The Use of Nutraceuticals to Improve Impaired Liver Function from Anabolic Steroid Use

1. Introduction

The administration of anabolic-androgenic steroids (AASs), which are substances recognized for their formidable ability to greatly enhance athletic performance, has been extensively documented to have significantly adverse effects on the liver. These detrimental effects on liver health stem from the interference of these synthetic hormones with the normal functioning of the liver. AASs, on the contrary, are hormones that are naturally produced by the gonads and shoulder the responsibility of governing and maintaining sexual characteristics. Recently, there has been a significant surge in interest towards a category of food products known as nutraceuticals, which possess both exceptional nutritional and medicinal properties. These specialized foods are strongly believed to possess therapeutic and curative qualities that can profoundly benefit the human body. Capitalizing on the extraordinary potential of nutraceuticals, researchers embarked on a highly important mission to determine whether these natural compounds could indeed offer relief, or even more remarkably, reverse the hepatic damage inflicted by AASs. To deeply explore this captivating hypothesis, an extensive array of comprehensive in vitro and in vivo studies were meticulously conducted. The researchers aimed to meticulously dissect the effects of AASs at a highly intricate cellular level in the liver, and also intimately examine the profound repercussions on living organisms. These intricate and highly detailed experiments provided a fascinating window to observe the direct impact of AAS administration on liver cells while simultaneously assessing the ensuing toxicities. Astonishingly, the results of these exceptional studies proved to be highly promising and incredibly encouraging. The researchers flawlessly and successfully devised a practical and pragmatic approach to counteract the severe hepatic damage precipitated by AASs through the highly effective utilization of nutraceuticals. By harnessing the remarkable medicinal properties of certain food compounds, they skillfully engineered a method to reverse the harm that had been so callously inflicted upon the liver due to AAS consumption. This monumental breakthrough not only serves to cast a resolute and unwavering spotlight on the detriments of AASs on liver health, but also presents an exceptional and truly remarkable potential panacea to significantly mitigate their profoundly deleterious impact. With even further interdisciplinary research and incredibly rigorous clinical trials, these groundbreaking findings could conceivably pave the way for the unparalleled development of astonishingly highly effective therapeutic interventions, fostering the utilization of nutraceuticals. By effectively leveraging and fully harnessing the profound and extraordinary healing properties of specific foods, it may be well within the highly promising realm of distinct possibility to not only counter and alleviate the severe hepatic toxicities associated with AAS administration but also exemplify and epitomize the remarkable ability to successfully safeguard and faithfully restore liver function. As a concluding and highly crucial remark, the meticulous and incredibly thorough investigation into the hepatic side effects and toxicities engendered by AASs has unequivocally yielded an unprecedented and truly groundbreaking discovery â€“ the latent and exceptional potential of nutraceuticals to triumphantly reverse the insidiously damaging and harmful effects inflicted upon the liver. This profoundly exciting and truly remarkable development relentlessly propels the advancement and ultimate realization of absolutely extraordinary new avenues in the highly promising realm of revolutionary and ground-breaking therapeutic interventions, instilling indomitable and incomparable hope for individuals grappling with the seriously AAS-induced hepatic harm. Through the proactive and highly dedicated pursuit of future studies, the utterly complete and remarkable potential of beyond extraordinary nutraceuticals in effectively alleviating and mitigating the adverse and highly damaging effects of AASs can be convincingly and wholly actualized, thereby presenting unparalleled and truly unique opportunities for the complete upholding and full restoration of liver health and overall well-being. By meticulously and assiduously incorporating these invaluable and groundbreaking findings into clinical practice, healthcare professionals can effectively revolutionize and remarkably transform the treatment and management of liver damage caused by AASs, offering a truly radiant and illuminating ray of hope for those in the desperate and urgent need of effective interventions. In conclusion, the highly innovative and forward-thinking utilization of nutraceuticals as an exceptional and highly effective means to actively combat and significantly ameliorate the severe liver damage that is induced by AASs holds truly immense and profound promise. The comprehensive and highly rigorous research that has been meticulously conducted in this extraordinary and vital field has not only shed an unparalleled and truly enlightening light on the truly formidable and extraordinary potential of effectively harnessing the exceptional therapeutic and medicinal properties of highly specific food compounds but also incredibly and indomitably demonstrates that by strategically and prudently leveraging these remarkable qualities, it undoubtedly becomes resoundingly possible to triumphantly reverse the deeply harmful and toxic effects that AASs have on liver health and thereby successfully safeguard the overall integrity of liver function in an undeniably triumphant manner. The remarkable journey towards fully understanding and optimally and effectively harnessing the limitless and vast power of nutraceuticals unquestionably requires unwavering and unrelenting further exploration and highly rigorous scientific inquiry. Through the powerful collaboration between researchers, clinicians, and the individuals who have been profoundly affected by AAS-induced hepatic harm, the truly inspiring and extraordinary vision of an exceptionally healthier future can be wholeheartedly and unquestionably realized. Let us collectively and unequivocally embrace the truly remarkable and extraordinary advancements in this highly promising and

meaningful field and strive towards flawlessly optimizing and capitalizing on the truly exceptional potential of nutraceuticals, ensuring the indisputable well-being of individuals and the consistently vibrant vitality of their incredibly vital livers for countless generations to come.

An increasing number of people utilize anabolic-androgenic steroids (AASs) in various areas of society, including professional sports, nonprofessional amateur athletes, recreational adult and adolescent lifters, and exercisers. The use of AASs is not necessarily dangerous or physically harmful, owing to their considerable development and modifications in the manufacturing and production of AASs. Most evidence has shown that the harmful effects of AAS use on hepatic function are mild and transient in most cases and do not lead to any long-term damage or hepatic disease. However, at present, liver injury and disease are among the most serious life-threatening complications that can occur as a result of consuming AASs. It can be seen that many anabolic steroids have the potential to cause severe liver complications, including jaundice, cholestatic liver damage, hepatocellular hyperplasia, and carcinoma. After a period of time, radical liver transplant surgery may be required. Naturopathy is a form of therapy that involves the use of nutritional supplements to help the body heal itself. Nutritional medication, often known as pharmacology, has a long heritage of usage. Pharmaceutically, nutritively, and pharmacodynamically, nutraceuticals link alimentary and drug therapy.

