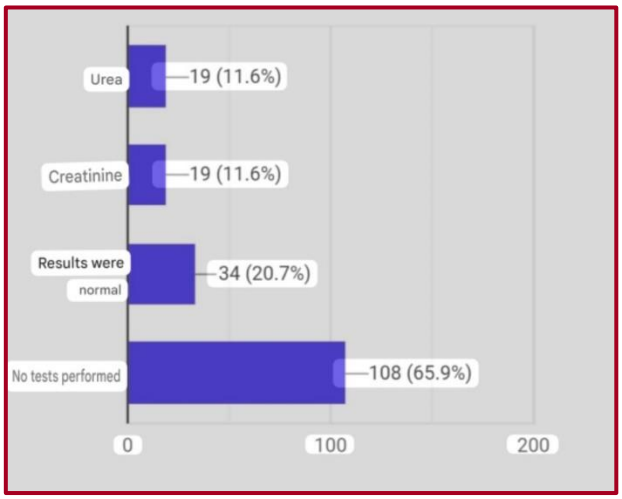


Figure 17: The Proportions of Elevated Levels in Laboratory Tests

Question (14): The image shows the kidney function test results for 164 people.

1. No tests performed: The largest percentage of participants (65.9%, or 108 people) did not undergo

any tests, which may indicate a lack of regular follow-up or a lack of awareness of the need for testing.

2. Normal results: 20.7% (34 people) reported that their results were within the normal range.

3. Elevated urea and creatinine: The percentage of participants who observed elevated urea and creatinine was equal, at 11.6% (19 people each).

5.1.15. Distribution of the Questionnaire by Symptom Onset During Dietary Supplement Intake

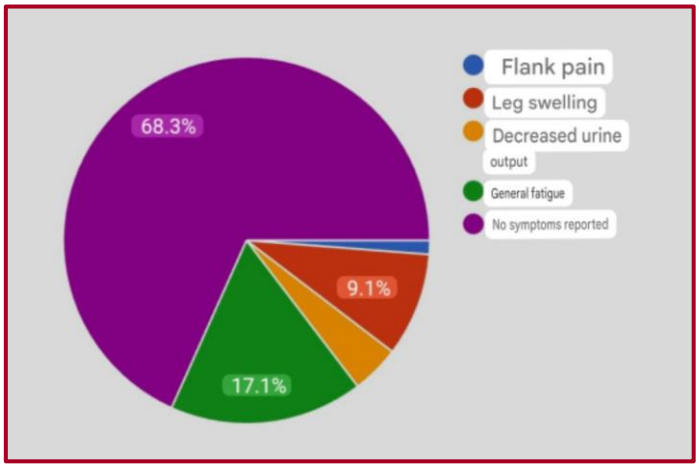


Figure 18: The Proportions of Symptoms Appearing After Taking Supplements

Question (15): The image below shows the results of a survey on side effects associated with taking dietary supplements, conducted on 164 people.

1. The majority (68.3%) reported no side effects (highlighted in purple), indicating that most participants experienced no immediate health problems.

2. General fatigue (17.1%) was the most common side effect reported (highlighted in green).

1. Leg swelling (9.1%) was the second most frequently reported side effect (highlighted in orange).

5.1.16 Distribution of the Questionnaire by Community Perceptions of the Effect of Supplements on Kidneys

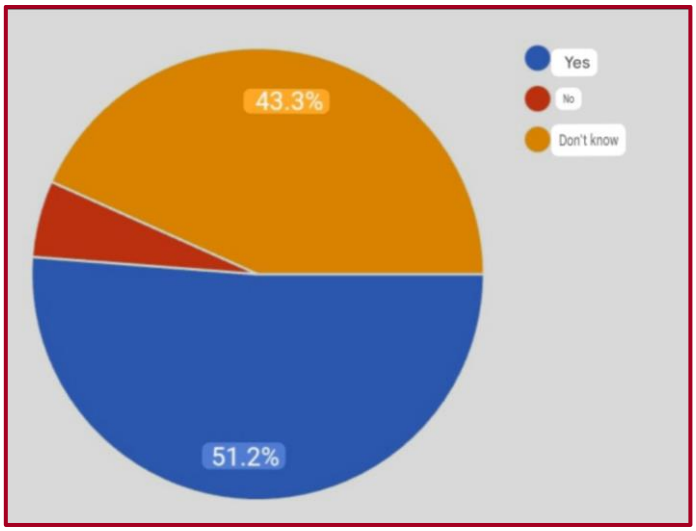


Figure 19: The Proportions of Supplements' Effect on the Kidneys

Question (16): Results show the potential effects of dietary supplements on the kidneys of 164 people.

Yes (51.2%): More than half of the participants believe that dietary supplements have an effect on kidney health, reflecting a general awareness or caution regarding the consumption of these substances.

Don't know (43.3%): A very large percentage, approaching half, is uncertain or lacks sufficient knowledge on this topic, indicating a need for greater health awareness.

No (approximately 5.5%): A very small minority asserts that there is no effect, which aligns with the general trend toward caution.

5.1.17. Distribution of the Questionnaire by Experiencing Health Problems After Taking Supplements

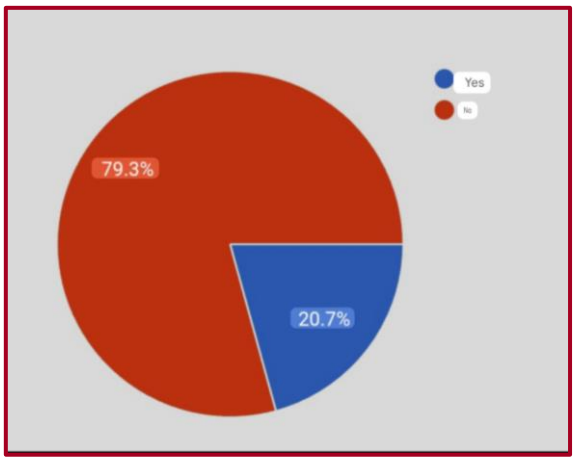


Figure 20: The Proportions of Suffering and Health Problems After Taking Supplements

Question (17): Results of the health effects of dietary supplements. 164 people

1. The majority (79.3% in red): answered "No," indicating that approximately 130 people in the sample did not experience any direct health problems.
2. The minority (20.7% in blue): answered "Yes," meaning that approximately 34 participants experienced complications or side effects.

5.1.18. Distribution of the Questionnaire by Support for Strict Regulation of Supplement Sales

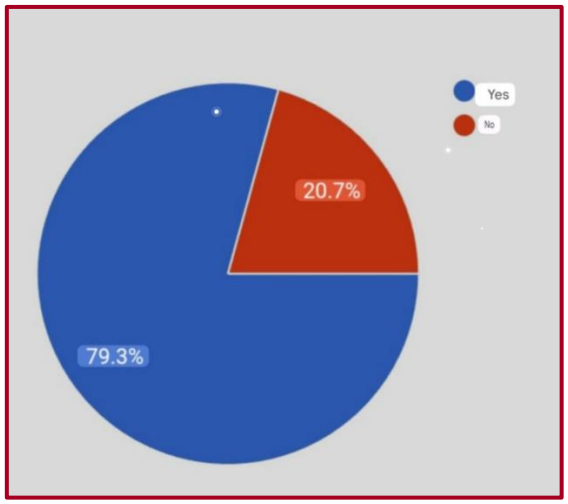


Figure 21: The Proportions of Support for Strict Regulation of Supplement Sales

Question (18): The pie chart shows a clear division of opinion regarding strict regulation of the sale of dietary supplements.

1. Supporters (Yes): Percentage: This option garnered the majority at 79.3%. Estimated number: Approximately 130 people out of the total participants.

2. Opponents (No): Percentage: 20.7%. Estimated number: Approximately 34 people.

5.1.19. Distribution of the Questionnaire by Kidney Function Testing After Dietary Supplement Intake

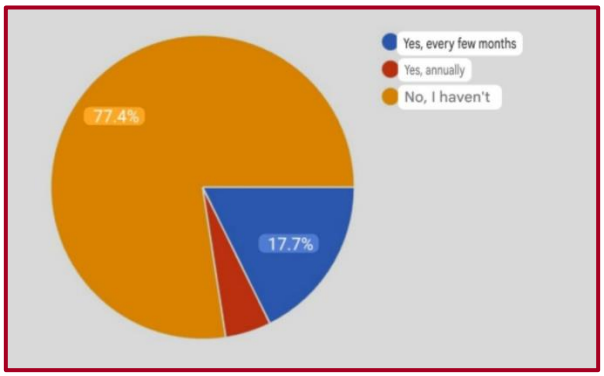


Figure 22: The Proportions of Undergoing Regular Kidney Function Tests After Taking Supplements

Question (19): Pie Chart Showing the Extent to Which Participants (164 Responses) Performed Kidney Function Tests After Using Supplements, Where the Percentage of "No, I Did Not Do That" Was 77.4%, While the Percentage of "Yes, Every Few Months" Was 17.7%, and the Percentage of "Yes, Annually" Was 4.9%.

5.1.20. Distribution of the Questionnaire by Use of Low-Dose Supplements and Their Safety

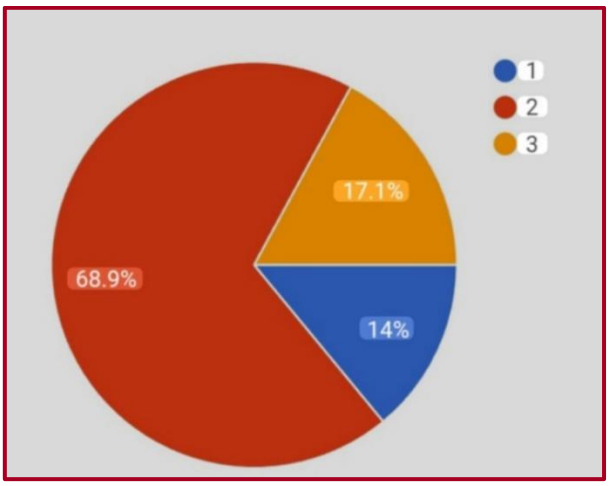


Figure 23: The Proportions of Safety of Taking Dietary Supplements at Low Doses

Question (20): Pie Chart Showing Participants' Opinions (164 Responses) Regarding the Safety of Dietary Supplements If Used at Low Doses, Where the Percentage of Option (2) Was 68.9%, While the Percentage of Option (3) Was 17.1%, and the Percentage of Option (1) Was 14%.

5.1.21. Distribution of the Questionnaire by Excessive Supplement Intake Leading to Kidney Damage

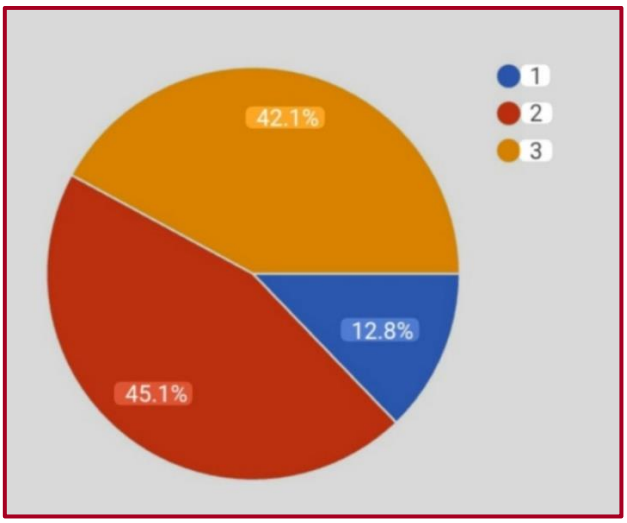


Figure 24: The Proportions of Excessive Dietary Supplement Intake and Its Harm to the Kidneys

Question (21): Pie Chart Showing Participants' Opinions (164 Responses) Regarding the Possibility That Excessive Use of Supplements May Lead to Renal Damage, Where the Percentage of Option (2) Was 45.1%, While the Percentage of Option (3) Was 42.1%, and the Percentage of Option (1) Was 12.8%.

