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Rooibos, a fake friend

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To

Pr Raoul Poupon
Edito in chief Clincs and Research in Hepatology and Gastroenterology

Limoges, April 23rd 2020

Dear Editor,

Please, find enclosed the manuscript entitled: **“Rooibos, a fake friend” submitted as “Case report”** in Clincs and Research in Hepatology and Gastroenterology.

Rooibos is available worldwide and is considered as a liver protector. Nevertheless, it can expose to severe liver damage. We think that clinicians must know this potential side effect.

I confirm that the manuscript is original research and is not under consideration elsewhere. I confirm that all the authors participated in the preparation of the manuscript and that they will sign a statement attesting authorship disclosing all potential conflicts of interest.

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We thank you for considering our manuscript for publication.

Yours sincerely,

Dr Paul Carrier.

Rooibos, a fake friend.

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Abbreviations.

ALT: Alanine aminotransferase.

AST: Aspartate aminotransferase.

HAV: Hepatitis A virus.

HBV: Hepatitis B virus.

HCV: Hepatitis C virus.

HEV: Hepatitis E virus.

Human Immunodeficiency Virus.

HSV: Herpes Simplex virus.

IgM: Immunoglobulin M.

Polymerase Chain Reaction.

VZV: Varicella Zona virus.

Key words.

Rooibos. Acute hepatitis. Drug Induced Liver Injury.

Rooibos, a fake friend.

Summary. 58 words.

Rooibos is consumed worldwide and its use considered safe. It contains scavengers of free radicals and is so is deemed to be a liver protector. Nevertheless, hepatic toxicity exists even if rare. It is probably underdiagnosed and clinicians should think about it in case of acute hepatitis. We report a case of liver injury attributed to Rooibos.

Introduction.

Tea consumption is worldwide diffused, with a wide variety of products available. Rooibos, a well-known South Africa tea plant grown in Cederberg region, in Western Cape province, is also known for its potential antioxidant properties and many studies interest these favorable effects [1]. Nevertheless, many herbal products are associated with liver toxicity and must be screened in case of acute hepatitis [2].

We report here a rare case of Rooibos toxicity.

Case report.

A 63-years old patient was admitted to our hospital for jaundice in September 2019. He usually took TADALAFIL and FESOSTERODINE for a prostatic adenoma, ESOMEPRAZOLE, ZOLPIDEM and PARACETAMOL on demand. He had no alcohol or tobacco consumption. Patient had no family history of liver disease.

The examination of the file made it possible to find a comparable episode fourteen months ago, requiring an hospitalization but with a favorable spontaneous evolution. The interrogation at the time had not highlighted any toxic cause. All the etiological explorations, including biological tests and morphological explorations, were normal. A liver biopsy was performed that didn't show specific lesions, except granuloma. After resolution of the acute episode, the liver function test remained normal without any other event until September 2019.

At admission, apart from jaundice, the patient did not have fever, itching, encephalopathy, bleeding signs or deterioration of general condition. Abdominal examination was normal. Blood tests showed elevated ALT (1345 IU/L, N<32), AST (795 IU/L, N<32). Alkaline phosphatase level was 128 IU/L (N<104), gamma-glutamyl-transferase 309 IU/L (N<36). Prothrombin time was 59% and factor V 103%. Lactate concentration was normal. Virus-associated hepatitis were screened, negative (IgM anti-HAV, HBsAg, anti-HCV antibodies, Parvovirus B19, VZV, HIV antibodies, anti-HEV IgM, PCR HEV and HSV PCR were negative. Autoimmune liver antibodies panel was negative and immunoglobulins level normal. Doppler-coupled ultrasound was normal. Testing for toxic substances in the blood and urine was negative. Patient had taken PARACETAMOL during the last 14 days, but at dose inferior to 3 grams per day. No new treatments susceptible to give hepatic lesions had been introduced. By resuming the interrogatory, we strongly suspected the role of red tea: in fact, the patient remembered having consumed red tea before his two hospitalizations for acute hepatitis, and had not taken any between the two periods. The commercial references of his red tea showed presence of Rooibos essentially. Extrinsic and intrinsic criteria were met concerning Rooibos. The clinical and biological course was favorable after stopping red tea consumption. No new liver biopsy was performed. Patient was discharged at day 5. Rooibos consumption was definitively excluded and liver tests were normal on subsequent controls during a 6-months follow-up.

Discussion.

Rooibos is a plant also called *Aspalathus linearis*. It is generally considered safe and worldwide available as red tea since 40 years [3]. It is popular as health beverage, because it contains neither harmful stimulants nor caffeine [4] and is considered as a

liver protector. Human experience is interesting. Rooibos contains a lot of hydroxylated and polyhydroxylated phenolic compounds, such as aspalalinin, aspalathin, or nathofagin, and flavonoids [5]. These compounds, particularly aspalathin, have antioxidant effects, and act as scavengers of free radicals [6][7][8]. They decrease oxidative stress and pro-cytokine inflammation proteins [9][10][11]. Antimutagenic and cancer modulating properties were also suggested, with preliminary studies in mice models [12][13][14]. They may have a favorable impact on metabolic syndrome, notably diabetes mellitus [4][15][16] and on cardiovascular diseases [17]. No liver injury signal was registered in these studies. More studies are necessary, particularly in humans. Studies were led in liver injury induced mice and suggested a potential interest in [5][9]. A role in hepatic insulinoreistance exists [18].

Beside this potential benefit, there is a very low number of reports about liver toxicity. To our knowledge, only three cases were previously described: patients were young (from 37 to 51 years old) and took Rooibos regularly [19][20][21]. After red tea discontinuation, liver enzymes returned to normal very rapidly in all patients. No fulminant hepatitis has been reported in the literature and mechanism of toxicity is not elucidated.

Liver toxicities have also been described with other South Africa teas: Buchu tea and its component, pennyroyal [22]. DILI associated to herbal medicines (kava,...) are also regularly reported [2].

To conclude, although Rooibos seems to be promising in insulinoreistance prevention, caution with regard to hepatic side effects remains necessary, notably in human studies and the potential risk of widely diffused many kinds of tea must be known by clinicians, enhancing once again the crucial importance of interrogation.

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