

# Hepatotoxicity of Kava: True or False

by Roy Upton, Herbalist AHG

## Introduction

Between 1990 and 2002, approximately 68 case reports of alleged hepatotoxicity associated with consumption of the anti-anxiety herb *Piper methysticum* (kava) were made worldwide. To date, no published medical reports regarding such an effect have been made from the South Pacific where kava consumption is most prominent. Most of the reports occurred in Germany and Switzerland where use of kava extracts is widespread. These reports stimulated a chain reaction of regulatory restrictions that has resulted in the banning or severe restriction of the sale of most kava products throughout much of the world, with the exception of the U.S. and the South Pacific.

In addition to the European reports, the Food and Drug Administration (FDA), in January 2002, reported having received 26 reports on kava-related adverse effects between May 1998 and December 2001, including 5 that were liver-related. Subsequently, FDA solicited additional reports from health professionals and reviewed their own existing files. To date, FDA has identified 51 total cases of adverse events due to kava, 21 of which include some liver-associated complaint. Currently, this issue is being investigated by FDA who has only thus far chosen to publish an "Advisory" to both health professionals and consumers, of the potential association between kava use and hepatotoxicity. This situation raises many issues with far-reaching ramifications regarding herbal medicine and the use of herbal supplements, both for the herb market and health professionals.

Following is a presentation of the original European reports that led to the current regulatory restrictions. Determining causality is a difficult process that is best left to toxicologists and statisticians. However, readers hopefully may draw their own conclusions based on the available information. A few formal toxicological reviews of the case reports have been

conducted, the findings of which are presented below. A comprehensive assessment of kava safety would have to weigh the relative benefits of kava use against its relative risk. Since concern about kava and hepatotoxicity has been raised, no formal benefit:risk assessment has been published, though a number of such reviews have been conducted. Some of these allude to a positive benefit:risk ratio for its use as an anxiolytic and others present a contrary opinion. This raises an interesting challenge for the US market which can only trade botanicals within the limitations of the dietary supplement health and education act (DSHEA) which only allows for disclosure of "statements of nutritional support" (structure and function claims). DSHEA does not allow for therapeutic claims to be made or implied. This has caused some to expect a risk tolerance of zero for botanicals, that is, if there are no intended benefits then any risk is unacceptable. All substances, including water, have a potential for toxicity and so it is the relative benefit:risk ratio that should determine the relative value of a substance. Given the current regulatory framework, the only benefit assessment that could be made would be within the construct of the structure and function parameters. Currently, there has been no definitive determination of what constitutes an acceptable structure and function claim for kava.

There have been many theories as to why kava may be associated with hepatotoxicity. Such theories have postulated that there is an increased potential for toxicity due to toxic solvents (acetone) being used in commercial preparations, use of relatively highly concentrated extracts (30-70% kavalactones), use of preparations that are inconsistent with historically used preparations, and use of kava forms traditionally not meant for long term use ("2-day kava"), among others. Prior to the acceptance of any theories as to why kava may be causing hepatotoxicity, if indeed it is, there must first be



**Roy Upton**

Roy Upton is trained in both Western and Traditional Chinese herbalism and has been working professionally as an herbalist for 18 years. He is the vice-president of the AHG, and serves on the board of directors of the Botanical Medicine Academy. He is also the executive director and editor of the *American Herbal Pharmacopoeia*. Roy is general manager of Planetary Formulas, and is a member of the Standards Committee of the American Herbal Products Association. Roy has also authored several books, including *St. John's Wort* and *Echinacea* and the *Botanical Safety Handbook*.

a critical assessment of the reports themselves.

### **Clinical Efficacy of Kava as an Anxiolytic**

From an efficacy perspective, the strongest data, in addition to traditional use, supporting the use of kava as an anxiolytic is derived from a meta-analysis by Pittler and Ernst (2000). In this review, a comprehensive literature search of all double-blind, placebo-controlled studies was conducted and included a total of 377 subjects. According to these researchers, kava was significantly superior to placebo for the treatment of anxiety. Of the studies they reviewed, one reported that synthetic kavain was equally effective as oxazepam for the treatment of anxiety (Ernst 2002; Lindberg and Pitule-Schoedel 1990). In these studies, only 14 subjects reported mild adverse effects. In 2 post-marketing surveillance studies involving a total of 6000 subjects taking 120-240 mg of kava extract (Laitan®) daily, mild adverse effects were reported in less than 2% of subjects (Pittler and Ernst 2000). In one clinical trial, kava was used successfully, with no reported adverse side effects, for benzodiazepine (BZD) withdrawal (Woelk et al 1993). In another (included in review of Ernst), efficacy for kava was reported with no development of tolerance over a period of 25 weeks (Volz and Kieser 1997).