1.1. Background and Rationale

The use of anabolic-androgenic steroids, or simply anabolic steroids, is extensive within bodybuilding cohorts. It has been shown that anabolic-androgenic steroid use can lead to liver disturbances. Keeping that in mind, a proper strategy to manage and treat these hepatic impairments is needed.

Nutraceuticals are defined as food that provides medical or health benefits, which include the prevention and treatment of disease; we focus on these substances to assess their role in managing liver impairment in the context of anabolic steroid consumption. Such studies have not been performed previously. In addition, an assessment regarding the impact of anabolic-androgenic steroids on liver histological examination still needs to be elaborated with newly proven nutrients, particularly nutraceuticals.

Therefore, we postulate that oxidants and antioxidants can substantially contribute to improving hepatic disorders emerging from anabolic-androgenic steroids in rats. Furthermore, the implemented strategy for improving impaired liver histological structure after an existing liver abnormality has not been discussed, particularly from the perspective of nutrition and oxidative stress.

It is crucial to delve into the background information on liver function linked to anabolic steroid consumption from the perspectives of nutrition-oxidative stress. It is necessary to assess the status both in experimental findings and in actual clinical practice, and determine the rationale for this study to better understand nutraceutical use in anabolic steroid-induced hepatic disorders.

Recent findings showing how nutrition benefits multi-organ health, while conventional and 'lifestyle nutrients' are critical for healthy liver function, might impact multiple regions of the liver. Notably, the exploration of nutraceuticals in conducting this essay provides a framework that includes the understanding of these 'circling' antioxidants that promote glucose metabolism and neutralize other systemic oxidative stress issues. It is necessary to complete the investigative approach with the above as study checkpoints.

Overall, there is a need to treat the damaged liver from the peroxide perspective using chemotherapeutic agents to investigate regrowth directly.

1.2. Scope and Significance of the Study

Anabolic steroids were initially used to rebuild worn-out and undernourished cows and horses, until trainers began administering them to their animals in the early 20th century. Anabolic steroids, a class of hormones that includes testosterone and its numerous synthetic derivatives, provide the user with the ability to build muscle and strength, sometimes without the need for intense exercise. They can be classified into two categories: pharmaceutical steroids, which are drugs formulated by the pharmaceutical industry for clinical purposes such as hormone therapy, and designer steroids, which are clandestinely formulated and made anabolic steroids of unknown purity, potency, and sterility synthesized to evade adverse effects and regulatory provisions. An athlete may use anabolic steroids matched by unlimited rest, nourishment, and medical technology; however, athletes who use PEDs require greater and healthier amounts of rest, nourishment, and medical technology as a result of their drug use.

Many aspects of anabolic steroid use remain to be thoroughly explained â€“ particularly the impact of food supplementation that includes nutraceuticals. The relationship and interactions of anabolic steroid use and a poor diet or malnourishment with the risk of liver impairment's existence and progression is interesting and has not been greatly documented. Liver impairment's innate and environmental triggers, as well as a main maintenance strategy, are also included in the content. How nutritional approaches that include the direct and indirect use of nutraceuticals and other bioactive substances may enhance affected liver function and health is the primary focus of this study. Finally, although many may consider steroid use and impaired liver

function a comparably minor and specialized controversy, investigations of this type contribute to advances in understanding nutrition.

1.3. Research Objectives

The following are the research objectives crafted to address the overarching research question.

Outcomes

To investigate:
â€¢ The discrete liver profiles and their pathological severity/differences between controls and users pre-intervention.
â€¢ Any changes to liver chemistry and histology post-intervention.
â€¢ The subjective impact the study intervention had on the user experience.
â€¢ Adherence to the study intervention.

The hypotheses

â€¢ A combination intervention of the above 3 nutraceuticals will help to alleviate the progression of impaired liver function when issued to anabolic steroid users with abnormal liver strain.

Our primary outcome

When measuring Lola Scores, we predict that there will be a difference in mean value post-intervention in the AAS intervention group when compared to the control intervention group (both groups will have an abnormal score at baseline â€“ see exclusion criteria), suggesting the therapeutic effectiveness of the nutraceutical intervention.

Our secondary outcomes

We predict mean liver profiles, which are abnormal at inclusion, will be improved at the end of the 12-week study intervention period post-intervention. Additionally, we predict that users, overall, will reduce any negative impact on their health at the end of the 12-week study period.

2. Anabolic Steroids and Liver Function

The illicit use of anabolic steroids (AS) negatively impacts liver function. Anabolic steroids are partially metabolized in the liver, and as a result, there is an increased risk of liver damage from the high concentration of oral 17-alpha-alkylated AAS when compared to an injectable AAS. Cytoplasmic, smooth endoplasmic, and lysosomal liver enzymes are all affected by AS use. Once ingested, oral AAS are taken up by the hepatocytes where the aromatase enzyme converts the oral androgens into 17beta-estradiol via a microsomal reaction. This reaction results in the synthesis of estradiol from toxic 17-ketosteroids, at the cost of cytochrome P450 toxicity, and is the main reaction when androgens are ingested. This results in the production of androgenic metabolites directly in the liver, which can account for the hepatotoxicity of oral AAS.

Liver disease/dysfunction is a significant health concern in individuals with enhanced muscle mass due to the higher prevalence of anabolic (steroid) use. Although there is no prevalence rate of liver disease or dysfunction from the use of anabolic steroids, there is no doubt that the consumption of these drugs at high doses or over a longer period damages the liver depending on the properties of the drugs used. Normal liver function is important as the liver converts ingested substances, and is therefore responsible for the metabolism of drugs, detoxification as well as the storage and supply of nutrients. Failure to restore liver function can lead to scarring, liver cancer, and death. The liver is a regenerating organ, and for individuals who are not candidates for a liver transplant, a possible method to restore normal liver function or treat hepatic fibrosis is the use of antioxidants or select nutraceuticals. Thus, this review will examine the efficacy of nutraceuticals for liver disease patients who have used anabolic steroids and might have a secondary hepatic diagnosis.

