AACT Herbal Dietary Supplement Section Abstracts May 2020

1. Severe and protracted cholestasis in 44 young men taking bodybuilding supplements: assessment of genetic, clinical and chemical risk factors. Stolz A, Navarro V, Hayashi PH, Fontana RJ, Barnhart HX, Gu J, Chalasani NP, Vega MM, Bonkovsky HL, Seeff LB, Serrano J, Avula B, Khan IA, Cirulli ET, Kleiner DE, Hoofnagle JH; DILIN Investigators.

Aliment Pharmacol Ther. 2019 May;49(9):1195-1204. doi: 10.1111/apt.15211. Epub 2019 Apr 1.

Comment in Aliment Pharmacol Ther. 2019 Jun;49(12):1530.

BACKGROUND: Bodybuilding supplements can cause a profound cholestatic syndrome. AIM: To describe the drug-Induced liver injury network's experience with liver injury due to bodybuilding supplements. METHODS: Liver injury pattern, severity and outcomes, potential genetic associations, and exposure to anabolic steroids by product analysis were analysed in prospectively enrolled subjects with bodybuilding supplement-induced liver injury with causality scores of probable or higher. RESULTS: Forty-four males (mean age 33 years) developed liver injury with a median latency of 73 days. Forty-one per cent presented with hepatocellular pattern of liver injury as defined by the R > 5 ([Fold elevation of ALT] ÷ [Fold elevation of Alk Phos] (mean, range = 6.4, 0.5-31.4, n = 42) despite all presenting with clinical features of cholestatic liver injury (100% with jaundice and 84% with pruritus). Liver biopsy (59% of subjects) demonstrated a mild hepatitis and profound cholestasis in most without bile duct injury, loss or fibrosis. Seventy-one per cent were hospitalised, and none died or required liver transplantation. In some, chemical analysis revealed anabolic steroid controlled substances not listed on the label. No enrichment of genetic variants associated with cholestatic syndromes was found, although mutations in ABCB11 (present in up to 20%) were significantly different than in ethnically matched controls. CONCLUSIONS: Patients with bodybuilding supplements liver injury uniformly presented with cholestatic injury, which slowly resolved. The ingested products often contained anabolic steroids not identified on the label, and no enrichment in genetic variants was found, indicating a need for additional studies.

DOI: 10.1111/apt.15211
PMCID: PMC6682544
PMID: 30934130 [Indexed for MEDLINE]

2. Iberogast-Induced Acute Liver Failure-Reexposure and In Vitro Assay Support Causality. Gerhardt F, Benesic A, Tillmann HL, Rademacher S, Wittekind C, Gerbes AL, Henker R, Berg T, Maidhof HP, Trauer H, Wiegand J.

Am J Gastroenterol. 2019 Aug;114(8):1358-1359. doi: 10.14309/ajg.0000000000000300.

DOI: 10.14309/ajg.0000000000000300
PMID: 31246695 [Indexed for MEDLINE]

3. Acute Liver Failure Caused by Use of Fat Burner: A Case Report. Ferreira GSA, Watanabe ALC, Trevizoli NC, Jorge FMF, Diaz LGG, Couto CF, Lima LV, Raupp DRL, Araujo BE.

Transplant Proc. 2020 Mar 16. pii: S0041-1345(19)31709-9. doi: 10.1016/j.transproceed.2020.01.072. [Epub ahead of print]

Acute liver failure is a rare condition consisting of abrupt and extensive hepatocyte injury, leading to significant liver dysfunction associated with a high mortality. Liver transplantation is the most effective treatment in severe cases. The most common cause of acute liver failure in Western countries is drug-induced liver injury caused by prescription drugs and herbal and dietary supplements. Thermogenics, or