In addition to the positive findings of these studies and review, the Commission E of Germany similarly conducted an extensive review of the literature regarding kava prior to 1990. This led to the generation of a positive monograph being issued for the use of kava for anxiety, agitation, and nervous tension. As is stated later in this discussion, numerous members of the Commission continue to support the use of kava according to the efficacy and safety review reflected in the current Commission E monograph despite the restrictive action taken by the German government.

### **Kava: Adverse Effects Review—Europe**

The most well established side effects associated with long-term ingestion of large amounts of kava are dermatological symptoms of dry, flaky, and yellowish discoloring of the skin known as kava dermatopathy. This is reported to occur at doses that are approximately 100 times the recommended therapeutic dose (Strahl et al 1998). Symptoms usually subside upon discontinuation of kava use. Additional predictable

symptoms include loss of motor function and slowed reaction times. However, the data regarding these actions are mixed.

Most of the regulatory actions taken in Europe were based on 27 case reports (originally reported as 30 but 3 were duplicates) made to health authorities in Germany and Switzerland. One of these included a fatality and four resulted in liver transplantation. The majority of others reported varying levels of hepatotoxicity such as jaundice, elevated liver enzymes, and hepatitis. It appears that the decision to ban kava sales was an emotional response to a potential health hazard before appropriate toxicity reviews were conducted. Since then, such reports have been done with some vindicating the use of kava in the general population and others finding a negative benefit to risk ratio, meaning that the risk outweighs the benefit. In Germany, the banning of kava did not have unilateral support. A number of the members of the German Commission E (see Commission E Monographs, American Botanical Council) expressed “their astonishment” at the decision to withdraw kava products from the market. Moreover, based on their earlier benefit:risk assessment, it is their opinion that the benefits outweigh the risks and therefore the products should be allowed on the market with certain limits proposed.

Despite this, as of July 2002, the German government suspended all product licenses for kava products, effectively removing them from the market. Initially, the Germany had been entertaining the idea of moving kava extract products to a prescription-only category but then chose a complete prohibition instead. Most companies had already removed their kava products from the market but had hopes of eventually being able to bring them back with approved labeling. This no longer seems to be the case. It is likely this conversation is not completely over. For the time being, however, Germany’s direction has been emulated in numerous countries, most of which have not made public any formal risk assessment.

In the European reports, a variety of preparations, at a variety of dosages (see Table 2) were consumed by a wide range of subjects (21-81 years of age) over a period of from 2 weeks to 2 years. Even a cursory review of the reports brings into direct question the validity of many of the

reports, while in most, a causative effect cannot be determined definitively. In what appears to be the most detailed review of the case reports by a government agency, the Medicines Control Agency (MCA) of the United Kingdom (UK) reported that none of 68 reports made worldwide could be attributed to kava with “certainty” (Breckenridge 2002) MCA further classified the various reports according to the relative level of causality that can be attributed to them including “probable”, “possible” and “unlikely”. When reviewing these data it is important to differentiate between adverse events that may be a direct result of kava alone, suggesting a potential for direct hepatotoxicity, concomitant factors that may be responsible for direct hepatotoxicity, such as ingestion of hepatotoxic drugs, and an interaction of the two.

As complete details as are available regarding the original 27 reports are presented in Table 2. A number of specific points are worthy of discussion and highlighting.

