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An Analysis of Kava Kava

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Kava has an interesting history. It has been safely consumed ceremonially in the South Pacific and other parts of the world. The earliest European knowledge of Kava dates back to the late 1700s, with the journeys of Captain Cook.

Today, usage of Kava beverages in tropical climates is similar to the use of alcoholic beverages in the West. However, the plant from which the beverage is made also has useful properties for anxiety, hyperactivity, stress, and restlessness.

Many studies have been conducted on Kava; below, we summarize just a few:

- In 2009, the journal *Psychopharmacology* published a 3-week placebo-controlled, double blind crossover trial that recruited 60 adult participants with 1 month or more of elevated generalized anxiety. They received five Kava tablets per day were prescribed containing 250 mg of kavalactones/day. The study found that participants' Hamilton Anxiety Scale scores were significantly reduced; Kava was also effective in reducing depression. Participants experienced no serious adverse effects and no clinical hepatotoxicity.[1]
- In 2010, the department of Zoology at Cairo University studied the effects of Kava on rats. They found no adverse effects on the liver and kidneys, and suggested that Kava might be preferred to treat anxiety, due to the lack of withdrawal and addictive properties.[2]
- In 2001, *CNS Spectrums* published an article examining the effects of 280 mg kavalactones administered each day over 4 weeks. No adverse effect differences were found between Kava and placebo.[3]
- In 2014, the University of Minnesota College of Pharmacy and Masonic Cancer Center found that Kava may prevent the development of tobacco-smoke induced lung cancer.[4]

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[1] J. Sarris et. al, "The Kava Anxiety Depression Spectrum Study (KADSS): A Randomized, Placebo-controlled Crossover Trial Using an Aqueous Extract of *Piper methysticum*," *Psychopharmacology* (2009) 205: 399, accessed June 8, 2017, doi:10.1007/s00213-009-1549-9.

[2] Neveen Noor, "Anxiolytic Action and Safety of Kava: Effect on Rat Brain Acetylcholinesterase Activity and Some Serum Biochemical Parameters," *African Journal of Pharmacy and Pharmacology* Vol. 4(11), pp. 823-828, November 2010, accessed June 8, 2017, https://www.researchgate.net/publication/228678736_Anxiolytic_action_and_safety_of_Kava_Effect_on_rat_brain_acetylcholinesterase_activity_and_some_serum_biochemical_parameters.

[3] Kathryn M. Connor, Jonathan R.T. Davidson and L. Erik Churchill, "Adverse-Effect Profile of Kava," *CNS Spectrums* 6, No. 10 (2001): 848-53, accessed June 8, 2017, doi:10.1017/S109285290000167X.

[4] Miranda Taylor, "U of M Research Finds Kava Plant May Prevent Cigarette Smoke-induced Lung Cancer," last modified January 7, 2014, accessed June 8, 2017, https://www.healthtalk.umn.edu/2014/01/07/u-m-research-finds-kava-plant-may-prevent-cigarette-smoke-induced-lung-cancer/.

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- In 2008, a study in *Cancer Prevention Research* found that Kava chalcone Flavokawain A exhibits "strong antiproliferative and apoptotic effects against human urinary bladder cancer cell lines derived from different stages of bladder cancer."[5]
- In 2005, the *Cochrane Database of Systematic Reviews* analyzed 7 studies on Kava, and concluded that Kava had a "significant treatment effect" on the Hamilton Anxiety Scale. Few adverse effects were reported, and even then, the adverse effects were mild, transient, and infrequent.[6]

Despite these benefits, there was a real struggle to bring Kava to the masses. In late 2001, the FDA investigated alleged Kava Kava-related liver toxicity[7]; the following year, Health Canada, among others, banned preparations containing Kava.[8] Interestingly, these issues only became known when it became a consumer product. Here's why:

- The plant cultivar – Traditionally used cultivars are expensive to import; therefore suppliers were using cultivars that had no history of safe use.
- The part of the plant – Traditionally the rhizome was used, with no hepatotoxic side effects; suppliers were using aerial parts as well.
- The age of the plant – The kava should be 5 years old before harvesting; suppliers were using very young plants.

Unlicensed Kava is still classified by Health Canada as high risk, and selling unlicensed kava possesses several liability risks for both suppliers and retailers, as well as the safety risk for consumers.

For three and half years, the parent company of Doctor's Choice, Life Choice, fought Health Canada's decision banning Kava Kava and was successful in March 2012 as the first to legally introduce Kava Kava supplements back onto the Canadian market, with a fully-approved Natural Product Number license

[5] Yaxiong Tang et. al, "Effects of the Kava Chalcone Flavokawain A Differ in Bladder Cancer Cells with Wild-type Versus Mutant P53," *Cancer Prevention Research* November 2008 Volume 1, Issue 6, accessed June 8, 2017, doi: 10.1158/1940-6207.CAPR-08-0165.

