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Disclosure forms are available with the article online.

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The Forbidden Fruit: A Case of Tejocote (*Crataegus mexicana*) Supplement Toxicity

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Keywords

Weight loss, Ingestion, Immune system, Idiopathic thrombocytopenic purpura, Disclosure, Bradycardia, Toxicity, Nausea, Heart rate, Tejocote, *Crataegus mexicana*

Abstract

Supplement use continues to increase throughout the United States and as these compounds are not approved by the Food and Drug Administration, the side effect profiles are not well studied. Tejocote (*Crataegus mexicana*) is part of the hawthorn family and is a Mexican root supplement that is marketed for weight loss. We describe the case of a patient who ingested tejocote and presented with weakness, nausea, bradycardia with an atrioventricular block, and drug-induced thrombocytopenia.

Background

Supplement use has increased over the past few decades and now constitutes an estimated \$151.9 billion industry with growth expected to be 5% to 7% in the next year and doubling in size by 2030 (1). These compounds are not regulated by the Food and Drug Administration and do not undergo stringent testing requirements, with their side effect profiles being virtually unknown. Questioning patients about supplement usage remains an important part of the history due to serious side effects.

Objective

Our objective is to help other providers be able to identify the side effects from ingestion of tejocote root supplementation and highlight the importance of asking about supplement use.

Case Report

A 55-year-old woman presented to the emergency department with symptoms of weakness, nausea, abdominal pain, and low heart rates she had noticed on her smart watch occurring for roughly a month. An electrocardiogram was obtained (Figure 1), the findings of which showed bradycardia at a rate of 48 beats/min and a prolonging PR interval followed by a nonconducted QRS complex, indicative of a second-degree atrioventricular block, Mobitz type 1. Laboratory testing was significant for a calcium of 11.1 mg/dL (8.4–10.2 mg/dL) and severe thrombocytopenia with platelet count of 22 000/ μ L ($150\text{--}450 \times 10^3/\mu\text{L}$). Further questioning of the patient revealed she was taking an herbal supplement for weight loss, tejocote. She had taken this supplement for 3 years but stopped 2 months before presentation at the advice of her primary care physician due to concerns about drug–drug interactions with her other medications. At that time, she was placed on semaglutide for prediabetes and to help with weight loss. However, due to worsening constipation, which she attributed to stopping the supplement, she restarted tejocote again 1 month before her presentation.

Work-up for her severe thrombocytopenia, including a hepatitis panel and HIV testing, was unremarkable, and she did not report any personal or family history of bleeding diathesis. A peripheral smear was performed, which was negative for schistocytes or platelet clumping. Cardiac enzymes were undetectable, and the findings of an echocardiogram showed an ejection fraction of 60% to 65%, normal chamber sizes, and no valvular abnormalities. While investigating the causes of the patient's symptoms, a brief review of tejocote root demonstrated

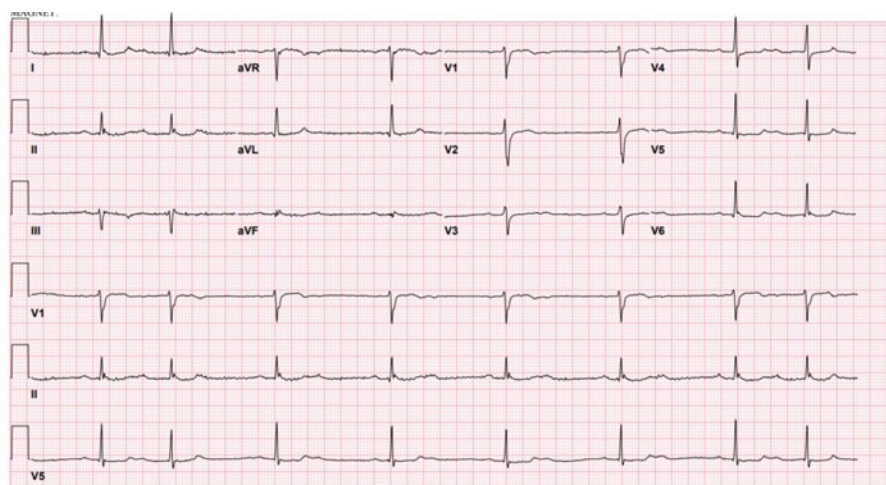


Figure 1. Initial electrocardiogram demonstrating a sinus bradycardia at a rate of 48 beats/min with a second-degree atrioventricular block, Mobitz type 1, narrow QRS morphology, and a normal QT interval with a QTc of 402 milliseconds.

the supplement can mimic digoxin. Therefore, a digoxin level was checked, which was low but detectable at 0.4 ng/mL (0.8–2.0 ng/mL). As the patient did not report taking digoxin, it was felt this was likely secondary to cross-reactivity with the tejocote supplement and the digoxin assay.

