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Review

Proposal for a Kava Quality Standardization Code

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ABSTRACT

Rare cases of hepatotoxicity emerged with the use of kava drugs and dietary supplements prepared from rhizomes and roots of the South Pacific plant kava (*Piper methysticum*). Their psychoactive, anxiolytic, relaxing, and recreational ingredients are the kavalactones kavain, dihydrokavain, methysticin, dihydromethysticin, yangonin, and desmethoxyyangonin, but there is little evidence that these kavalactones or the non-kavalactones pipermethystine and flavokavain B are the culprits of the adverse hepatic reactions. It rather appears that poor quality of the kava material was responsible for the liver toxicity. Analysis of existing kava quality standardizations with focus on chemical, agricultural, manufacturing, nutritional, regulatory, and legislation backgrounds showed major shortcomings that could easily explain quality problems. We therefore suggest a uniform, internationally accepted device for kava quality standardizations that are in the interest of the consumers because of safety reasons and will meet the expectations of kava farmers, pharmaceutical manufacturers, regulators of agencies, and legislators. The initial step resides in the establishment of Pan-Pacific kava quality legislation as an important part of the proposed Kava Quality Standardization Code. In conclusion, a sophisticated approach to establish kava quality standardizations is needed for safe human use of kava as relaxing traditional beverages, the anxiolytic drugs, and recreational dietary supplements.

Contents

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1. Introduction

Kava refers to the plant *Piper methysticum* Forster f. of the South Pacific region and the psychoactive products, derived from its rhizomes and roots. Among the various kava products are traditional aqueous kava beverages (Lebot et al., 1997), acetonic and ethanolic kava drugs (Teschke et al., in press-b, 2011b), medicinal aqueous kava extracts (Sarris et al., 2011a), and kava dietary supplements (FDA, 2002a). Kavalactones, also called kavapyrones, are the active ingredients of kava products (Fig. 1) and responsible for their relaxing, sedative, and anxiolytic properties (Lebot et al., 1997). Traditional aqueous kava beverages are part of religious, ceremonial, and social events, whereas acetonic and ethanolic kava drugs and medicinal aqueous kava extracts serve as anxiolytic herbal remedies (Lebot et al., 1997; Sarris and Kavanagh, 2009). The calming and recreational properties are the basis for kava use as dietary supplements (FDA, 2002a).

In the past few years, considerable international interest in kava emerged in various countries, such as the US (Brown et al., 2007), Canada (Ulbricht et al., 2005), the United Kingdom (Ernst, 2007; Richardson and Henderson, 2007), Germany (Schmidt et al., 2005; Teschke et al., in press-a), France (Lasme et al., 2008), Switzerland (Lüde et al., 2008), China (Zhou et al., 2010), Japan (Xuan et al., 2008), Australia (Sarris et al., 2010, 2011a; Tang et al., in press), New Zealand (Rasmussen, 2005), New Caledonia (Russmann et al., 2003), Vanuatu (Lebot, 2006), and other South Pacific countries (Codex Alimentarius, 2010). Some of these publications have been the result of international scientific cooperations, with an additional kava report provided by the WHO (2007). The international interest focused on hepatotoxic adverse reactions reported in association with the use of all types of kava products in the South Pacific Islands, Australia, Europe, and the US (Lebot, 2006; WHO, 2007). These findings were unexpected and created concern. Indeed, kava hepatotoxicity was substantiated following exclusion of numerous alternative diagnoses and based on a liver specific, structured, and quantitative causality assessment method in a few cases (Teschke, 2010a; Teschke et al., 2008a,b, 2009). Following final and thorough analysis in 14 patients with liver disease described worldwide, causality for kava ± comedication was highly probable and probable in 1 and 4 patients, respectively, though in nine patients causality was only possible in line with a weak association (Teschke, 2010a). Risk factors included daily overdose, prolonged treatment, and comedication with synthetic drugs and dietary supplements comprising herbal ones in most of these 14 patients. Various typical features of kava hepatotoxicity as a disease and herb-induced liver injury have been described in detail with classification as a hepatocellular rather cholestatic or mixed type of injury based on an idiosyncratic reaction (Teschke, 2010a,b).

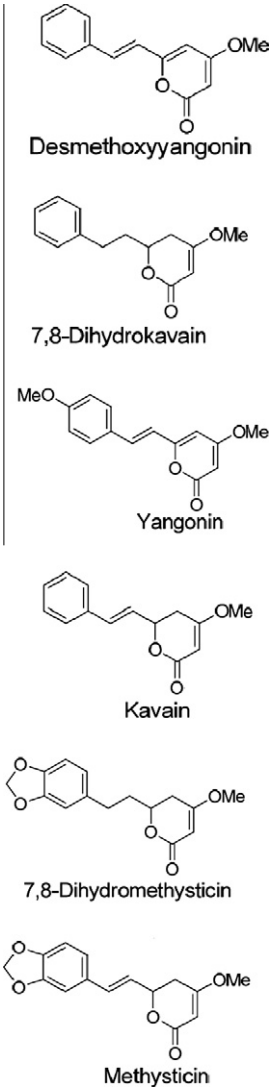

Fig. 1. The six major kavalactones are quantified by HPLC and used for the chemotype identification. The chemotype is of utmost importance for assessment of kava quality standards (Lebot et al., 1997, 2006; Teschke et al., 2011b).

The WHO kava report summarized the evidence for kava hepatotoxicity and efficacy (WHO, 2007). It alluded also to at least 16 well-controlled, double-blind studies that showed efficiency of