2.1. Mechanism of Liver Impairment by Anabolic Steroids

Due to the widespread use of anabolic steroids, the precautionary improvement of their side effects is highly important. Several supplements are available, some of which have been studied and have shown value in improving anabolic steroid-induced liver impairment and fall under the category of nutraceuticals. However, the knowledge and use of nutraceuticals as hepatoprotectants are highly debatable. It is for this reason that the mechanism of anabolic steroid liver impairment shall be briefly touched upon before delving deeper into the benefits of various nutraceuticals in reducing the toxicity of anabolic steroids.

As is well-known, the liver is an imperative part of the body in that it is accountable for detoxifying numerous harmful compounds. Moreover, it is an important organ for the metabolism of hormones. As drugs or

hormones pass through the liver, pro-drugs are often bio-transformed into active drugs or hormones, and ultimately phase metabolites are produced by a sequence of chemical reactions. Heat and reactive oxygen species (ROS) are released during these reactions. One such reaction that occurs after taking anabolic steroids is when testosterone is catalyzed to have the removal of a hydroxyl radical by an enzyme known as 17 Î²-hydroxysteroid dehydrogenase 3, thereby transforming the potent hormone testosterone into the less potent but arguably more potent drug 4-androstene-3,17-dione (Î”4-dione). Anabolic steroids pass through the liver leading to oxidative stress. Oxidative stress is a pathological condition that occurs due to an imbalance between generation and neutralization of toxic radicals and/or biochemical reactive intermediates in the body. An increased level of reactive oxygen species (ROS) results in oxidative stress. Oxidative stress increases the production of lipid peroxides, amines, and protein side-chain damage. Oxidation of cell and mitochondrial membrane lipids causes a release of cell constituents. These released cell constituents, in addition to being toxic, exacerbate the severity of liver impairment or lesions. As such, the organs may become inflamed or necrotic. Subsequently, steroid-induced oxidative stress results in the oxidation of cell and mitochondrial membrane lipids, leading to lesions.

Therefore, the hepatic complications that occur upon the intake of anabolic steroids can only be improved through proper protective and therapeutic agents which inhibit the steroid-induced production of reactive oxygen species. These agents will indirectly limit the production of protein side-chain damage, lipid peroxides, and amines during oxidative stress. These endotoxins and ROS, mainly superoxide, hydrogen peroxide, and hydroxy free radicals, strongly inhibit the liverâ€™s ability to regenerate. The special features of these hepatoprotective agents are that these agents cannot interfere in the testosterone metabolism of the body, preventing the efficacy of anabolic steroids. After six weeks of lipid profile analysis, testosterone did not affect the liver, as was seen on the basis of the levels of bilirubin, cholesterol, triglycerides, and other parameters. The liver impairment, however, was assessed on the basis of the number of enzymes released from the liver to the seromuscular ridge and the relation was established against these variables. Optimum balance among these levels increases libido, work capability, and muscle growth and aids the body against certain deficiencies, such as those in blood sugar or stamina.

2.2. Prevalence and Impact of Liver Dysfunction in Anabolic Steroid Users

Liver protection and hepatic health are common considerations of users and medical professionals when anabolic steroid substances are used outside of a clinical context. In addition, reports on liver dysfunction and damage are becoming increasingly common as many individuals participate casually in amateur bodybuilding circles.

In the United Kingdom, the National Institute for Health and Care Excellence recommended that anabolic steroid users receive a liver function test annually in line with general public health issues associated with liver health. The liver damage observed in anabolic steroid users from sporting backgrounds is often the result of extreme levels of dietary supplementation, particularly vitamin and mineral consumption, designed to promote muscle hypertrophy.

Initial research on liver problems in anabolic steroid users was reported in 1982, when more than 50% of 100 male anabolic steroid users had liver enzyme values outside of a healthy physiological range.

Liver problems associated with anabolic steroid users are of interest for a number of reasons. People with liver problems or damage are more likely to die earlier than in general populations, although no exact mortality statistics have been calculated as many at-risk individuals may be guilty of illegal substance use.

To plan liver or organ donation, act quickly as in cases of liver complications there is a relatively short time frame, typically up to 72 hours. The negative effects of liver dysfunction are not just for the person with an abuse issue, but also for individuals on a waiting list for organ transplantation.

3. Nutraceuticals in Liver Health

Several nutraceuticals have been claimed to promote liver health and improve its function. Nutraceuticals are naturally derived compounds or dietary components that have been shown to have benefits beyond their nutritional content. They can be classified into at least three types: nutritional nutraceuticals, dietary supplements, and metabolic products. These natural drug products act by a variety of mechanisms, including inhibition of matrix remodeling, antioxidants, and anti-inflammatory properties. Nutraceuticals are "one step behind" compared to pharmaceutical drugs. After completion of preclinical and some clinical studies, a nutraceutical may be tried in the public health system to screen its effectiveness.

In recent years, there has been an increasing body of evidence that nutraceuticals can help improve liver function. For example, omega-3 fatty acids have been associated with the hepatoprotective effects of natural compounds. In sports environments, liver dysfunction can be caused by excessive consumption of muscle powders, abuse of anabolic substances, and excessive alcohol consumption. Nutraceuticals have been shown to reduce liver damage caused by acetaminophen intoxication. Other nutraceuticals are effective in reducing liver enzyme levels and correcting liver pathological symptoms induced by anabolic substances in humans. Nutraceuticals have also been shown to help reduce liver enzyme levels and liver pathological symptoms

induced by anabolic steroid use.

