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Proceeding Paper

Impure Nephrotic Syndrome in a Young Weightlifter Induced by a Plant-Based Dietary Supplement: A Case Report †

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Abstract: Numerous weight loss preparations emerge without medical or pharmaceutical supervision, thereby accentuating the risk to public health. Recent data shed light on the extent of the problem, with an increase in cases of nephrotoxicity associated with the use of plant-based dietary supplements (DSs). A 22-year-old patient, a smoker with no significant medical history, was admitted to the nephrology department of EHU Oran for the management of impure nephrotic syndrome complicated by acute renal failure, edema, and proteinuria. During interrogation, the patient admitted to incorporating the following products into his weight loss and muscle gain program: a plant-based DS named "Animal cuts®", composed of 38 plant extracts, supplementation with "Whey protein" at a dosage of 300 g/day, and creatine. Two samples, blood and urine, were sent to the toxicology department of EHU Oran. Since we did not receive the DS sample, a screening for various drugs was negative. An in-depth literature search on the toxic potential of the various components of "Animal cuts®" allowed us to identify five components posing a risk to renal function, namely dandelion root extract (*Taraxacum* sp.), juniper berries (*Juniperus* sp.), green tea leaf extract (*Camelia sinensis*), and ginger (*Zingiber officinale)*. Cases of renal dysfunction related to creatine supplementation have been reported in the literature. However, numerous studies indicate that "Whey protein" may not pose any nephrotoxic risk in individuals with normal renal function. This case adds to the growing number of reports of nephrotoxicity following the use of plant-based DSs and underscores the importance of strengthening regulations governing their production.

Keywords: Animal cuts®; whey protein; creatine; nephrotoxicity; plant-based dietary supplement

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1. Introduction

As weight-related concerns intensify, there is a notable increase in the demand for bodybuilding and weight loss products. This trend has prompted industries to expand their offerings, catering to the diverse needs of consumers seeking to sculpt their bodies and manage their weight effectively. Herbal dietary supplements, largely unregulated by the United States Food and Drug Administration (FDA), have gained substantial popularity due to their perceived safety and reduced likelihood of adverse side effects compared to synthetic alternatives such as Whey protein [1]. However, some are associated with severe toxicities, including nephrotoxicity. The current report describes a case of acute renal failure in a young healthy male taking a herbal dietary complement (DS) called "Animal cuts®", as well as protein supplementation, opting for a powdered form of "Whey protein" and "Creatine".

2. Patients and Methods

We report a 22-year-old male patient with no significant medical history except for a smoking habit admitted to the nephrology department of the University Hospital Establishment (EHU) of Oran for the management of an impure nephrotic syndrome complicated by acute renal failure.

The patient presented with generalized bilateral and symmetrical pitting edema. However, no prior renal complications or familial history of renal diseases were detected. Upon admission, laboratory investigations unveiled marked proteinuria and hypoalbuminemia.

During the interrogation, the patient denied the use of non-steroidal anti-inflammatory drugs (NSAIDs) or any other medication. However, he revealed a two-month history of consistent consumption of a herbal-based dietary supplement (DS) known as Animal cuts®, with the intention of promoting fat burning and assisting his bodybuilding journey.

This DS, widely marketed for its purported benefits in performance enhancement, represents a multifaceted blend of botanical constituents. It is composed of 42 packs, each containing nine (9) gel capsules. Within each capsule, approximately eight (8) different plant extracts are evenly distributed, resulting in a cumulative total of 38 distinct plant extracts throughout the entirety of the supplement [2].

Notably, the patient had been ingesting Animal cuts® concomitantly with other dietary supplements, specifically Whey protein, administered orally in powdered form alongside creatine supplementation at a dosage of 300 g and 5 g per day, respectively, for one month.

Two specimens, blood and urine, were forwarded to the toxicology department of the EHU of Oran for comprehensive analysis, aiming to ascertain potential toxicological contributions to the patient's renal pathology. However, we were unable to obtain a sample of the dietary complement consumed in the present report, namely Animal cuts®, Whey protein, and creatine.

A literature search using Google scholar was undertaken to explore the impact of the 38 plant extracts present in the DSs Animal cuts®, Whey protein, and creatine on renal and other functions.

3. Results

3.1. Results of Toxicological Analysis: Drugs in Blood and Serum

A toxicological screening of various drugs was conducted on the patient's blood and urine samples, including for the detection of benzodiazepines, THC (delta-9-tetrahydrocannabinol), ecstasy, barbiturates, cocaine, and opioids. The results obtained from the different assays are presented in the table below (Table 1).

Table 1. Toxicological screening results obtained from the patient's urine and blood samples.