1. According to the review of MCA, none of the reports could be correlated with kava use with certainty.
2. According to the review of MCA, 12 of the reports were classified as “unlikely” or “unassessable.”
3. According to the review of MCA, 15 of the reports were considered “probable” or “possible”.
4. Of MCA’s 15 “probable” or “possible”, all but three were consuming conventional medications with reported hepatotoxicity. Of these three subjects, one consumed 60 g of alcohol (specific details were lacking) in a single drinking episode, while the hepatic impairment of another was reported as possibly being caused by prior alcohol consumption.
5. In at least 18 of the total 27 cases, the subjects were also taking medications that have been associated with hepatotoxicity (see note 7 below).
6. Liver transplants were reported in 4 subjects. According to the MCA review, kava as a contributory factor was considered “certain” in zero cases; “probable” in one case; “possible” in two cases; and “unlikely” in the remaining case.
7. In the single transplant reported as “probable”, the subject was also taking acetaminophen. Acetaminophen is highly toxic to the liver and is commonly used in studies to induce hepatotoxicity. Large doses can cause liver necrosis in as little as five days. It is the most common overdose reported to the American Association of Poison Control Centers and is the most common cause of liver failure requiring liver transplantation in the United States (US) and United Kingdom (UK). Between 1996 and 2001 in the UK, acetaminophen use alone was associated with 159 liver transplants. Alcohol consumption increases the risk of acetaminophen toxicity. This subject reported concomitant moderate intakes of alcohol.
8. Of the three remaining subjects requiring transplants, all were taking conventional medications that have been associated with hepatotoxicity. One subject consumed 4 times the recommended dose of kava.
9. A number of the co-medications used were prescribed for severe gastric reflux, migraines, diabetes, and depression suggesting potentially already existing serious conditions in these subjects.
10. In total, there were two positive rechallenges and one relatively strong temporal association of liver toxicity with kava use. These appear to be the strongest of the European cases linking kava with hepatotoxicity.
11. There were a total of six positive dechallenges in which symptoms resolved upon discontinuation of kava, five were considered possible or probable, and one was classified as unlikely. It is likely that an interaction was responsible for the event in these cases.
12. Swiss health authorities (IKS) estimated that eight cases of hepatotoxicity, including all of those discussed above, have occurred in a total of 40 million daily doses or one case per 170,000 courses of treatments of 30 days duration (Stoller 2000). In the review of Ernst (2002) hepatotoxic effects due to kava use was estimated to have occurred in less than one case per one million

**Table 1 Characterization and dosage of products used (Europe)**

Product	Dosage
Acetone extract	70-210 mg kavalactones daily
Ethanol extract (dry)	25-500 mg kavalactones daily
Kavain (synthetic)	400 mg daily
Kava	95 mg kava, 190 mg guarana
Kava (30% lactones) w/ passion flower, hops, and German chamomille	250 mg kava (100 mg blend of other ingredients)

daily doses. Since 1991, approximately 200 million daily doses of ethanolic kava extracts and 40 million daily doses of the acetone extract have been sold worldwide. This appears to establish that reports of serious adverse events have been rare.

**Toxicological Reviews**

Subsequent to these reports and regulatory actions, a number of toxicological reviews were conducted. Some are still underway. According to one review (Schmidt 2002), it was believed that an assertion of kava causing hepatotoxicity based on the reports in Germany and Switzerland was largely “incomprehensible and arbitrary”. The American Herbal Products Association (AHPA) commissioned a toxicological review by Donald Waller, PhD, professor of pharmacology and toxicology, University of Illinois-Chicago. After reviewing all of the available reports and medical histories to that date, Dr. Waller (2002) agreed with the review of Schmidt and further stated that “kava, when taken in appropriate doses for reasonable periods of time, has no scientifically established potential for causing liver damage.” He did, however, acknowledge the potential for drug interactions and idiosyncratic reactions to occur with any pharmacologically active substance.

FDA has now compiled a total of 51 adverse events reports dating from 1995 to 2002, 21 of

which include liver-related events, including one fatality and one liver transplant. No causative assessment, such as that conducted by MCA, has been done with all of the FDA reports. The one liver-related fatality occurred in 1996 in a 24-year old male who was consuming seven products, one of which was a multi-ingredient body building product that listed kava as the primary herb ingredient in a six-herb combination (total herbs = 200 mg). The serving size and total amount of kava consumed were not disclosed. In the others, elevation of liver enzymes resolved after discontinuation of kava in four subjects. No reference to concomitant hepatotoxic drug use was made in these subjects. In one of

