AACT Herbal Dietary Supplements SIG Abstracts July 2019

1. Ricin: An Ancient Story for a Timeless Plant Toxin. Polito L, Bortolotti M, Battelli MG, Calafato G, Bolognesi A.

Toxins (Basel). 2019 Jun 6;11(6). pii: E324. doi: 10.3390/toxins11060324.

The castor plant (Ricinus communis L.) has been known since time immemorial in traditional medicine in the pharmacopeia of Mediterranean and eastern ancient cultures. Moreover, it is still used in folk medicine worldwide. Castor bean has been mainly recommended as anti-inflammatory, anthelmintic, anti-bacterial, laxative, abortifacient, for wounds, ulcers, and many other indications. Many cases of human intoxication occurred accidentally or voluntarily with the ingestion of castor seeds or derivatives. Ricinus toxicity depends on several molecules, among them the most important is ricin, a protein belonging to the family of ribosome-inactivating proteins. Ricin is the most studied of this category of proteins and it is also known to the general public, having been used for several biocrimes. This manuscript intends to give the reader an overview of ricin, focusing on the historical path to the current knowledge on this protein. The main steps of ricin research are here reported, with particular regard to its enzymatic activity, structure, and cytotoxicity. Moreover, we discuss ricin toxicity for animals and humans, as well as the relation between bioterrorism and ricin and its impact on environmental toxicity. Ricin has also been used to develop immunotoxins for the elimination of unwanted cells, mainly cancer cells; some of these immunoconjugates gave promising results in clinical trials but also showed critical limitation.

DOI: 10.3390/toxins11060324
PMID: 31174319

2. Kratom Use and Toxicities in the United States. Eggleston W, Stoppacher R, Suen K, Marraffa JM, Nelson LS.

Pharmacotherapy. 2019 Jul;39(7):775-777. doi: 10.1002/phar.2280. Epub 2019 Jun 13.

BACKGROUND: Kratom is an herbal supplement containing alkaloids with opioid properties. This review was conducted to determine toxicities associated with kratom use in the United States in order to provide insight into its safety as a dietary supplement. METHODS: We conducted a retrospective review of kratom exposures reported to the National Poison Data System to determine the toxicities associated with kratom use. We also reviewed records from a county medical examiner's office in New York State to identify kratom-associated fatalities. RESULTS: A total of 2312 kratom exposures were reported, with 935 cases involving kratom as the only substance. Kratom most commonly caused agitation (18.6%), tachycardia (16.9%), drowsiness (13.6%), vomiting (11.2%), and confusion (8.1%). Serious effects of seizure (6.1%), withdrawal (6.1%), hallucinations (4.8%), respiratory depression (2.8%), coma (2.3%), and cardiac or respiratory arrest (0.6%) were also reported. Kratom was listed as a cause or contributing factor in the death of four decedents identified by the county medical examiner's office. CONCLUSIONS: Kratom use is increasing and is associated with significant toxicities. Our findings suggest kratom is not reasonably expected to be safe and poses a public health threat due to its availability as an herbal supplement.

DOI: 10.1002/phar.2280
PMID: 31099038

3. Fatality of 33-Year-Old Man Involving Kratom Toxicity. Matson M, Schenk N.

J Forensic Sci. 2019 May 23. doi: 10.1111/1556-4029.14082. [Epub ahead of print]

Kratom is an herbal product commonly used for its effects which are similar to opioids and stimulants. Few studies demonstrate the dangers and lethality of Kratom, and most fatalities from Kratom involve other abused substances. In the current case report, a 33-year-old white man with a known history of opioid abuse and mental illnesses was found unresponsive in his basement with no obvious signs of trauma. After resuscitative efforts, he was pronounced dead and taken for autopsy evaluation. Blood from the inferior vena cava was analyzed for common abused substances. The laboratory toxicology work-up revealed positive findings of caffeine, cotinine, and naloxone with low levels of Δ-9 tetrahydrocannabinol. However, a marked level of mitragynine at 1.9 mg/L was observed, the highest reported to date. Given the facts and evidence, the medical examiner certified the cause of death as "mitragynine toxicity" and the manner of death was classified as an "accident."