[6] Max H Pittler and Edzard Ernst, "Kava Extract for Treating Anxiety," *Cochrane Database of Systematic Reviews* 2003 No. 1, accessed June 8, 2017, doi: 10.1002/14651858.CD003383.

[7] Mark Blumenthal, "Kava Safety Questioned Due to Case Reports of Liver Toxicity," HerbalGram, 2002; 55:26-32, American Botanical Council, accessed July 5, 2017, http://cms.herbalgram.org/herbalgram/issue55/article2147.html.

[8] "Kava Kava Products Ordered Off the Shelves Over Liver Concerns," *CBC News*, August 21, 2002, accessed July 5, 2017, http://www.cbc.ca/news/canada/kava-kava-products-ordered-off-the-shelves-over-liver-concerns-1.341900.

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from Health Canada. This had a ripple effect on the international Kava market, as afterwards, Germany lifted their Kava ban[9], determining that such a ban based on perception over data was not only unfair, but also illegal.[10] As the American Botanical Council notes, the German ban reversal ruling was based on the following factors:

(1) The number of hepatotoxicity case reports was inflated by the inclusion of duplicates.
(2) The ad hoc process used to make the risk assessment is likely to produce different results if applied by different assessors.
(3) The majority of the reports could be more easily explained by known co-medications or alcohol abuse.
(4) The application of a suitable method for assessing liver damage in clinical research reduced the number of cases to three reports where the liver damage was possibly caused by kava, as there were not any obvious, more likely alternative explanations.
(5) The number of possible cases was so small (less than one case/one million monthly doses) that it did not justify the ban.
(6) Risk assessments must be performed in the context of their therapeutic environment. "A drug must not be removed from the market if all possible replacements for it carry (or might potentially carry) an even higher risk." Pharmaceutical alternatives to kava have known significant adverse effects that might be more harmful than those caused by kava.
(7) A case report is not proof of causality. The regulatory authority cannot act on the mere suspicion of potential danger; it has the obligation to provide evidence for both the alleged dangers and the causal relationship with the suspected medication.
(8) Once the regulatory authority has accepted clinical proofs of efficacy, a company having a licensed drug on the market is not obliged to continuously provide new evidence of efficacy, and the regulator cannot withdraw its approval just because new standards are published at a later date.[11]

While some seem to believe that Health Canada lifted the Kava ban on a whim, in reality, it was the result of many hours of hard work. All Kava products being sold in Canada today are in a direct response of Life Choice pioneering for the consumer's rights to purchase the product without discrimination and to remove the negative stigma associated with lesser quality Kava. Still, as kava supplements have flooded the market, problems have occurred, as well.

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[9] "The Kava Ban," Richters Herbs, accessed July 5, 2017, https://www.richters.com/show.cgi?page=Issues/kava.html.

[10] Kenny Kuchta, Mathias Schmidt, and Adolf Nahrstedt, "German Kava Ban Lifted by Court: The Alleged Hepatotoxicity of Kava (*Piper methysticum*) as a Case of Ill-Defined Herbal Drug Identity, Lacking Quality Control, and Misguided Regulatory Politics," Planta Med 2015; 81: 1647–1653, accessed July 4, 2017, doi: http://dx.doi.org/10.1055/s-0035-1558295.

[11] Heather S. Oliff, PhD, "RE: German Court Lifts Kava Ban; Hepatotoxicity May Be Linked to Kava Cultivar," American Botanical Council, last modified February 29, 2016, accessed July 4, 2017, http://cms.herbalgram.org/herbclip/539/021651-539.html.

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Just this year, it was reported that Dr. Mathias Schmidt in Germany and the Vanuatu Ambassador to the European Union, Roy Mickey Joy, in Brussels, have both expressed concerns about the quality of Vanuatu Kava that is currently bombarding the US. Both men previously fought to defend Vanuatu's export market in Europe. Dr. Schmidt received a complaint from the US stating that the country was being overwhelmed by "tudei" kava, as well as leaves and stalks being marketed as "kava." After analyzing the numbers, Dr. Schmidt stated, "That's almost 60 tons of non-noble non-root material sold as kava in 2016 by just one exporter. I thought the Vanuatu Kava Act had been changed, but if someone like [this single supplier] can sell such quantities without any consequences, there must be more than just one person closing their eyes."[12] As a result of these concerns, a new Kava Export Standard was scheduled to be implemented March 1; this standard would penalize those using "tudei" kava and kava mixed with "*makas.*"[13] What are these strains, and why are they of such concern?