5.1.22. Distribution of the Questionnaire by Mandatory Medical Supervision for Supplement Intake

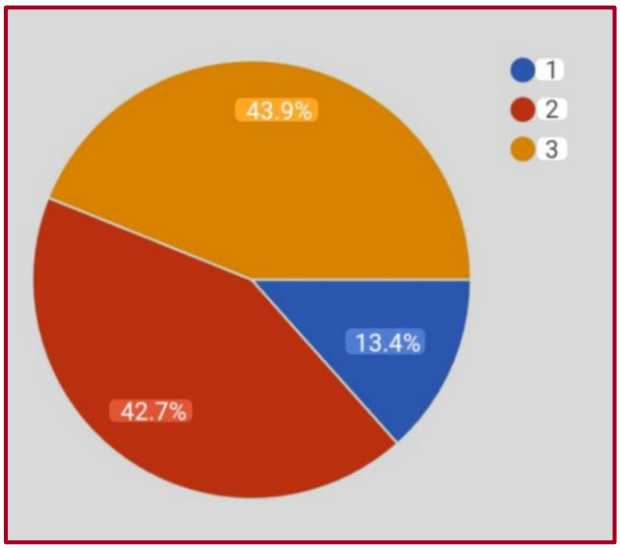


Figure 25 The Proportions of Mandating Consumption of Dietary Supplements Under Medical Supervision

Question (22): Pie Chart Showing Participants' Opinions (164 Responses) Regarding the Necessity for Supplements to Be Under Continuous Medical Supervision, Where the Percentage of Option (3) Was 43.9%, While the Percentage of Option (2) Was 42.7%, and the Percentage of Option (1) Was 13.4%.

Table 5. Perceived Health Risks of Uncontrolled Dietary Supplement Consumption

Health Risk	Percentage
Kidney damage and kidney failure	36%

General illnesses and health problems	18%
Liver damage and poisoning	15%
Side effects and bodily disorders	11%
Don't know	6%
Overdoses and poisoning	5%
Heart and hormonal disorders	5%
Drug interactions	2%
Supplement addiction	2%

Table (5) shows participants' opinions regarding the health risks of uncontrolled consumption of dietary supplements, where "Kidney Damage and Failure" topped the perceived harms at a rate of (36%), followed by "General Diseases" at a rate of (18%) and "Liver Damage" at a rate of (15%), while "Drug Interactions and Supplement Addiction" constituted the lowest pessimistic views at a rate of (2%) for each.

Table 6. Recommended Measures to Avoid Risks of Dietary Supplements

Recommended Measure	Number (out of 164)	Percentage
Consult a doctor or pharmacist and undergo medical tests before use	96	58.50%
Use supplements only with a prescription and under medical supervision	31	18.90%
Adhere to the recommended dosages and avoid overuse	17	10.40%
Rely on a healthy and balanced diet and natural alternatives	10	6.10%
Impose controls on the sale of dietary supplements and promote health awareness	4	2.40%
Take supplements only when necessary or reduce their use	3	1.80%
Don't know / Unclear answers	3	1.80%

Table (6) shows the proposed measures to avoid the risks of dietary supplements, where "Medical Consultation and Tests" topped the procedures at a rate of (58.50%), followed by "Prescription and Medical Supervision" at a rate of (18.90%) and "Adherence to Doses" at a rate of (10.40%), while "Reducing Use" and "Unclear Answers" received the lowest percentage at (1.80%) for each.

5.2.Analysis of Questionnaire Data from Patients

5.2.1. Distribution of the Questionnaire by Gender

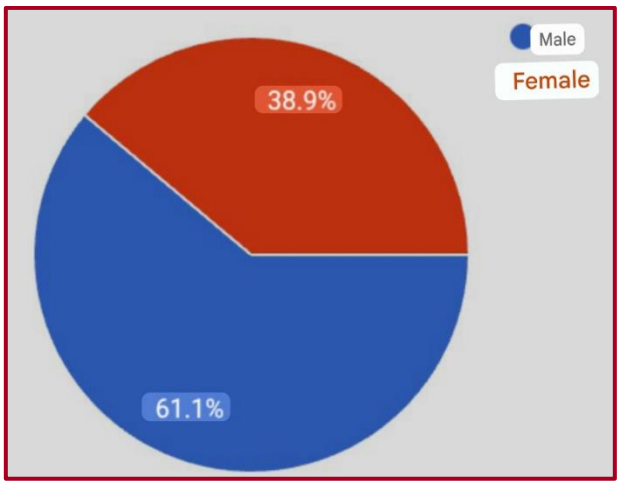


Figure 26: The Proportions of Genders For Patients

Question (1): The results show that males represented the majority of the participants with a percentage of 61.1%, while females represented 38.9% of the total sample.

5.2.2. Distribution of the Questionnaire by Age

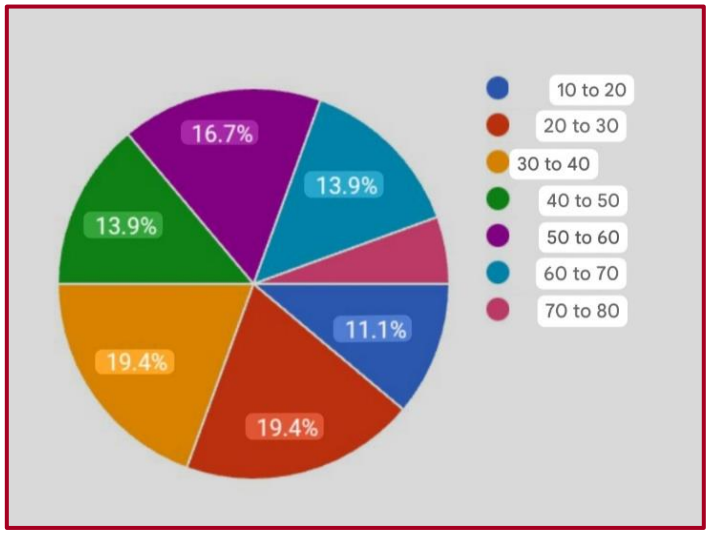


Figure 27: The Proportions of Age Groups For Patients

Question (2): The age groups between 20-30 years and between 30-40 years represented the highest percentages with 19.4% each. Participants aged 50-60 years represented 16.7%. The age groups 40-50 years and 60-70 years each represented 13.9%, while the age group 10-20 years represented 11.1%. The lowest percentage was recorded for the age group 70-80 years.

5.2.3. Distribution of the Questionnaire by Educational Level

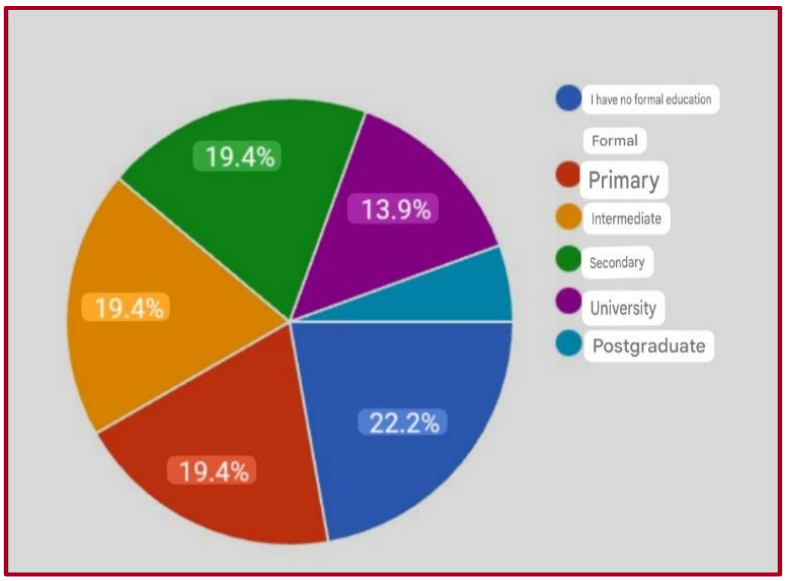


Figure 28: The Proportions of Educational Levels For Patients

Question (3): The findings indicate that participants without formal education represented the highest percentage with 22.2%. Primary, middle, and secondary education levels each represented 19.4%. University level represented 13.9%, while postgraduate studies recorded the lowest percentage.

5.2.4. Distribution of the Questionnaire by Occupation or Activity

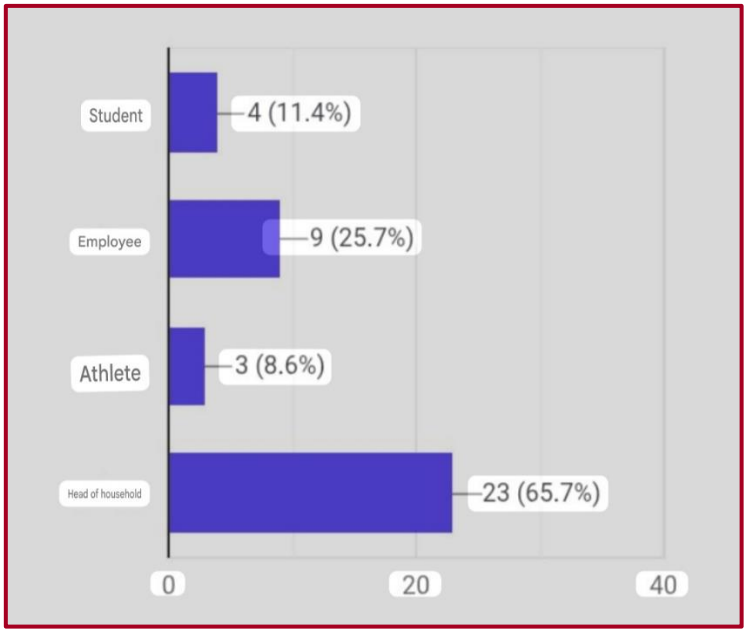


Figure 29: The Proportions of Occupation or Activity For Patients

Question (4): The majority of participants were housewives, representing 65.7%. Employees represented 25.7%, students represented 11.4%, and athletes represented 8.6%.

5.2.5. Distribution of the Questionnaire by Chronic Health Condition

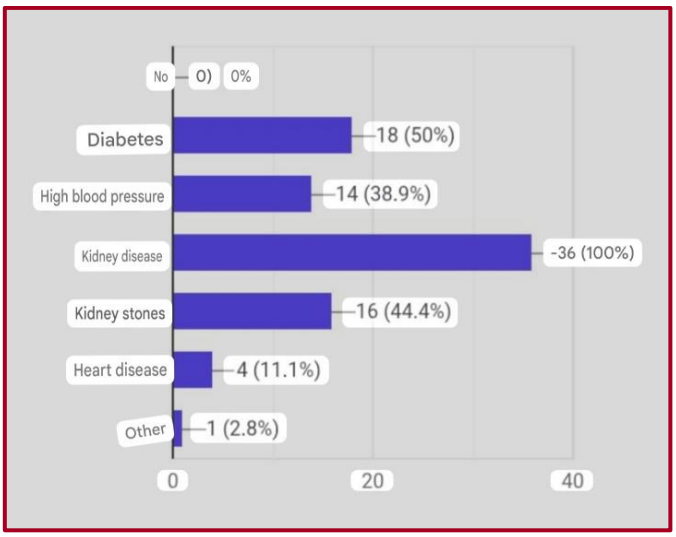


Figure 30: The Proportions of Chronic Health Conditions For Patients

Question (5): All participants suffered from kidney disease, representing 100% of the sample. Diabetes was reported by 50% of participants, kidney stones by 44.4%, and high blood pressure by 38.9%. Heart diseases represented 11.1%, while other diseases represented 2.8%.