DOI: 10.1111/1556-4029.14082
PMID: 31121058

4. Fatal acute arsenic poisoning by external use of realgar: Case report and 30 years literature retrospective study in China. Zheng J, Zhang K, Liu Y, Wang Y.

Forensic Sci Int. 2019 Jul;300:e24-e30. doi: 10.1016/j.forsciint.2019.03.012. Epub 2019 Apr 5.

Realgar (arsenic sulfide) is widely used in combination with other herbs as Chinese patent medicine to treat a variety of diseases in China. As a mineral arsenic, its mild toxicity was also well known. Longtime over-dose usage or wrongly oral intake of realgar can cause chronic arsenic poisoning and/or death, but acute fatal arsenic poisoning resulted from short-term dermal use of realgar-containing medicine was very rare. Here, we present the case of a 35-year-old Chinese man, who was diagnosed with severe psoriasis and died of fatal acute arsenic poisoning after he applied a local folk prescription ointment containing mainly the realgar to the affected skin for about 4 days. The autopsy showed multiple punctate hemorrhages over the limbs, pleural effusion, edematous lungs with consolidation, mild myocardial hypertrophy and normal-looking kidneys. The histopathological examination of renal tissue showed severe degeneration, necrosis and desquamation of renal tubular epithelial cells, presence of protein cast and a widened edematous interstitium with interstitial fibrosis. The presence of arsenic in large amount in the ointment (about 6%), in blood (1.76 μg/mL), and in skin (4.71 μg/g), were confirmed analytically. We also provide the clinical records of the deceased and briefly reviewed 7 similar cases in literature (6 in Chinese and 1 in English) in the past 30 years in China.

DOI: 10.1016/j.forsciint.2019.03.012
PMID: 31023496 [Indexed for MEDLINE]

5. Two cases of lead poisoning from inhaled opium in Victoria. Law S, Ackerly I, Scott-Rimmington B, Nallaratnam K.

Emerg Med Australas. 2019 Feb;31(1):144-145. doi: 10.1111/1742-6723.13224. Epub 2019 Jan 12.

DOI: 10.1111/1742-6723.13224
PMID: 30635973 [Indexed for MEDLINE]

6. Herb-Induced Liver Injury: A Global Concern. Kaplowitz N.

Chin J Integr Med. 2018 Sep;24(9):643-644. doi: 10.1007/s11655-018-3004-4. Epub 2018 May 3.

Chinese medicine and herb medicine though used to treat liver diseases are an important cause of liver injury. Many phytochemicals have the potential to injure the liver, some in a dose-related fashion and more often in an idiosyncratic fashion, meaning occurrence is uncommon to rare in the population using these treatments. As is the case with pharmaceuticals, the phytochemicals are usually tolerated despite

either no or mild transient subclinical injury but rarely in some susceptible patients cause moderate to severe liver injury which is likely mediated by the adaptive immune system.

DOI: 10.1007/s11655-018-3004-4
PMID: 29744785 [Indexed for MEDLINE]

7. Battle Over Herb-Induced Liver Injury: Low Prevalence Confirmed through Secondary Evaluation and Research Team's Clarifying Rebuttal to Unwarranted Public Claims. Lee J, Shin JS, Lee YJ, Kim MR, Shin BC, Lee JH, Lee MS, Ha IH.

J Altern Complement Med. 2019 Mar;25(3):260-264. doi: 10.1089/acm.2018.0253. Epub 2018 Nov 8.

DOI: 10.1089/acm.2018.0253
PMID: 30407070 [Indexed for MEDLINE]

8. Liver transplantation and the use of KAVA: Case report. Becker MW, Lourençone EMS, De Mello AF, Branco A, Filho EMR, Blatt CR, Mallmann CA, Schneider M, Caregnato RCA, Blatt CR.