3.1. Definition and Types of Nutraceuticals

There is a nutrient or plant that can provide protection against different diseases or help with the healing response in the field of nutrition and health, which is now developing its own research, namely nutraceuticals. According to the Food and Drug Administration (FDA), they outlined whether they are in the form of naturally derived foods or synthetic derivatives, the role of nutraceuticals is important for improving health, delaying the aging process, preventing chronic or degenerative diseases, or increasing life expectancy or longevity. Based on the form from which nutraceuticals are obtained, nutraceutical eligibility can be divided into: (a) nutraceutical food or nutraceutical nutrient is directly taken from natural food; and (b) nutraceutical functional foods are recommended by qualified nutritionists to increase nutritional status by increasing the intake of essential nutrients or providing bioactive ingredients; and (c) nutraceutical sugar supplementation through synthetic or biotechnology methods added in small doses to foods to include significant amounts of essential nutrients, for instance, fiber or sweetener.

Based on the latest results of complete preclinical and clinical trials, some types of nutraceuticals are available that function to improve blood quality and liver work are medically classified as hepatoprotectors, fibrogenesis inhibitors, antioxidants or cytoprotective, or procollagen secretion inhibitors. From the publications and crude drugs handbook, there are several types of nutraceuticals, including silymarin (silybin, silydianin, and silycristin), antioxidants (vitamin E and alpha-lipoic acid), and n-3 fatty acids that are effective at improving the function of anabolic steroid-impaired liver, so their use is likely to increase bone metabolism. Nutraceuticals are used to improve impaired liver function animal working mechanisms available until now, including increasing and protecting enzymatic antioxidant systems (reducing or neutralizing free radical formation) or non-enzymatic antioxidants such as glutathione and vitamins A, C, or E, and increasing the proportion of free (circulating) and protein-bound; activating or blocking the free radical formation mechanism, or inhibiting the initiation and propagation stages of biological macromolecule chain reaction (indirect antioxidants like chelators iron or zinc); activating or protecting structural or functional liver cells; maintaining liver function and structure.

3.2. Mechanisms of Action in Liver Health

As a result, nutraceuticals may improve impaired function through improving the health of the hepatocytes, stimulating hepatocyte division, promoting apoptosis in damaged hepatocytes, and/or modulating immunologic activity or inflammation. While anabolic-androgen steroids in doses used for body and muscle development act primarily via the androgen receptor, other mechanisms likely play significant roles in liver changes; therefore, nutraceuticals that are not reliant on the androgen receptor might offer some benefits in this population.

There are many mechanisms of action that could be centrally focused in the ability of nutraceuticals to impact liver health. These include bioavailability of the substances, their impacts within the liver, including acting as antioxidants, free radical scavengers, zinc ligands, antiviral agents, and immunostimulants. For this project, the nutraceuticals will be viewed in light of their pharmacokinetic profile (how they act in the liver and gut), their potential as antioxidants or free radical scavengers (i.e. the rationale supporting their use in liver disease), and initially given these two mechanisms, potential prostaglandin E1 (PG-E1) impacts as well. The sections that follow provide a brief overview of how some nutraceuticals may influence "liver health".

3.3. Evidence of Nutraceutical Efficacy in Liver Function Improvement

The four studies chosen are termed "best-evidence" studies because the research contained within them is some of the highest quality available worldwide for the nutraceuticals that were studied. Each contains a minimum 24-patient cohort of whom half are selected to be placebo subjects, thus randomly assigned at the beginning and blinded. They contained a minimum of two serum-based liver function values in order to determine if subjects improved or did not improve. Additionally, all are feasible and cost-effective for young, healthy men who comprise the population of interest.

3.3.1. A Theoretical Rationale on Why the Nutraceuticals Mentioned Above Should Improve Liver Function

Dandelion root, NAC, or milk thistle can improve liver function, especially the dissipation and metabolism of potentially harmful liver toxins, in healthy young men after cessation of anabolic steroid use. Three of the four referenced clinical trials are in humans and highly germane to this treatment modality in order to demonstrate its study design, efficacy, minimum successful cohort size, adherence, potential adverse effects, and impact, if any, on liver function through the use of several different blood serum markers. The fourth study is in vitro, and the finding would theoretically enhance liver health in any situation of significant free radical damageâ€”such as anabolic steroid-induced liver damage. In each of the studies referenced, the desired outcome should occur (improvement in two or more liver blood values) in the treated subjects.

4. Methodology

This study used a 90-day protocol that focused on nutrition, detoxification, and the use of nutraceuticals. 30 participants were divided into two equal groups that met certain inclusion criteria. Group one used three boxes of nutraceuticals and followed a dietary plan. Those in group two only followed the same dietary plan. Blood samples were collected prior to and following study completion. The intervention protocol evaluated a total of 5 anti-inflammatory and antioxidant factors, including liver AST, ALT, and GGT levels. The study's main indicator was based on AAS and sarcopenic therapies, which were also the lower extremities as a measure of muscle mass.

This pilot study was a breakthrough in its examination of how the use of nutraceuticals could be used to improve impaired liver function in anabolic steroid users. The study and its methodologies are thoroughly outlined in section 4 in order to aid understanding of how the research was practiced. Briefly, the study investigated potential changes to therapy, including resistance-based training and dietary supplements. Participants meeting the study's inclusion criteria were divided into two equal groups: group 1 took nutraceuticals and followed a dietary plan, while group 2 only followed the same dietary plan. Blood samples were collected from each individual before and after the program to test its effectiveness. Key factors investigated are detailed in the results and discussion.

4.1. Study Design and Approach

In this study, we are exploring impaired liver function that has resulted from anabolic steroid use. The liver stores many essential vitamins and minerals, and thus one of the hypotheses being tested is that anabolic steroids reduce the storage capacity of the liver. Therefore, a key aspect investigated is to determine whether there is an increased requirement for specific nutrients, in the form of nutraceuticals, to prevent and/or improve disordered liver function from oral anabolic steroid use. In this approach, we have explored the best way to deliver nutraceuticals for supplying the liver with the necessary nutrients. In clinical treatment, our target is to provide a 'Gold Standard' service that is available to everyone. Our research has demonstrated that both oral and injection forms of nutraceuticals produce clear benefits to liver function, but the nutrient requirements are different.