5.2.6. Distribution of the Questionnaire by Family History of Kidney Disease

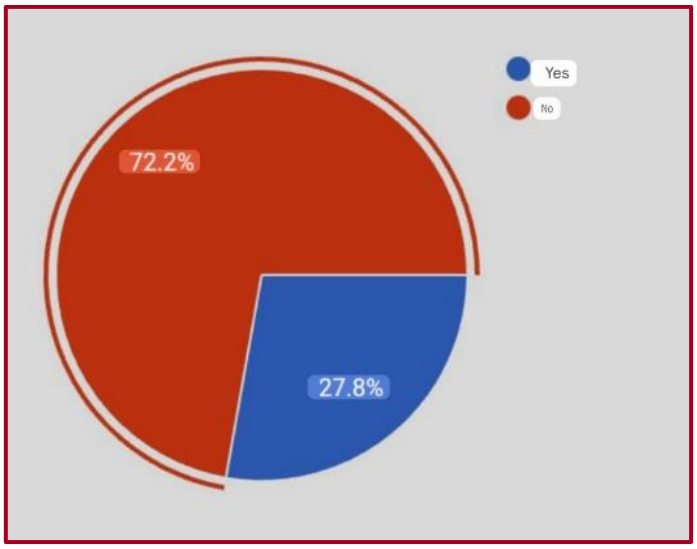


Figure 31: the Proportions of Family History of Kidney Disease For Patients

Question (6): The results show that 72.2% of participants did not have a family history of kidney diseases, whereas 27.8% reported having a family history of kidney diseases.

5.2.7. Distribution of the Questionnaire by Previous Dietary Supplement Intake

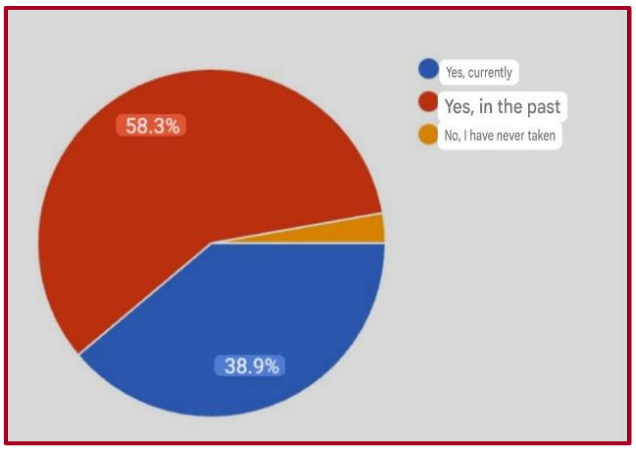


Figure 32: The Proportions of Previous Dietary Supplement Use For Patients

Question (7): The pie chart shows the proportions of participants' responses (36 responses) regarding dietary supplement intake, where the percentage of those who had taken them previously was 58.3%, currently 38.9%, compared to a small percentage who had never taken them.

5.2.8. Distribution of the Questionnaire by Dietary Supplement Use

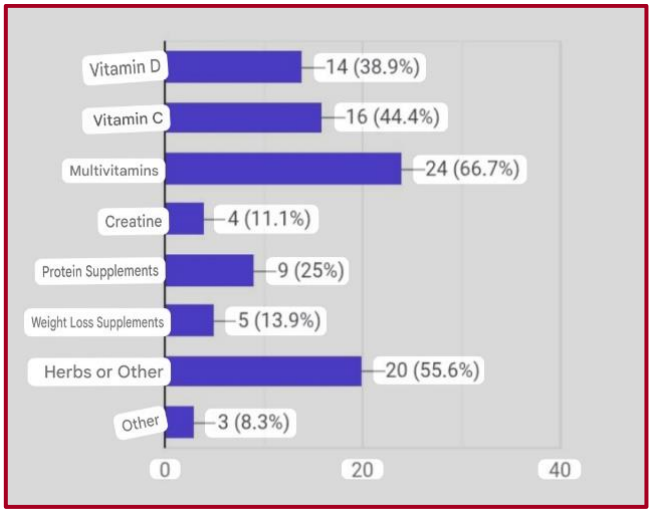


Figure 33: The Proportions of Types of Dietary Supplements Used For Patients

Question (8): The horizontal bar chart shows the types of dietary supplements used by participants (36 responses), where multivitamins ranked first at 66.7%, followed by herbs and extracts at 55.6%, and vitamin C at 44.4%.

5.2.9. Distribution of the Questionnaire by Duration of Dietary Supplement Intake

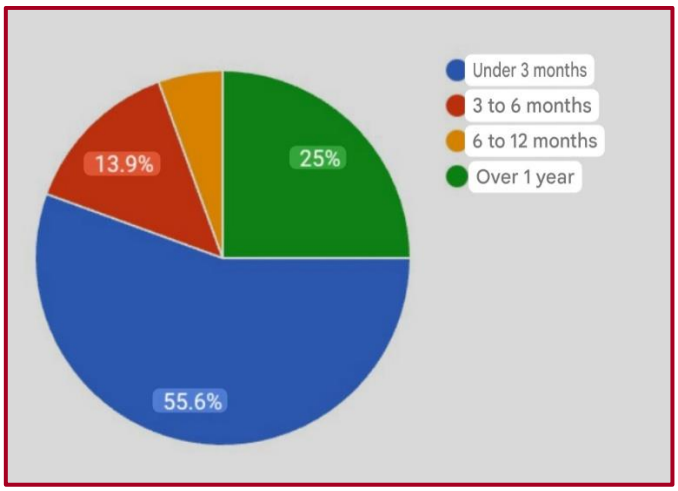


Figure 34: The Proportions of Duration of Dietary Supplement Use For Patients

Question (9): The pie chart shows the duration of dietary supplement use by participants (36 responses), where the category of less than 3 months constituted the largest proportion at 55.6%, followed by the category of more than a year at 25%, then the category of 3 to 6 months at 13.9%.

5.2.10. Distribution of the Questionnaire by Mode of Dietary Supplement Intake

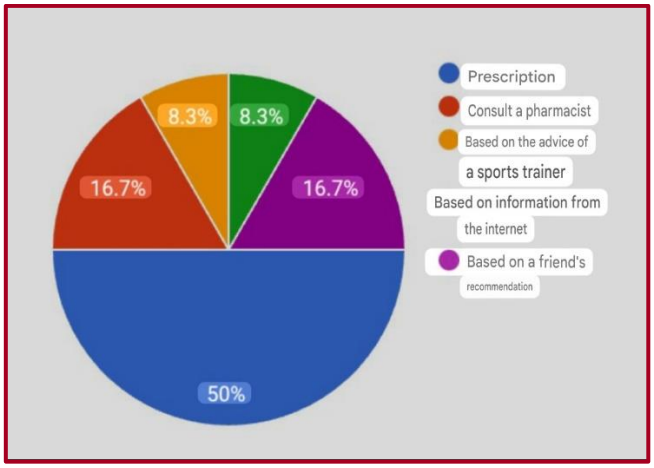


Figure 35: The Proportions of Dietary Supplement Administration Methods For Patients

Question (10): The pie chart shows how participants (36 responses) made the decision to take dietary supplements, where "Medical Prescription" accounted for half of the responses at 50%, followed equally by "Based on Pharmacist Consultation" and "Based on Friends' Recommendation" at 16.7% each.

5.2.11. Distribution of the Questionnaire by Recommended Dosage of Dietary Supplements

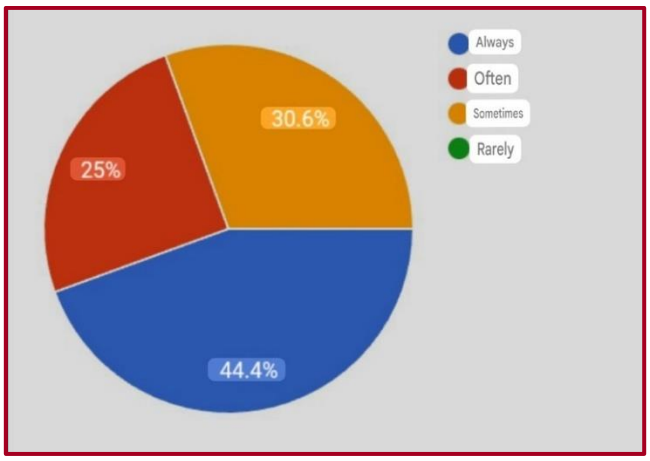


Figure 36: The Proportions of Adherence to Recommended Dietary Supplement Dosages For Patients

Question (11): The pie chart shows the extent of participants' (36 responses) adherence to the recommended dosage of dietary supplements, where the percentage of those who adhered "Always" was 44.4%, followed by the category "Sometimes" at 30.6%, then the category "Often" at 25%.

5.2.12. Distribution of the Questionnaire by Exceeding the Recommended Dosage

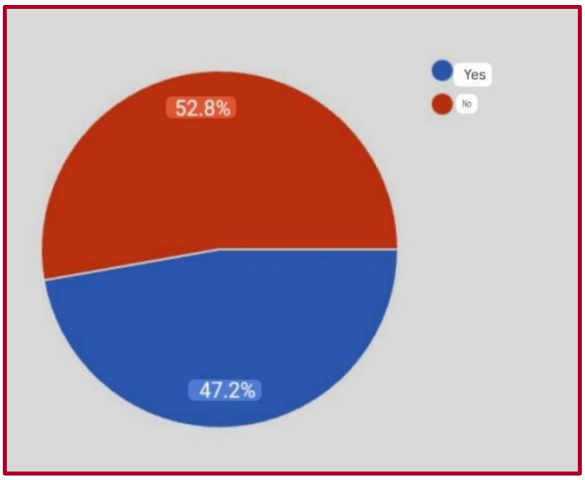


Figure 37: The Proportions of Exceeding the Recommended Dietary Supplement Dosage For Patients

Question (12): The pie chart shows the extent to which participants (36 responses) exceeded the recommended dosage of dietary supplements, where 52.8% of them answered "No", while the percentage of those who exceeded the dosage "Yes" was 47.2%.

5.2.13. Distribution of the Questionnaire by Kidney Function Tests

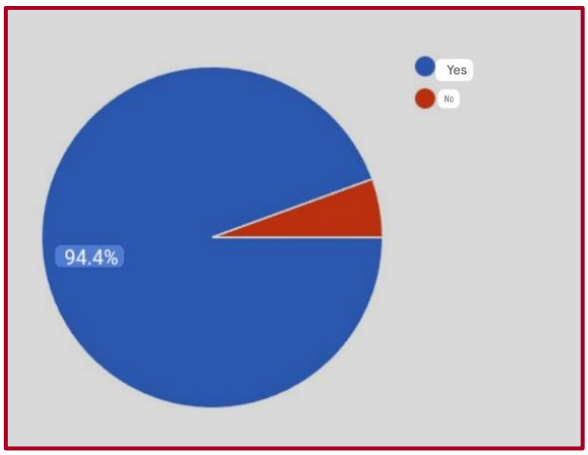


Figure 38: The Proportions of Kidney Function Tests Performed in the Past Year For Patients

Question (13): The pie chart shows the extent to which participants (36 responses) underwent kidney function tests during the past year, where the percentage of those who answered "Yes" was 94.4% (34 people), while the percentage of those who did not undergo them was 5.6% (2 people).

5.2.14. Distribution of the Questionnaire by Kidney Tests

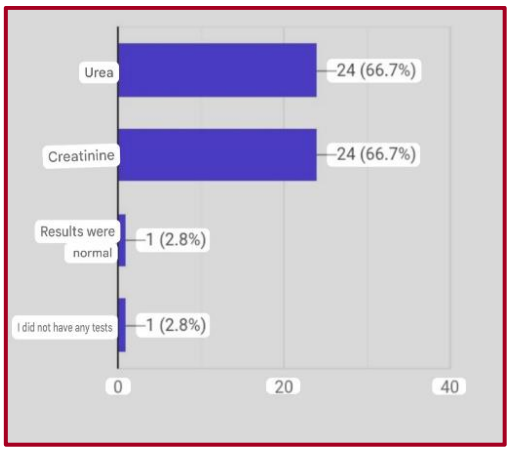


Figure 39: The Proportions of Elevated Levels in Laboratory Tests For Patients

Question (14): The graph shows the responses of 36 participants regarding whether they noticed an increase in certain indicators. The results were distributed as follows: Urea: 24 participants (66.7%) reported an increase. Creatinine: 24 participants (66.7%) also reported an increase. Normal results: Only one participant (2.8%) reported normal results. No tests performed: One participant (2.8%) indicated that they did not undergo any tests.