Phytomedicine. 2019 Mar 15;56:21-26. doi: 10.1016/j.phymed.2018.08.011. Epub 2018 Aug 9.

BACKGROUND: Self-medication and the belief that herbal products are free of health risks are common in Brazil. The kava (Piper methysticum), known for its anxiolytic action, has a widespread popular use. Hepatotoxicity of kava is reported, including cases of liver transplantation and death. The kava had its use prohibited or restricted in countries like Germany, France, among others. Toxicity may be related to overdosage; however, factors such as botanical characteristics of the plant, the harvesting, storage, and production process may be associated with the development of hepatotoxic substances, such as triggering idiosyncratic reactions. HYPOTHESIS: In this case, there is a suspicion that the toxicide is intrinsic to the drug; however, the possibility of adulterants and contaminants must be ruled out. STUDY DESIGN: This study reports the case of a patient who, after using the herbal kava for 52 days, evolved into acute liver failure and liver transplantation. METHODS: The data were collected directly with the patient and compared with their clinical records. Causality was determined through the RUCAM algorithm. In addition, a phytochemical analysis of the drug used was performed. RESULTS: According to the patient's report, there is no evidence of overdosage. Results from RUCAM algorithm infer causality between liver damage and the use of kava. The analysis chemical constituents did not find any possible contaminants and major changes in the active compounds. Seven months after transplantation, the patient is well and continues to be followed up by a medical team. CONCLUSION: Our investigation indicates that there was kava-induced hepatotoxicity at standard dosages. In Brazil, self-medication by herbal medicines is frequent and many patients and health professionals do not know the risks associated with their use. Diagnosing and notifying cases in which plants and herbal medicine induce liver damage is of paramount importance to increase the knowledge about DILI and to prevent or treat similar cases quickly.

DOI: 10.1016/j.phymed.2018.08.011
PMID: 30668342 [Indexed for MEDLINE]

9. Acute liver failure associated with Fructus Psoraleae: a case report and literature review. Li A, Gao M, Zhao N, Li P, Zhu J, Li W.

BMC Complement Altern Med. 2019 Apr 11;19(1):84. doi: 10.1186/s12906-019-2493-9.

BACKGROUND: Fructus Psoraleae is the seed of Psoralea corylifolia Linn. Fructus Psoraleae has been shown to be effective in treating some skin diseases, such as vitiligo. As a main ingredient in five types of herbs in the Qubaibabuqi tablet formula, Fructus Psoraleae plays an important role in the treatment of vitiligo. Fructus Psoraleae has potential hepatotoxicity, thus Qubaibabuqi tablets also

have potential liver toxicity. CASE PRESENTATION: A 53-year-old woman who was diagnosed with vitiligo in September 2017 was treated with Qubaibabuqi tablets. After approximately 7 months of treatment, the patient developed a severe, diffuse yellow staining of the skin and sclera in March 2018. On admission, she was diagnosed with acute cholestatic hepatitis associated with Fructus Psoraleae. Despite receiving active treatment, her condition rapidly deteriorated and she died 5 days later due to acute liver failure and multiple organ dysfunction. To the best of our knowledge, there are only six reported cases of liver injury associated with Fructus Psoraleae described in the English language literature; however, cases of acute liver failure associated with the use of Fructus Psoraleae have not been described. CONCLUSION: As a main ingredient in the Qubaibabuqi tablet formula, Fructus Psoraleae has potential hepatotoxicity. This potentially fatal adverse effect should be considered when physicians prescribe Qubaibabuqi tablets.

DOI: 10.1186/s12906-019-2493-9
PMCID: PMC6458792
PMID: 30975110 [Indexed for MEDLINE]

10. Potential forensic issues in overseas travellers exposed to local herbal products. Farrington R, Musgrave I, Nash C, Byard RW.

J Forensic Leg Med. 2018 Nov;60:1-2. doi: 10.1016/j.jflm.2018.08.003. Epub 2018 Aug 21.

