



## The activities of the International Kava Executive Council IKEC to remove the kava ban in Europe



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# Traditional and Medicinal Use of Kava



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- ✓ Has taken place for centuries with no occurrence of liver problems
- ✓ There are no obvious cases of liver toxicity seen in hospitals in the Pacific
- ✓ When prepared according to traditional methods, kava cannot commonly cause severe acute liver toxicity; otherwise it would have been noticed by now
- ✓ Drug in Europe/Germany for more than 50 years

# Regulatory Measures



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- ✓ April 2001 - Recall of the registration of a kava product in Switzerland
- ✓ Nov 2001 - „Stufenplan-Verfahren“ in Germany
- ✓ June 2002 - Withdrawal of 97 kava products by 49 companies in Germany by the Drug Regulatory authority BfArM
  - Complaints by Commission E
  - ZÄN (Central Committee of physicians for complementary treatment) lawsuit against the decision
  - Withdrawal in other European countries: Austria, Belgium, France, Greece, Netherlands, UK
  - Withdrawal of kava products by Singapore, Canada, Malaysia
  - Voluntary recall: Australia, New Zealand (traditional kava products not concerned)
  - FDA warning

# International Usage Before/After Ban



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Country	Before	After
Europe	Drugs/Supplements	banned
Singapore	Supplements	banned
Canada	Supplements	banned
USA	Supplements	Supplements + traditional form
Australia	Supplements	Traditional form OK, extracts banned
New Zealand	Supplements	Traditional form OK, extracts banned
Brazil	Drugs	Drugs
Pacific Islands	Traditional form	Traditional form

# Socio-Economical Impact on the South Pacific Islands



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The increasing popularity of kava in Europe and the US led to:

- ✓ A tremendous increase in kava demand
- ✓ An increase in land planted with kava  
(e.g. from 353 acres in 1998 to 2600 in 2002 in Samoa)
- ✓ Development of a strong kava industry
- ✓ High dependency of the South Pacific Islands economy and the livelihood of many rural communities on the kava market

# Socio-Economical Impact in the Pacific



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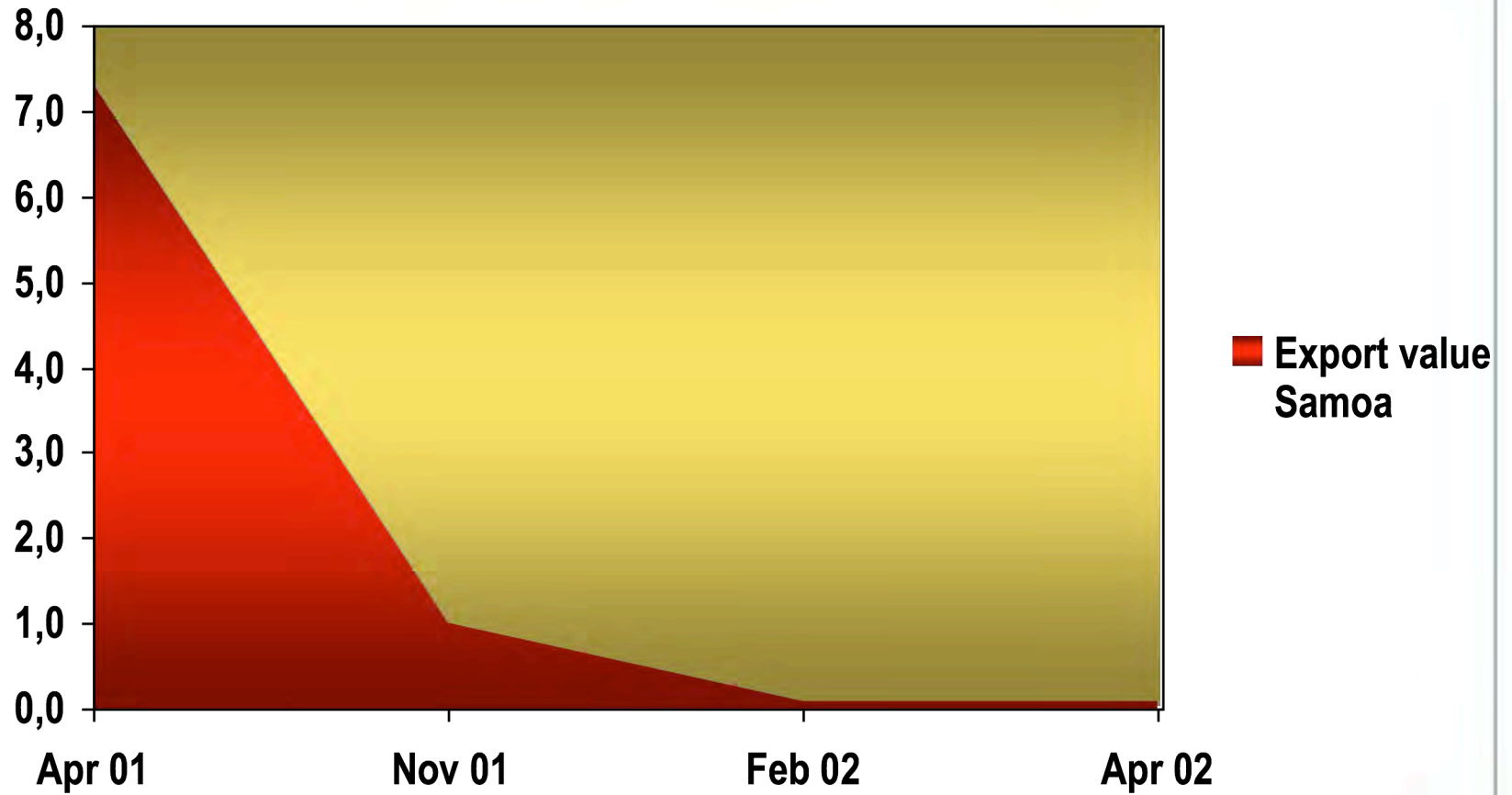
- ✓ The ban on kava products in most EU countries and others led to an economic disaster
- ✓ Exports of kava decreased dramatically
- ✓ In all of the Pacific Island states and Hawaii export rates in 2002 were reduced up to 75 % compared to 2001

