We report Apetamin (cyproheptadine lysine and vitamin syrup), a non-US Food and Drug Administration-approved weight gain supplement, causing drug-induced autoimmune hepatitis. A 40-year-old previously healthy woman presented with fatigue, right-sided abdominal discomfort, and jaundice 6 weeks after starting Apetamin, which she learned from social media for figure augmentation. Labs were significant for elevated transaminases, positive smooth muscle antibody, and increased immunoglobulins. Biopsy indicated drug-induced autoimmune hepatitis. Symptoms improved with prednisone, azathioprine, and stopping Apetamin which contains cyproheptadine, a known hepatotoxin. The case reveals the influence of social media and its impact on health and the importance of a complete drug history.

INTRODUCTION

Drug-induced autoimmune hepatitis (DIAIH) is a rare hepatotoxicity. It is characterized by the presence of autoantibodies (antinuclear, antismooth muscle, or anti-liver-kidney-microsomal antibodies), raised immunoglobulins, and a hepatocellular pattern of serum enzyme elevations. Liver biopsy has features of autoimmune hepatitis (AIH), including interface hepatitis with a lymphocytic or lymphoplasmacytic infiltrate and hepatic rosette formation. Symptoms can be insidious and may include fatigue, nausea, rash, arthralgias, abdominal discomfort, jaundice, and pruritis. DIAIH responds to corticosteroids and immune suppressors. Hepatitis resolves with the withdrawal of the inciting drug. Associated drugs include antimicrobials (nitrofurantoin and minocycline), interferon, infliximab, and statins. We report a rare case of Apetamin (cyproheptadine, lysine, and vitamin syrup) causing DIAIH. The supplement, manufactured by TIL Healthcare PVT (Chennai, India), a pharmaceutical company based in India, is composed of active ingredient cyproheptadine 2 g and L-lysine 150 mg, and B vitamins dexamethasone 4.5 g, nicotinamide 15 mg, thiamine 2 mg, and pyridoxine 1 mg, per 5 mL of syrup. The drug is unregulated in the United States and marketed for selective weight gain.

CASE REPORT

A 40-year-old previously healthy woman was found to have elevated transaminases on pre-employment laboratory work. Outpatient workup revealed elevated smooth muscle antibody and negative viral hepatitis serology. She was admitted to the hospital, where she complained of fatigue, right-sided abdominal discomfort, and jaundice of a few weeks. Her history was significant for alcohol consumption of 2–3 drinks 3 nights per week. She denied taking prescription medications but reported taking an over-the-counter-supplement called Apetamin (cyproheptadine, lysine, and vitamin syrup). She started taking the supplement 6 weeks before to enhance her figure. She revealed that she consumed more than the 5 mL recommended daily dose and instead drank from the bottle to maximize effects. She learned of the drug on social media, where it was promoted as a nonsurgical body augmentation alternative.
Laboratory work on presentation was significant for aspartate aminotransferase (AST) 838 U/L, alanine transaminase (ALT) 997 U/L, and alkaline phosphate 90 U/L. Smooth muscle antibody was 5 times the upper limit of normal and IgG 2 times the upper limit of normal (3,162 mg/dL), concerning for AIH. Viral hepatitis serology was negative for hepatitis A IgM, hepatitis B core IgM, hepatitis B surface antigen, and hepatitis C antibody. Human immunodeficiency viruses, Epstein-Barr virus, and Cytomegalovirus, QuantiFERON, and mitochondrial antibody were negative; iron and ceruloplasmin were normal. Right upper quadrant ultrasound showed mild echogenicity of the liver seen with hepatic steatosis, normal portal and hepatic veins, and no biliary dilatation. Percutaneous liver biopsy performed on day 2 of admission showed active hepatitis with increased fibrosis, cholestasis, cholangiolar metaplasia, lymphoplasmacytic inflammation, lobular inflammation, disarray, hepatocyte necrosis, and multinucleated hepatocytes (Figure 1). The patient scored a 16 on the AIH scale, with a pretreatment likelihood of definite AIH. On the Roussel Uclaf Causality Assessment Method scale, assessing causality between offending drugs and liver damage, the patient scored 11 indicating highly probable adverse drug reaction. Findings indicated DIAIH, and the patient was started on prednisone 40 mg oral daily with rapid improvement in liver function.

She was discharged after 5 days with down-trending transaminases, counseled to stop Apetamin and alcohol, and prescribed prednisone 40 mg oral daily. At the 1-week discharge follow-up, she reported an increase in energy and denied jaundice, itching, or abdominal pain. Transaminases continued to downtrend to AST 104 U/L and ALT 247 U/L, and azathioprine 50 mg by mouth once daily was started. At the 3-month follow-up, transaminases had normalized, and prednisone was tapered to 30 mg daily. However, her course was complicated by missed medication doses and an increase in transaminases. She was closely followed, and at the 8-month follow-up, laboratory test results showed AST 24 U/L and ALT 30 U/L. She remained on azathioprine 50 mg, and prednisone was further tapered to 20 mg daily.

**DISCUSSION**

This case reveals the dangerous of Apetamin (cyproheptadine, lysine, and vitamin syrup) causing DIAIH. The supplement is not Food and Drug Administration-approved for over-the-counter use in the United States. The active ingredient, cyproheptadine, can only be purchased legally with a prescription. Still, this supplement is easily purchased illegally over the internet and on social media.

Cyproheptadine is a first-generation antihistamine indicated for allergic reactions. It can be prescribed off label for cyclic vomiting and appetite stimulation. In the United States, cyproheptadine is prescribed in a tablet form with standard dosing between 4 and 20 mg/d. The maximum daily dosing is 0.25 mg/kg for children and 0.5 mg/kg in adults or 32 mg. Apetamin contains 2 mg per 5 mL serving, but it is taken in an unmonitored setting without provider supervision or counseling. It is purchased without a prescription.