5.2.15. Distribution of the Questionnaire by Symptom Onset During Dietary Supplement Intake

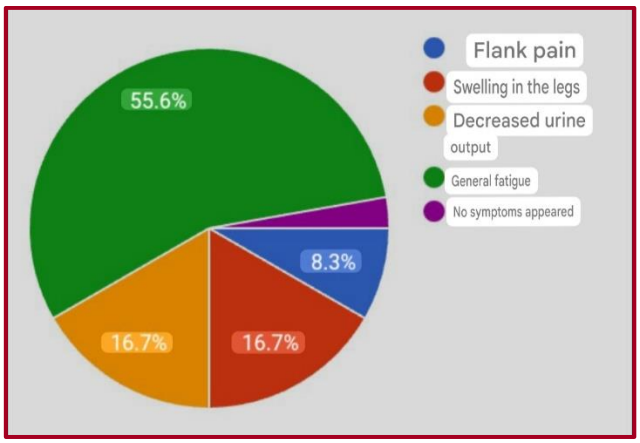


Figure 40: The Proportions of Symptoms Appearing After Taking Supplements For Patients

Question (15): The results illustrate the following: Most Common Symptom: General fatigue topped the list of symptoms with 55.6%, indicating it was the most prominent side effect among participants. Moderately Common Symptom: Leg swelling and decreased urine output were equally prevalent, each at 16.7%. Least Common Symptom: Flank pain was the least common among the options presented, at 8.3%.

5.2.16. Distribution of the Questionnaire by Community Perceptions of the Effect of Supplements on Kidneys

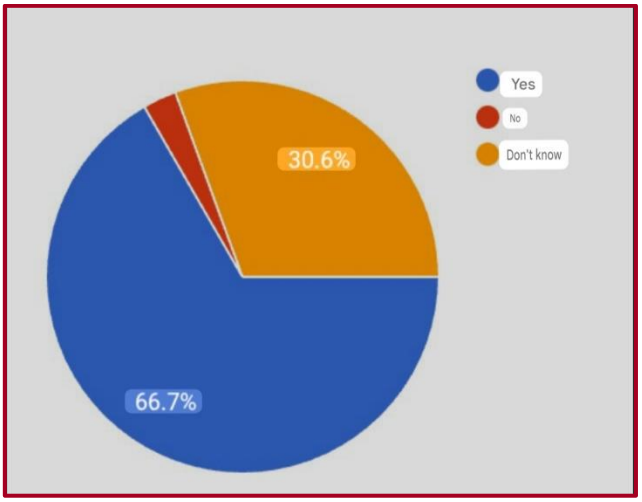


Figure 41: The Proportions of Supplements' Effect on the Kidneys For Patients

Question (16): Yes (Majority): 66.7% of respondents believe that supplements have an effect on the kidneys. This indicates a high level of awareness among two-thirds of the sample regarding the risks of unsupervised supplement use. Don't know (Second): 30.6% came in second place, representing approximately one-third of the participants, highlighting the need for this group to receive more awareness and accurate medical information. No (Minority): The remaining percentage of approximately 2.7% is very small and represents those who believe that supplements do not pose any risk or have any effect on the kidneys.

5.2.17. Distribution of the Questionnaire by Experiencing Health Problems After Taking Supplements

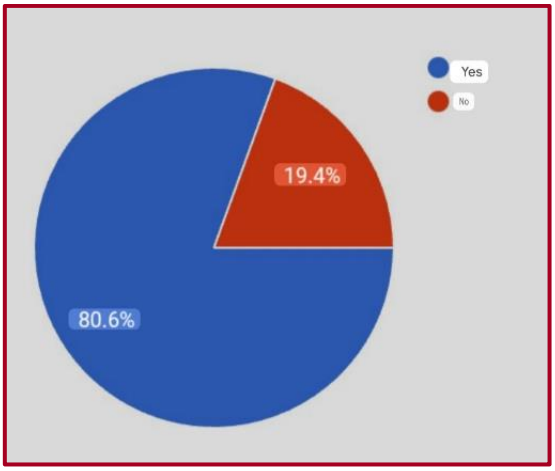


Figure 42: The Proportions of Suffering and Health Problems After Taking Supplements For Patients

Question (17): Yes (Majority - 80.6%): A very high percentage indicating that most of the sample experienced negative experiences or health complications resulting from the use of dietary supplements. No (Minority - 19.4%): Meaning that less than one-fifth of the participants did not experience any health problems.

5.2.18. Distribution of the Questionnaire by Support for Strict Regulation of Supplement Sales

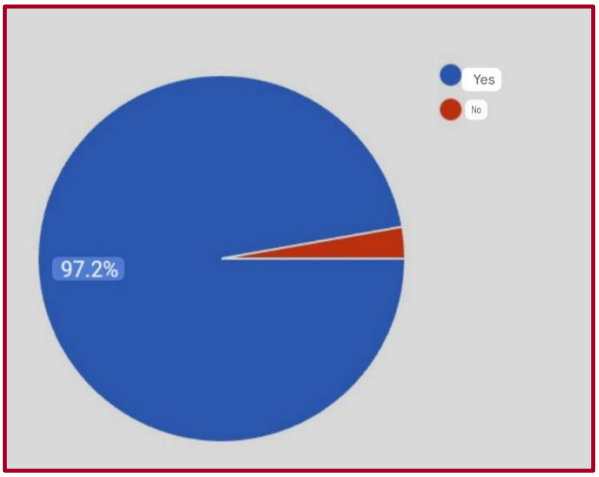


Figure 43: The Proportions of Support for Strict Regulation of Supplement Sales For Patients

Question (18): Supporters (Yes): This category represents the overwhelming majority at 97.2%, meaning that approximately 35 out of 36 people support regulation. Opponents (No): This category is very small, representing approximately 2.8%, which is equivalent to only one response.

5.2.19. Distribution of the Questionnaire by Kidney Function Testing After Dietary Supplement Intake

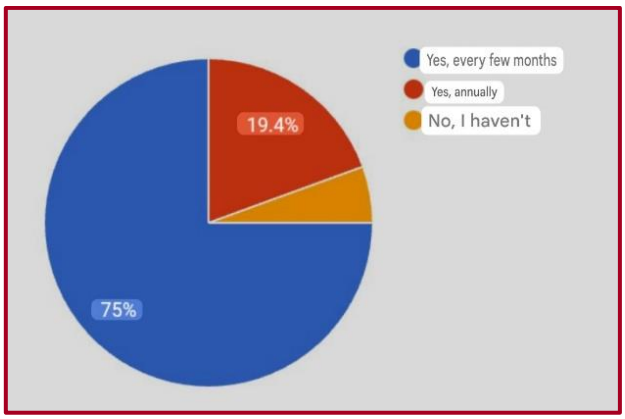


Figure 44: The Proportions of Undergoing Regular Kidney Function Tests After Taking Supplements For Patients

Question (19): Every few months: 75% of respondents reported that they undergo kidney function tests every few months. Annually: 19.4% stated that they do so annually. Never: Only 5.6% indicated that they have never performed such tests.

5.2.20. Distribution of the Questionnaire by Use of Low-Dose Supplements and Their Safety

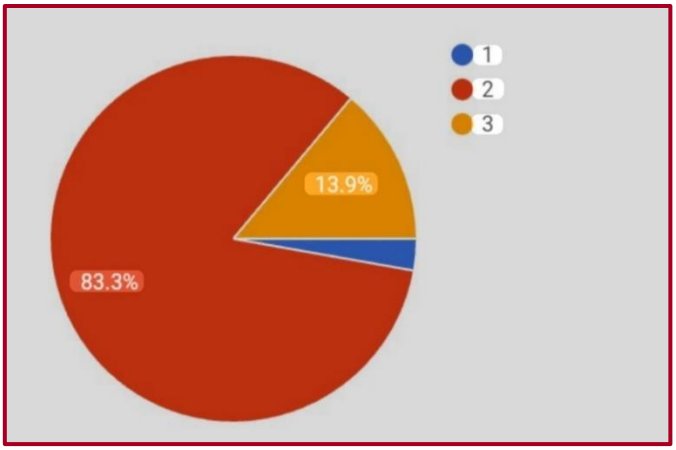


Figure 45: The Proportions of Safety of Taking Dietary Supplements at Low Doses For Patients

Question (20): Agree (Option 2): 83.3% of respondents selected this option. Strongly Agree (Option 3): 13.9% chose this option. Disagree (Option 1): Only 2.8% selected this option.

5.2.21. Distribution of the Questionnaire by Excessive Supplement Intake Leading to Kidney Damage

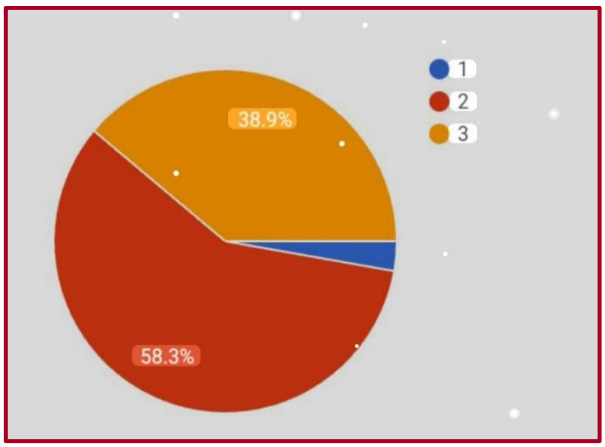


Figure 46: The Proportions of Excessive Dietary Supplement Intake and Its Harm to the Kidneys For Patients

Question (21): Agree (Option 2): 58.3% of respondents selected this option. Strongly Agree (Option 3): 38.9% chose this option. Disagree (Option 1): Only 2.8% selected this option.

5.2.22. Distribution of the Questionnaire by Mandatory Medical Supervision for Supplement Intake

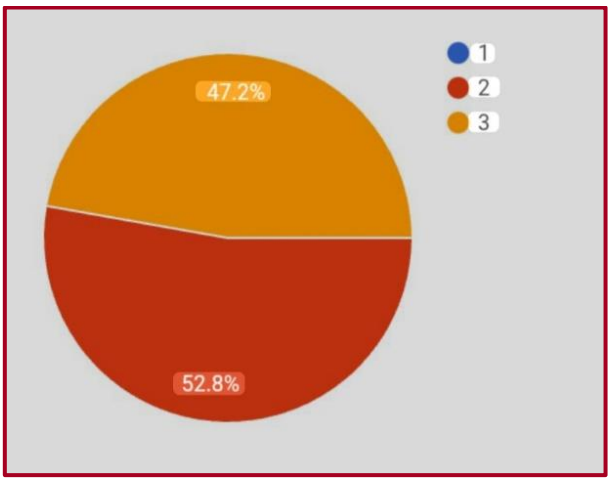


Figure 47: The Proportions of Mandating Consumption of Dietary Supplements Under Medical Supervision For Patients

Question (22): Agree (Option 2): 52.8% of respondents selected this option. Strongly Agree (Option 3): 47.2% chose this option. Disagree (Option 1): No participants selected this option.

Table 7: Potential Consequences of Excessive or Improper Use of Dietary Supplements

Consequence	Number of Participants
Chronic diseases such as kidney failure	8
Body poisoning	8
General fatigue and serious illnesses	7
Addiction to supplements	3
Reliance on supplements instead of food	3
Stomach pain and nausea	3
Vitamin and mineral deficiencies/excesses	3

Death	1

Table (7) shows the potential consequences of excessive use of dietary supplements, where "Chronic Diseases and Body Intoxication" topped the consequences at a rate of (22.22%) for each, followed by "General Fatigue and Serious Diseases" at a rate of (19.44%), while the remaining symptoms and diseases received a rate of (8.33%), whereas "Death" recorded the lowest rate at (2.78%).

