

CPD

Acute cutaneous toxicity with kava: an inflammatory sebotropic reaction and urticaria

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Kava is prepared from the plant *Piper methysticum*. It has been used for centuries in South Pacific communities, and dried kava root is exported internationally. We report a case of an acute inflammatory sebotropic eruption and urticaria in a patient following kava consumption.

A 23-year-old white woman presented with a 5-day history of a widespread, pruritic, erythematous rash, which had started on her right forearm. The patient's medical history included anxiety. She used no regular medication, and denied the use of any herbal medications or supplements.

On physical examination, urticated, erythematous plaques were seen, which were most prominent on the trunk and proximal arms (Fig. 1a–d). Scattered pustules were present on the upper back and face, with some facial swelling and scaling. The patient was febrile (temperature 38.0 °C) with palpable cervical lymphadenopathy. Other vital signs were normal.

The differential diagnosis included early pustular psoriasis, pityriasis rubra pilaris, acute generalized eruptive pustulosis and viral exanthem.

An incisional biopsy was taken from the right arm, and histological examination revealed folliculocentric inflammation, rich in neutrophils (Fig. 2a–c). Fungal yeast forms were detected deep in the follicle (Fig. 2d), mimicking a fungal folliculitis.

Laboratory investigations showed a significantly raised alanine aminotransferase level (297 U/L; normal range 7–35 U/L), with normal bilirubin and alkaline phosphatase levels. Mild lymphopenia ($0.6 \times 10^9/L$;

$1.0\text{--}3.0 \times 10^9/L$) was present, but white blood cell, neutrophil and eosinophil counts were normal. Blood cultures and a throat swab for respiratory viruses were negative.

The initial treatment plan was topical steroids and oral histamine. One week later the patient presented with acute facial swelling and a history of transient, urticated plaques on the limbs. On this occasion the patient reported that she had been using a kava supplement, which she had purchased online as an anxiolytic. Oral prednisolone was given for 5 days, and the patient was advised to stop taking kava. Liver function tests normalized and at the 3-month follow-up, there had been no subsequent episodes.

Kava has been used for centuries in South Pacific communities for medicinal, social and cultural purposes. Prepared from the roots of *P. methysticum*, its active ingredients (kavalactones) have anxiolytic and euphoric effects.¹ Kava became more widely available in Western countries in the 1990s, and by the early 2000s, sales were worth approximately US\$200 million a year.² However, kava was soon implicated in several cases of acute liver failure, and it was banned afterwards in many countries, including the UK in 2003. This toxicity was unexpected from its use in the Pacific Islands, and debate exists whether this represents medical undersurveillance in the Pacific Islands or differences in use in Western countries.¹

In 2007, a World Health Organization (WHO) report concluded that kava-induced hepatotoxicity was rare. In our case, the RUCAM (Roussel Uclaf Causality Assessment Method) score was 6,³ suggesting probable causality for the supplement. The WHO report suggested that chemicals other than kavalactones may have been responsible for hepatotoxicity. Potential causes include use of substandard kava due to high demand (including aerial parts of the plant, which contain toxic alkaloids), adulteration of kava products

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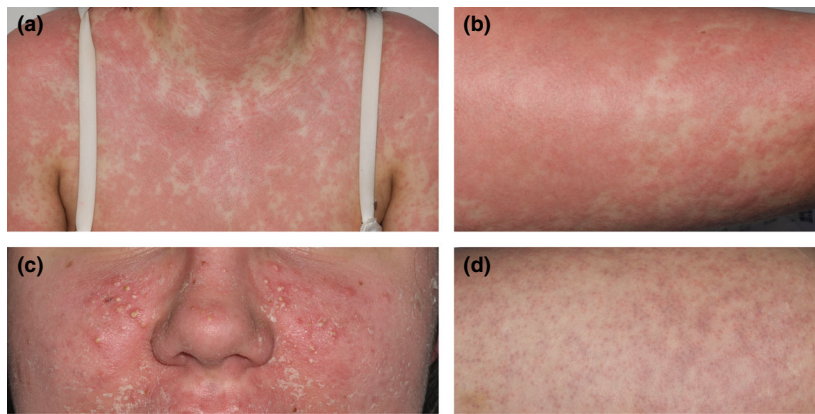


Figure 1 Urticated, erythematous plaques most confluent on (a) the chest and (b) proximal arms; and (c) pustules, scaling, and swelling on the face. (d) There was a marked follicular prominence on the legs.