# Export values



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metric tons



# Socio-Economical Impact in the South Pacific



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- ✓ Due to a mass cessation of exports domestic prices dropped severely
  - Breakdown of the local kava industry, and bankruptcy for many farmers
  - Unemployment
  - Increased poverty for the kava dependant rural communities
  - Decreased tax income for the affected countries

# Scientific Evaluation



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- ✓ The German BfArM as well as other national health authorities stated that the ban on kava was justified because:
  - Kava intake can cause severe adverse events
  - The efficacy for the claimed indication can not be regarded as proven
  - This led to a negative benefit/risk assessment

# Our Scientific Evaluation



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- ✓ Expert Report on the Clinical Documentation
- ✓ Expert Report on the Pharmacological-Toxicological Documentation
- ✓ Comprehensive Case Analysis of the reported cases of severe adverse events

# Efficacy



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1. The efficacy of kava in the treatment of conditions of nervous anxiety, stress and restlessness was approved by
  - 12 randomized controlled (11 placebo, 1 reference), double-blind clinical trials with approximately 1000 patients
  - Various non-controlled trials including approximately 10,000 patients
2. The Cochrane Institute stated in a meta-analysis of controlled clinical trials that:
  - The vast majority of the clinical trials that been carried out are of high methodological value
  - The efficacy of kava in the claimed indication has to be regarded as proven

# Efficacy



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3. The German Commission E, an independent expert commission implemented by the German Ministry of Health, has confirmed the efficacy of kava in the claimed indication
4. Another independent expert commission implemented by the German Ministry of Health (Institut für die Arzneimittelverordnung in der gesetzlichen Krankenversicherung) included kava in the main section of the “Positive List”
  - Kava is considering to conform to the criteria of evidence based medicine
  - Confirming the efficacy of kava

# Safety



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## ✓ Traditional use:

- During the nearly 1000 years of traditional kava use in the South Pacific region, no severe adverse effects have been reported

## ✓ Clinical trials:

- In all the clinical trials, entailing approximately 10,000 patients, no severe adverse events have been observed
- Less than 1 % of patients reported adverse events, most of which were gastrointestinal complaints



## ✓ Post-marketing experience

- About 250 million daily doses have been sold during the last 10 years
- Until 1998 no severe adverse events have been reported
- Assuming that all of the reported 39 cases, which the BfArM decision was based on, were related to kava intake, the incidence for hepatic AEs would be: 0.15 cases/one million doses
- ⇒ a very low risk potential

