

Hepatitis induced by traditional Chinese herbs; possible toxic components

J A Kane, S P Kane, S Jain

Abstract

Traditional Chinese herbal remedies are widely available in the United Kingdom for the treatment of chronic skin disorders. Their benefits are considerable, but their use is completely unregulated. Two patients are described here who suffered an acute hepatic illness related to taking traditional Chinese herbs. Both recovered fully. The mixtures that they took included two plant components also contained within the mixture taken by a previously reported patient who suffered fatal hepatic necrosis. These cases highlight the need for greater awareness of both the therapeutic and toxic potential of herbal remedies, as well as greater control of their use.

(Gut 1995; 36: 146-147)

Keywords: hepatitis, Chinese herbs.

Chinese 'herbs' are increasingly being used in western Europe to treat skin diseases, particularly eczema and psoriasis. The mixture, which may contain eight or more varieties of dried root, root bark, rhizome or herb, and sometimes insect fragments, is boiled and the decoction taken daily. The 'tea' is usually unpleasant to drink and can cause diarrhoea. Anecdotally, and in controlled trials, this form of treatment can effectively control these skin conditions.^{1,2} There are a growing number of Chinese herb shops and clinics in the United Kingdom, where the usual practice is to tailor a wide variety of herbs to the perceived needs of the individual patient.³ While reported toxic reactions are few, two children taking Chinese herbs developed reversible abnormalities of the standard serum tests of liver function,² and a nine year old girl taking Chinese herbs for eczema suffered a hepatic illness that relapsed with reintroduction of the treatment.⁵ Adults with hepatitis related to similar treatment have also been reported,^{6,7} as has been one fatal case where hepatitis was complicated by massive hepatic necrosis.⁸

We report two further such cases of hepatitis in adults, which permit identification of the probable toxic components of the herbal mixture.

Case report 1

A 39 year old white woman presented to her general practitioner in September 1991 with a short history of anorexia, nausea, and fatigue, without abdominal pain. Her urine had been dark and her sclerae yellow

for one day. She was receiving no regular prescribed drugs, and drank less than one unit of alcohol per week. She had not received any injections or blood transfusions in the preceding two years. Examination was unremarkable apart from jaundice and 3 cm hepatomegaly.

Investigations showed serum bilirubin of 139 rising to 444 $\mu\text{mol/l}$ (0-17), alanine transaminase 2440 IU/l (0-30), alkaline phosphatase 261 IU/l (55-220). A provisional diagnosis of viral hepatitis was made, but hepatitis A IgM antibody was negative, as was serology for hepatitis B and C performed three months later. An auto-antibody screen was also negative.

Her liver function returned to normal over two months, but after a further six weeks she again complained of malaise, itching, and dark urine and was noted to be mildly icteric with a serum bilirubin of 31 $\mu\text{mol/l}$, alanine transaminase 1314 IU/l, alkaline phosphatase 300 IU/l. On close questioning she admitted to having taken a Chinese herbal decoction for her psoriasis on a daily basis for two months preceding the onset of her first bout of jaundice. She had restarted this three days before the second episode of jaundice as her psoriasis had recurred.

After a further two months her liver function was again normal, and she has remained well for the subsequent 18 months.

The Table shows the contents of the herbal mixture taken by the patient. Contamination by fungi or heavy metals was sought but not found.

Case report 2

A 61 year old Chinese woman became unwell in November 1992 with nausea, malaise, weight loss, dark urine, and jaundice. For 11 months her severe eczema had been treated with a Chinese herbal preparation, with significant improvement after six months of treatment. There was no other relevant past history, nor any known exposure to hepatitis viruses or other toxins. She drank very little alcohol, and her only prescribed treatment had been a short course of terfenadine. Physical examination showed jaundice but no other abnormality. Her serum bilirubin was 221 $\mu\text{mol/l}$, aspartate transaminase was >1000 IU/l (0-40), and alkaline phosphatase was 311 IU/l (65-300). Hepatitis A, B, and C serology was negative, as were smooth muscle and anti-nuclear antibodies. Hepatobiliary ultrasonography was normal. She was advised to stop the herbal treatment, and after a few days all of her symptoms disappeared. Her serum liver func-

Canbury Medical
Centre, Kingston upon
Thames, Surrey
J A Kane

West Middlesex
University Hospital,
Isleworth, Middlesex
S P Kane

Luton and Dunstable
Hospital, Luton,
Bedfordshire
S Jain

Correspondence to:
Dr S Kane, West Middlesex
University Hospital,
Twickenham Road,
Isleworth, Middlesex
TW7 6AF.

Accepted for publication
17 February 1994

Plant components of the Chinese herbal preparations taken by cases 1 and 2, and by the patient reported by Perharic-Walton and Murray⁸ who suffered fatal hepatic necrosis

Case 1	Case 2	Fatal case ⁸
<i>Dictamnus dasycarpus</i>	<i>Dictamnus dasycarpus</i>	<i>Dictamnus dasycarpus</i>
<i>Paeonia suffruticosa</i>	<i>Paeonia suffruticosa</i>	<i>Paeonia</i> spp
<i>Rehmannia glutinosa</i>	<i>Shisandra chinensis</i>	<i>Rhemannia glutinosa</i>
<i>Hedyotis diffusa</i>	<i>Angelica sinensis</i>	<i>Cocculus trilobus</i>
<i>Sophora subprostrata</i>	<i>Bupleurum chinese</i>	<i>Eurysolen gracilis</i>
<i>Gentiana scabra</i>	<i>Phellodendron chinese</i>	<i>Glycyrrhiza</i> spp
<i>Smilax glabra</i>	<i>Tribulus terrestris</i>	<i>Lophatherum</i> spp
<i>Paris polyphylla</i>	<i>Shizonepeta tenuifolia</i>	<i>Potentilla</i> spp
	<i>Saposhnikovia divaricata</i>	

tion tests returned to normal within three months.