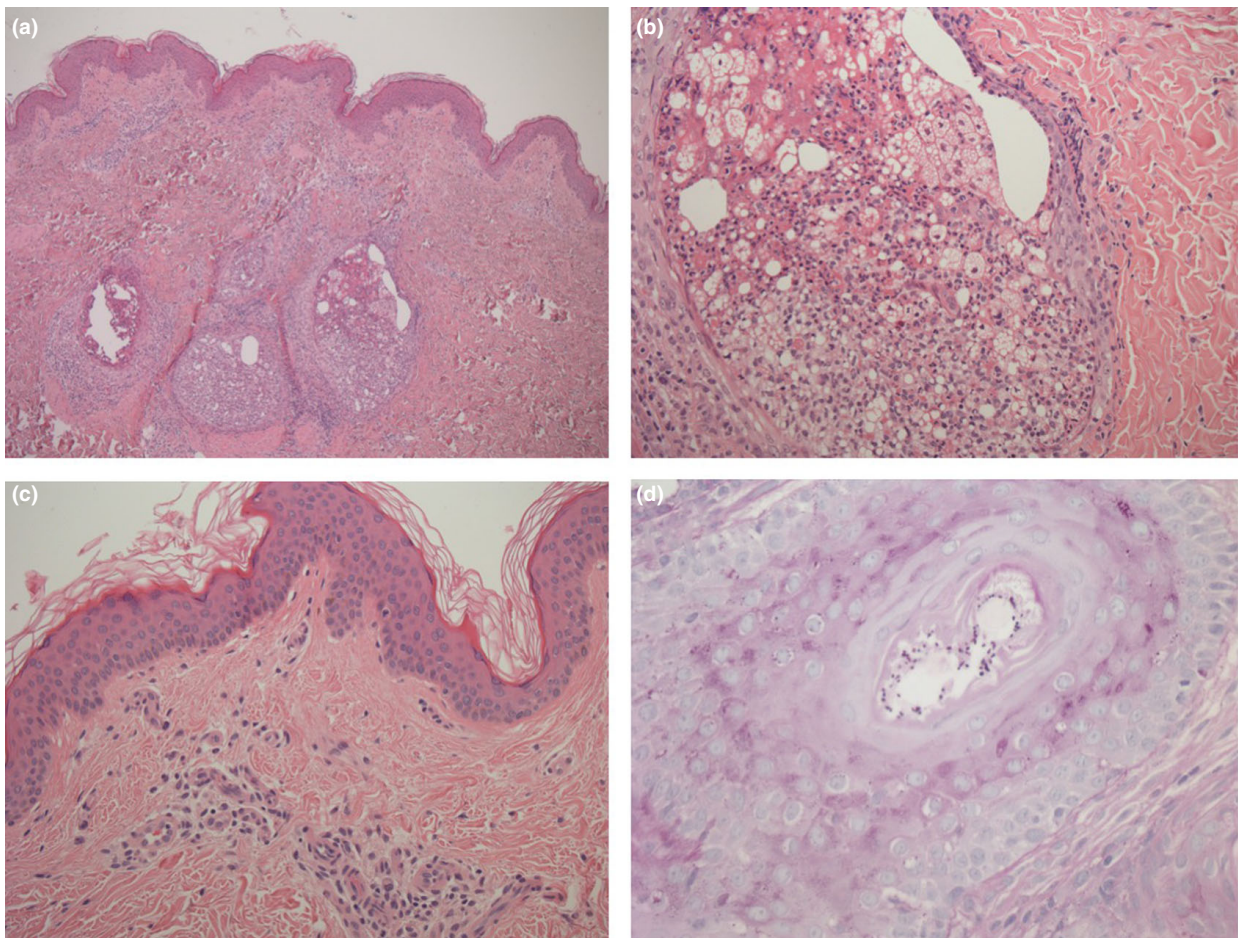


Figure 2 (a) Mixed follicular and perifollicular inflammatory infiltrate affecting the whole pilosebaceous unit, rich in neutrophils, with some mononuclear cells and eosinophils also present. (b) Folliculocentric inflammation. (c) Mild perivascular lymphocytic infiltrate was present in the dermis with an unremarkable epidermis. Haematoxylin and eosin, original magnification (a) $\times 2.5$; (b) $\times 10$; (c) $\times 10$. (d) Fungal spores were visible, although these may have been commensal (periodic acid–Schiff $\times 20$).

with synthetic kavain and mycotoxins present in the kava root when not consumed fresh.¹ The latter has been deemed the working hypothesis for kava hepatotoxicity in Western countries, and such toxins have been detected on exported kava root.¹ The cutaneous adverse effects of kava also vary by region. In the Pacific Islands, almost half of regular kava consumers develop a chronic ichthyosiform eruption (45%). However, this has not been reported in Europe and the USA, where instead an acute sebotropic inflammatory reaction has been reported. This sebotropic eruption has consistent clinical (pruritic, erythematous plaques with or without facial swelling, fever and lymphadenopathy),^{6,7} histological (folliculocentric inflammation, either neutrophilic or lymphocytic) and biochemical (neutrophilia and transaminitis) features.^{6,7} Urticaria has been reported in both populations.⁸

The absence of this sebotropic eruption in the Pacific Islands may suggest a similar aetiology to kava-induced hepatotoxicity. In our case, we observed yeasts on histological examination, which mimicked fungal folliculitis, although these may have been commensal. Analysis of the kava product for potential contaminants, such as mycotoxins, was not possible.

To our knowledge, this is the first report of acute cutaneous toxicity to kava in the UK. Although kava is banned in the UK, herbal products are often marketed and sold online with limited regulation, and thus pose a much greater safety risk.

Acknowledgement

We thank Dr A. Nagy for kindly providing the histology photos.

Learning points

- Kava use is commonly associated with a chronic ichthyosiform eruption in the Pacific Islands, whereas in the USA and the UK an acute sebotropic inflammatory eruption has been observed.
- The sebotropic distribution of the eruption induced by kava is thought to reflect the lipophilic nature of the kavalactones within kava.
- These may accumulate in the lipids of sebaceous glands, which then leads to folliculocentric inflammation.

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CPD questions

Learning objective

To gain up-to-date knowledge of kava dermatopathy.

Question 1

Which of the following adverse effects led to restriction of use of kava in many countries in the early 2000s?

- (a) Nephrotoxicity.
- (b) Peripheral neuropathy.
- (c) Chronic ichthyosiform eruption.
- (d) Hepatotoxicity.
- (e) Seizures.

Question 2

Which of the following is the most common adverse effect of kava?

- (a) Acute sebotropic reaction.
- (b) Chronic ichthyosiform eruption.
- (c) Urticaria.

A memorable patient

- (d) Hepatotoxicity.
- (e) Lichenoid eruption.

Instructions for answering questions

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- Read the article in print or online, paying particular attention to the learning points and any author conflict of interest disclosures
- Reflect on the article

- Register or login online at <http://www.wileyhealthlearning.com/ced> and answer the CPD questions
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