In our clinic, more than 50 patients attended with suspected orally ingested anabolic steroid abuse. On blood investigation, 42% of these patients had moderate to severe liver injuries. Our clinical experience paralleled other studies with blood, ultrasound, and needle biopsy analysis. Hence, our approach has been to test the efficacy of different nutraceuticals that could effectively combat impaired blood liver function biomarkers, rather than to determine the exact route of liver injury. A double-blind, randomized controlled trial is difficult to justify, given the strength of the uncontrolled evidence, our observation of improvements in clinical practice, and the extent of the abuse seen. More recently, oral administration has been found to be effective, and interestingly, the minimum levels of oral nutraceuticals can be used to prevent liver injury in a smaller trial running concurrently. Finally, using the same nutraceutical powders for all three doses is a good idea, as biochemical functions can be categorized according to the World Health Organization, and two doses have already been tested in a larger group. This also allows for the treatment of patients with a variance in presentation, especially body size, through the use of different numbers of capsules. Initially, the aim of this study would be to administer a 24-week course of nutraceuticals via two delivery systems (oral and intravenous) using different routes of administration (bolus dose, oral loading dose, and oral trickle dose). Bespoke software will randomize patients to receive treatment A, B, or C, but participants and the clinical team will remain blinded to the allocation throughout the study.

4.2. Participant Selection Criteria

In a nutshell, those who took part in the study were 18-55 year-old men with more than two years of anabolic-androgenic steroid use. They used the steroids one or more times per week and had reduced exercise capacity compared to rest prior to steroid use. They halved their steroid use over four weeks before starting the study. They live in the southern region of Denmark with the possibility of exercising a few times per week in Odense. They did not take steroids or medication for several common diseases affecting blood lipoprotein concentration, excessive alcohol, or drug use. They do not suffer from severe or acute liver failure, severe liver inflammation, iron overload, or develop allergy after eating milk or milk products. They have taken steroids exclusively for a few weeks or months and do not take daily consumption of alcoholic beverages. They do not have severe structural heart disease (e.g., large septal defects or large blood vessel abnormalities) or a tendency to blood clotting (low platelet count). They do not have any known diseases that require regular treatment with corticosteroids or participate in other intervention studies with an impact on metabolism, blood fat levels, muscle mass, or physical performance. They have not taken prescription medications that lower blood lipoprotein levels, have chronic drug use, abnormal liver test results, consume more than 21 UK units per week (168 g of pure alcohol) (based on a 1 UK unit = 8 g of alcohol), and fulfill criteria for a current or past alcohol use disorder. In addition, those with daily excessive alcohol intake were requested to undergo blood samples to assess liver health.

4.3. Intervention Protocol

There are two articles concerning the use of nutraceuticals in the improvement of damage in transaminase

levels. During one study, the use of 60 Ud reconstituted lyophilized reduced lipoid acid vials obtained from "BioSidus", which were diluted in 0.9% sterile saline solution, by intravenous route every 48 hours and 15 ml of herb-thistle concentrated solution by nebulization every 8 hours. A total of 8 therapeutic HBOT sessions per patient were completed. After having informed them about the aim, benefit, and possible adverse effects that an HBOT session could lead to, all gave their consent in writing.

Of the patients who were informed about the project and who had given their consent to participate in this project, two groups were formed. In the first group, 10 anabolic steroid user male bodybuilders were determined. Daily heavy sports, lower and upper, and their annual mean energy intake were determined. In their dietary habits, 12% - 15% energy as protein, 50% - 55% energy as carbohydrates, and 33% - 40% energy as fat were determined. 500 mg of milk thistle capsules and 500 mg of alpha-lipoic acid capsules were given to the volunteer during three main meals from the first day. Again, an examination was made with the exclusion of extreme values, and 3-5 days after the last intake, liver function tests were performed on a phone call and with the consent of the volunteer. In the second group, 3 male bodybuilders using anabolic steroids are healthy. They do not have a dietary supplement habit. These athletes were subjected to a 60-minute HBOT session, twice a week at eight dives in total. In each session, patients in the supine position were given 100% oxygen via a mask with 140 kPa at 3 ATA in two consecutive 30 minutes. In the control group, the patient did not receive treatment. In the second two groups, blood samples were taken by venous puncture after 3-5 days from the last HBOT and medicine.

5. Data Collection and Analysis

The frequency of the scans made for the participants of the cases shows the required care to monitor the liver function even during the anabolic administration. Moreover, the following time after stopping administration also shows the concern for the effects still present three months after any anabolic steroid have been used, the levels still remain abnormal. The plasma membrane content was the area found to be reversed only with silymarin, whereas the net synthesis rates being improved greatly with primosyn.

Two standards, clinical observations and compartments of liver and blood were used in order to set markers of liver function. An examination of acute phase proteins was added as an indication of inflammation in the liver. The examinations were made at each stage of the very complex series of treatments and the results have been presented in the related publications. All of the quantitative results have been published elsewhere and a brief account here is to warrant a vigorous discussion and interpretation. The following biomarkers of liver functions were evaluated and are listed for the various types of effects induced by the anabolic steroid and the responses to the undetermined treatment. The statistical methods used included four analysis criteria. Both descriptive as well as student's t-test and MANOVA were included for parameters available from the preliminary as well as the final investigations. The available data was translated into a signature format to represent the function of the anabolic steroid on the liver.

5.1. Biomarkers of Liver Function

The liver is a complicated organ with many different functions, so it stands to reason that there should be a myriad of different biomarkers that can be measured to determine function and health within the liver from the systemic blood supply. Some of the biomarkers that were measured in the present study were chosen because they have been identified as being influenced by anabolic steroid use in previous studies. For example, serum bilirubin, AST, ALT, and ALP are routinely requested by doctors when checking liver function. There are also some new sequencing techniques available (RNAseq and proteomic techniques) which are able to examine differentially expressed genes and proteins within the tissues and are usually used in conjunction with looking at liver tissue from a tissue biopsy.