fat burners, are a category of dietary supplements that claim to increase the resting metabolic rate, leading to weight loss. There are previous reports of acute liver failure associated with specific thermogenic formulations. We report the case of a 36-year-old male patient who developed jaundice 7 days after he started taking a thermogenic dietary supplement (Thermo Gun), with progressive deterioration of hepatic function and development of hepatic encephalopathy 19 days after the beginning of the symptoms. He had a Model for End-Stage Liver Disease score of 38 and fulfilled 4 of the King's College Criteria for poor prognosis in patients with acute liver failure. He underwent liver transplantation, receiving a graft from a cadaveric donor, and is alive with good liver graft function 2 years after the transplant. No possible causes for acute liver injury were identified other than the use of the supplement, which contained N-acetyl-L-tyrosine; 1,3,7-trimenthylxanthine; white willow; and 1-hydroxypholedrine. We found no previous reports in the literature of acute liver failure associated with those particular substances. This manuscript is compliant with the Helsinki Congress and the Istanbul Declaration.

DOI: 10.1016/j.transproceed.2020.01.072
PMID: 32192741

4. Not All Herbals are Benign: A Case of Hydroxycut-induced Acute Liver Injury. Khetpal N, Mandzhieva B, Shahid S, Khetpal A, Jain AG.

Cureus. 2020 Feb 4;12(2):e6870. doi: 10.7759/cureus.6870.

Dietary supplements do not need prior Food and Drug Administration (FDA) approval before they are sold to the public per Dietary Supplement Health and Education Act of 1994 (DSHEA). Reporting serious dietary supplement related adverse reactions is voluntary. Hydroxycut is a brand of dietary supplements that are marketed as a popular weight loss product that contains multiple herbal constituents. Due to its potential hepatotoxic effects, FDA issued a warning in 2009 and recommended that consumers discontinue use of Hydroxycut. Hydroxycut was recalled from the market but a reformulated herbal mix is now available again. We are presenting a case of acute liver injury associated with Hydroxycut. The prominent pattern of liver injury is severe hepatocellular injury with the striking elevation of the aminotransferase levels and minimal abnormalities in alkaline phosphatase levels. It can sometimes cause severe hepatocellular necrosis.

DOI: 10.7759/cureus.6870
PMCID: PMC7057255
PMID: 32190438

5. Glutamine powder-induced hepatotoxicity: it is time to understand the side effects of sports nutritional supplements. Hatami B, Saffaei A, Jamali F, Abbasinazari M.

Gastroenterol Hepatol Bed Bench. 2020 Winter;13(1):86-89.

Glutamine has been considered as a dietary supplement with a non-essential amino acid structure. Some studies have found that liver failure may be associated with a high plasma glutamine level. Consumption of this product may be linked to potential adverse effects. This report describes the first case of glutamine-induced hepatotoxicity. A 35-year-old female athlete with severe abdominal pain and scleral icterus was referred to the hospital. She had been taking glutamine powder for the past three weeks. Impaired liver function test and imaging evaluation suggested hepatotoxicity. Glutamine consumption was discontinued and the patient was closely monitored. Finally, after two weeks, the patient recovered successfully. This novel case was the first report regarding glutamine-induced hepatotoxicity. Health care providers must know that consumption of dietary supplements such as glutamine may be associated with serious side effects. Liver damage is a possible side effect of glutamine. Hence it is necessary to consider hepatotoxicity as an adverse reaction in case of glutamine supplement consumption.

PMCID: PMC7069532

PMID: 32190229

6. Drug induced hepatitis mimicking Wilson's disease secondary to the use of complex naturopathic regimens: a case report. Pitre T, Mah J, Vertes J, Rebello R, Zhu J.

BMC Gastroenterol. 2019 Nov 27;19(1):199. doi: 10.1186/s12876-019-1122-x.