"Tudei kava" is called such because the effects last two days. Some suppliers have suggested that "Tudei kava" (called such because the effects last two days) is a safe variety with no liver concerns. They suggest it is practically interchangeable with other varieties[14]—which is true in that once dried and ground, Tudei and noble kavas are indistinguishable.[15] However, they are not interchangeable. Tudei kava is actually a wild type of kava which is unsuitable for consumption.[16] Even historically, native Pacific Islanders only consumed Tudei occasionally, as Tudei cultivars were known to have side effects of nausea and lethargy (called a "kava hangover" by some). Flavokawain B (FKB) is a chalcone from kava root that is toxic to some liver cells.[17] In fact, Tudei kava has been banned for export because it is so dangerous; yet, there are still those advocating for its safety.[18] Interestingly, even those promoting Tudei kava recognize that kava extracted certain ways, such as with solvents, would be wise to avoid. With normal preparation, extraction, and consumption, the amount of FKB in kava is almost non-

[12] Len Garae, "Vanuatu Company Accused of Exporting Kava 'Trash' Throws Industry in Turmoil," last modified January 15, 2017a, accessed June 6, 2017, https://asiapacificreport.nz/2017/01/15/vanuatu-company-accused-of-exporting-kava-trash-throws-industry-in-turmoil/.

[13] Len Garae, "2015 Amendments to Vanuatu Kava Laws Gazetted; Exports to Be Improved," last modified January 30, 2017b, accessed June 6, 2017, http://www.pireport.org/articles/2017/01/30/2015-amendments-vanuatu-kava-laws-gazetted-exports-be-improved.

[14] Kona Kava Farm, "Tudei Kava," accessed June 6, 2017, https://www.konakavafarm.com/kava-tudei.html.

[15] Kalm with Kava, "Noble Kava vs Tudei Kava: An Overview on the Differences," accessed June 6, 2017, https://kalmwithkava.com/noble-kava-vs-tudei-kava/.

[16] The Plant List (2013), Version 1.1, Published on the Internet, accessed July 4, 2017, http://www.theplantlist.org/tpl1.1/record/tro-50299918.

[17] Kalm with Kava.

[18] Kava Guru, "Emerging Controversy Around Tudei Kava," accessed June 6, 2017, http://kava.guru/getting-started/emerging-controversy-around-tudei-kava/.

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existent. Tudei kava, however, can contain 20 times the FKB as noble kava, and if the product is improperly extracted, that amount can go even higher.[19]

Makas are the hard fibers that remain in ground, micronized kava; they are known to cause nausea. This could be for similar reasons as Tudei, that undesirable kavalactones are concentrated there. Most kava processors will not remove Makas from their product, because it results in a 50% loss of volume, and therefore, a loss of revenue. The consequences of this, though, include nausea and dermopathy[20]—a scaly skin rash that occurs in those who are heavy kava consumers.[21]

The Kava (Amendment) Act passed in 2015 sought to crack down on risky kava import practices. Now, all kava must be noble root, clean, and healthy of any defect or disease.[22] A study published by Planta Medica in Germany could not find any toxicity for noble Kava, but suggested Tudei kava needs to be investigated. The German study is available in full here (original is referenced below).[23]

Table 1. Kavalactone and pipermethystine content of the three kava extracts

Component	Methanolic root	Acetonic root	Methanolic leaves
Methysticin	16.6	17.3	0.6
Dihydromethysticin	12.0	12.4	11.3
Kavain	16.2	14.4	0.4
Dihydrokavain	13.4	13.7	10.2
Yangonin	13.6	13.1	1.1
Demethoxyyangonin	9.8	10.6	0.5
Total kavalactones	81.6	81.4	24.1
Pipermethystine	0.011	0.011	1.34

Kavalactones were analyzed with reversed phase HPLC and pipermethystine by GC–MS as described in Materials and methods. Units are % of dried extract (w:w).

Extracted from:
Hepatocellular toxicity of kava leaf and root extract
Phytomedicine. 2008 Jan;15(1-2):120-31
Lüde S, et al.

[19] Kalm with Kava.

[20] Chris Allen, "The Secret to Good Micronized Kava," *The Kava Blog*, accessed June 6, 2017, http://www.kavalibrary.com/Micronized_Kava.html.

[21] Georgina Harvey, "Kava Dermopathy," *DermNet New Zealand*, last modified March 2017, accessed June 6, 2017, https://www.dermnetnz.org/topics/kava-dermopathy/.

[22] Garae, 2017b.

[23] Rolf Gebhardt and Mathias Schmidt, "Impact of Kava Cultivar, Plant Part and Extraction Medium on In-vitro Cytotoxicity of Kava (*Piper methysticum)* in HEPG2 and HEP3B Cells," *Planta Med* 2006; 72, accessed July 4, 2017, doi: 10.1055/s-2006-950146.