Table 8: Recommended Measures to Avoid Risks Associated with Dietary Supplement Use

Recommended Measure	Number of Participants
Consult a doctor	10
Adhere to a good, healthy diet	6
Take supplements only as prescribed by a doctor	6
Impose strict controls on the sale of supplements	5
Adhere to the prescribed dosage	4
Have regular kidney function tests	3
Stop taking supplements if any abnormal symptoms appear	2

Table (8) shows the recommended measures to avoid the risks of dietary supplements, where "Doctor Consultation" topped the procedures at a rate of (27.78%), followed by "Healthy Nutrition" and "Medical Prescription" at a rate of (16.67%) for each, followed by "Strict Regulation" at a rate of (13.89%), while "Stopping When Symptoms Appear" recorded the lowest rate at (5.56%).

6. Discussion and Analysis of Results:

6.1 Dietary Supplement Consumption Pattern Among Healthy Individuals:

The theoretical and statistical data reviewed in this study have shown that dietary supplements are no longer limited to diseased groups, but have become a common routine behavior among a huge proportion of the healthy population, with the percentage of adult users in some developed countries reaching approximately 57.6% (Mishra et al., 2021). Upon analyzing the motivations and types of supplements most consumed by this group (multivitamins, vitamin D, and vitamin C), the following toxicological and physiological points can be derived and discussed:

1. Consumption for Prevention Purposes and Absence of Medical Supervision: Healthy individuals are mostly driven by the motivation of "health promotion" or "prevention of nutrient deficiency", a behavior driven by intensive commercial promotion (Dietary Supplement Health and Education Act [DSHEA], 1994). Although the use of these compounds at the Recommended Dietary Allowances (RDAs) is considered safe, the biological problem lies in the absence of medical supervision (self-consumption), which opens the door to the risk of "chronic excessive doses" without the healthy individual being aware (Institute of Medicine, 2006).

2. The Dilemma of Fat-Soluble Vitamins and the Risk of Renal Toxicity (Vitamin D): The results indicate that vitamin D is one of the most common supplements among healthy individuals. From a toxicological perspective, and because this vitamin is fat-soluble, it has a high capacity for bioaccumulation in tissues (Marcinowska-Suchowierska et al., 2018). This continuous accumulation as a result of unstudied selfconsumption leads to exceeding the "Tolerable Upper Intake Level (UL)", paving the way for hypervitaminosis D, the physiological consequences of which directly affect the kidneys by causing hypercalcemia and nephrocalcinosis, threatening the glomerular filtration function of the kidney (Galior et al., 2018).

3. Renal Filtration Load and Oxalate Nephropathy (Vitamin C): Although vitamin C is classified as a watersoluble and safe compound consumed by healthy individuals to enhance immunity, the high doses excessively taken by healthy individuals (more than 2 g/day) lead to increased metabolism within the body and its conversion into "oxalate" (Oxalate) (Ferraro et al., 2016). This increase in oxalate excretion in urine in a healthy individual turns the kidney environment into a saturated environment, leading to the formation of calcium oxalate stones, or what is more dangerous such as "acute oxalate nephropathy" as a result of renal tubular obstruction (Lumlertgul et al., 2018).

4. The Effect of Polypharmacy and Absence of Pre-Market Regulation: The absence of mandatory premarket screening of dietary supplements before they are introduced to the market allows healthy

individuals to fall under the influence of advertising misinformation. This drives the healthy individual to consume multiple compounds simultaneously (Polysupplementation), which increases the probability of chemical interactions and increases the metabolic and filtration burden on the renal units (Nephrons), which are forced to deal with high concentrations of xenobiotics and excrete them, which may cause long-term renal cellular stress (Ashar & Miller, 2020).

6.2 Clinical and Renal Toxicological Indicators Among the Patient Group:

The statistical and laboratory indicators derived from the study sample (n=36) show explicit clinical signs confirming the close correlation between the random consumption pattern of dietary supplements and the deterioration of renal function. When analyzing these data from the perspective of Nephrotoxicity, the results can be interpreted and discussed according to the following physiological axes:

1. Correlation Between Dose Randomness and Laboratory Renal Failure

47.2% of patients acknowledged exceeding the recommended doses, while 55.6% do not regularly adhere to safe doses. This randomness in consumption directly explains the shocking laboratory result where 66.7% of the sample recorded a sharp and combined elevation in both blood urea and creatinine indicators. From a physiological standpoint, creatinine and urea are nitrogenous wastes eliminated exclusively via glomerular filtration. The sharp elevation in their serum concentrations is conclusive laboratory evidence of a decreased Glomerular Filtration Rate (GFR) and Kidney Injury resulting from chronic chemical stress caused by accumulation of supplement metabolites at Supra-physiological doses (Bargnoux et al., 2018).

2. Correspondence of Clinical Symptoms with Toxic Mechanisms

The study recorded the appearance of clear clinical symptoms in patients during the period of supplement intake; flank pain ranked first at 55.6%, followed by leg swelling at 16.7%, and Oliguria at 16.7%. These clinical signs correspond exactly with targeted tubular cytotoxicity (Tubular Necrosis); acute flank pain is often associated with obstruction of renal tubules by oxalate or calcium crystals resulting from overuse of supplements such as vitamin C, vitamin D, and herbs, which were consumed by the sample at high rates of 44.4%, 38.9%, and 55.6% respectively (Lumlertgul et al., 2018). Moreover, the appearance of leg swelling accompanied by oliguria physiologically reflects the inability of the damaged kidney to excrete water and salt, causing Fluid retention within the body, which is an advanced clinical sign of Acute Kidney Injury (Ostermann et al., 2020).

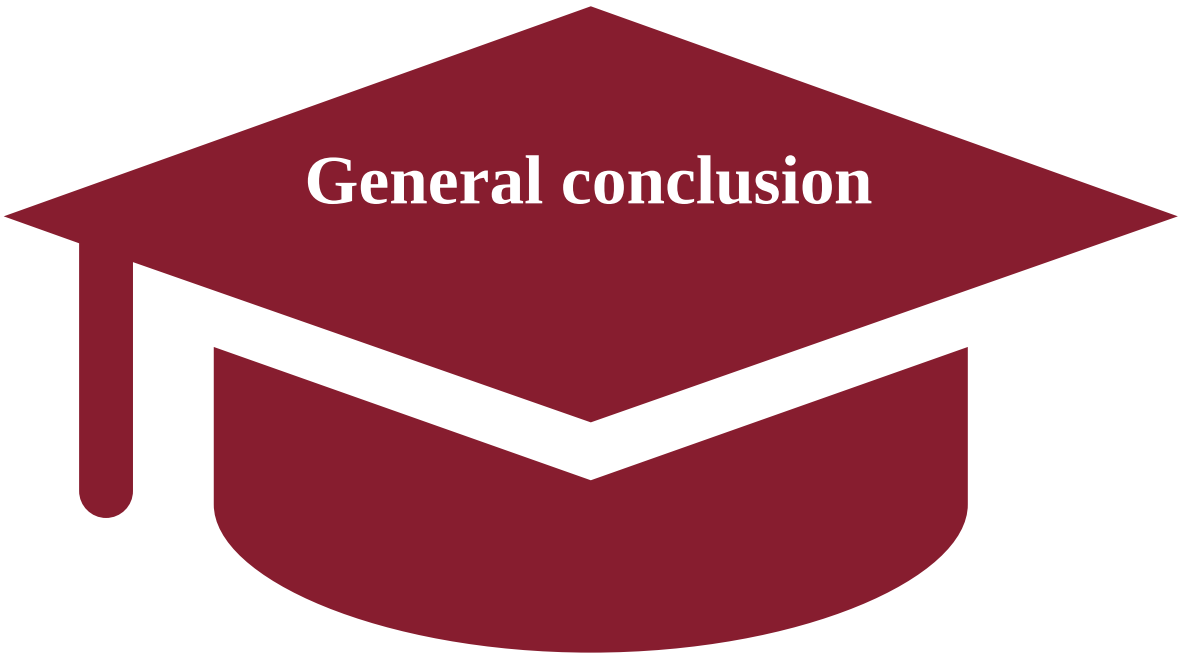
3. Polysupplementation and Risk of Herbal Toxicity

The results showed that 66.7% of patients consume multivitamins, and shockingly, 55.6% rely on herbs

and natural extracts for long periods exceeding one year in 55.6% of them. In toxicology, the random combination of vitamins and herbs constitutes a dual metabolic burden on renal Nephrons. Herbs and extracts of unknown origin often contain biologically active phytochemicals or contaminants with heavy metals, causing direct toxicity in the renal tubulointerstitial tissue (Tubulointerstitial nephritis) (Yang et al., 2018). This chronic and combined consumption increases the probability of Synergistic toxicity interactions, accelerating the process of programmed renal cell death (Apoptosis).

4. Absence of Periodic Follow-up and Patient Risk Assessment

Although 80.6% of patients acknowledged suffering from direct health problems after consumption, 75% of them confirmed that they did not perform any periodic kidney function tests during the period of use. This result clinically explains why renal toxicity transforms from an acute and temporary condition (which can be remedied by stopping supplement intake) into permanent chronic renal disease; the kidney is an organ with high compensatory capacity, and tissue damage occurs silently without loud symptoms in the early stages, preventing early detection of kidney injury until function deteriorates acutely (Ghimire et al., 2021). This is what led patients to agree in their open-ended answers (questions 23 and 24) that the major risks are kidney failure and body intoxication, recommending the necessity of consulting a physician and periodic laboratory follow-up.



General conclusion

General conclusion

This thesis has conducted a comprehensive, multi-dimensional investigation into the nephrotoxic effects of unregulated dietary supplement consumption, integrating systematic literature review with original field research conducted in the Wilaya of El Oued. The cumulative evidence demonstrates unequivocally that excessive and medically unsupervised consumption of dietary supplements constitutes a serious and underappreciated threat to renal integrity, operating through a diverse array of both direct and indirect nephrotoxic mechanisms.

At the physiological level, protein supplements consumed at doses exceeding 2.5 g/kg/day induce glomerular hyperfiltration, accelerating the progressive deterioration of renal function in individuals with limited renal reserve. High-dose vitamin C supplementation (>1 g/day) is statistically associated with increased urinary oxalate excretion and calcium oxalate nephrolithiasis, while chronic vitamin D toxicity (>10,000 IU/day) precipitates hypercalcaemia, nephrocalcinosis, and irreversible acute kidney injury in documented cases. Aristolochic acid nephropathy — the most dramatic example of herbal supplement-induced renal disease — causes rapidly progressive interstitial fibrosis and progression to end-stage renal disease, accompanied by an alarming incidence of urothelial carcinoma reaching 50% in some reported series.

Heavy metal contamination — particularly lead, cadmium, arsenic, and mercury in substandard herbal preparations — has been firmly linked to proximal tubular injury, Fanconi syndrome, and progressive decline in glomerular filtration rate. Creatine supplementation, while not directly nephrotoxic at recommended doses in healthy individuals, predictably elevates serum creatinine and may mask early chronic kidney disease by creating a false impression of stable renal function. Taken together, the evidence establishes a clear dose-dependent, mechanism-driven continuum from subclinical renal stress to end-stage renal failure attributable to unmonitored supplement use.

The field survey conducted among 200 participants across Ben Ammar Djilani Hospital, sports halls, pharmacies, and family networks in the Wilaya of El Oued revealed two parallel and equally alarming phenomena. The first concerns young athletes, many of them preoccupied with external physical appearance, who consume protein powders and creatine in doses far exceeding recommended levels without any medical prescription or specialist guidance, thereby imposing an enormous filtration burden on the kidneys and elevating intraglomerular capillary pressure. The second concerns elderly individuals who rely on traditional herbal remedies as substitutes for evidence-based medicine, often unaware that several of these preparations harbour compounds of potent nephrotoxic potential.

Direct observation in the dialysis units of local hospitals documented young patients experiencing renal failure attributable to supplement overuse — a lived reality that transforms this thesis from an academic exercise into a call for urgent, multi-level public health action. The fact that 68% of supplement users in comparable populations identify social media as their primary information source, while only 9% consult a medical professional before initiating use, underscores the magnitude of the educational deficit that must be addressed.