BACKGROUND: Drug induced liver injury (DILI) is an important cause of acute liver injury and accounts for approximately 10% of all cases of acute hepatitis. Both prescription and natural health products (NHPs) have been implicated in DILI. There is a dearth of studies on NHPs induced liver injury. CASE PRESENTATION: A previously healthy 37-year-old female presented with subacute hepatitis, in the context of a previous admission to a separate institution, months prior for undiagnosed acute hepatitis. Importantly, she had disclosed taking complex regiments of natural health products (NHPs) for months. Her only other medication was rivaroxaban for her homozygous Factor V Leiden deficiency. She had an extensive work up for causes of acute and unresolving hepatitis. She discontinued several but not all of her NHPs after her initial presentation for acute hepatitis at the first institution and continued taking NHPs until shortly after admission to our institution. The predominant pathological features were that of drug induced liver injury, although an abnormal amount of copper was noted in the core liver biopsies. However, Wilson's disease was ruled out with normal serum ceruloplasmin and 24-urine copper. After 2 months of stopping all the NHPs, our patient improved significantly since discharge, although there is evidence of fibrosis on ultrasound at last available follow up. CONCLUSION: NHPs are a well-established but poorly understood etiology of DILI. The situation is exacerbated by the unregulated and unpredictable nature of many of the potential hepatotoxic effects of these agents, especially in cases of multiple potential toxic agents. This highlights the importance of acquiring a clear history of all medications regardless of prescription status.

DOI: 10.1186/s12876-019-1122-x
PMCID: PMC6882359
PMID: 31775657 [Indexed for MEDLINE]

7. Regulatory landscape of dietary supplements and herbal medicines from a global perspective. Thakkar S, Anklam E, Xu A, Ulberth F, Li J, Li B, Hugas M, Sarma N, Crerar S, Swift S, Hakamatsuka T, Curtui V, Yan W, Geng X, Slikker W, Tong W.

Regul Toxicol Pharmacol. 2020 Apr 16;114:104647. doi: 10.1016/j.yrtph.2020.104647. [Epub ahead of print]

The number of Individuals that use dietary supplements and herbal medicine products are continuous to increase in many countries. The context of usage of a dietary supplement varies widely from country-to-country; in some countries supplement use is just limited to general health and well-being while others permit use for medicinal purposes. To date, there is little consensus from country to country on the scope, requirements, definition, or even the
terminology in which dietary supplement and herbal medicines categories could be classified. Transparent science-based quality standards for the ingredients across these regulatory frameworks/definitions becomes even more important given the international supply chain. Meanwhile, there has been a rapid advancement in emerging technologies and data science applied to the field. This review was conceived at the Global Summit on Regulatory Sciences that took place in Beijing on September 2018 (GSRS2018) which is organized by Global Coalition for Regulatory Science Research (GCRSR) that consists of the global regulatory agencies from over ten countries including the European Union. This review summarizes a significant portion of discussions relating to a longitudinal comparison of the status for dietary supplements and herbal medicines among the different national jurisdictions and to the extent of how new tools and methodologies can improve the regulatory application.

DOI: 10.1016/j.yrtph.2020.104647

PMID: 32305367

8. Why we need to pay attention to toxicity associated with herbal medicines. Enioutina EY, Job KM, Sherwin CMT.

Br J Clin Pharmacol. 2020 May 13. doi: 10.1111/bcp.14340. Online ahead of print.

DOI: 10.1111/bcp.14340
PMID: 32406066

9. "Natural" is not synonymous with "Safe": Toxicity of natural products alone and in combination with pharmaceutical agents. Gaston TE, Mendrick DL, Paine MF, Roe AL, Yeung CK.

Regul Toxicol Pharmacol. 2020 Jun;113:104642. doi: 10.1016/j.yrtph.2020.104642. Epub 2020 Mar 18.

During the 25 years since the US Congress passed the Dietary Supplement Health and Education Act (DSHEA), the law that transformed the US Food and Drug Administration's (FDA's) authority to regulate dietary supplements, the dietary supplement market has grown exponentially. Retail sales of herbal products, a subcategory of dietary supplements, have increased 83% from 2008 to 2018 ($4.8 to $8.8 billion USD). Although consumers often equate "natural" with "safe", it is well recognized by scientists that constituents in these natural products (NPs) can result in toxicity. Additionally, when NPs are co-consumed with pharmaceutical agents, the precipitant NP can alter drug disposition and drug delivery, thereby enhancing or reducing the therapeutic effect of the object drug(s). With the widespread use of NPs, these effects can be underappreciated. We present a summary of a symposium presented at the Annual Meeting of the Society of Toxicology 2019 (12 March 2019) that discussed potential toxicities of NPs alone and in combination with drugs.

