

Khat-related liver disease in sub-Saharan Africa: neglected, yet important

Authors' reply

We thank Stian Orlien and colleagues for raising attention to the issue of khat use as a recreational drug in sub-Saharan Africa in response to our Comment.¹ Although we mentioned the fact that traditional herbal medicine could contribute to the burden of cirrhosis in this region, as the use of khat is associated with a substantial increase in liver fibrosis,² we do not think that the available evidence shows that khat is a major contributor to chronic liver disease. Khat is used in parts of east Africa, including Djibouti, Ethiopia, Somalia, Somaliland, Kenya, Sudan, Uganda, and Madagascar. Apart from its long-standing popularity as a recreational drug, it can be used for the treatment of erectile dysfunction, malaria, influenza, vomiting, and headache.³ The Central African Republic, Gabon, and Côte d'Ivoire were in the top 10% of countries for cirrhosis-related deaths in 2010 but khat use is uncommon in west or central Africa.⁴

The question of khat's liver toxicity is complex. It contains numerous compounds, including alkaloids, terpenoids, flavonoids, sterols, glycosides, tannins, amino acids, vitamins, and minerals.⁵ Research into the deleterious effects of khat has largely concentrated on the pharmacological effects of cathinone and cathine on the cardiovascular system and CNS, and studies on possible liver toxicity in humans are restricted to Ethiopia and Somaliland and to reports from western Europe almost exclusively involving Somali men. Additional research is necessary to establish the prevalence of liver toxicity in people who chew khat in Ethiopia versus Djibouti (where liver toxicity is apparently not observed)⁶ and Yemen (which has the highest

proportion of users worldwide),⁷ and in Kenya, Uganda, and Madagascar, where studies have not been done. Also necessary is investigating the mechanisms and progression of liver damage induced by khat, the effects of gender (khat toxicity is observed much more frequently in males)⁸ and genetics (genetic variants in CYP2D6 might play a role in liver toxicity),⁹ and the contribution of other compounds found in khat and of contaminating herbicides and pesticides to liver disease.¹⁰

Current evidence shows that hepatitis viruses and alcohol are the main contributors to the incidence of liver cirrhosis throughout sub-Saharan Africa¹ and efforts should continue to curb their effects.

We declare no competing interests.

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- 1 Vento S, Dzudzor B, Cainelli F, Tachi K. Liver cirrhosis in sub-Saharan Africa: neglected, yet important. *Lancet Glob Health* 2018; **6**: e1060–61.
- 2 Orlien SMS, Ismael NY, Ahmed TA, et al. Unexplained chronic liver disease in Ethiopia: a cross-sectional study. *BMC Gastroenterol* 2018; **18**: 27.
- 3 WHO. Assessment of khat (*Catha edulis* Forsk). 2006. https://www.who.int/medicines/areas/quality_safety/4.4KhatCritReview.pdf (accessed Oct 25, 2018).
- 4 Acuda W, Othieno CJ, Obondo A, Crome IB. The epidemiology of addiction in sub-Saharan Africa: a synthesis of reports, reviews, and original articles. *Am J Addict* 2011; **20**: 87–99.
- 5 Kalix P, Braenden O. Pharmacological aspects of the chewing of khat leaves. *Pharmacol Rev* 1985; **37**: 149–64.
- 6 Coton T, Simon F, Oliver M, Kraemer P. Hepatotoxicity of khat chewing. *Liver Int* 2011; **31**: 434.
- 7 Al-Mugahed L. Khat chewing in Yemen: turning over a new leaf. *Bull World Health Organ* 2008; **86**: 741–42.

- 8 Orlien SMS, Sandven I, Berhe NB, et al. Khat chewing increases the risk for developing chronic liver disease: a hospital-based case-control study. *Hepatology* 2018; **68**: 248–57.
- 9 Sharma A, Orlien SMS, Abdosh AT, et al. PWE-082 genetic variants in CYP2D6 and the propensity to chronic liver disease in men chewing khat. *Gut* 2018; **67**: A113.
- 10 Al-Akwa AA, Shafer M, Al-Akwa S, Aleryani SL. Free radicals are present in human serum of *Catha edulis* Forsk (khat) abusers. *J Ethnopharmacol* 2009; **125**: 471–73.