the liver transplant cases, a subject was taking the conventional medication Asiphex, (rabeprazole) for gastric reflux, a drug that has been associated with fulminant liver failure in at least one case. Another was undergoing conventional chemotherapy and liver enzymes returned to normal after both chemo and kava were discontinued. There was one report believed to represent a positive correlation between kava use and hepatotoxicity. This subject was reported to have a cytochrome P450 deficiency (Strahl et al 1993), and therefore may have been unable to metabolize kavalactones. Recently, the ability of kava and kava lactones to inhibit cytochrome P450 in in vitro assays was demonstrated (Mathews et al 2002). In this study, either kava or individual lactones were dissolved in acetone at a concentration of 1 or 10 µM and the acetone was evaporated. Human liver microsomes pretreated with the kava solution were assayed for their effects on various cytochrome P450 enzymes. Significant inhibition of a number of enzymes was seen suggesting that kava may have an effect of inhibiting the clearance of drugs that are metabolized through these enzyme systems (such as benzodiazepines), thereby increasing their potential for toxicity.

According to Waller, two examples of chronic and high dose consumption of kava that were not associated with any significant liver damage provide some evidence that kava itself is not a

direct hepatotoxin, even in extremely high concentrations. In one of the US reports of general kava adverse effects, the subject consumed up to 10-15 pills (150 mg each) daily for a year with occasional use of up to 300 pills (45,000 mg) in one day and did not exhibit hepatotoxicity. Moreover, this subject had a history of alcohol abuse, depression, anxiety, and social phobic disorder. Another was a 13-year-old girl who attempted suicide with kava (4000-5000 mg) and similarly exhibited no hepatic abnormalities, only deep sleep, and was released from the hospital the following day.

Two non-hepatic related fatalities were reported. One subject was an 86-year old man with congestive heart failure who drank 1 cup of an herbal tea that contained kava with 6 other botanicals and died in his sleep; the other was a 28-year old female who died of cerebral hemorrhage due to capillary-venous malformation. She was also consuming 2 weight loss products (Mini-Thins and Yellow Jackets) containing a total of 50 mg of ephedrine semi-continuously for 10 years and regularly for 2 years, coupled with oral contraceptives, an antiemetic (prochlorperazine), and ibuprofen.

A detailed analysis of the FDA reports is beyond the scope of this discussion as the primary decisions leading to regulatory restrictions on kava were based primarily on the original 27 reports from Germany and Switzerland. However, in the review of the original 26 FDA case reports by Waller, it was similarly concluded that “there is no scientifically supported association of liver disease with the use of kava which can be found using the US FDA adverse reaction case reports.” Still, a few cases showed a clear resolution of symptoms upon dechallenge suggesting that, at least in some individuals, kava may be a contributory factor in some hepatotoxic events. While Dr. Waller’s report included an evaluation of the first 26 reports provided by FDA in January of 2002, no assessment has been done on the remaining cases.

Of three cases reported in the UK, two appear to be associated with kava use. The elevated liver enzymes of one subject who consumed 6 bottles of wine per week and an undisclosed amount of kava for three months returned to normal after

discontinuation of kava suggesting the possibility of potentiation, unless he also stopped consumption of wine, which was not noted. A second case of raised liver enzymes also returned to normal after discontinuation of kava. This subject was also taking an antihypertensive medication (bendrofluazide). In the last case, liver enzymes remained elevated despite discontinuation of kava.

There are two cases, one that appears to not have been included in the review of MCA (Escher et al 2001) and another very recent report (Campo et al, in press). In the first, a 50-year-old man consumed 210-280 mg of kavalactones daily for two months. Liver function tests showed a 60 to 70-fold increase in enzymes and subsequently required a liver transplant. Upon histological examination, the liver showed extensive and severe hepatocellular necrosis. In the recent report, a 14-year-old girl developed fulminant hepatitis and hepatic failure requiring liver transplantation after ingestion of kava at recommended doses over a three month period. These subjects reportedly had no pre-existing condition which would have given rise to such an event. These cases appear to be among the only relatively definitive reports of direct hepatotoxicity due to kava use.