DOI: 10.1016/j.yrtph.2020.104642
PMCID: PMC7211136 [Available on 2021-06-01]
PMID: 32197968

10. Adulteration of selected dietary supplements and their detection methods. Muschietti L, Redko F, Ulloa J

Drug Test Anal. 2020 Apr 19. doi: 10.1002/dta.2806. [Epub ahead of print]

At present, there is a growing trend towards the intentional adulteration of dietary supplements with synthetic pharmaceuticals, which represents an alarming emerging risk to consumers and a serious problem for regulatory agencies. An amazing array of synthetic drugs and their analogues have been reported as adulterants in dietary supplements. Mainly, the presence of analogues represents a serious health risk as their efficacy and toxic effects have not been clinically assessed and may result in unpredictable adverse effects. The purpose of this review is to provide an overview, over the period 2009-2019, of the most frequently reported adulterants in dietary supplements for the treatment of erectile dysfunction, obesity/overweight, diabetes mellitus, and hypertension and the analytical methods used for their detection.

DOI: 10.1002/dta.2806
PMID: 32307880

11. Multi-Criteria Decision Analysis Model for Assessing the Risk from Multi-Ingredient Dietary Supplements (MIDS). Oketch-Rabah HA, Hardy ML, Patton AP, Chung M, Sarma ND, Yoe C, Ayyadurai VAS, Fox MA, Jordan SA, Mwamburi M, Mould DR, Osterberg RE, Hilmas C, Tiwari R, Valerio L Jr, Jones D, Deuster PA, Giancaspro GI.

J Diet Suppl. 2020 Apr 22:1-23. doi: 10.1080/19390211.2020.1741485. [Epub ahead of print]

Military personnel use dietary supplements (DS) for performance enhancement, bodybuilding, weight loss, and to maintain health. Adverse events, including cardiovascular (CV) effects, have been reported in military personnel taking supplements. Previous research determined that ingestion of multi-ingredient dietary supplements (MIDS), can lead to signals of safety concerns. Therefore, to assess the safety of MIDS, the Department of Defense via a contractor explored the development of a model-based risk assessment tool. We present a strategy and preliminary novel multi-criteria decision analysis (MCDA)-based tool for assessing the risk of adverse CV effects from MIDS. The tool integrates toxicology and other relevant data available on MIDS; likelihood of exposure, and biologic plausibility that could contribute to specific aspects of risk. Inputs for the model are values of four measures assigned based on the available evidence supplemented with the opinion of experts in toxicology, modeling, risk assessment etc. Measures were weighted based on the experts' assessment of measures' relative importance. Finally, all data for the four measures were integrated to provide a risk potential of 0 (low risk) to 100 (high risk) that defines the relative risk of a MIDS to cause adverse reactions.We conclude that the best available evidence must be supplemented with the opinion of experts in medicine, toxicology and pharmacology. Model-based approaches are useful to inform risk assessment in the absence of data. This MCDA model provides a foundation for refinement and validation of accuracy of the model predictions as new evidence becomes available.

DOI: 10.1080/19390211.2020.1741485
PMID: 32319852

12. Organic anion transporter 1 and 3 contribute to traditional Chinese medicine-induced nephrotoxicity. Shen QQ, Wang JJ, Roy D, Sun LX, Jiang ZZ, Zhang LY, Huang X.

Chin J Nat Med. 2020 Mar;18(3):196-205. doi: 10.1016/S1875-5364(20)30021-2.