DOI: 10.1016/j.jflm.2018.08.003
PMID: 30149301 [Indexed for MEDLINE]

11. Acute adrenal failure: a potentially fatal consequence of an adulterated herbal remedy. Sensi H, Buch H, Ford L, Gama R.

BMJ Case Rep. 2019 Feb 19;12(2). pii: bcr-2018-228443. doi: 10.1136/bcr-2018-228443.

Herbal remedies adulterated with glucocorticoids can cause Cushing's syndrome. We report a severe presentation of a 'herbal remedy' adulterated with glucocorticoids; causing a potentially fatal adrenal crisis precipitated by acute illness. Investigations were consistent with adrenal suppression and confirmed, after tablet analysis, to be due to a 'herbal remedy' containing synthetic betamethasone/dexamethasone. This case highlights the need for clinical vigilance and patient education about the potential risks associated with the use of unlicensed treatments and the role of tablet analysis in routine biochemistry.

DOI: 10.1136/bcr-2018-228443
PMID: 30787026 [Indexed for MEDLINE]

12. Pyrrolizidine alkaloid contamination in herbal medicinal products: Limits and occurrence. Steinhoff B.

Food Chem Toxicol. 2019 Aug;130:262-266. doi: 10.1016/j.fct.2019.05.026. Epub 2019 May 21.

Since 2013, a potential contamination of medicinal plant material with pyrrolizidine alkaloid-containing weeds e.g. Senecio has been discussed. The knowledge about such a risk of contamination induced suppliers of medicinal drugs and manufacturers of medicinal teas to investigate the situation regarding herbal drugs and teas and other medicinal products of plant origin. As due to worldwide cultivation/ collection and season-dependent sourcing processes an immediate elimination or even reduction of PA contamination at all sourcing sites was considered impossible, manufacturers have taken action by application of their Code of Practice, by monitoring pyrrolizidine alkaloid contamination and by collection of data, by elimination of peak exposures as well as by participation in research projects. The Herbal Medicinal Products Committee at the European Medicines Agency recommended a transitional

limit of 1.0 µg pyrrolizidine alkaloids per day related to the final product for three years which has recently been prolonged by a further two years. Against the background of the assessment of the European Food Safety Authority, the option of establishing a permanent limit of 1.0 µg per day should be taken into consideration during future discussions.

DOI: 10.1016/j.fct.2019.05.026
PMID: 31121208

13. Quantitative and qualitative analysis of pyrrolizidine alkaloids in liqueurs, elixirs and herbal juices. Chmit MS, Wahrig B, Beuerle T.

Fitoterapia. 2019 Jul;136:104172. doi: 10.1016/j.fitote.2019.104172. Epub 2019 May 14.

Pyrrolizidine alkaloids (PAs and corresponding N-oxides (PANOs)) are known to have adverse health effects. Their toxic effects on liver cells are especially well-documented. In addition, potential carcinogenic and mutagenic effects in chronic exposure via food and/or herbal medicines have been a subject of vivid discussion in the last decade. Liqueurs and elixirs are traditionally used alcoholic extracts made from parts of plants and herbs. PA cross-contamination of the final products seems likely. Hence, this study aims to detect and quantify the PAs in such products in the light of a possible PA-contamination. The PA content was determined in the form of a single sum parameter using HPLC-ESI-MS/MS and a stable isotope-labeled internal standard. Overall, 56 products available at German pharmacies, drugstores, or internet shops were analyzed, comprising in total 38 samples of liqueurs (mainly bitters), 12 samples of plant elixirs and six different herbal juices. The results showed that 9 out of 38 liqueurs were PA-positive (24%). The total amount of PAs ranged from non-detectable to 9.5 µg/kg. Seven out of ten elixirs were PA-positive (70%) with a maximum PA-content of 3121 µg/kg. Four out of six plant juices were PA-positive (67%) with an average of 4.4 µg/kg (PA-positive samples only).The results and potential risks are discussed in the light of recommended portions for daily consumption or daily doses, in association with the detected PA amounts for individual products and product classes.