### Conclusion

Despite the severity of the regulatory actions taken by governments internationally, the available data raises numerous doubts as to any definitive correlation between kava and hepatotoxicity. The most significant limitation of a review such as this is the limited availability of information, especially with regards to the presence of pre-existing conditions for which the subjects are being medicated, the timing of administration of conventional medications and kava, and the underlying imbalances that led to ingestion of kava in the first place. More information could help in making a clearer assessment.

Thus far, the US FDA has not taken a restrictive action pending further investigation and review of the collected reports. Because of this, product liability insurance issues aside, kava is still available on the American market. However, product liability for these products may be

**Table 2 Liver related adverse events reported by German and Swiss Health Authorities**

Age/Sex	Event	Preexisting Condition	Product & Dose	Concomitant Medications	Side Effects of Concomitant Medications	Outcome and MCA Classification
37/f	Hepatitis	—	2 x 70 mg dry acetone extract [Laitan®]	Microdiol (5 yrs), Diclofenac	Diclofenac associated with severe hepatic reactions in 15% of those using; marked elevation of liver enzymes requiring monitoring 4-8 weeks after initiation of therapy; reports of fulminant hepatitis, liver necrosis, jaundice, fatal hepatitis, and liver transplant.	Recovery after 3 mos. Negative rechallenge.  Unlikely
62/f	Liver cell impairment	—	60 mg (?) dry ethanol extract [Kavatino]	None noted	—	Recovered on withdrawal of all drugs. Positive rechallenge with kava.  Probable
33/f	Bilirubinaemia, hepatitis, increased liver enzymes, cirrhosis of the liver	—	Dry ethanol extract [Kavatino] for approximately 4 mos	Cisapride (begun same time as kava)	Cisapride removed from US market after 11 deaths. Hepatic side-effects reported.	Unassessable
46/f	Severe liver damage with jaundice	—	2 x 70 mg/d dry acetone extract [Laitan®] for 4.5 mos	Propranolol, HCT, Valsartan	Elevated liver enzymes associated with both drugs. Propranolol contraindicated in patients with impaired liver function. Valsartan slows hepatic clearance of drugs.	Possible
33/f	Cholestatic hepatitis with jaundice	—	3 x 70 mg/d dry acetone extract [Laitan®] for 2-3 mos	Acute consumption of 60 g alcohol	—	Recovery after 6 weeks. Lab confirmed drug-induced hepatic damage and ruled out alcohol despite acute exposure.  Probable
60/f	Increased bilirubin and transaminases, indolent jaundice	Depression	70 mg/d dry acetone extract [Laitan®]	Celebrex	Hepatic side effects associated with concomitant medication. Celebrex inhibits cytochrome P-450(2D6). Increased liver enzymes and abnormal liver function reported.	Recovery after 2 weeks.  Possible
50/m	Acute necrotizing hepatitis, irreversible liver damage	Nervous tension	3-4 x 70 mg/d dry acetone extract [Laitan®] for 2 months	Moderate alcohol intake; acetaminophen, Nachtkerzensam enol	Highly toxic to liver; in UK 159 liver transplants associated with drug (1996-2001).	Transplant  Probable
21/f	Increased liver enzymes, jaundice, hepatitis	8-10 x 50 mg (Kavain Harras Plus).  Dose 4-6 times over recommended dose.	—	Acetaminophen, Paspertin, Pantoprazol, Basilikum-Tropfen  Concomitant drugs prescribed for mild-severe gastric reflux.	Acetaminophen highly toxic to liver; in UK 159 liver transplants associated with drug (1996-2001).	Unassessable

