GETTING TO THE BOTTOM OF ALCOHOL AND KRATOM: A POSSIBLE SYNERGISTIC MECHANISM TO HEPATOCELLULAR LIVER INJURY

TRIPTI NAGAR[1], VATSAL KHANNA[1], PADMINI GIRI[1], RANIM CHAMSEDDIN[1], AHMAD REFAI[1], ABDULLAH YESILYAPRAK[1], ISSAM TURK[2]

[1]Wayne State University School of Medicine Department of Internal Medicine, [2]Ascension Providence Rochester

WAYNE STATE
School of Medicine

INTRODUCTION

- Kratom is a herbal derivative of an evergreen species, Mitragyna speciosa. Extracts have been used as an opioid replacement in treating chronic pain as they contain partial mu-opioid receptor activity
- Although rare, chronic kratom use has been seen to cause a cholestatic pattern of liver injury with severe hyperbilirubinemia. Our case presents a 36-year-old male who presented with drug-induced hepatocellular liver injury due to chronic kratom use.

CASE REPORT

- We report a case of a 36-year-old male with a history of alcohol dependence who presented to the hospital for evaluation of intermittent chest pain.
- He reported continued alcohol use of 1 pint of vodka per day and was drinking regularly for the past 17 years. Over the week prior to admission, he endorsed nausea and vomiting
- He began taking kratom supplements as it was an opioid-type medication that helped him discontinue chronic Vicodin and oxycodone use
- On admission, the patient's vital signs were stable. Physical examination revealed mild epigastric tenderness without palpable masses or organomegaly. No stigmata noted of chronic liver disease

INVESTIGATIONS

- Electrocardiogram showed normal sinus rhythm without ST-T wave changes.
- Clinical laboratory results showed significant transaminitis in a pure hepatocellular pattern with aspartate aminotransferase (AST) 1182 and alanine aminotransferase (ALT) 909, representing an R factor of 55.9. Gamma-glutamyl transferase (GGT) level was 208. Total and direct bilirubin levels were normal. The coagulation profile and hepatitis panel were unremarkable.
- Hepatitis panel was negative
- Prior evaluation four months ago showed AST of 111 and ALT of 132 (table 1)
- Computed Tomography (CT) of the abdomen and ultrasonography showed evidence of hepatic steatosis.
- Abdominal US significant for diffuse hepatic steatosis. No biliary ductal dilation and normal evaluation of the hepatic and splenic vasculature

MANAGEMENT

- Discontinuation of kratom during the hospital course showed improvement in transaminase levels, and the patient was discharged with continued liver function monitoring outpatient.

FIGURE 1 – CT ABDOMEN

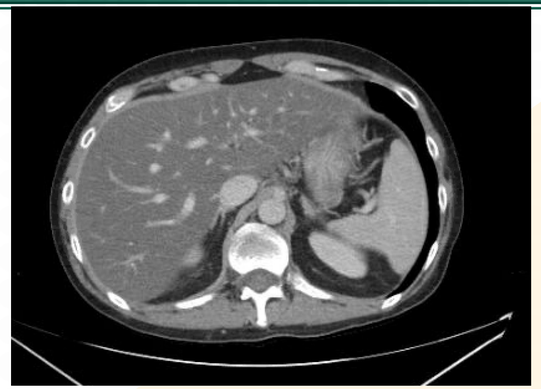
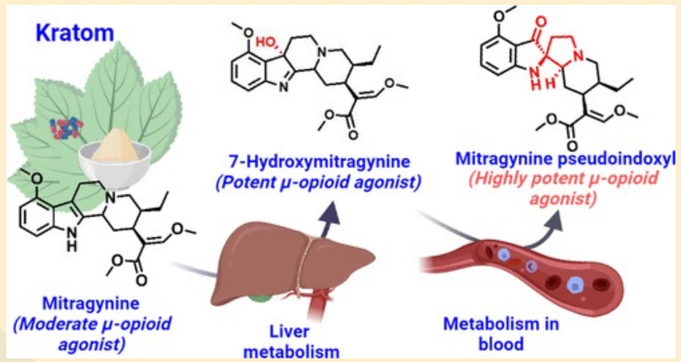


TABLE 1 – LIVER ENZYME COMPARISON

	Prior Kratom	After Kratom
AST	79	1182
ALT	94	909
Total Bilirubin	0.25	0.9
INR	0.9	0.9
R factor	5.9	55.9

FIGURE 2 – KRATOM METABOLISM



DISCUSSION

- The interaction of alcohol and kratom has not been well studied. The literature review demonstrated case reports showing a cholestatic pattern of liver injury; however, our patient's case did not align with these findings, most notably with normal total and direct bilirubin levels.
- Drug-induced liver injury is usually dose-dependent, as seen with improved liver function with kratom abstinence in our case.
- Kratom metabolism involves the formation of mitragynine which functions as a moderate opioid mu-receptor agonist. This is then hydroxylated to a more potent mu-receptor agonist in the liver itself
- Further metabolism in the bloodstream leads to the development of a highly potent mu-agonist that is approximately 10-fold more potent than mitragynine
- The mechanism of injury due to regular kratom use has not been well established; however, recent studies show hepatic upregulation of a ligand-gated transcription factor leading to increased toxic metabolite formation.

CONCLUSION

- Hepatic toxicity in cases of multiple substance use disorder must be considered with lesser-known herbal supplemental products
- In our patient case, we hypothesize the combination of kratom and alcohol is potentially synergistic in causing acute drug-induced liver injury.
- Robust medical profiles of herbal supplementation are lacking yet crucial in clinical awareness and patient education

REFERENCES

Schimmel J, Dart RC. Kratom (Mitragyna Speciosa) Liver Injury: A Comprehensive Review. *Drugs*. 2020
Ahmad J, Odin JA, Hayashi PH, et al. Liver injury associated with kratom, a popular opioid-like product: Experience from the U.S. drug induced liver injury network and a review of the literature. *Drug and Alcohol Dependence*. 2021
Fernandes CT, Iqbal U, Tighe SP, Ahmed A. Kratom-Induced Cholestatic Liver Injury and Its Conservative Management. *Journal of Investigative Medicine High Impact Case Reports*. 2019
Osborne CS, Overstreet AN, Rockey DC, Schreiner AD. Drug-Induced Liver Injury Caused by Kratom Use as an Alternative Pain Treatment Amid an Ongoing Opioid Epidemic. *Journal of Investigative Medicine High Impact Case Reports*. 2019
Tayabali K, Bolzon C, Foster P, Patel J, Kalim MO. Kratom: a dangerous player in the opioid crisis. *Journal of Community Hospital Internal Medicine Perspectives*. 2018
Kratom. PubMed. Published 2012.
ACS Pharmacol. Transl. Sci. 2020, 3, 6, 1063–1068
Publication Date:July 31, 2020https://doi.org/10.1021/acsptsci.0c00075

CORRESPONDENCE

tripti@wayne.edu