The regulatory framework governing dietary supplements in most jurisdictions — including those shaping the Algerian market — is characterised by a fundamental asymmetry: the burden of proving harm rests with regulators after market entry rather than with manufacturers prior to commercialisation. This post-market surveillance model has created a permissive environment in which dangerous products may circulate for years before regulatory action is triggered. Documented evidence demonstrates that over 32% of tested supplement products do not contain declared ingredients in stated amounts, while 20% of Ayurvedic preparations have been found to contain lead, mercury, and arsenic at levels exceeding acceptable daily intake thresholds.

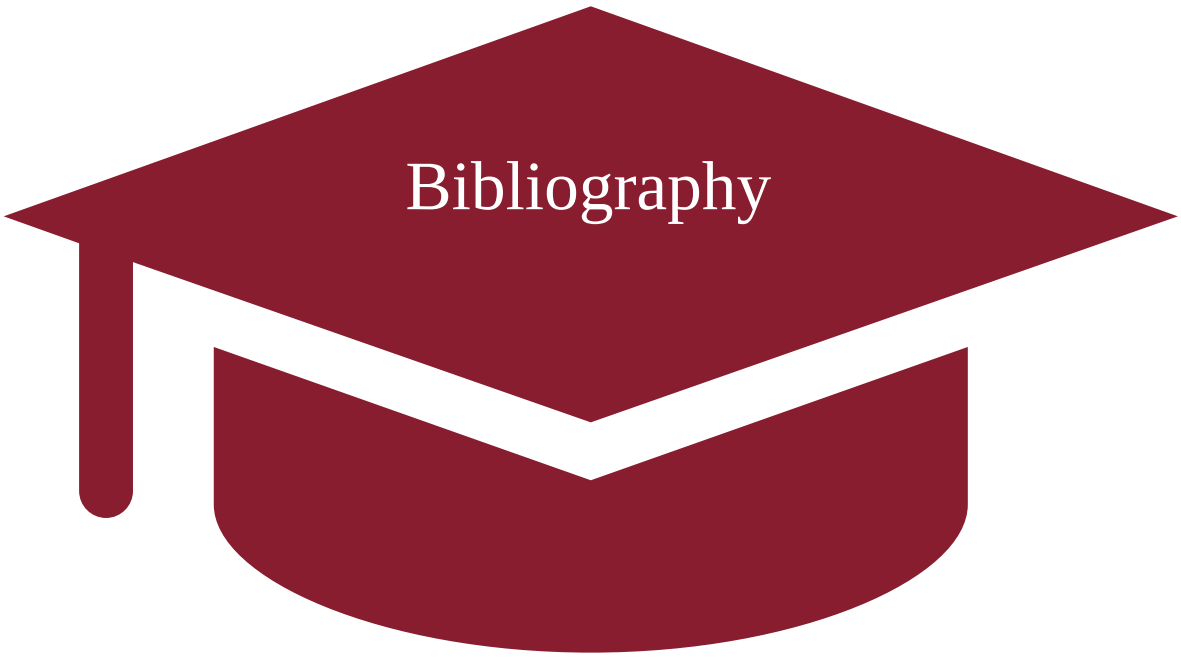
The globalisation of supplement distribution through online channels further enables regulatory arbitrage, allowing products prohibited in one jurisdiction to be freely marketed in another. The convergence of these regulatory failures with the pervasive influence of social media health marketing creates an environment of systematic misinformation in which consumers — particularly young athletes and elderly individuals reliant on traditional medicine — are uniquely vulnerable to supplement-induced renal harm.

Recommendations and Future Perspectives

On the basis of the totality of scientific and field evidence, this study advances the following strategic recommendations:

- First: Enactment of binding pre-market safety legislation requiring manufacturers to demonstrate product safety and compositional accuracy prior to commercialisation, coupled with mandatory adverse event reporting systems to enable real-time pharmacovigilance.
- Second: Integration of evidence-based supplement safety education into school health curricula and clinical training programmes for healthcare practitioners, with emphasis on systematic elicitation of supplement use history in patients presenting with renal dysfunction.
- Third: Implementation of targeted periodic renal screening programmes for high-risk populations — particularly competitive athletes, chronic herbal medicine users, and the elderly — with emphasis on sensitive early biomarkers including urinary KIM-1, NGAL, and microalbuminuria to detect renal injury before GFR decline becomes clinically apparent.
- Fourth: Conduct of longitudinal epidemiological studies encompassing populations with pre-existing renal insufficiency — the subgroup at greatest risk and most systematically under-represented in existing supplement safety literature — to establish robust evidence-based tolerable intake thresholds for this vulnerable cohort.

In summation, this thesis affirms that a dietary supplement is not inherently safe by virtue of being labelled 'natural'. It is the dose that makes the poison — a principle articulated by Paracelsus five centuries ago and as clinically relevant today as ever. The kidneys, as the body's central filtration organ, ultimately bear the cost of every unmonitored excess. Those who have witnessed young dialysis patients at first hand understand that no supplement in the world is worth the price of irreversible renal failure. Prevention, education, and rigorous regulatory oversight are not optional complements to clinical nephrology — they are its most powerful tools.



Bibliography

References

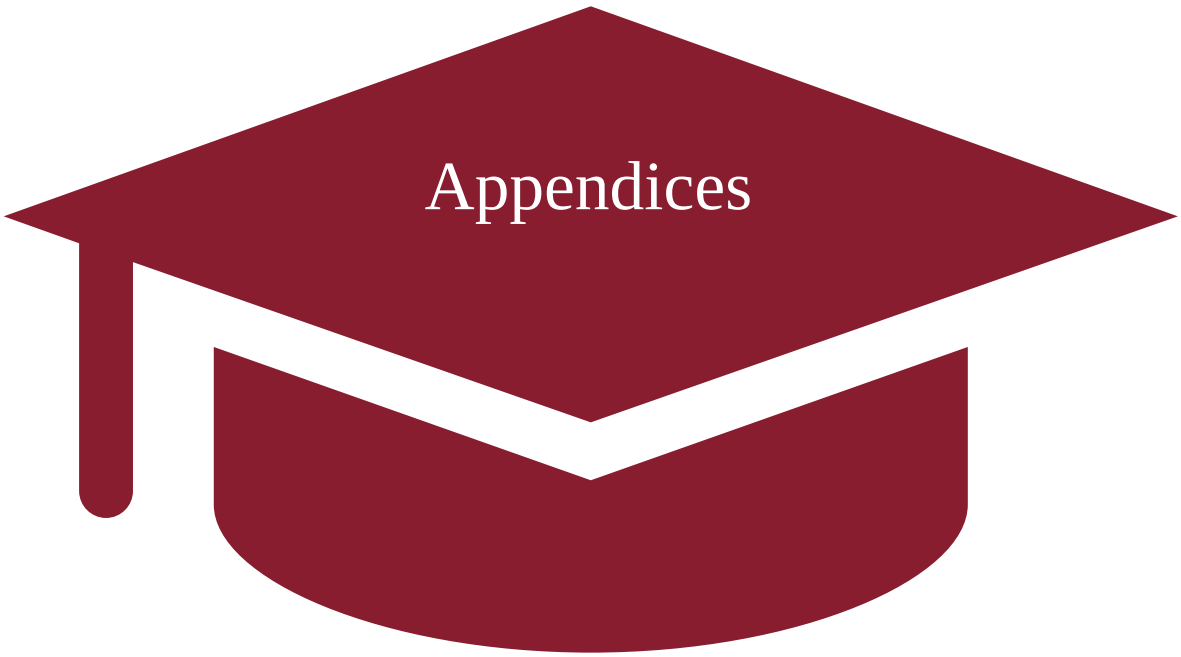
- Antonio, J., & Ciccone, V. (2013). The effects of pre versus post workout supplementation of creatine monohydrate on body composition and strength. Journal of the International Society of Sports Nutrition, 10(1), 36. https://doi.org/10.1186/1550-2783-10-36
- Antonio, J., Ellerbroek, A., Silver, T., Orris, S., Scheiner, M., Gonzalez, A., & Peacock, C. A. (2016). A high protein diet (3.4 g/kg/d) combined with a heavy resistance training program improves body composition in healthy trained men and women. Journal of the International Society of Sports Nutrition, 13(1), 16. https://doi.org/10.1186/s12970-016-0121-9
- Bacchi Modena, A., Taddei, S., & Ambrosioni, E. (2012). Inhibitors of the renin-angiotensin system and prostaglandin metabolism. Journal of Cardiovascular Pharmacology, 19(Suppl. 6), S69–S75. https://doi.org/10.1097/00005344-199200006-00012
- Bailey, R. L., Gahche, J. J., Miller, P. E., Thomas, P. R., & Dwyer, J. T. (2013). Why US adults use dietary supplements. JAMA Internal Medicine, 173(5), 355–361. https://doi.org/10.1001/jamainternmed.2013.2299
- Bankir, L., Roussel, R., & Bouby, N. (2016). Protein- and diabetes-induced glomerular hyperfiltration: Role of glucagon, vasopressin, and urea. American Journal of Physiology-Renal Physiology, 309(1), F2–F23. https://doi.org/10.1152/ajprenal.00531.2014
- Barbier, O., Jacquillet, G., Tauc, M., Cougnon, M., Poujeol, P., & Motais, R. (2005). Effect of heavy metals on, and handling by, the kidney. Nephron Physiology, 99(4), 105–110. https://doi.org/10.1159/000083981
- Barregard, L., Fabricius-Lagging, E., Lundh, T., Mölne, J., Wallin, M., Olausson, M., Modigh, C., & Sallsten, G. (2010). Cadmium, mercury, and lead in kidney cortex of living kidney donors: Impact of different exposure sources. Environmental Research, 110(1), 47–54. https://doi.org/10.1016/j.envres.2009.10.002
- Bauer, J. M., Biolo, G., Cederholm, T., Cesari, M., Cruz-Jentoft, A. J., Morley, J. E., Phillips, S., Sieber, C., Stehle, P., Teta, D., Visvanathan, R., Volpi, E., & Boirie, Y. (2013). Evidence-based recommendations for optimal dietary protein intake in older people: A position paper from the PROT-AGE Study Group. Journal of the American Medical Directors Association, 14(8), 542–559. https://doi.org/10.1016/j.jamda.2013.05.021
- Bender, D. A. (2014). Nutritional biochemistry of the vitamins (2nd ed.). Cambridge University Press.
- Bent, S. (2008). Herbal medicine in the United States: Review of efficacy, safety, and regulation. Journal of General Internal Medicine, 23(6), 854–859. https://doi.org/10.1007/s11606-008-0632-y
- Bertram, J. F., Douglas-Denton, R. N., Diouf, B., Hughson, M. D., & Hoy, W. E. (2011). Human nephron number: Implications for health and disease. Pediatric Nephrology, 26(9), 1529–1533. https://doi.org/10.1007/s00467-011-1843-8
- Bianco, A., Mammina, C., Paoli, A., Bellafiore, M., Battaglia, G., Caramazza, G., Palma, A., & Jemni, M. (2014). Protein supplementation in strength and conditioning adepts: Knowledge, dietary behavior and practice in Palermo, Italy. Journal of the International Society of Sports Nutrition, 11(1), 30. https://doi.org/10.1186/1550-2783-11-30
- Biesalski, H. K., Bischoff, S. C., Puchstein, C., & Wichert, B. (Eds.). (2017). Nutritional medicine: According to the curriculum of nutritional medicine of the German Medical Association. Georg Thieme Verlag.
- Bikbov, B., Purcell, C. A., Levey, A. S., Smith, M., Abdoli, A., Abebe, M., ... & Bhatt, S. (2020). Global, regional, and national burden of chronic kidney disease, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. The Lancet, 395(10225), 709–733. https://doi.org/10.1016/S0140-6736(20)30045-3
- Bilezikian, J. P., Brandi, M. L., Eastell, R., Silverberg, S. J., Udelsman, R., Marcocci, C., & Potts, J. T. (2020). Guidelines for the management of asymptomatic primary hyperparathyroidism. The Journal of Clinical Endocrinology & Metabolism, 99(10), 3561–3569. https://doi.org/10.1210/jc.2014-1413
- Carr, A. C., & Vissers, M. C. (2013). Synthetic or food-derived vitamin C: Are they equally bioavailable? Nutrients, 5(11), 4284–4304. https://doi.org/10.3390/nu5114284