Age/Sex	Event	Preexisting Condition	Product & Dose	Concomitant Medications	Side Effects of Concomitant Medications	Outcome and MCA Classification
69/f	Cholestatic hepatitis	—	2 x 200 mg synthetic kavain (Neuronika)	Aspirin, dehydrosanol, renylin (pentoxifyllin)	Hepatic side effects reported for all medications.	Unassessable
35/m	Cholestatic hepatitis	Anxiety	2 x 200 mg synthetic kavain (Neuronika)	—	—	Recovery after discontinuation of kava. Unassessable
68/f	Increased liver enzymes	Liver enzymes raised prior to kava use	3 x 70 mg acetone extract [Laitan®]	—	—	Enzymes did not go higher with kava use Unlikely
39/f	Upper abdominal pressure, nausea, vomiting, jaundice	Depressive neurosis	3 x 70 mg acetone extract [Laitan®] (2 mos)	Diazepam, Gravistat (estradiol), L-thyroxin	Liver tumors, cholestasis, and anicteric hepatitis associated with Gravistat.	Recovery after discontinuation of all medications. Probable
68/f	Cholestatic hepatitis, jaundice	Depression	3 x 70 mg acetone extract [Laitan®] (2 yrs)	Neuroplant forte, Maaloxan if required.	Sporadic reports of increased liver enzymes with Maaloxan;	Diagnosed as immunological hypersensitivity reaction resulting in idiosyncratic hepatic damage. Recovered after 97 days. Possible
50/f	Increased liver enzymes, liver cell impairment, acute hepatitis with jaundice	—	3 x 70 mg acetone extract [Laitan®] (2 mos)	Furosemide, Atenolol, Terfenadine	Jaundice associated with Furosemide; Terfenadine contraindicated in patients with hepatic liver dysfunction.	Possible
72/f 75/f (reported twice)	Cholestatic hepatitis, liver cell impairment	—	25 mg dry ethanol extract [Phytogeriatrikum] (6 mos)	Eunova (herbal?)	—	Unassessable
81/f	Toxic hepatitis with fatal liver failure, acute yellow liver dystrophy	Anxiety, restlessness	2 x 60 mg dry ethanol extract 9 mos [Kavatino]	Hydrochlorothiazide, hawthorn extract	—	Death. Hepatic impairment due to alcohol possible; pathology showed damage started 18 months prior to death. Probable
39/f	Severe hepatitis with confluent necrosis	—	60 mg (?) (6 mos)	Paroxetine, St. John's wort, hormonal ovulation inhibitors (6 yrs)	Paroxetine associated with infrequent or rare reports of abnormal liver function, elevated liver enzymes, and hepatitis. Not to be used with MAO or SSRI.	Onset of symptoms at 6 mos and again 14 days after re-exposure. Probable
59/f	Liver cell impairment	Anxiety	2 x 120 mg dry extract [Limbao] (4 mos)	Buscopan (derivative of Datura for treatment of irritable bowel syndrome).	Sporadic reports of hepatotoxicity.	Unassessable

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\* MCA = Medicines Control Agency, United Kingdom

phased out over the next several years and will eventually impact availability more than it already has. In the US, many companies have discontinued the use of kava in their products due to the lack of product insurance. Insuring that such situations are not repeated with other botanicals will be a challenge to the entire herbal community in the future. Thus far, AHPA has taken the lead on defending the herbal products category and has recommended specific label warnings for kava products (see AHPA Kava Label Warning). However, in the future, practitioners will have to have a louder voice in these debates if our materia medica is to be preserved.

**Kava and Product Liability**

Despite the inconclusiveness of the case reports presented, the severity of the current regulatory restrictions placed on kava worldwide is severely impacting its current and future accessibility as an herbal supplement and medicine. For the past 30 years in the United States, there have been relatively few problems with herbal products and thus relatively few insurance claims against the product category overall. This is quickly changing as attorneys are actively seeking any way they can to initiate legal action when an issue has been raised regarding an herbal product as well as other commodities. In the state of California, there are very strict limits on the level



Michael Balick

**Table 3 Assessment Criteria of Medicines Control Agency (MCA)**

Criteria	Assessment	#
Certain	Clinical event that occurs in a plausible time relation to drug administration; event not coincidental and not related to current condition or medications; recovery upon dechallenge; recurrence on rechallenge.	0
Probable	Clinical event that occurs in a plausible time relation to drug administration; event unlikely to be related to current condition or medications; recovery upon dechallenge; rechallenge not necessary to fulfill this criteria.	14
Possible	Clinical event that occurs in a plausible time relation to drug administration; event may be caused by current condition or medications.	30
Unlikely	Clinical event with temporal relation to drug administration but which makes a causal relation improbable and in which other medications or disease conditions provide a plausible explanation.	5
Unassessable	Report can not be judged due to insufficient or contradictory information that can not be supplemented or verified.	19