Drug	Dose	Interpretation
Benzodiazepine	<15 µg/mL	Negative
THC	0 µg/mL	Negative
Ecstasy	<75 µg/mL	Negative
Barbiturates	<28 µg/mL	Negative
Cocaine	0.099 ng/mL	Negative
Opioids	<16 µg/mL	Negative

3.2. Results of Dietary Complement Analysis: Literature Review

3.2.1. Animal Cuts®

An in-depth literature review on the composition of the dietary supplement "Animal cuts®", as well as its impact on renal function and other physiological processes, enabled us to obtain the following results, as presented in the table below (Table 2).

Table 2. Composition and metabolites of Animal cuts® supplement: Impacts on renal and other functions.

Composition	Main Chemical Metabolites	Impact on Renal Function	Impact on Other Functions
Stimulant complex (750 mg)			
Caffeine anhydrous	Caffeine	May be nephrotoxic [3]	-
Kola nut (seeds)	1–3% caffeine/theobromine	-	Oral and gastrointestinal cancer [4]
Guarana (seeds)	Caffeine/tannins/theobromine	-	Pancreatitis/Hepatic cytolysis [5]
Yerba mate (leaf)	0.9–1.7% caffeine	-	-
Raspberry ketones	Substituted phenol	-	Hepatotoxicity [6]
Coleus forskohlii extract (root)	Forskoline	-	Genotoxicity [7]
Evodiamine	-		-
Metabolic complex (750 mg)			
Green tea leaf extract	Epigallocatechin gallate	Theoretic nephrotoxic [8]	Hepatotoxicity [8]
Oolong tea leaf extract	Epigallocatechin gallate	-	Hepatotoxicity [8]
Black tea leaf extract	Epigallocatechin gallate	-	Hepatotoxicity [8]
Coffee bean extract	Caffeine/tannins	-	-
Thyroid complex (350 mg)			
L-thyrosine	Dopamine/adrenaline precursor	-	-
Olive leaf extract	Oleuropein/ligstroside	-	-
Salvia officinalis leaf	-	-	Intestinal toxicity [9]
Water-shedding complex (750 mg)			
Dandelion (*Taraxacum officinale*) (root)	-	Contraindication in cases of renal colic [10]	-
Uva ursi leaf	-	-	Hepatotoxicity [8]
Juniper berry fruit	-	Nephrotoxicity [8]	-
Buchu leaf	-	-	-
Celery seeds	-	-	-
Nootropic complex (500 mg)			
Cocoa powder (bean)	-	-	-
DMAE bitartrate	Dimethyaminoethanol	-	Hepatotoxicity [8]
Huperzia serrata extract	Huperzine A	-	-
Cortisol-inhibiting complex (300 mg)			
Ashwagandha extract (leaf)	Withanolides Eleuthersid	-	-
Eleutherococcus senticosus (root) *Magnolia* sp.	Neolignan (Magnolol)	-	-
Phosphatidylserine	-	-	-
CCK-boosting complex (300 mg)			
Cha-de-bugre (*Cordia salicifolia*)	Allantoin/ caffeine	-	-
Apple cider vinegar powder	-	-	-
Cinnamon (*Cinnamomum* sp.)	Eugenol and others	-	-
Bioavailability complex (500 mg)			
Ginger (*Zingiber officinale*) (root)		Theoretic nephrotoxic potential [8]	-
Cayenne (fruit)	-	-	-
Grapefruit (6,7-dihydroxyber-gamottin) (peel)	-	-	-
Naringin (*Citrus maxima*)	-	-	-
Black pepper extract (fruit)	Piperine	-	Hepatic cytolysis [5]
Quercetin	-	-	-

3.2.2. Whey Protein

The chemical composition of Whey protein and its impact on renal and other functions are presented in the table below (Table 3).

Table 3. Composition of Whey protein and its impact on renal and other functions.

	Composition (%)	Impact on Renal Function	Impact on Other Functions
Whey protein	50% alpha lactalbumin 25% beta lactoglobulin 7% bovine serum albumin 5% immunoglobulin Branched chain amino acid	High risk of nephrolithiasis [11]	Hepatotoxicity (increase in ALA/AST enzymes) [11] Reduced intestinal microbiota: *Bacteroides phylum* [11]

3.2.3. Creatine

The chemical composition of creatine and its impact on renal and other functions are presented in the table below (Table 4).

Table 4. Composition of creatine and its impact on renal and other functions.

Dietary Supplement	Composition	Form of Acute Kidney Injury	Other Adverse Events
Creatine	Methionine Glycine Arginine	Acute interstitial nephritis (AIN) [12]	Hypertension Rhabdomyolysis [12]

4. Discussion

Dietary supplements are widely used by the public for perceived health benefits, but some of them have been associated with kidney disease [8].