![Figure 1](image_url)

**Figure 1.** The biopsy demonstrates (A) a vitamin expansion of portal areas by inflammation, (B) many plasma cells in clusters, scattered eosinophils, and macrophages, (C) lobules indicating hepatocyte damage with rarefied cytoplasm, lobular inflammation, cholestasis, hepatocyte drop out, and (D) a trichrome stain showing increased fibrosis with focal areas of bridging.
and marketed as a “vitamin syrup,” suggesting a pro-health benefit. Without regulation and consumer awareness of side effects, consumers, such as our patient, are more at risk of exceeding daily dosing and experiencing adverse reactions.

Cyproheptadine has been shown to be a safe, well-tolerated medication that helps facilitate weight gain. Studies in underweight populations show that it is effective in young children with poor feeding and cystic fibrosis but less successful in malignancy and human immunodeficiency virus. Under controlled settings, common side effects include sedation, irritability in young children, and anticholinergic reactions. Cyproheptadine has also been linked to hepatitis. Only a few cases have reported hepatoxicity, developing 1–6 weeks after exposure in patients with no previous liver or biliary disease. A cholestatic or mixed pattern of liver enzyme elevations have been described, and acute liver failure is rarely documented. Patients recovered within weeks of discontinuation. The pathway of injury is unknown but believed to be related to the chemical structure. Cyproheptadine has not been known to induce an autoimmune reaction, as observed in this case.

The popularity of cyproheptadine-based weight gain supplements is concerning, given the severe risks and limited knowledge in the general and medical community. This product exploits the cultural ideals of beauty and society’s willingness to achieve such standards. It is marketed to women for selective weight gain to augment buttocks, hips, and thighs. However, there is no data on the prevalence of cyproheptadine use for body augmentation in the United States; only a study in the Democratic Republic of Congo found significant misuse in young women. Given the influence of social media and targeted advertising, the prevalence may be on the rise.

This case highlights the changing environment in which medications are advertised, distributed, and sold. Social media is a powerful tool to selectively target and lure patients into purchasing drugs that can negatively impact health. In response, healthcare providers must take a complete drug history. Furthermore, providers must be familiar with such trends and side effects to counsel and treat patients effectively.

DISCLOSURES
Author contributions: V. Garland wrote this manuscript and reviewed the literature. A. Kumar edited the manuscript and is the article guarantor. B. Theisen provided the images. M. Borum edited and revised the manuscript for intellectual content.

Financial disclosure: None to report.
Informed consent was obtained for this case report.
Received September 20, 2019; Accepted March 31, 2020

REFERENCES
1. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury. National Institute of Diabetes and Digestive and Kidney Diseases: Bethesda, MD, 2012. Autoimmune hepatitis.
2. Bjornsson E, Talwalkar J, Treeprasertsuk S, et al. Drug-induced autoimmune hepatitis: Clinical characteristics and prognosis. Hepatology. 2010; 51(6):2040–8.
3. Martine-Casas O, Diaz-Ramierz G, Marin-Zuluaga O. Differential characteristics in drug-induced autoimmune hepatitis. JGH Open. 2018;2(3):97–104.
4. Danan G, Benichou C. Causality assessment of adverse reactions to drugs—II. A novel method based on the conclusions of international consensus meetings: Application to drug-induced liver injuries. J Clin Epidemiol. 1993;46(11):1323–30.
5. LiverTox: Clinical and Research Information on DrugInduced Liver Injury. National Institute of Diabetes and Digestive and Kidney Diseases: Bethesda, MD. Cyproheptadine.
6. Cyproheptadine: Drug information. UpToDate (https://www.uptodate.com/contents/cyproheptadine-drug-information?search=cyproheptadine&source=panel_search_result&selectedTitle=1~44&usage_type=rw&panelkp_tab=drug_general&display_rank=1). Accessed March 14, 2020.
7. Harrison ME, Norris ML, Robinson A, Spettigue W, Morrisey M, Iserlin L. Use of cyproheptadine to stimulate appetite and body weight gain: A systematic review. Appetite. 2019;137:62–72.
8. Sant’Anna AM, Hammes PS, Porporino M, Martel C, Zygmuntowicz C, Ramsay M. Use of cyproheptadine in young children with feeding difficulties and poor growth in a pediatric feeding program. J Pediatr Gastroenterol Nutr. 2014;59(5):674–8.
9. Chinuck R, Dewar J, Baldwin DR, Hendron E. Appetite stimulants for people with cystic fibrosis. Cochrane Database Syst Rev. 2014;(7):CD008190.
10. Chertoff J, Alam S, Clark V. Cyproheptadine-induced acute liver failure. ACG Case Rep J. 2014;1(4):212–3.
11. Freneaux E, Larrey D, Berson A, et al. Hepatitis caused by cyproheptadine (Periactine): A case report and review of the literature. Gastroenterol Clin Biol. 1988;12(6-7):573–5.
12. Henry D, Lowe J, Donnelly T. Jaundice during cyproheptadine treatment. Br Med J. 1978;1(6115):753.
13. Larrey D, Geneve J, Pessayre D, et al. Prolonged cholestasis after cyproheptadine-induced acute hepatitis. J Clin Gastroenterol. 1987;9(1):102–4.
14. Lulebo A, Bavuidibo C, Mafuta E, et al. The misuse of cyproheptadine: A non-communicable disease risk behaviour in Kinshasa population, Democratic Republic of Congo. Subst Abuse Treat Prev Policy. 2016;11:7.