Ref: *Lancet* 2000; 356: 1255-1259

**Table 4 International Regulatory Actions**

Australia	Investigated safety of kava. Initially felt only an advisory warning was necessary. August 2002, issued a voluntary recall to consumer level of all medicines containing kava on sale in Australia. Manufacturers given a period of time to submit safety data for their products.
Canada	Banned sale of kava-containing products.
Fiji	Issues international memorandum stating that evidence does not support a ban of kava products.
France	Suspended sales of products.
Germany	Revoked product licenses for kava extracts.
Ireland	Voluntary removal of all kava-containing products.
New Caledonia	Ban of pharmaceutical but not traditional kava products.
Portugal	Suspension of sale of kava products for 1 year.
Switzerland	Concluded that risks do not outweigh benefit; acetone extracts recalled; ethanol extracts limited to sales in pharmacies.
United Kingdom	Banned sale of kava-containing products.
United States	Issued advisory to health professionals to actively look for kava-hepatotoxicity reactions; consumers notice recommending discontinuation of kava use.

of the number of “contaminants” or toxic compounds such as heavy metals, that are allowed in foods without appropriate warning labeling. Some of these levels are so low that a large number of commercial food products, even of organically cultivated foods, are in violation. This sets the stage for the arbitrary testing of products in hopes of finding those that are in violation in anticipation of receiving a quick settlement. Such actions have led to numerous Chinese herbal companies either going out of business or relocating to other states where such a law is not in place. The litigious nature of the American public and the extravagant financial penalties awarded by in-court and out-of-court settlements create a significant challenge for the future of the herbal products industry and the practice of herbal medicine.

On the insurance side of the equation, insurance providers hear about such actions and create a running list of botanicals for which they will no longer provide product liability insurance, regardless of whether the initial complaint against the botanical was justified or not. This

has been most evident with an importation restriction notice against Chinese botanicals put out by FDA a number of years ago. There has been long-term confusion in the Chinese herb trade of *Stephania tetrandra* (han fang ji) with *Aristolochia fang ji* (guang fang ji), which contains the known renal toxin aristolochic acid (AA; also present in wild ginger *Asarum* spp.). Numerous other herbs have been implicated as potential adulterants, some justifiably, others not and have been included on the list even though they do not contain AA. While the FDA’s standing policy is that the botanical(s) can remain in trade as long as the manufacturer or marketer can show it is free of AA, many insurance providers have chosen not to provide product liability insurance for any of the herbs on the list regardless of their safety or the confirmed lack of toxic compounds.

Kava is included on the restriction list of a number of insurance carriers. This raises an important issue for manufacturers as to whether they should discontinue use of the herb(s) in their products or continue selling uninsured products. In an environment rife with ambulance chasers,

the latter choice is not very appealing and many manufacturers have chosen to remove anywhere from 3 to 20 herbs from their product mix. While this has thus far not significantly impacted herbal practitioners it nevertheless has the potential to do so, especially for those who continue to wildcraft or may not be aware of the current regulatory reality. Thus far there has been at least one case against an herbal practitioner for prescribing a formula that turned out to contain AA. Moreover, continued use of these botanicals by practitioners potentially increases their liability, even in absence of a patient being injured. More challenges for the herbalist community, unfortunately, are on the horizon if the environment does not change dramatically. At the very least, the herbalist community is at risk of watching its materia medica be whittled down as issues regarding herb purity, herb toxicity, and herb-drug interactions become more and more apparent.

#### AHPA Kava Label Warning

“US FDA advises that a potential risk of rare, but severe, liver injury may be associated with kava-containing dietary supplements. Ask a healthcare professional before use if you have or have had liver problems, frequently use alcoholic beverages, or are taking any medication. Stop use and see a doctor if you develop symptoms that may signal liver problems, including jaundice (yellowing of the skin or whites of the eyes) and brown urine. Other nonspecific symptoms can include nausea, vomiting, light-colored stools, unexplained tiredness, weakness, stomach or abdominal pain, and loss of appetite. Not for use by persons under 18 years of age, or by pregnant or breastfeeding women. Not for use with alcoholic beverages. Excessive use, or use with products that cause drowsiness, may impair your ability to operate a vehicle or heavy equipment.”

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