The patient's clinical course and the results of toxicological screenings are strongly suggestive of a toxic injury caused by the dietary supplements reported in the present case, notably Animal cuts®, Whey protein and creatine.

In light of the absence of the dietary supplement sample provided by the patient, direct analyses could not be carried out. Nonetheless, we conducted an extensive investigation aiming to examine the association between the nephrotic syndrome induced in the reported case and the intake of DS.

Some of the ingredients in the patient's supplements have been reported as nephrotoxic in contemporary studies, including recent review articles on herbal remedies. In addition, none of the supplements that he was taking contained mefenamic acid and/or Aristolochia, which have been identified as adulterants in herbal products and implicated in interstitial nephritis [8,13].

The consumption of caffeine, the main chemical compound in Kola nuts, Guarana (seeds), and Yerba mate (leaf) contained within Animal cuts®, increases the urinary excretion of calcium, magnesium, potassium, sodium, and chloride. Due to adenosine having a renal protective effect, its antagonism by caffeine has led to a suspicion of renal toxicity. A study conducted in vivo in obese and diabetic rats showed an increase in proteinuria, intrarenal resistances, and an acceleration of renal function degradation with caffeine administration [3].

Moreover, some DS therapies that are not associated with renal dysfunction warrant discussion. Green tea leaf extract (*Camelia sinensis*) and Ginger (*Zingiber officinale)* have the potential to be nephrotoxic because of their mechanisms or adverse event profiles. The lack of evidence does not mean that these DS are safe, and renal function should be monitored in all patients who consume these agents. The review led by Steven G. et al. on dietary-supplement-induced renal dysfunction confirms that these plant extracts, through their mechanism of COX inhibition, alter renal hemodynamics, thus potentially being nephrotoxic [8].

Likewise, the volatile oil distilled from the berries of *Juniperus communis* (juniper) can cause renal damage at excessive doses [14].

Furthermore, among the variety of plants known for their possible diuretic actions is Dandelion (*Taraxacum officinale* L. Weber) [15]. The acute toxicity of this plant appears to be low, with LD50 values estimated at 36.8 g/kg and 28.8 g/kg for the root and whole plant, respectively [16]. Adverse or complex toxic effects of *T. officinale* have not yet been reported.

Regarding whey protein, studies have linked the consumption of a high-protein diet with the development of renal issues, utilizing both animal and human models. Short-term intake of a diet supplemented with whey protein has been shown to lead to elevated levels of plasma urea, increased urinary volume, and higher urinary calcium excretion. Additionally, there is a reduction in urinary pH and citrate levels. The concurrent decrease in urinary pH, along with hypocitraturia and hypercalcemia, is acknowledged as a risk factor for nephrolithiasis [11,17].

The ingestion of creatine likely results in an increase in serum creatinine, since creatine is spontaneously and irreversibly converted into serum creatinine. Consequently, a falsely positive diagnosis of renal insufficiency may be made in an individual consuming creatine when only blood tests are considered [18]. The current state of knowledge does not allow us to assert that creatine exerts a deleterious effect on the kidney in the long term. However, several cases of worsening renal pathologies have been described in the literature and attributed to creatine intake.

Based on current research findings, the use of creatine supplementation seems to pose no significant safety concerns for healthy adults when adhering to recommended loading (20 g per day for five days) and maintenance doses (up to 3 g per day). However, individuals with a prior history of kidney disease or those using nephrotoxic medications may face an elevated risk of renal dysfunction when using creatine [19].

In addition, some dietary supplements may contain compounds that are directly toxic to the kidneys, leading to acute or chronic kidney injury. The purity of dietary supplements may be compromised due to the inadvertent inclusion of undisclosed substances, or through contamination by heavy metals or microorganisms.

A study involving 121 substances reveals that such contaminations are prevalent and can occur at various stages, particularly during production, and particularly in regions with less stringent regulatory oversight. Nephrotoxicity induced by heavy metals manifests as chronic tubulointerstitial nephritis progressing to chronic kidney disease (CKD), proximal tubulopathy (characterized by glycosuria, aminoaciduria, hyperphosphaturia, hypercalciuria), or glomerular involvement, often associated with occupational exposures [20].

5. Conclusions

The present case adds to the increasing number of reports of nephrotoxicity induced by dietary supplements and highlights that herbal extracts may not be free of adverse effects.

In our review of the literature concerning the potential effects of the constituents of the DS Animal cuts®, five (5) components exhibited a non-negligible nephrotoxic potential. Similarly, supplementation with whey protein and creatine is not devoid of risks for renal function.

Until these products are more closely regulated and their advertising better scrutinized, physicians and patients should become more familiar with herbal products that are commonly used as weight lose supplements and recognize those that are potentially harmful.

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