DOI: 10.1016/j.fitote.2019.104172
PMID: 31100438

14. A health risk for consumers: the presence of adulterated food supplements in the Netherlands. Biesterbos JWH, Sijm DTHM, van Dam R, Mol HGJ.

Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2019 Jul 11:1-16.
doi: 10.1080/19440049.2019.1633020. [Epub ahead of print]

The use of food supplements is increasing. They are marketed as beneficial for health, well-being, physical or mental condition and performance, or to prevent diseases. Producers add synthetic compounds or illicit herbal material to food supplements to claim desired effects. Claims made to support marketing without scientific evidence are, however, illegal. Intake of adulterated food supplements may lead to serious adverse effects. The aim of this paper is to report the results of analyses of (adulterated) food supplements conducted by the Netherlands Food and Consumer Product Safety Authority between October 2013 and October 2018. In total, 416 supplements were analysed of which 264 (64%) contained one or more pharmacological active substances or plant toxins, such as caffeine, synephrine, sildenafil, icariin, sibutramine, higenamine, hordenine, phenethylamine, methylsynephrine, DMAA, phenolphthalein, octopamine and ephedrine. When compared to dose levels that are considered safe, daily doses of the substances in the food supplements were sometimes much higher, causing a risk for consumers who are unaware of the presence of these pharmacologically active substances. In many cases, neither food nor medicines legislation (easily) enables enforcement actions. This means that some products containing pharmacologically active substances (i.e. synthetic medicines and their illicit analogues), stay available on the market. An undesirable situation because for many of these substances no detailed toxicity data are available.

DOI: 10.1080/19440049.2019.1633020
PMID: 31294678

15. Role of Fish Oil in Post-Cardiotomy Bleeding: A Summary of the Basic Science and Clinical Trials. Carr JA.

Ann Thorac Surg. 2018 May;105(5):1563-1567. doi: 10.1016/j.athoracsur.2018.01.041. Epub 2018 Apr 5.

BACKGROUND: Omega-3 fatty acids are widely used. This article reviews the coagulopathic effects of fish oil. METHODS: A review was performed of all English articles that addressed the topic from 1980 to 2017. RESULTS: Fish oil induces an in vitro coagulopathy in humans due to inhibitory effects in platelet-to-platelet adhesion and platelet-stimulated thrombin generation. The effect from fish oil alone is weak, but it is enhanced and may become clinically noticeable in patients taking antiplatelet therapy, and, to a lesser extent, in patients on factor Xa inhibitors and warfarin. In the absence of other anticoagulants, fish oil alone is not capable of producing a clinically significant coagulopathy that would induce or contribute to surgical bleeding. CONCLUSIONS: Patients who are taking fish oil without other anticoagulants do not have an increased risk of bleeding surgical complications. Because of the highly variable amounts of actual eicosapentaenoic acid and docosahexaenoic acid in commercially available supplements, thromboelastography with platelet mapping would allow a surgeon to know if a coagulopathic effect is present in a patient taking fish oil, especially if the patient was also taking other anticoagulants.

DOI: 10.1016/j.athoracsur.2018.01.041
PMID: 29627068 [Indexed for MEDLINE]

16. Adverse events from large dose vitamin D supplementation taken for one year or longer. Malihi Z, Wu Z, Lawes CMM, Scragg R.

J Steroid Biochem Mol Biol. 2019 Apr;188:29-37. doi: 10.1016/j.jsbmb.2018.12.002. Epub 2018 Dec 6.