- Carpenter, K. J. (2012). The discovery of vitamin C. Annals of Nutrition and Metabolism, 61(3), 259–264. https://doi.org/10.1159/000343121
- Coates, A. E., Hardman, C. A., Halford, J. C. G., Christiansen, P., & Boyland, E. J. (2019). Social media influencer marketing and children's food intake: A randomized trial. Pediatrics, 143(4), e20182554. https://doi.org/10.1542/peds.2018-2554
- Coca, S. G., Yalavarthy, R., Concato, J., & Parikh, C. R. (2012). Biomarkers for the diagnosis and risk stratification of acute kidney injury: A systematic review. Kidney International, 73(9), 1008–1016. https://doi.org/10.1038/ki.2008.14
- Cohen, P. A. (2016). The supplement paradox: Negligible benefits, robust consumption. JAMA, 316(14), 1453–1454. https://doi.org/10.1001/jama.2016.14252
- Curthoys, N. P., & Moe, O. W. (2014). Proximal tubule function and response to acidosis. Clinical Journal of the American Society of Nephrology, 9(9), 1627–1638. https://doi.org/10.2215/CJN.10391012
- De-Regil, L. M., Peña-Rosas, J. P., Fernández-Gaxiola, A. C., & Rayco-Solon, P. (2015). Effects and safety of periconceptional oral folate supplementation for preventing birth defects. Cochrane Database of Systematic Reviews, (12), CD007950. https://doi.org/10.1002/14651858.CD007950.pub3
- Diehl, K., Thiel, A., Zipfel, S., Mayer, J., Litaker, D. G., & Schneider, S. (2012). How healthy is the behavior of young athletes? A systematic literature review and meta-analyses. Journal of Sports Science & Medicine, 11(2), 201–220.
- Domingo, J. L., Nadal, M., & Bocio, A. (2015). Human exposure to metals through seafood consumption. In R. Merkel & J. Hamre (Eds.), Seafood toxicants and health (pp. 247–281). Nova Science.
- European Commission. (2002). Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements. Official Journal of the European Communities, L183, 51–57.
- FDA CFSAN. (2023). CFSAN adverse event reporting system (CAERS). U.S. Food and Drug Administration. https://www.fda.gov/food/compliance-enforcement-food/cfsan-adverse-event-reporting-system-caers
- Ferraro, P. M., Curhan, G. C., Gambaro, G., & Taylor, E. N. (2016). Total, dietary, and supplemental vitamin C intake and risk of incident kidney stones. American Journal of Kidney Diseases, 67(3), 400–407. https://doi.org/10.1053/j.ajkd.2015.09.005
- Gabardi, S., Munz, K., & Ulbricht, C. (2007). A review of dietary supplement-induced renal dysfunction. Clinical Journal of the American Society of Nephrology, 2(4), 757–765. https://doi.org/10.2215/CJN.00500107
- Global Wellness Institute. (2023). The global wellness economy: Country rankings 2022. Global Wellness Institute.
- Gokmen, M. R., Cosyns, J. P., Arlt, V. M., Stiborova, M., Phillips, D. H., Schmeiser, H. H., Nortier, J. L., & Lord, G. M. (2013). The epidemiology, diagnosis, and management of aristolochic acid nephropathy: A narrative review. Annals of Internal Medicine, 158(6), 469–477. https://doi.org/10.7326/0003-4819-158-6-201303190-00005
- Gomez, R. A., Pentz, E. S., Jin, X., & Cordaillat, M. (2014). CBP and p300 are essential for renin cell identity and morphological integrity of the kidney. American Journal of Physiology-Heart and Circulatory Physiology, 296(5), H1455–H1464. https://doi.org/10.1152/ajpheart.00912.2008
- Grand View Research. (2023). Sports nutrition market size, share & trends analysis report, 2023–2030. Grand View Research. https://www.grandviewresearch.com/industry-analysis/sports-nutrition-market
- Hall, J. E. (2021). Guyton and Hall textbook of medical physiology (14th ed.). Elsevier.
- Haraldsson, B., Nyström, J., & Deen, W. M. (2008). Properties of the glomerular barrier and mechanisms of proteinuria. Physiological Reviews, 88(2), 451–487. https://doi.org/10.1152/physrev.00055.2006
- Hathcock, J. N., Shao, A., Vieth, R., & Heaney, R. (2007). Risk assessment for vitamin D. American Journal of Clinical Nutrition, 85(1), 6–18. https://doi.org/10.1093/ajcn/85.1.6
- Hendricks, B. B., Neff, R. A., & Poole, M. D. (2020). Social media influencer effect on dietary supplement consumption and health-related beliefs. Nutrients, 12(3), 759. https://doi.org/10.3390/nu12030759
- Holick, M. F. (2017). The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. Reviews in Endocrine and Metabolic Disorders, 18(2), 153–165. https://doi.org/10.1007/s11154-017-9424-1

- Hughes, M. F. (2002). Arsenic toxicity and potential mechanisms of action. Toxicology Letters, 133(1), 1–16. https://doi.org/10.1016/S0378-4274(02)00084-X
- Jabeen, S., & Naeem, M. (2019). Creatine-induced nephropathy in a young bodybuilder: A case report. Journal of Medical Case Reports, 13(1), 152. https://doi.org/10.1186/s13256-019-2104-z
- Jager, R., Purpura, M., Shao, A., Inoue, T., & Kreider, R. B. (2014). Analysis of the efficacy, safety, and regulatory status of novel forms of creatine. Amino Acids, 40(5), 1369–1383. https://doi.org/10.1007/s00726-011-0874-6
- Kalantar-Zadeh, K., Kramer, H. M., & Fouque, D. (2017). High-protein diet is bad for kidney health: Unleashing the taboo. Nephrology Dialysis Transplantation, 32(2), 195–197. https://doi.org/10.1093/ndt/gfw296
- KDIGO. (2012). KDIGO clinical practice guideline for acute kidney injury. Kidney International Supplements, 2(1), 1–138. https://doi.org/10.1038/kisup.2012.1
- KDIGO. (2013). KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International Supplements, 3(1), 1–150. https://doi.org/10.1038/kisup.2012.73
- Knapik, J. J., Steelman, R. A., Hoedebecke, S. S., Austin, K. G., Farina, E. K., & Lieberman, H. R. (2016). Prevalence of dietary supplement use by athletes: Systematic review and meta-analysis. Sports Medicine, 46(1), 103–123. https://doi.org/10.1007/s40279-015-0387-7
- Lanhers, C., Pereira, B., Naughton, G., Trousselard, M., Lesage, F. X., & Dutheil, F. (2017). Creatine supplementation and upper limb strength performance: A systematic review and meta-analysis. Sports Medicine, 47(1), 163–173. https://doi.org/10.1007/s40279-016-0571-4
- Lentferink, Y. E., Koffijberg, H., Merry, A. H. H., & van Stel, H. F. (2017). Drivers of health behaviour in young adults: A systematic literature review. Preventive Medicine, 94, 74–83. https://doi.org/10.1016/j.ypmed.2016.11.007
- Marcinowska-Suchowierska, E., Kupisz-Urbanska, M., Lukaszkiewicz, J., Pludowski, P., & Jones, G. (2018). Vitamin D toxicity: A clinical perspective. Frontiers in Endocrinology, 9, 550. https://doi.org/10.3389/fendo.2018.00550
- Maret, W., & Sandstead, H. H. (2006). Zinc requirements and the risks and benefits of zinc supplementation. Journal of Trace Elements in Medicine and Biology, 20(1), 3–18. https://doi.org/10.1016/j.jtemb.2006.01.006
- Martin, W. J., & Sherrell, Z. (2006). Chromium picolinate-induced rhabdomyolysis and acute renal failure. Southern Medical Journal, 99(3), 323–324. https://doi.org/10.1097/01.smj.0000197440.26027.4c
- Mathews, N. M. (2018). Prohibited contaminants in dietary supplements. Sports Health, 10(1), 19–30. https://doi.org/10.1177/1941738117727736
- Maughan, R. J., Burke, L. M., Dvorak, J., Larson-Meyer, D. E., Peeling, P., Phillips, S. M., Rawson, E. S., Walsh, N. P., Garthe, I., Geyer, H., Meeusen, R., van Loon, L. J. C., Shirreffs, S. M., Spriet, L. L., Stuart, M., Vernec, A., Currell, K., Ali, V. M., Budgett, R. G. M., ... Engebretsen, L. (2018). IOC consensus statement: Dietary supplements and the high-performance athlete. British Journal of Sports Medicine, 52(7), 439–455. https://doi.org/10.1136/bjsports-2018-099027
- Mehta, R. L., Cerdá, J., Burdmann, E. A., Tonelli, M., García-García, G., Jha, V., Susantitaphong, P., Rocco, M., Vanholder, R., Sever, M. S., Cruz, D., Jaber, B., Lameire, N. H., Lombardi, R., Lewington, A., Feehally, J., Finkelstein, F., Correa-Rotter, R., Murray, M., ... Remuzzi, G. (2015). International Society of Nephrology's 0by25 initiative for acute kidney injury. The Lancet, 385(9987), 2616–2643. https://doi.org/10.1016/S0140-6736(15)60126-X
- Mena, P., González-Mey, U., de la Concepción, M. L. R., Fernández-González, M. D., & Sevillano-Fernández, J. A. (2018). Herbal and dietary supplement induced acute kidney injury in children and teenagers. Pediatric Nephrology, 33(7), 1205–1212. https://doi.org/10.1007/s00467-018-3920-5
- Mishra, S., Stierman, B., Gahche, J. J., & Potischman, N. (2021). Dietary supplement use among adults: United States, 2017-2018 (NCHS Data Brief No. 399). National Center for Health Statistics. https://doi.org/10.15620/cdc:101131
- Moore, K. L., Dalley, A. F., & Agur, A. M. R. (2019). Clinically oriented anatomy (8th ed.). Wolters Kluwer.