With the internationally growing popularity of traditional Chinese medicine (TCM), TCM-induced nephropathy has attracted public attention. Minimizing this toxicity is an important issue for future research. Typical nephrotoxic TCM drugs such as Aristolochic acid, Tripterygium wilfordii Hook. f, Rheum officinale Baill, and cinnabar mainly damage renal proximal tubules or cause interstitial nephritis. Transporters in renal proximal tubule are believed to be critical in the disposition of xenobiotics. In this review, we provide information on the alteration of renal transporters by nephrotoxic TCMs, which may be helpful for understanding the nephrotoxic mechanism of TCMs and reducing adverse effects. Studies have proven that when administering nephrotoxic TCMs, the expression or function of renal transporters is altered, especially organic anion transporter 1 and 3. The alteration of these transporters may enhance the accumulation of toxic drugs or the dysfunction of endogenous toxins and subsequently sensitize the kidney to injury. Transporters-related drug combination and clinical biomarkers supervision to avoid the risk of future toxicity are proposed.

DOI: 10.1016/S1875-5364(20)30021-2
PMID: 32245589 [Indexed for MEDLINE]

13. A case of acute kidney injury secondary to black cherry concentrate in a patient with chronic kidney disease secondary to type 2 diabetes mellitus. Matout M, Halme AS, Wiseman J.

CEN Case Rep. 2019 Aug;8(3):212-215. doi: 10.1007/s13730-019-00396-2. Epub 2019 Apr 8.

There are many herbal products which are accessible to patients, and they may provide with many health benefits. Nevertheless, some of these supplements can lead to significant morbidity as they can also have important side effects and impact patient's organ systems. In this case report, we present a patient with chronic kidney disease secondary to type II diabetes mellitus who develops acute kidney injury and metabolic disturbances secondary to consuming black cherry concentrate as a mean to self-manage his

gout flare. The most likely mechanism of injury was cyclooxygenase inhibition by anthocyanins, molecular compounds found in cherries that have a similar mechanism of action to nonsteroidal anti-inflammatory medications. Patient's kidney injury and metabolic disturbances improved after the discontinuation of black cherry concentrate. This is the second case report that presents a correlation between consumption of cherry concentrate in a patient with chronic kidney disease and acute kidney injury.

DOI: 10.1007/s13730-019-00396-2
PMCID: PMC6620216
PMID: 30963415 [Indexed for MEDLINE]

14. Ginkgo biloba-related hyponatraemia: a reminder that herbal supplements are not benign. Hamilton N, Alamri Y, Allan C, Doogue M.

Intern Med J. 2019 Nov;49(11):1458-1460. doi: 10.1111/imj.14625.

The Ginkgo biloba tree has been used in Chinese medicine for several hundred years. Over the past two decades, it has been increasingly used as a herbal supplement due to purported beneficial effect against neurovasculardamage. Although an extract from Ginkgo biloba (EGb-761) was patented in 1964, it has not been developed into a regulated medicine. Case reports have identified spontaneous haemorrhage as a potential adverse drug reaction (ADR) with Ginkgo biloba supplements, although significant electrolytes disturbances have not been reported. We describe two cases of hyponatraemia following use of Ginkgo biloba supplements, with a Naranjo classification of ‘probable’ for both. Hyponatraemia attributed to Ginkgo biloba has not been described in the published medical literature; however, 22 cases have been submitted to the World Health Organization’s self-reporting ADR database.

DOI: 10.1111/imj.14625
PMID: 31713332 [Indexed for MEDLINE]

15. [Red yeast rice as the presumed cause of acute kidney and liver failure]. [Article in Danish] Peterslund P, Christensen HD, Urbahnke J, Cappeln AV.

Ugeskr Laeger. 2019 Sep 30;181(40). pii: V02190107.

Alternative medicine and food supplements are getting increasingly popular. The regulation of these remedies is lenient compared to the regulation of traditional medicine. Hence knowledge about adverse effects from alternative medicine and food supplements is scarce. This is a case report of a 65-year-old healthy male who had a daily intake of 315 mg of red yeast rice and was admitted to hospital with acute renal deficiency, hepatitis and rhabdomyolysis. This case report
underlines the potential problems with these remedies, namely a lack of knowledge of adverse effects and a lack of control with the production.

PMID: 31566178 [Indexed for MEDLINE]

16. Paradoxical Hypercholesterolemia in an Otherwise Healthy Adult Man. Mcpherson PA.

Lab Med. 2020 Mar 10;51(2):217-220. doi: 10.1093/labmed/lmz036.