# Our Case Analysis



Classification	Number of reports
Double or triple entries	4
No connection to kava	13
Probably connected to concurrent medication	22
Connection to kava doubtful	6
Connection to kava not assessable	31
Possible connection to over-dosage of kava	2
Possible connection to kava at monograph conform dosage	1

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# Results of the Our Case Analysis



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- ✓ Regarding the available data, our findings do not agree with the findings of the German BfArM
- ✓ Many of the AERs lack important details and can not be included in the evaluation
- ✓ As seen in the table there are only 3 out of 79 cases of severe adverse events that can be related to kava intake
- ✓ Therefore the revised incidence for hepatic AEs would be: 0.012 cases/one million doses

# Automatic Blaming Of Herbal Medicine



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- ✓ An 81 year old woman who died from liver failure had taken a kava product prior to the incident (BfArM identifier 98004297)
- ✓ Post-mortem examination: early liver cirrhosis started well before the first intake of kava. Probably caused by alcohol abuse. German authorities denying the intake of alcohol by the patient, and use this case report as a dramatic example for the alleged side effects of kava

# Kava Use Internationally Today



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- ✓ Kava is sold as drug in Brazil
- ✓ Kava is sold as supplement in the USA
- ✓ Kava is broadly used in the Pacific
- ✓ Kava in traditional form is used in Australia and New Zealand
- ✓ Intensive internet and mail-order sales

# Status of Kava Science (1)



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- ✓ A publication by Dr. U. Hagemann from the German Health Authorities summarizes the decision:
  1. **Benefit:** only 2 studies fulfilled the required criteria for drug registration, to be double-blind and placebo-controlled and a dosage between 60 and 120 mg kava lactones, but these two publications had other flaws.  
**Comment:** In total there are 11 controlled studies and 2 meta analyses. The international scientific community regards Kava's efficacy as proven.
  2. **Risk:** 40 reports about suspected hepatotoxic reaction, 7 severe cases, 2 of which died  
**Comment:** 3 of them can be directly related only to Kava

# Status of Kava Science (2)



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## Conclusion Dr. U. Hagemann:

- Kava related severe liver damage is very rare
- Dosage in most cases was higher than recommended 60 – 120 mg kava lactones per day or had longer exposure
- This means that there must be a dosage below which no liver toxicity is probable or even can be excluded
- A deficit for the patients was not to be expected – there are alternatives for treatment

## Comment:

- The alternatives for treatment primarily are Benzodiazepines, these have a high dependency risk as well as a higher risk of liver toxicity with 0.9 – 2.1 cases per 1 million dosages. Kava only has a risk of 0.012 cases per 1 million dosages.

# Status of Kava Science (3)



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- ✓ Several publications in Germany from
  - Teschke, Loew, Schmidt, Schilcher, Siegers, Gaus, Nahrstedt
- ✓ In the USA from
  - Waller

criticize the German decision and are pushing for a re-evaluation of the data and the consequences.

One alternative proposes to preliminary put kava under prescription as a drug before reaching a final decision

# Status of Kava Science (4)



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## New data / new publications since the Kavas ban 2002 - Summary

Over 50 new scientific publications:

- ✓ 1 Meta-Analysis
- ✓ 1 Controlled clinical trial
- ✓ 1 Drug monitoring study
- ✓ 2 Epidemiological study
- ✓ 3 Case reports
- ✓ 4 Pharmacological studies
- ✓ 3 Analytical/composition studies
- ✓ 35 Reviews/theoretical publications

# Proposal for Optimised Quality Control to Guarantee Safest Kava



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- ✓ Selection on best varieties
  - Screen for certain varieties which meet the criteria
  - No so called “two day kava” for export
- ✓ Rootstock use only
  - No usage of aerial parts, peelings or leaves
- ✓ Approved quality control system
  - Development of a SOP system
  - Development of a government controlled quality seal (Prime Pacific Kava)
- ✓ Usage of traditional form or ethanolic extracts only
- ✓ Define an optimum composition of single kavapyrones
  - M + DM controlled extracts
- ✓ Dose and time limitation of use, warnings

# Goals of International Kava Executive Council IKEC



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- ✓ To guarantee consumers and patients a safe usage of kava kava
- ✓ Re-activation of the kava trade between the kava producing ACP states and the states of Europe
- ✓ Reduction of financial damage for the kava exporting countries