The Table shows the plant contents of this patient's herbal mixture. The preparation also contained insect fragments (*Cryptotympane pustulata*).

Neither patient was subjected to liver biopsy.

Discussion

In case 1 there was clear recurrence both of symptoms and of biochemical evidence of hepatocellular damage shortly after resuming treatment with the Chinese herbs. In case 2, the rapid symptomatic and biochemical improvement on stopping treatment, and the absence of evidence for any other causes of hepatitis, also strongly incriminates the Chinese herbal mixture as the cause for her hepatitis.

Many herbs and plant extracts including germander, comfrey, and mistletoe are known to be hepatotoxic.^{9 10} Traditional Chinese medicinal herbs are used to treat numerous conditions as well as skin disorders, and have been reported as causing interstitial renal fibrosis when incorporated into a slimming regimen.¹¹ While the two cases described here are not the only ones in which Chinese herbal preparations may be implicated in causing hepatitis, it is difficult to pinpoint the plant component or components responsible for hepatocellular damage because of the large number of potential ingredients that may be used. The Table shows the ingredients of the herbal mixtures taken by our two patients, as well as those of the mixture taken by the one patient reported elsewhere who died.⁸ The root

bark of *Dictamnus dasycarpus* and of *Paeonia* are the only two plant materials common to all three preparations: in our two cases *Paeonia suffruticosa* was identified, while in the fatal case the *Paeonia* species was not categorised. Of particular interest is the suggestion that *Paeonia* (the paeony), a common medicinal plant, could be providing the therapeutically active moiety of some Chinese herbal mixtures used for treating skin diseases.¹²

In conclusion, while Chinese herbal preparations clearly have a place in the treatment of certain common skin diseases, their use in the United Kingdom is completely unregulated, as are their contents. Herbalists prescribing and dispensing these preparations, and medical practitioners whose patients may be reluctant to admit that they are taking them, should be aware of their potential for occasional serious hepatotoxicity. There is some evidence from the cases reported here that either *Dictamnus dasycarpus* or *Paeonia* species could be the toxic agent.

We are grateful to Professor J D Phillipson and his colleagues in the Department of Pharmacognosy, School of Pharmacy, University of London, for examining and analysing the herbal preparations taken by our two patients, and to Drs L Perharic-Walton and V Murray at the National Poisons Unit, Guy's Hospital, London, for their help with case 1.

- 1 Sheehan MP, Rustin MHA, Atherton DJ, Buckley C, Harris DJ, Brostoff J, *et al*. Efficacy of traditional Chinese herbal therapy in adult atopic dermatitis. *Lancet* 1992; **340**: 13-7.
- 2 Sheehan MP, Atherton DJ. A controlled trial of traditional Chinese medicinal plants in widespread non-exudative atopic eczema. *Br J Dermatol* 1992; **126**: 179-84.
- 3 Rustin MHA. The pharmacology of Chinese herbs [Book Review]. *Lancet* 1993; **342**: 38.
- 4 Sheehan MP, Atherton DJ. One year follow-up of children with atopic eczema treated with traditional Chinese medicinal plants. *Br J Dermatol* 1992; **127** (suppl 40): 13.
- 5 Davies EG, Pollock I, Steel HM. Chinese herbs for eczema. *Lancet* 1990; **336**: 177.
- 6 Carlsson C. Herbs and hepatitis. *Lancet* 1990; **336**: 1068.
- 7 Graham-Brown R. Toxicity of Chinese herbal remedies. *Lancet* 1992; **346**: 674.
- 8 Perharic-Walton L, Murray V. Toxicity of traditional Chinese herbal remedies. *Lancet* 1992; **346**: 674.
- 9 Larrey D, Vial T, Pauwels A, Castot A, Blour M, Martine D, Michel H. Hepatitis after Germander (*Teucrium chanaedrys*) administration: another instance of herbal medicine toxicity. *Ann Intern Med* 1992; **117**: 129-32.
- 10 MacGregor FB, Abernethy VE, Dahabra S, Cobden I, Hayes PC. Hepatotoxicity of herbal remedies. *BMJ* 1989; **299**: 1156-7.
- 11 Vanherweghem J-L, Depierreux M, Tielemans C, Abramowicz D, Dratwa M, Jadoul M, *et al*. Rapidly progressive interstitial renal fibrosis in young women: association with slimming regimen including Chinese herbs. *Lancet* 1993; **341**: 387-91.
- 12 Galloway JH, Marsh ID, Bittiner ID, Messenger AG, Gawkrödger DJ, Glet R, *et al*. Chinese herbs for eczema, the active compound? *Lancet* 1991; **337**: 566.