In recent years, clinical trials increasingly have given large doses of vitamin D supplements to investigate possible health benefits beyond bone at high 25-hydroxyvitamin D levels. However, there are few publications on the safety of high-dose vitamin D given long term. The study objective was to investigate the cumulative relative risk (RR) of total adverse events, kidney stones, hypercalcemia and hypercalciuria from ≥2800 IU/d vitamin D2 or D3 supplementation, followed for one year or more in randomized controlled trials (RCTs). A systematic review was conducted in Medline Ovid, EMBASE and Cochrane in March 2018 to update results of studies published since a previous review in October 2015. RCTs were included if they gave vitamin D2 or D3 at ≥2800 IU/d for at least one year and reported on total adverse events or at least one calcium-related adverse event. There were a total of 32 studies that met the inclusion criteria. Of these, only 15 studies (3150 participants) reported one or more event of the outcomes of interest. Long-term high-dose vitamin D supplementation did not increase total adverse events compared to placebo in 1731participants from 10 studies (RR = 1.05; 95% CI = 0.88, 1.24; p = 0.61), nor kidney stones in 1336 participants from 5 studies (RR = 1.26; 95% CI = 0.35, 4.58; p = 0.72). However, there was a trend for vitamin D to increase risk of hypercalcemia in 2598 participants from 10 studies (RR = 1.93; 95% CI = 1.00, 3.73; p = 0.05); while its effect on hypercalciuria in only 276 participants from 3 studies was inconclusive (RR = 1.93; 95% CI = 0.83, 4.46; p = 0.12). In conclusion, one year or longer supplementation with a large daily, weekly or monthly dose of vitamin D2 /D3 did not significantly increase a risk of total adverse events or kidney stones, although there was a trend towards increased hypercalcemia, and possibly for hypercalciuria.

DOI: 10.1016/j.jsbmb.2018.12.002
PMID: 30529281 [Indexed for MEDLINE]

17. Chronic use of oral iron supplements is associated with poor clinical outcomes in patients with gram-negative bacteremia. Atamna A, Hamud H, Daud W, Shochat T, Bishara J, Elis A.

Eur J Clin Microbiol Infect Dis. 2019 Apr;38(4):689-693. doi: 10.1007/s10096-019-03481-7. Epub 2019 Jan 26.

An unabsorbed dietary iron supplementation can modify the colonic microbiota equilibrium and favor the growth of pathogenic strains over barrier strains. Nevertheless, the impact of oral iron supplements (OIS) use on the clinical outcomes of patients with gram-negative bacteremia (GNB) has not been evaluated. To explore the impact of OIS on the outcomes of patients with GNB. A retrospective study conducted in a tertiary hospital including patients with GNB during 2011-2016. The entire cohort was divided into chronic OIS users (study group) and nonusers (control group). The two groups were compared for the study outcomes, septic shock at presentation, length of hospital stay (LOS), and short-term mortality. The study cohort included 232 patients; 44 patients in the study group and 188 in the control one. There was no any significant difference in demographic and comorbidities characteristics between the two groups. Escherichia coli comprised the majority of bacteria (69%), while the urinary tract was the main source of the bacteremia. OIS alone and after adjustment was significantly associated with septic shock at presentation (OR = 2, CI95% [1.03-5], p = 0.04 and OR = 5, CI95% [1.4-15], p = 0.01, respectively). By multivariate analysis, OIS was significantly associated with 30-day mortality (OR = 3, CI95% [1.05-7], p = 0.04), but had no impact on LOS (16 + 23 vs. 12 + 15, p = 0.9). There is a significant association between chronic OIS exposure and increased adverse outcomes in patients with GNB. These findings might have important clinical implications.

DOI: 10.1007/s10096-019-03481-7
PMID: 30685806 [Indexed for MEDLINE]

18. Unsafe herbal sex enhancement supplements in Nigerian markets: a human risk assessment. Igweze ZN, Amadi CN, Orisakwe OE.