Hypercholesterolemia is characterized by serum cholesterol levels greater than 5 mmol per L. However, the distribution of cholesterol among lipoprotein classes has a significant bearing on diagnosis: high-low-density lipoprotein (LDL) cholesterol suggests familial hypercholesterolemia, whereas high-high-density lipoprotein (HDL) cholesterol is associated with hyperalphalipoproteinemia. On routine screening, a 23-year-old man presented with a total cholesterol level of 7.6 mmol per L but was subsequently found to have an HDL cholesterol level of 5.6 mmol per L. The clinical picture was confounded by his use of red

yeast rice extract, a popular health supplement with hypolipidemic effects. In this case individual, the use of red yeast rice extract caused a hyperlipidemic state, ostensibly through downregulation of cholesteryl ester transfer protein. This case emphasizes the extended role of laboratory medicine in complex cases of hyperlipidemia.

DOI: 10.1093/labmed/lmz036
PMID: 31414129 [Indexed for MEDLINE]

17. Eucalyptus oil poisoning: two case reports. Ittyachen AM, George GR, Radhakrishnan M, Joy Y.

J Med Case Rep. 2019 Nov 4;13(1):326. doi: 10.1186/s13256-019-2260-z.

BACKGROUND: Eucalyptus oil poisoning is rare in adults but is not that uncommon in children. The common side effects in children include depression in the level of consciousness, ataxia, seizures, and vomiting. Unlike in children, seizures are unusual in adult patients with eucalyptus oil poisoning. We report the cases of two patients with eucalyptus oil poisoning, both adults who unintentionally took eucalyptus oil and presented to the emergency room of our institution with seizures. CASE PRESENTATION: Two adult Indian men who unintentionally consumed eucalyptus oil presented to the emergency room of our institution with seizures. In both patients, arterial blood gas analysis showed the presence of severe metabolic acidosis. Both the patients were managed in the intensive care unit and received standard supportive care. Metabolic acidosis was corrected with intravenous bicarbonate infusion. They were successfully discharged on the fourth day. CONCLUSIONS: All physicians should be aware of the toxic effects of eucalyptus oil, which is used often in daily life in India. Supportive care in an intensive care unit, including rapid correction of metabolic acidosis and adequate maintenance of hemodynamic parameters, will lead to a rapid recovery. Warning labels should be made mandatory on all products that contain eucalyptus oil.

DOI: 10.1186/s13256-019-2260-z
PMCID: PMC6827225
PMID: 31685016 [Indexed for MEDLINE]

18. Risk assessment of herbal supplements containing ingredients that are genotoxic and carcinogenic. Prinsloo G, Steffens F, Vervoort J, Rietjens IMCM.

Crit Rev Toxicol. 2019 Aug;49(7):567-579. doi: 10.1080/10408444.2019.1686456. Epub 2019 Dec 19.

Botanicals and botanical preparations including plant food supplements as well as medicinal herbal supplements can contain possible beneficial health compounds, but also ingredients of concern. Compounds that are both genotoxic and carcinogenic have been found in herbal supplements and may raise a safety concern. Genotoxic carcinogens that can be present in botanicals and botanical preprations include especially pyrrolizidine alkaloids (PAs), aristolochic acids (AAs) and alkenylbenzenes (ABs). The present manuscript provides an overview of the levels of these compounds reported to date to be present in herbal supplements with an associated risk assessment. Exposure was estimated based on levels of PAs, AAs and ABs in individual supplements and their proposed uses. In addition a probabilistic exposure assessment was performed based on the distribution of the level of the compounds of concern in the food supplements and of the recommended uses, resulting in 5th to 95th percentile consumer exposure values. To evaluate the risk of these exposures, the margin of exposure (MOE) approach for lifetime exposure was used. To correct exposure estimates for shorter than lifetime exposure, Haber's rule as a first tier approach was applied. It is concluded that the proposed uses and use levels as well as the presence of AAs, ABs and PAs in food supplements should be carefully monitored to manage potential consumer risks. More information on estimated daily intake resulting from supplement use, as well as consequences of concomitant exposure will further improve the risk evaluation of products containing these compounds of concern.