- Nasr, S. H., Kashtanova, D., Kasimov, M., Said, S. M., Cornell, L. D., & Fidler, M. E. (2020). Oxalate nephropathy due to gastrointestinal disorders. Clinical Journal of the American Society of Nephrology, 15(5), 639–646. https://doi.org/10.2215/CJN.14231119
- Navarro, V. J., Khan, I., Björnsson, E., Seeff, L. B., Serrano, J., & Hoofnagle, J. H. (2017). Liver injury from herbal and dietary supplements. Hepatology, 65(1), 363–373. https://doi.org/10.1002/hep.28813
- Nigam, S. K., Wu, W., Bush, K. T., Hoenig, M. P., Blantz, R. C., & Bhatt, D. L. (2015). Handling of drugs, metabolites, and uremic toxins by kidney proximal tubule drug transporters. Clinical Journal of the American Society of Nephrology, 10(11), 2039–2049. https://doi.org/10.2215/CJN.02440314
- Nordberg, G. F., Fowler, B. A., & Nordberg, M. (Eds.). (2015). Handbook on the toxicology of metals (4th ed.). Academic Press.
- Nortier, J. L., Pozdzik, A., Roumeguere, T., & Vanherweghem, J. L. (2015). Aristolochic acid nephropathy ('Chinese herb nephropathy'). Nephrologie & Therapeutique, 11(7), 574–588. https://doi.org/10.1016/j.nephro.2015.07.481
- Perazella, M. A., & Markowitz, G. S. (2010). Drug-induced acute interstitial nephritis. Nature Reviews Nephrology, 6(8), 461–470. https://doi.org/10.1038/nrneph.2010.71
- Pline, K. A., & Smith, C. L. (2005). The effect of creatine intake on renal function. Annals of Pharmacotherapy, 39(6), 1093–1096. https://doi.org/10.1345/aph.1E52
- Posadzki, P., Watson, L., & Ernst, E. (2013). Contamination and adulteration of herbal medicinal products (HMPs): An overview of systematic reviews. European Journal of Clinical Pharmacology, 69(3), 295–307. https://doi.org/10.1007/s00228-012-1353-z
- Remuzzi, G., & Bertani, T. (1998). Pathophysiology of progressive nephropathies. New England Journal of Medicine, 339(20), 1448–1456. https://doi.org/10.1056/NEJM199811123392007
- Ross, A. C., Manson, J. E., Abrams, S. A., Aloia, J. F., Brannon, P. M., Clinton, S. K., Durazo-Arvizu, R. A., Gallagher, J. C., Gallo, R. L., Jones, G., Kovacs, C. S., Mayne, S. T., Rosen, C. J., & Shapses, S. A. (2011). The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: What clinicians need to know. The Journal of Clinical Endocrinology & Metabolism, 96(1), 53–58. https://doi.org/10.1210/jc.2010-2704
- Saper, R. B., Phillips, R. S., Sehgal, A., Khouri, N., Davis, R. B., Paquin, J., Thuppil, V., & Kales, S. N. (2008). Lead, mercury, and arsenic in US- and Indian-manufactured Ayurvedic medicines sold via the internet. JAMA, 300(8), 915–923. https://doi.org/10.1001/jama.300.8.915
- Scales, C. D., Smith, A. C., Hanley, J. M., & Saigal, C. S. (2012). Prevalence of kidney stones in the United States. European Urology, 62(1), 160–165. https://doi.org/10.1016/j.eururo.2012.03.052
- Semba, R. D. (2012). The discovery of the vitamins. International Journal for Vitamin and Nutrition Research, 82(5), 310–315. https://doi.org/10.1024/0300-9831/a000124
- Smith, R., Jones, M., & Campbell, E. (2021). Social media as a dietary supplement information source: A survey of UK university students. Public Health Nutrition, 24(15), 4991–4999. https://doi.org/10.1017/S1368980021001361
- Standring, S. (Ed.). (2020). Gray's anatomy: The anatomical basis of clinical practice (42nd ed.). Elsevier.
- Stickel, F., Kessebohm, K., Weimann, R., & Seitz, H. K. (2005). Review of liver injury associated with dietary supplements. Liver International, 31(5), 595–605. https://doi.org/10.1111/j.1478-3231.2011.02519.x
- Stiborova, M., Arlt, V. M., & Schmeiser, H. H. (2016). Balkan endemic nephropathy: An update on its aetiology. Archives of Toxicology, 90(11), 2595–2615. https://doi.org/10.1007/s00204-016-1819-3
- Stokes, T., Hector, A. J., Morton, R. W., McGlory, C., & Phillips, S. M. (2018). Recent perspectives regarding the role of dietary protein for the promotion of muscle hypertrophy with resistance exercise training. Nutrients, 10(2), 180. https://doi.org/10.3390/nu10020180
- Taylor, E. N., & Davies, M. J. (2016). Vitamin D and the kidney. Current Opinion in Nephrology and Hypertension, 25(4), 338–344. https://doi.org/10.1097/MNH.0000000000000237
- U.S. Food and Drug Administration. (2022). Dietary supplements. FDA. https://www.fda.gov/food/dietary-supplements
- Watanabe, F., Yabuta, Y., Bito, T., & Teng, F. (2014). Vitamin B12-containing plant food sources for vegetarians. Nutrients, 6(5), 1861–1873. https://doi.org/10.3390/nu6051861

- Whitaker, L., Long, J., Petróczi, A., & Backhouse, S. H. (2018). Using the prototype willingness model to predict doping and supplement use intention. Scandinavian Journal of Medicine & Science in Sports, 28(3), 865–877. https://doi.org/10.1111/sms.12981
- Wolf, G. (2004). The discovery of vitamin D: The contribution of Adolf Windaus. Journal of Nutrition, 134(6), 1299–1302. https://doi.org/10.1093/jn/134.6.1299
- World Health Organisation. (2021). Food safety and quality: Dietary supplements. WHO. https://www.who.int/foodsafety/areas_work/food-technology/supplements/en



Appendices

Study on the Nephrotoxic Effects of Uncontrolled Dietary Supplement Intake on Kidney Function:

1. Sex:

☐ Male

☐ Female

2. Age group (select the appropriate category):

☐ 10–20 years

☐ 20–30 years

☐ 30–40 years

☐ 40–50 years

☐ 50–60 years

☐ 60–70 years

☐ 70–80 years

3. Educational level:

☐ No formal education

☐ Primary

☐ Intermediate

☐ Secondary

☐ University

☐ Postgraduate studies

4. Occupation or activity:

☐ Student

☐ Employee

☐ Professional athlete

☐ Head of household

☐ Unemployed

5. Have you been diagnosed with any chronic health condition? (Multiple answers possible)

☐ No

☐ Diabetes mellitus

☐ Hypertension

☐ Kidney disease

☐ Kidney stones

☐ Cardiovascular diseases

☐ Other: ……

6. Do you have a family history of kidney disease?

☐ Yes

☐ No

7. Have you ever taken dietary supplements?

☐ Yes, currently

☐ Yes, in the past

☐ No, never

8. Type of supplements you use or have used (multiple selections possible)

☐ Multivitamins

☐ Vitamin D

☐ Vitamin C

☐ Protein supplements

☐ Creatine

☐ Weight-loss supplements

☐ Herbs or natural extracts

☐ Other: ...

9. For how long have you been taking supplements?

☐ Less than 3 months

☐ 3–6 months

☐ 6–12 months

☐ More than 1 year

10. How do you take supplements?

☐ By medical prescription

☐ On a pharmacist’s advice

☐ Based on a fitness trainer’s advice

☐ Based on information from the internet

☐ Based on friends' recommendations

11. Do you adhere to the recommended supplement dosage?

☐ Always

☐ Often

☐ Sometimes

☐ Rarely

12. Have you ever exceeded the recommended dosage?

☐ Yes

☐ No

13. Have you had kidney function tests (creatinine, urea) performed during the past year?

☐ Yes

☐ No

14. If yes, did you notice an elevation in:

☐ Creatinine

☐ Urea

☐ I did not undergo testing

☐ Results were normal

15. Did you experience any symptoms while taking supplements?

☐ Flank pain

☐ Leg swelling

☐ Decreased urine output

☐ General fatigue

☐ No symptoms appeared

16. Do you believe that dietary supplements can affect the kidneys?

☐ Yes

☐ No

☐ I don't know

17. Where do you get your information about supplements?

☐ Physician

☐ Pharmacist

☐ Fitness trainer

☐ Internet

☐ Friends

18. Do you support strict medical regulation of dietary supplement sales?

☐ Yes

☐ No

19. Have you ever experienced health problems after taking a dietary supplement?

☐ Yes

☐ No

20. Do you perform periodic kidney function tests after using supplements?

☐ Yes, annually

☐ Yes, every few months

☐ No, I have not

Please indicate your degree of agreement from 1 to 3 (1 = Disagree, 2 = Agree, 3 = Strongly agree)

20. Dietary supplements are safe if used at low doses.

☐ 1 ☐ 2 ☐ 3

21. Excessive use of supplements may lead to kidney damage.

☐ 1 ☐ 2 ☐ 3

22. Supplements should be under continuous medical supervision.

☐ 1 ☐ 2 ☐ 3

23. In your opinion, what is the greatest risk resulting from the random use of supplements?

.....
.....

24. What recommendations do you think are necessary to reduce the risks associated with dietary supplements?

.....
.....

دراسة التأثير السام لتناول المكملات الغذائية بشكل غير منضبط على نشاط الكلى

1. الجنس

☐ذكر

☐أنثى

2. الفئة العمرية (إختر الفئة المناسبة)

☐من 10 إلى 20 سنة

☐من 20 إلى 30 سنة

☐من 30 إلى 40 سنة

☐من 40 إلى 50 سنة

☐من 50 إلى 60 سنة

☐من 60 إلى 70 سنة

☐من 70 إلى 80 سنة

3. المستوى التعليمي

☐لا أملك تعليمًا رسميًا

☐ابتدائي

☐متوسط

☐ثانوي

☐جامعي

☐دراسات عليا

4. المهنة أو النشاط

☐طالب

☐موظف

☐رياضي محترف

☐رب أسرة

☐بدون عمل

5. هل تم تشخيصك بمشكلة صحية مزمنة؟ (يمكن اختيار أكثر من إجابة)

☐لا

☐داء السكري

☐ارتفاع ضغط الدم

☐مرض كلوي

☐حصى الكلى

☐أمراض قلبية

☐أخرى.....

6. هل لديك تاريخ عائلي لأمراض الكلى؟

☐نعم

☐لا

7. هل سبق لك أن تناولت مكملات غذائية؟

☐نعم، حالياً

☐نعم، في الماضي

☐لا، لم أتناول أبداً

8. نوع المكملات التي تستخدمها أو استخدمتها (يمكن اختيار أكثر من نوع)

☐فيتامينات متعددة

☐فيتامين د

☐فيتامين هـ

☐مكملات البروتين

☐كرياتين

☐مكملات إنقاص الوزن

☐أعشاب أو مستخلصات طبيعية

☐أخرى..... :

9. منذ متى وأنت تتناول المكملات؟

☐أقل من 3 أشهر

☐3 – 6 أشهر

☐6 – 12 شهراً

☐أكثر من سنة

10. كيف تتناول المكملات؟

☐بوصفة طبية

☐باستشارة صيدلي

☐بناءً على نصيحة مدرب رياضي

☐بناءً على معلومات من الإنترنت

☐بناءً على توصية الأصدقاء

11. هل تلتزم بجرعة المكملات الموصى بها؟

☐دائماً

☐غالباً

☐أحياناً

☐نادراً

12. هل سبق أن تجاوزت الجرعة الموصى بها؟

☐نعم

☐لا

13. هل أجريت تحاليل لوظائف الكلى (كرياتينين، يوريا) خلال العام الماضي؟

☐نعم

☐لا

14. إذا كانت الإجابة نعم، هل لاحظت ارتفاعاً في: (يمكن اختيار أكثر من إجابة)

☐الكرياتينين

☐اليوريا

☐كانت النتائج طبيعية

☐لم أجري تحليل

15. هل ظهرت لديك أعراض خلال تناول المكملات؟ (يمكن اختيار أكثر من إجابة)

☐ألم في الخاصرة

☐تورم في الساقين

☐انخفاض في كمية البول

☐إرهاق عام

☐لا أعراض ظهرت

16. هل تعتقد أن المكملات الغذائية يمكن أن تؤثر على الكلى؟

☐نعم

☐لا

☐لا أعلم

17. من أين تحصل على معلوماتك حول المكملات؟

☐طبيب

☐صيدلي

☐مدرب رياضي

☐الإنترنت

☐أصدقاء

18. هل تؤيد فرض رقابة طبية صارمة على بيع المكملات الغذائية؟

☐نعم

☐لا

19. هل سبق أن عانيت من مشكلات صحية بعد تناول مكمل غذائي؟

☐نعم

☐لا

20. هل تقوم بإجراء فحوصات دورية لوظائف الكلى بعد استخدام المكملات؟

☐نعم، سنوياً

☐نعم، كل بضعة أشهر

☐لا، لم أقم بذلك

(يرجى تحديد درجة موافقتك من 1 إلى 3، حيث 1 = لا أوافق، 2 = أوافق إلى حد ما، 3 = أوافق بشدة)

21. المكملات الغذائية آمنة إذا تم استخدامها بجرعات منخفضة

☐ 3 ☐ 2 ☐ 1

22. الإفراط في المكملات قد يؤدي إلى ضرر كلوي

☐ 3 ☐ 2 ☐ 1

23. يجب أن تكون المكملات تحت إشراف طبي دائم

☐ 3 ☐ 2 ☐ 1

24. في رأيك، ما هو الخطر الأكبر الناتج عن الاستخدام العشوائي للمكملات؟

.....

.....

25 .ما التوصيات التي تعتقد أنها ضرورية للحد من المخاطر المرتبطة بالمكملات الغذائية؟

.....

.....