Kava for Generalized Anxiety Disorder

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Q. What is kava?

A. Kava, or kava kava, is an herbal drug from the kava plant (*Piper methysticum*), native to the Pacific Islands. The root of the plant is traditionally used to create a drink with sedative effects, and kava drinking is important in Pacific Islander culture. Kava extracts are also exported for use in Western societies as an anxiolytic, and pharmaceutical and herbal supplement companies extract kavalactones, the active ingredients in kava, to produce an herbal drug with anxiolytic effects. In the early 2000s, safety concerns over risks of hepatotoxicity led to temporary bans in several countries. A 2007 report by the World Health Organization (WHO) concluded that hepatic adverse reactions are rare, and are associated with excessive dose, drug interactions, and other factors such as excessive alcohol intake or pre-existing liver disease. There may also be risk of hepatotoxicity associated with products made using acetonic and ethanolic extracts (WHO, 2007). This report puts forth a recommendation for a pharmacopoeia standard that addresses issues around quality, dosage, and preparation. Bans have been lifted in most countries as a result of the lack of direct causal evidence of harm, but there are still concerns associated with increased risk of liver injury.

Q. What are the potential mechanisms of action underlying kava?

A. Kavalactones are responsible for the clinical effects of kava. The exact mechanisms of action by which kavalactones exert their anxiolytic effect is not known, but it is thought that kavalactones potentiate gamma-aminobutyric acid (GABA) type A receptors, reducing the release of excitatory neurotransmitters and limiting neuronal uptake of dopamine and norepinephrine (Ooi, Henderson, & Pak, 2018; Chua et al., 2016).

Q. Is kava recommended as a treatment for generalized anxiety disorder (GAD) in the Military Health System (MHS)?

A. There is no VA/DoD clinical practice guideline (CPG) on the treatment of GAD.

The MHS relies on the VA/DoD clinical practice guidelines (CPGs) to inform best clinical practices. However, in the absence of an official VA/DoD recommendation, clinicians should look to CPGs published by other recognized organizations, and may rely on knowledge of the literature and clinical judgement.

Q. Do other organizations with CPGs for the treatment of GAD recommend kava?

A. No. CPGs published by other organizations do not recommend the use of kava for GAD.

- The United Kingdom's National Institute for Health and Care Excellence (NICE) does not include kava in their guideline on management of GAD in adults (NICE, 2011).
- The Canadian Psychiatric Association does not include kava in their CPGs on management of anxiety disorders (Canadian Psychiatric Association, 2006).

Q. Do other authoritative reviews recommend kava as a treatment for GAD?

A. No. Other authoritative reviews have not substantiated the use of kava for GAD.

Several other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using similar grading systems as the VA/DoD CPGs. These include the Agency for Healthcare Research and Quality (AHRQ) and Cochrane.

- AHRQ: No reports on GAD were identified.
- Cochrane: A 2003 systematic review of kava extract versus placebo for treating anxiety included 12 double-blind randomized controlled trials (RCTs; Pittler & Ernst, 2003). Seven of these studies were included in a meta-analysis, which found "significant effects towards a reduction" of scores on

the Hamilton Anxiety (HAM-A) scale in participants receiving kava extract versus placebo at post-treatment. Adverse events reported in the studies were mild and infrequent. Participants were not required to have a diagnosis of GAD for studies to be included in this review, and this review does not include grading of the certainty of evidence.

Q. Is there any recent research on kava as a treatment for GAD?

A. A June 2019 literature search identified a recent systematic review and meta-analysis on kava for GAD (Ooi et al., 2018). This review included 10 studies, six of which were double-blind randomized placebo-controlled trials. Three of the double-blind randomized placebo-controlled trials reported change in HAM-A scores from baseline to post-treatment, and were included in a meta-analysis, which demonstrated that kava treatment did not result in statistically significant decreases in HAM-A anxiety score compared to placebo. This review found that kava was well tolerated in the included studies, and liver function tests found no differences between treatment groups.

No additional trials were identified as published since this systematic review. A multisite double-blind randomized placebo-controlled trial evaluating kava for the long-term (18 week) treatment of GAD was recently completed, but results are not yet available (Savage et al., 2015).

Q. What conclusions can be drawn about the use of kava as a treatment for GAD in the MHS?

A. There is some emerging evidence that kava may be effective in the short-term reduction of anxiety symptoms. However the body of evidence is insufficient to support kava as a treatment for GAD. Due to concerns of hepatic adverse reactions, there are a number of considerations that need to go into the decision to use kava as an herbal drug. These include patient history and risk factors (liver disease and excessive alcohol use), interactions with other drugs or herbal preparations, and the drug itself (quality, plant parts used, methods of preparation, dosage). It is important to note that kava is considered a psychoactive substance and Department of Defense Instruction 1010.04 prohibits improper use of any psychoactive substance (Office of the Under Secretary of Defense for Personnel and Readiness, 2014).

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