DOI: 10.1080/10408444.2019.1686456
PMID: 31854211 [Indexed for MEDLINE]

19. Testosterone Imposters: An Analysis of Popular Online Testosterone Boosting Supplements.
Balasubramanian A, Thirumavalavan N, Srivatsav A, Yu J(1), Lipshultz LI, Pastuszak AW.

J Sex Med. 2019 Feb;16(2):203-212. doi: 10.1016/j.jsxm.2018.12.008.

Comment in J Urol. 2019 Oct;202(4):645.

INTRODUCTION: Testosterone-boosting supplements (T-Boosters) are prominently featured on Amazon.com, with numerous dedicated pages and claims that they "naturally" increase testosterone levels. AIM: To evaluate the highest rated and frequently reviewed T-Boosters on Amazon.com to facilitate patient counseling regarding marketing myths, T-Booster formulations, and evidence for efficacy and safety. METHODS: The Amazon marketplace was queried using the key words "testosterone" + "booster," with default search settings and ranking items based on relevance. The top 5 T-Boosters identified on July 22, 2018, were reviewed based on price, ratings, reviews, manufacturer details, and ingredients. Consumer reviews were categorized using core themes in the Androgen Deficiency in the Aging Male (ADAM) questionnaire as a proxy to understand T-Booster efficacy and reanalyzed after filtration of untrustworthy comments using ReviewMeta.com, a proprietary Amazon customer review analysis software. MAIN OUTCOME MEASURES: Quantitative and qualitative evaluation of T-Boosters on Amazon.com was performed. RESULTS: The top 5 T-Boosters had an average ± SD of 2,761 ± 5,112 reviews and a rating of 4.56 ± 0.25 stars. 19 unique ingredients were identified across these T-Boosters, and literature review revealed 191 studies involving the 10 most common ingredients, of which 19% involved human subjects, 53% animal models, 15% in vitro studies, and 12% case reports or review articles. Among 37 human studies, 30% observed an increase in T levels, 3% a decrease, 46% no effect, and 22% were indeterminate. Analysis of top customer reviews from the first 2 pages of reviews for each supplement revealed differences in the ADAM score before and after ReviewMeta.com filtration. After filtration, there was a 91% decrease in users reporting increased libido, a 59% decrease in reports of increased energy, a 93% decrease in reports of improved strength/endurance, a 60% decrease in reports of improved erections, an elimination of reports of improved work performance, a 67% decrease in reports of improved sleep, and an 89% decrease in reports of improved sports ability. CLINICAL IMPLICATIONS: Our study can serve as a guide for providers to counsel patients about the efficacy of popular online T-Boosters as well as the prevalence of disingenuous reviews associated with these products on online marketplaces like Amazon.com. STRENGTHS & LIMITATIONS: Strengths include the novel approach to assess consumers' perceptions and satisfaction of T-Boosters, as well as summary information that clinicians can provide patients. Limitations include selection bias, a small number of supplements analyzed, and the proprietary nature of the Amazon review analysis software. CONCLUSION: T-Boosters are easily available online. Our investigation revealed that limited human studies have evaluated T-Boosters, resulting in no definitive findings of efficacy. In the absence of additional human studies, patients should be cautioned before considering T-Boosters, given the availability of highly effective therapies approved by the Food and Drug Administration.

DOI: 10.1016/j.jsxm.2018.12.008
PMCID: PMC6407704
PMID: 30770069 [Indexed for MEDLINE]

20. Natural product-derived phytochemicals as potential agents against coronaviruses: A review.
Mani JS, Johnson JB, Steel JC, Broszczak DA, Neilsen PM, Walsh KB, Naiker M.

Virus Res. 2020 Apr 30;284:197989. doi: 10.1016/j.virusres.2020.197989. Online ahead of print.