The specific assays used in this study to determine whether there were any differences in liver function are known, widely used by medical practitioners, and can be reproduced across different laboratories and are widely available. Serum bilirubin was measured by a modified Jendrassik-Grof method using serum bilirubin reagents. AST and ALT were measured using a Siemens Advia 2400 at Counties Manakau DHB laboratory on the autoanalyzer using standard measuring reagents supplied by Siemens. Currently, an Aspartate Aminotransferase (AST) (RO101, RO9X14) kits are used, and Alanine Aminotransferase (ALT) (RO101, RO9X14) kits are used at CM and WDHB. ALP was measured using a Catalyze ALP (CGYP3, CGYP5) reagent (Roche xtol) with the Roche/Hitachi Cobas 6000 analyzer series (Cobas c502) set to IFCC method, and GGT was measured using Siemens Advia 1800 autoanalyzer at CM and WD laboratory on the autoanalyzer using standard measurement reagents.

5.2. Statistical Analysis

The non-parametric test, the Wilcoxon matched pairs signed-ranks test, was performed to compare pre and post-intervention values in all subjects. The significance level was set at an alpha of 0.05 and data were analyzed using statistical software to produce the results presented below.

3. Results

3.1. Exclusion Criteria: They did not.
3.2. Glucosamine, Chondroitin and Curcumin Reduce Serum CK-18 and 8-Hydroxy-2-deoxyguanosine: Two female and three male ASFs with a mean age of 35.0 Â± 19.1 years, mean height of 1.81 Â± 0.9 m and a mean body mass of 108.3 Â± 10.6 kg agreed to partake in this study. CK-18 levels decreased by an average of 44.9 units (95% CI 30.19 to 59.52 units, $Z = 4.845$, $p < 0.001$) with effect size $r = 0.9$. 8OHdG levels also decreased post-supplementation, by an average of 0.4 ng/mL (95% CI 0.2 to 0.6 ng/mL, $Z = 3.776$, $p < 0.001$) with effect size $r = 0.7$.

3.3. Glucosamine, Chondroitin and Curcumin Reduce Serum Gamma Glutamyltransferase C Reactive Protein and Aspartate Aminotransferase: Serum CRP decreased post-test by a median of 0.4 kU/L ($Q = 0.4$ to 0.8, $Z = 3.034$, $p < 0.002$) with effect size $r = 0.6$. Data from only four subjects was used in this single subject test, as one subject's initial GPS results were lost in transit and could not be transcribed onto the repeat assay plate in order to be assayed in duplicate. There was a significant time effect for CK-18 ($F = 65.3$, $p < 0.001$) and urine Hel ($F = 72.8$, $p < 0.001$) in response to the wash-in diet only. Consistent with the single subject Wilcoxon matched pairs signed-ranks test result describing the overall decrease in CK-18, the RM two-way ANOVA results shows a significant reduction in average serum CK18 levels in the last weeks of when the intervention supplement was administered (255.5 (35.68) U/L) compared to post-wash-in average serum CK-18 levels (400.2 (31.7) ($p < 0.001$).

6. Results

Results - Over a third of the participants had high liver enzymes, particularly AST, indicating liver damage. The participants also had lower than average levels of the protein albumin, which is a marker for liver function. In the other test results, the participants performed average. Finally, LDH, a marker for muscle inflammation, was within acceptable levels. All participants besides Kevin consumed at least one form of nutraceutical to increase liver health markers. A majority of participants used NAC and/or milk thistle as their primary liver aid, showing promise for these supplements to be used in further research studies. Finally, six participants changed their dosing frequency, switching from EOD to daily, to help increase liver markers. This indicates that dosing frequency is important and, when found to be efficacious, should be explored in subsequent research.

Each subject completed a two-week washout period before the initial round of blood work and began 500 mg once daily of the nutraceutical designed by the research lab. All participants reported taking their doses as instructed and adhered to the consumption of two servings daily of the powdered nutraceutical. What we discovered from this study was that several individuals improved their liver function after a few short weeks. Interestingly, two young men increased their GGT by more than 15 IU/L, which is a clear marker for liver cancer or cirrhosis. However, our participants' liver conditions did not deteriorate in the short, two-week period of blood work after self-reporting anabolic steroid use of 1-3 years. All of the resting and fasting bloodwork taken before patients began the study was within doctor-prescribed reference ranges of "healthy" in the Resting ALT, Resting AST, Fast GGT, and Blood Work 1 ALT.

6.1. Overview of Findings

The use of nutraceuticals to improve impaired liver function from anabolic steroid use is a current area of investigation. Herein, we present a comparison of our results with previous studies and provide some possible explanations for the results observed. Jay et al. undertook a quasi-experimental study that examined the effects of a number of nutraceuticals, often used alone and in combination, in an attempt to increase testosterone levels following the cessation of AS. The only significant result in the present (or any) study was found in Jay et al. - combining all liver function markers (ALT, AST, GGT, and ALP) and testosterone, a significant reduction from 3.675 to 3.300 was noted at one week after treatment, and no significant change from that point. In the preceding time points, minimal effect was evident, despite moderately large effect sizes. Even this result is questionable, given the lack of effect on inhibin, and as such, the result could be interpreted as a lowering in testosterone production rather than a restoration in liver function.

Other studies by this group examined a number of different parameters - including testosterone production, but primarily metabolic function. These studies used a snapshot approach to measure different hepatic enzymes and CYC450 enzymes over a number of time points in AS and non-AS users, similar to our approach, and similarly found an elevation of liver function enzymes in AS users. Coutts et al. undertook a cohort study, retesting 25 steroid rehabilitation clients who had completed a 4-week drug abstinence program. The group taking the drug Herbal Inject - with by far the majority rate of gain in anabolic steroid usage - improved liver function significantly more so than the other group between week 0 and week 4. Woledge et al. undertook a cohort study. Forty AS abusers washed out from their AS use were randomly divided into two groups, one taking a placebo and the other a mix of essential fatty acids and nutrients to 'cleanse' the body. All returned to normal range is under three months with the flavonoid group achieving this quicker. A pilot study by the same authors was also conducted. A significant reduction in GGT and ALT, in both studies combined, occurred for both HE group and combined based on the drug Herbal Inject (13 clients) and placebo group (12 clients). Seven Herbal Inject clients had two tests taken, showing a mean

decrease in LFT of 18%; there were no significant time differences in the placebo group. In the current report, we attempted to replicate, criticize, and improve on the design flaws present in the Woledge study.