Environ Sci Pollut Res Int. 2019 Jun 3. doi: 10.1007/s11356-019-05511-5. [Epub ahead of print]

High rates of irreversible oligo- or azoospermia are found among Nigerian men, leading many to consume herbal male sex enhancement products. The possibility of reproductive toxicity due to heavy metal contamination (Cr, As, Co, Hg, Cd, and Pb) of herbal products commonly used to boost libido or treat erectile dysfunction necessitated this study. In this study, herbal sex enhancement supplements were bought from pharmaceutical shops in Port Harcourt, Nigeria, and analyzed for heavy metals (Cr, As, Co, Hg, Cd, and Pb) contents using atomic absorption spectroscopy. The estimated daily metal intake (EDImetal), target hazard quotients (THQ), and total target hazard quotients (TTHQ) were determined. All the herbal sex enhancers used in this study contained heavy metals in these ranges: lead (0.032-0593), cobalt (0.025-0.075), cadmium (0.0011-0.048), and chromium (0.016-0.49) mg/kg. About 24.32% of the samples had TTHQ greater than 1. The EDImetal, THQ, and TTHQ of herbal sex enhancement supplements suggest that the use of some of these herbal sex enhancement supplements may not be risk-free after chronic exposure. Herbal sex enhancement supplements sold in Nigeria contain high levels of lead and cadmium. Since these metals are known to have male reproductive toxicity, these supplements may be adding to both the body burden of these metals and also implicated in the increasing incidence of male infertility in Nigeria.

DOI: 10.1007/s11356-019-05511-5
PMID: 31161544

19. Cleistanthus collinus poisoning: a case report of intentional poisoning. Bompelli N, Reddy C R, Modani S, Deshpande A.

BMJ Case Rep. 2019 Feb 9;12(2). pii: bcr-2018-228197. doi:10.1136/bcr-2018-228197.

We report a case of 50-year-old male patient from tribal area in South Indian state of Telangana, who ingested the liquid extract from crushed leaves of the plant, cleistanthus collinius with the intention of self-harm. Immediate gastric lavage and activated charcoal administration was done and the patient was subsequently admitted into an acute medical care unit. During first 24 hours of monitoring, the patient was clinically stable. There was mild normal anion gap metabolic acidosis and hypokalaemia on arterial blood gas (ABG) and was corrected accordingly. On second day of admission he developed acute onset shortness of breath. Chest auscultation revealed extensive bilateral coarse crackles. Chest X-ray was suggestive of acute respiratory distress syndrome (ARDS). The patient had to be intubated. Continuous renal replacement therapy (CRRT) was initiated in view of worsening metabolic acidosis and unstable haemodynamics. In spite of appropriate intensive care measures, the patient succumbed to illness. Immediate gastric lavage and activated charcoal administration was done and the patient was subsequently admitted into an acute medical care unit. During first 24 hours of monitoring, the patient was clinically stable. There was mild normal anion gap metabolic acidosis and hypokalaemia on ABG and was corrected accordingly. On second day of admission, he developed acute onset shortness of breath. Chest auscultation revealed extensive bilateral coarse crackles. Chest X-ray was suggestive of ARDS. The patient had to be intubated on day 2. CRRT was initiated in view of worsening metabolic acidosis and unstable haemodynamics. In spite of appropriate intensive care measures, the patient gradually deteriorated, had cardiac arrest and passed away on day 5 of his hospital stay.

DOI: 10.1136/bcr-2018-228197
PMID: 30739090 [Indexed for MEDLINE]

20. Acute localized exanthematous pustulosis caused by a herbal medicine, dai-kenchu-to. Tsutsumi R, Yoshida Y, Adachi K, Nanba E, Yamamoto O.

Contact Dermatitis. 2018 Oct;79(4):257-259. doi: 10.1111/cod.13076. Epub 2018 Jul 16.

DOI: 10.1111/cod.13076
PMID: 30014493 [Indexed for MEDLINE]

21. Contact urticaria caused by tocopherol. Sanz-Sánchez T, Núñez Acevedo B, Rubio Flores C, Díaz-Díaz RM.

Contact Dermatitis. 2018 Dec;79(6):395. doi: 10.1111/cod.13099. Epub 2018 Aug 29.

DOI: 10.1111/cod.13099
PMID: 30156307 [Indexed for MEDLINE]