# IKEC

## International Kava Executive Council

### Pacific Co-Chair

Edward L. Wilson

### Executive Director

Joerg Gruenwald

### European Co-Chair

Anthony Bush

**Josateki Nawalowalo**

(Fiji)

**Eddie Wilson**

(Samoa)

**To'imoana Takataka**

(Tonga)

**John Aruhuri**

(Vanuatu)



CDE

**Anthony Bush**

EHMP (UK)

**Dr. Carlo Sessa**

ASSOERBE (I)

**Dr. Barbara Steinhoff**

BAH (D)

**Dr. Mathias Schmidt**

Extractor (D)

# Update on International Activities

## Activities of the IKEC



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- ✓ Discussion with Deputy Health Minister Dr. Schroeder and politicians of different parties
  - Meeting with Deputy Health Minister Dr. Schroeder together with Dr. Steinbeck-Klose (SPD)
  - Meeting with Green Parliamentarian Birgit Bender, responsible for health issues
- ✓ Organization of meetings with representatives of national health authorities Germany, UK
  - Meeting with Dr. Keller
  - Pre-meeting with several representatives within the MHRA



# Recent Activities



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## International Kava Conference 2004 (IKC 2004)

Nov. 30 - Dec. 2, 2004 in Suva (Fiji)

- o Organised by: the University of the South Pacific, the Fiji School of Medicine, the Pacific Islands Forum Secretariat and the International Kava Executive Council
- o Supported by the Governments of Fiji, Tonga, Samoa and Vanuatu as well as local and international organisation committees
- With 120 participants from 16 countries
- Chaired by Prof. Dr. Ralph Edwards, WHO Drug Monitoring Center Uppsala

# IKC 2004

IKC  2004

Support the fight against the kava ban

#### Major Conference Goals:

- To provide an international forum for discussions on the scientific and regulatory situation of kava
- To evaluate new scientific data on toxicity and efficacy of Kava
- To create an improved quality control systems for kava raw material from the South Pacific
- To identify ways to secure the future of the local kava industry



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## International **30 NOVEMBER - 2 DECEMBER 2004** SUVA, FIJI AT THE PIFS Kava Conference 2004

[www.ikec.org](http://www.ikec.org)

#### An international conference organized by

- International Kava Executive Council (IKEC) • University of the South Pacific (USP)
- Fiji School of Medicine (FSM) • Republic of the Fiji Islands • Pacific Island Forum Secretariat (PIFS)

#### IKC 2004 who will attend:

Reknown International Scientists: Scientific Experts from 12 countries covering Europe, North America and the South Pacific

Representatives of the Governments of Fiji, Samoa, Tonga and Vanuatu

International Organizations: European Unions Centre for Development of Enterprise (CDE) and PRO INVEST, World Health Organization (WHO), Pacific Islands Forum Secretariat (PIFS)

Private Sector: Kava Growers, Traders, Extractors, Intentional Neutraceutical and Pharmaceutical Companies and Associations

#### Local Conference Office

**Chairman**  
Ratu Josefa Namanimalo  
Fiji Kava Council

**Secretary**  
Henry Banzag  
Pacific Island Forum Secretariat  
Trade and Investment Division

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#### The IKC is supported by

The Governments of



The EU Centre for Development of Enterprise (CDE)  
PROINVEST  
Italian Medicinal and Aromatic Plants Producer and Trader Association (ASSOERBE)  
The American Herbal Product Association (AHPA)  
Bundesverband der Arznei- und Heilpflanzen (BAH)

#### International Conference Office

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c/o Phytopharm Consulting

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13687 Berlin  
Germany

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Fax: +49 30 4200 8500

Travel funds for Pacific kava growers, traders and exporters are available, please apply to the local or international organizing committee.



# Recent New Research



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- ✓ In-vitro toxicological research  
by Prof. Gebhardt, University of Leipzig  
in human hepatocytes
- ✓ In-vivo toxicological research  
by Prof. DiSilvestro, Ohio State University  
in rats

# WHO Report



World Health  
Organization

## Assessment of the risk of hepatotoxicity with kava products



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# Summary



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- ✓ The kava ban is scientifically not justified
- ✓ New toxicological trials confirm the safety of kava
- ✓ WHO gives directions to improve quality control and bring kava back to Europe
- ✓ The German authorities are the only to request more clinical data
- ✓ Kava will make its way back to Europe, it is only a matter of time
- ✓ If we don't react in this case, in future most herbals can easily disappear from the market

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