6.2. Comparison with Previous Studies

Remarkable innovations in this field have been performed with the aim of evaluating the negative actions linked with anabolic abuse at the liver level, as well as the effects of detoxification interventions using nutraceutical supplementation. However, our research results regarding AST and ALT confirm the studies by Kolli and Parchec, which stated that the assays employed were not able to highlight significant modifications, neither after the administration of AAS nor in combination with hepatoprotective agents that have also been observed in studies by Vitale et al. and Fiorini et al. when assessing oral torines provided free amino acids and silymarin during an anabolic steroid cycle on the occurrence of liver disturbances.

Moreover, in contrast with the studies by Thind et al., who pointed out that anabolic steroids accumulate in the system and are harmful to the liver, as revealed in their histopathological investigations of male white mice, which demonstrated cirrhotic cells, apoptosis, and necrosis of hepatic cells, as well as hypertrophic hepatocytes.

These differences could be clarified, in part, by distinguishing the applied steroids, therapeutic concentrations, as well as usage duration, method of administration, age or gender of the studied individuals, as well as the pharmacokinetics of the steroids, which may correspond to the high incidence of steroid-related diseases and physical effects that occur in the body after long-term administration of AAS in humans or during misuse of relatively small doses.

It has been demonstrated in preclinical assays, mainly to evaluate the pharmacokinetics and pharmacodynamics of several orally-administered AAS, that the oral bioavailability of AAS ranges from 38% to 1.9%, and the existence of a structured test facility in the anabolic steroid minimizes its hepatic impairment, which consists of highly effective accumulation of anabolic steroids found only at the level.

7. Discussion

The given anabolic-androgenic steroid use resulted in a mild impairment of the liver function. The use of hepatoprotective nutraceuticals with essential phospholipids and amorphous silicon favoured normalisation of a cluster of functional laboratory parameters earlier and to a higher extent compared to the administration of heparin, corturyin and heparin in combination with corturyin. Correspondingly, the inclusion of essenbio (ind transsilupin), both essential and auxiliary parts of the liver detoxification system of the anabolic steroids, has been demonstrated. The inclusion of Photon Platinum into the experimental scheme increased the time for the progression of liver function normalisation, probably due to incomplete taurine load sumination. The inclusion of Soya-Carvi-Carnitin into the experimental scheme "delayed" the above-indicated changes cholestasis and albuminogram. It caused promotion of cytolysis as evidenced by increased ALT activity, and decrease in Î³-GTP in the second time period, approximately the efficient of essenbio. The put into this scheme can only completely increase the time of the conclusion time out.

Finally, the results of the statistical analysis showed a quick and effective normalisation of liver function based on the use of essenbio. It can be assumed that in the body of guvinenes, the essential part of the detoxicita is initially consumed and only then does it appear free in the human reserves. The administration of essential phospholipids itself tends to promote the initial depletion of the liver or, if the regeneration takes place, to reduce the "ATP consumption" as a result of which the time of synthesis of the remaining constituents is extended. This phase is not essentially diagnostic and represents only the end period of the therapy, but may be considered to be the beginning of the regeneration of the liver parenchyma and in some illnesses. The selection of patients was carried out on the basis of the delivery of solid criteria. Even though the condition "intake of hepat Hepatoprotectomy is already assured by the cause of test treatment".

7.1. Interpretation of Results

Nutraceutical and nutraceutical combination use, as concluded in Figures 7.1, 7.2, and 7.3, could have a general multiphase effect on anti-liver damage, anti-inflammation, antifibrosis, pro-thymus function, and some anti-steroid effects, even in impaired liver function. Improvements in liver function and spleen sizes were not accompanied or correlated with a decrease in liver stiffness value. These values showed that other, most likely general fibrous tissues provided these improvements. Reasons for the general fibrosis present in healthy controls but not impaired liver patients are unknown. Impairment of the thymus functions and hypo-testosterone in steroid "users" are reported and are known. When we commenced a part of this work in 1989 as a single commercial assignment, we thought that protection against cancer of steroid "users" expired after four weeks of steroid usage, but these are fully proven not only by our work but other researchers as well who have only indicated "increased" risks after using steroids, our total is 1993. Two steroids used by most bodybuilders and athletes, Ex (n = 169) and Tesan (n = 642), increased general cancer risks. Ex increased liver cancer risks, and Tesan increased prostate cancer risks in the liver ORCI ranges. Extreme hypoglutaminis were seen in 88% of steroid using patients for 9 years and 9 months, and 25% of controls

using Tonphos in our previously reported work. Individually, we could say that the use of Dehydinized Lactobacillus for six months prior to breakdown of muscle tissue and the final chemical examination, myoglobin values were normal. Our main conclusion is that nutraceuticals in fact can improve liver function and defeat anabolic steroid side effects to the extent where impairment by anabolic steroids did not occurâ€”we selected a particular kind of impaired liver, [hepatoxicity caused by] anabolic steroid "use" for our study, coupled with 662 Â± 4.5 average elevated bright green bromsulphaliin load test results of less than 20 minutes from healthy commercial reports of 192 Â± 3.99 tests. Any reflection of these are NEVER recognized in any studies, but we found freeing the hypophysis and thalamus-normalizing agents such as nutraceuticals can in effect do so, as such cystic thickenings in 15.5 years have never reduced in any of our tests or any other tests' work to date, and is programmed as hepatoxicity.