She was placed on telemetry and monitored for 4 days, during which time her symptoms improved. Her heart rate normalized, and her platelet count increased to 95 000/ μ L ($150\text{--}450 \times 10^3/\mu\text{L}$). On day of discharge, a repeat digoxin level was undetectable, and her electrocardiogram findings showed normal sinus rhythm with resolution of the second-degree atrioventricular block. She was discharged in stable condition with instructions to stop taking the tejocote supplement. At her follow-up appointment a week later, she stated her nausea, abdominal pain, and weakness had completely resolved, and her smart watch showed normalization of her heart rate to the 70s.

Discussion

Crataegus mexicana is a common hawthorn species in Mexico (2). The term “tejocote” refers to the fruit of the tree, traditionally used to make jellies, marmalades, and candies (3). A preparation of the dried root has emerged as an herbal supplement marketed for weight loss, with the postulated mechanism to be secondary to its high pectin content, leading to early satiety and decreased appetite (2).

There are more than 300 species of hawthorn that have been used for centuries as remedies for cardiovascular and gastrointestinal disease (4). The clinical effects are thought to occur due to active organic compounds called phenols. These phenols have similar structures to cardiac glycosides and have been shown to bind to digoxin assays, causing a falsely elevated digoxin level (5), as demonstrated in our patient.

Cardiovascular effects of hawthorn extracts, including positive inotropy and antiarrhythmic properties, are thought to be

from cyclic adenosine monophosphate inhibition of sodium–potassium–ATPase (6). The Survival and Prognosis: Investigation of *Crataegus* Extract WS 1442 in congestive heart failure study looked at the safety and efficacy of *Crataegus* WS1442 in advanced heart failure. This failed to show a significant difference in the composite end points of cardiac death, nonfatal myocardial infarction, and hospitalization but suggested a reduction in sudden cardiac death in patients with a reduced left ventricular ejection fraction (7). Although most data concerning cardiovascular effects of hawthorn seem to be protective, *C mexicana* was reported to cause cardiotoxicity after ingestion in a pediatric patient, leading to severe bradycardia and second-degree heart block, Mobitz type 1, as seen in our patient (8). Tejocote supplement overdose also was implicated to cause dysrhythmias, bradycardia, and pulseless electrical activity in a previously healthy young man (9). *C mexicana* also has been demonstrated to cause acute pericarditis (10), although the mechanism remains unclear.

Hematologic effects are not well-documented. *C mexicana* was reported to cause drug-induced immune thrombocytopenia after ingestion of the tejocote supplement in a female patient using it for weight loss, with improvement after stopping the supplement (11). Drug-induced thrombocytopenia is a diagnosis of exclusion and requires clinical investigation regarding recent medication changes. Drug-induced thrombocytopenia causes are vast and encompass more than 300 medications and supplements. Treatment is discontinuation of the drug, with recovery of the platelet count seen within 4 to 5 half-lives of the medication (12). We suspect drug-induced thrombocytopenia to be the cause of our patient’s severe thrombocytopenia, as her platelet count normalized without any intervention other than discontinuation of the tejocote supplement.

Gastrointestinal effects of hawthorn preparations are the most common adverse events reported, such as mild abdominal pain and nausea. However, more serious side effects, such as severe abdominal pain, vomiting, diarrhea, and upper gastrointestinal bleeding, have been recorded (13). It is thought that the tannins

and flavonoids found in hawthorn extracts lead to variable side effects, including irritation of the gastric lining (14).

As with most herbal supplements, literature regarding the full side effect profile of *C mexicana* extracts, including tejocote, is sparse. In addition, there are no data on interactions of tejocote supplements with other medications, including glucagon-like peptide 1 inhibitors, as seen in our patient. Glucagon-like peptide 1 inhibitors (semaglutide) delay gastric emptying, which can alter the pharmacokinetics of medications and supplements, leading to increased absorption (15). We postulate the addition of semaglutide increased absorption of the tejocote supplement, thus precipitating the clinical effects that prompted hospitalization.

Our patient presented with severe hematologic and cardiovascular complications, including drug-induced thrombocytopenia and bradycardia with a Mobitz Type 1 second-degree atrioventricular block, along with gastrointestinal upset. With supportive care and time to allow clearance of the tejocote supplement, these complications resolved. Further research is needed to evaluate the effectiveness of active treatments and medications in life-threatening circumstances of tejocote supplement ingestion. Finally, patient and provider education regarding the potential severe adverse effects of tejocote supplements is paramount for early identification of these adverse outcomes.

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