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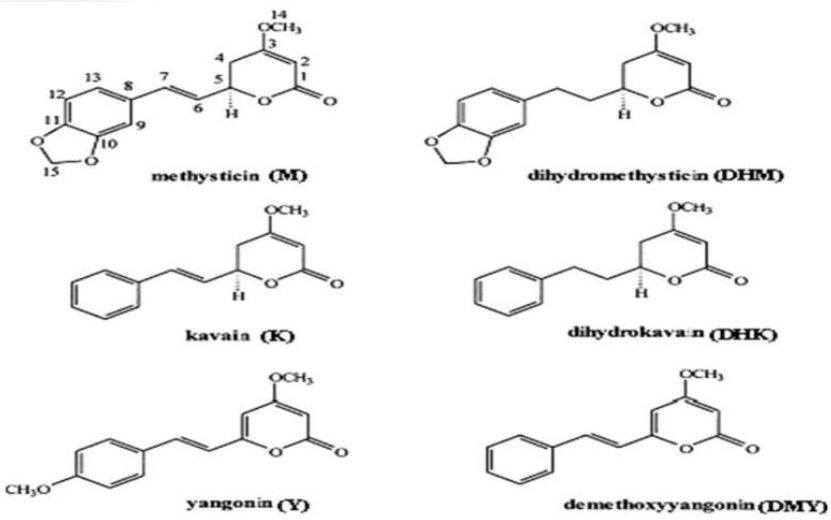
The above chart gives more insight into the difference mature Kava roots can make. Life Choice and Doctor's Choice only use 5 year noble Kava roots. For the leaves and stems, it should first be noted that Pipermethystine is present; this is a toxic alkaloid that can contaminate kava products during high volume production and/or low quality control.[24] It should also be noted that dihydrokawain is around 40% of the total kavalactones and kavain represents 10% of the total kavalactones. This means that the evaluation of the HPLC fingerprint of the kava root and extract gives different kavalactones profiles and the part of the plant can be easily distinguished. On the other hand, extract of 30-70% cannot be produced if the roots are not used.

The chart to the right demonstrates what Kava levels should be using a high quality 5 year noble root Kava strain.

When true 5 year noble Kava roots are used, the product is perfectly safe and very effective for treating anxiety and stress. True 5 year noble root powder or liquid will cause a numbing effect when placed on the tongue. This is just one test to use when choosing kava. Sadly, just licensing the product does not guarantee that all Kava products are using the top quality material; the consumers will decide on what quality they purchase, now that they are given the freedom of choice. We advise customers to choose Kava from trusted suppliers, such as Doctor's Choice, as lesser qualities may jeopardize the product's health benefits.

Doctor's Choice is very concerned with the questionable global quality of kava. Our scientific team has invested hundreds of hours of research and lab analysis in order to produce the therapeutic quality of kava. Shortcuts are being taken in the harvesting stage, and the greed for added profits is being overlooked as kava filler material is being blended with root material. The



Materials and methods

Raw materials

All solvents were of high-performance liquid chromatography (HPLC) grade from Fisher Scientific (Fairlawn,

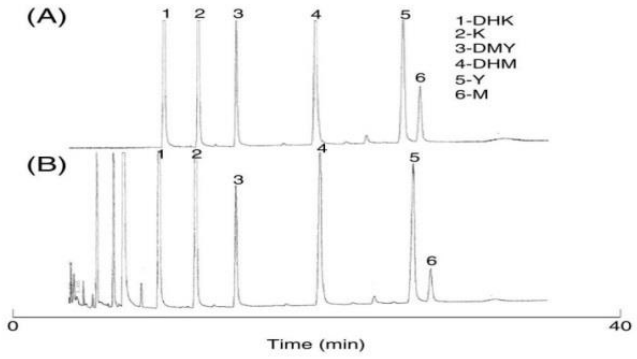


Fig. 2 GC chromatograms of six kavalactone standards (**A**) and a typical kava extract (**B**)

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[24] LD Dinh, et. al, "Interaction of Various *Piper methysticum* Cultivars with CNS Receptors in Vitro," *Planta Med* 2001 Jun;67(4), accessed July 4, 2017, doi: 10.1055/s-2001-14334.

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extraction process is also of concern, as harsh chemicals are being used with chemical residue left on the finished material. Noble kava roots of 5 years have a long and safe history of use when prepared the traditional way. As with all good things, they can be manipulated for added profit, and as a result, the lesser quality jeopardizes not only the poor product, but also casts doubt on those of high quality. The global kava industry has already experienced the negative press and public perception of substandard kava, and through the efforts of companies like Doctor's Choice, this stigma has been removed, but the memories remain.

It is crucial to preserve at all costs the quality and integrity of kava so future generations can safely use this amazing plant without the fear of contamination or ill health. When choosing to purchase a kava product support, only use those companies that prove they are using quality 5 year noble roots that have been prepared ethically and backed by clinical studies. When consumers demand to purchase products that use 5 year noble roots, they ensure the growth and longevity of the kava industry.

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