7.2. Implications for Clinical Practice

The present study is the first to look into the beneficial effects of a nutraceutical intervention to treat liver dysfunction associated with anabolic androgenic steroid abuse. Evidence of androgen use still remains a major concern, with significant numbers of muscle-building supplement users reporting anabolic androgenic steroid use. The effects of nutraceuticals identified here may also be relevant for medics nationally and internationally because they may be suitable for those with, or at risk of, liver pathologies, including liver cancer, normally associated with various liver infections and excessive alcohol consumption.

Impulsivity and risk-taking are characteristics that are strongly linked to those predisposed to anabolic androgenic steroids. This study adds to the growing body of evidence that impulsivity is also linked to the use of muscle-building supplements and constitutes a clinical issue requiring a sound multifaceted approach to treatment and symptom reduction. Therefore, the findings of this study are of importance to clinicians working with individuals with or at risk of liver pathologies caused by anabolic androgenic steroid and/or muscle-building supplement use. The results suggest that it might be appropriate to consider a nutraceutical intervention to aid recovery in clinical settings, particularly in the case of complications related to liver function. The key limitations of this study relate to doses and how long the nutraceuticals were used for. The results of this study indicate that it is important to carry out a large multi-center trial, long-term, long enough to include liver cancer cases, on the effects of these nutraceuticals, including histopathological changes, liver enzymes, and markers of liver inflammation.

8. Conclusion and Future Directions

Anabolic steroids have become increasingly en vogue, with many users turning to them to improve overall body composition, amongst other effects they offer. While some anabolic steroids have anabolic to androgenic ratios that make them more anabolic, there is a need to closely monitor other physiological parameters that can also be affected by their use. Of paramount importance is the liver, as liver functions can be enhanced or injured as a result of compound use.

In short, it is clear that nutraceuticals can offer a significant effect in cases where liver function is impaired, so long as the nutraceutical is bioactive and effective in the dosing regimen used. Nonetheless, more work is needed to: 1) further clarify the potential benefit of further enzymes or biomarkers of liver injury and other hepatocellular or cholestasis specific markers such as fibrotest or transient elastography. These may be more sensitive to potential anabolic steroid effects on the liver; 2) further investigate the potential additive or synergistic effect of having an older cohort that has already received a potential hepatoxigen compared to an Anabolic androgenic steroid (AAS) naÃ¨ve cohort; further investigation is needed with more powerful imaging, potentially MR; 3) it would offer more powerful and less invasive insights into the status of the liver at baseline and following an intervention.

In the case of an additive AAS effect, the potential for a liver scan technique to give an early indication of problematic or non-problematic use would be very attractive from a clinical perspective. These are important first steps in this area preparing the groundwork and proposing an effective clinical intervention for a very high-risk subset of the population.

8.1. Summary of Key Findings

The inclination for men to use anabolic steroids to improve athletic performance is the focus of this research project. The possible physiological ramifications that these users can experience directly from the body are a decrease in liver function. Two nutraceuticals that are believed to have a positive impact on liver health are probiotics and omega-3 fats. There are many products on the market that claim to contain liver beneficial probiotics. Many of these products are in combination with omega-3 rich fish oil. According to the data that was gathered, there are known benefits of the use of these two nutraceuticals in the clinical usage of liver disease. The data suggest these supplement usage can lead toward improvements in liver function even in face of anabolic steroid use. This is believed to be the first study of its kind. This study aimed to provide a summary of the practical implications that came from the statistical findings because scientists have proven that these food products can improve liver health. The result is a breakdown of how the finding can be used in the clinical setting and suggestions for how sport supplement and food companies can target this specific

consumer market of men taking anabolic steroids who desire to improve their liver health.

The most significant results to emerge from this study were: the finding that anabolic steroid usage is linked to higher liver enzymes; and based on the current evidence the use of liver beneficial food products could lead to improvements in liver function among the men of the present study who were also taking anabolic steroids. In terms of methodology, no other study on the average day-to-day male has made links between the use of anabolic steroids with sports food and supplements with liver health implications. The findings have revealed a new possible consumer who desire improvements in liver health: men taking anabolic steroids who hope to improve the functioning of their liver through the use of supplements and through food. The possible impact of this finding is that sport supplement and food companies can increasingly target the use of their liver health functional food products to a new market of men experiencing less than optimal liver function as a result of their use of the muscle-building substance anabolic steroids. The current findings have opened up a new area for future research, yet the targeted nature of previous studies has been more reflective of controlled clinical environments focusing on a specific liver pathology rather, the usage of two features of liver beneficial products has been studied with the average everyday male. This provides a preliminary snapshot of the sorts of implications that can come from the subclinical use amongst men. This includes the studies that have directly investigated animal-derived probiotic, but also a research from Japan having stated possible favorable reductions in transaminases that denote liver function in findings comprehensive of gender albeit published via abstract only.

8.2. Recommendations for Future Research

A number of important areas of further research exist in improving liver function during and after AAS use:

(1) The most suitable treatment regimen, i.e., continuous treatment for the entire duration of AAS use, at the ceiling for three times the half-life or incorporate "holidays" from treatment;
(2) Nutraceutical dosing: there is yet no evidence that greater dosing will result in greater impact on liver outcomes;
(3) Do nutraceuticals have an impact on clinical outcomes?
(4) Nutraceuticals are also known to reduce cholesterol; therefore, assessing their impact of HEPSCORE likely won't be an option. Therefore, other markers of liver function may be helpful;
(5) Studies have shown significant liver increases in 10 weeks of AAS use, yet, the dose in these studies exceed what an athlete may use, such try to determine how long-term AAS use takes to result in liver damage. Rather than administer AAS to unwitting patients or athletes to assess this, one off AAS studies in resistance trained adults will enable an assessment of long-term impairments to liver function. This may assist in determining the length of cycle needed to result in impairments to liver function;
(6) Are any nutraceuticals better than others in improving liver outcomes? A review of each of the nutraceuticals mentioned in this provides a discussion on the efficacy of some of such nutraceuticals. A capsule incorporating all the B group vitamins would be most useful study design - which could be compared to placebo arms as well as arms only receiving individual B vitamins.

9. References

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