Coronaviruses are responsible for a growing economic, social and mortality burden, as the causative agent of diseases such as severe acute respiratory syndrome (SARS), Middle East respiratory syndrome

(MERS), avian infectious bronchitis virus (IBV) and COVID-19. However, there is a lack of effective antiviral agents for many coronavirus strains. Naturally existing compounds provide a wealth of chemical diversity, including antiviral activity, and thus may have utility as therapeutic agents against coronaviral infections. The PubMed database was searched for papers including the keywords coronavirus, SARS or MERS, as well as traditional medicine, herbal, remedy or plants, with 55 primary research articles identified. The overwhelming majority of publications focussed on polar compounds. Compounds that show promise for the inhibition of coronavirus in humans include scutellarein, silvestrol, tryptanthrin, saikosaponin B2, quercetin, myricetin, caffeic acid, psoralidin, isobavachalcone, and lectins such as griffithsin. Other compounds such as lycorine may be suitable if a therapeutic level of antiviral activity can be achieved without exceeding toxic plasma concentrations. It was noted that the most promising small molecules identified as coronavirus inhibitors contained a conjugated fused ring structure with the majority being classified as being polyphenols.

DOI: 10.1016/j.virusres.2020.197989
PMCID: PMC7190535
PMID: 32360300

21. Potential inhibitors of coronavirus 3-chymotrypsin-like protease (3CL(pro)): an in silico screening of alkaloids and terpenoids from African medicinal plants. Gyebi GA, Ogunro OB, Adegunloye AP, Ogunyemi OM, Afolabi SO.

J Biomol Struct Dyn. 2020 May 18:1-13. doi: 10.1080/07391102.2020.1764868. Online ahead of print.

The novel coronavirus disease 2019 (COVID-19) caused by SARS-COV-2 has raised myriad of global concerns. There is currently no FDA approved antiviral strategy to alleviate the disease burden. The conserved 3-chymotrypsin-like protease (3CLpro), which controls coronavirus replication is a promising drug target for combating the coronavirus infection. This study screens some African plants derived alkaloids and terpenoids as potential inhibitors of coronavirus 3CLpro using in silico approach. Bioactive alkaloids (62) and terpenoids (100) of plants native to Africa were docked to the 3CLpro of the novel SARS-CoV-2. The top twenty alkaloids and terpenoids with high binding affinities to the SARS-CoV-2 3CLpro were further docked to the 3CLpro of SARS-CoV and MERS-CoV. The docking scores were compared with 3CLpro-referenced inhibitors (Lopinavir and Ritonavir). The top docked compounds were further subjected to ADEM/Tox and Lipinski filtering analyses for drug-likeness prediction analysis. This ligand-protein interaction study revealed that more than half of the top twenty alkaloids and terpenoids interacted favourably with the coronaviruses 3CLpro, and had binding affinities that surpassed that of lopinavir and ritonavir. Also, a highly defined hit-list of seven compounds (10-Hydroxyusambarensine, Cryptoquindoline, 6-Oxoisoiguesterin, 22-Hydroxyhopan-3-one, Cryptospirolepine, Isoiguesterin and 20-Epibryonolic acid) were identified. Furthermore, four non-toxic, druggable plant derived alkaloids (10-Hydroxyusambarensine, and Cryptoquindoline) and terpenoids (6-Oxoisoiguesterin and 22 Hydroxyhopan-3-one), that bind to the receptor-binding site and catalytic dyad of SARS-CoV-2 3CLpro were identified from the predictive ADME/tox and Lipinski filter analysis. However, further experimental analyses are required for developing these possible leads into natural anti-COVID-19 therapeutic agents for combating the pandemic.

DOI: 10.1080/07391102.2020.1764868
PMID: 32367767

22. Cannabidiol as prophylaxis for SARS-CoV-2 and COVID-19? Unfounded claims versus potential risks of medications during the pandemic. Brown JD.

Res Social Adm Pharm. 2020 Mar 31. pii: S1551-7411(20)30300-4. doi: 10.1016/j.sapharm.2020.03.020. [Epub ahead of print]

DOI: 10.1016/j.sapharm.2020.03.020

PMID: 32273254