Toxicon 55 (2010) 81–86

Contents lists available at ScienceDirect

Toxicon

journal homepage: www.elsevier.com/locate/toxicon

Clinical Report

Double lethal coconut crab (*Birgus latro* L.) poisoning

C. Maillaud [a,*], S. Lefebvre [a], C. Sebat [a], Y. Barguil [b,c], P. Cabalion [d], M. Cheze [e], E. Hnawia [c], M. Nour [c], F. Durand [a]

[a] SAMU/SMUR/SAU/UHCD [Emergency Department], Territorial Hospital of New Caledonia, P.O. Box J5, 98849 Noumea, New Caledonia
[b] Biochemistry Laboratory, Territorial Hospital of New Caledonia, P.O. Box J5, 98849 Noumea, New Caledonia
[c] L.I.V.E. & Laboratory for Chemistry of Natural Substances, University of New Caledonia, P.O. Box R4, 98851 Noumea Cedex, New Caledonia
[d] Laboratory for Natural Substances of Terrestrial Origin and Traditional Knowledge, US 084, "Institute of Research for Development", Noumea Centre, 101 Promenade Roger Laroque, Anse Vata, P.O. Box A5, 98848 Noumea Cedex, New Caledonia
[e] Laboratoire Toxlab, 7 rue Jacques Cartier, F – 75018 Paris, France

ARTICLE INFO

Article history:
Received 2 November 2008
Received in revised form 4 January 2009
Accepted 15 June 2009
Available online 8 July 2009

Keywords:
Coconut crab
Birgus latro L.
Poisoning
Cardiorespiratory arrest
Hyperkaliemia
Cerbera manghas L.
Cardenolide
Neriifolin
Loyalty Islands
New Caledonia

ABSTRACT

We report a double lethal coconut crab *Birgus latro* L. poisoning in New Caledonia. Both patients died after showing gastro-intestinal symptoms, major bradycardia with marked low blood pressure, and finally asystolia. Both had significative hyperkaliemia, suggesting a digitaline-like substance intoxication. Traditional knowledge in the Loyalty Islands relates coconut crab toxicity to the consumption of the *Cerbera manghas* fruit by the crustacean. Elsewhere previous descriptions of human poisoning with the kernel of fruits of trees belonging to the genus *Cerbera*, known to contain cardiotoxic cardenolides, appear to be very similar to our cases. Cardenolides assays were performed on patient's serum samples, fruit kernel and on the crustacean guts, which lead us to suppose these two fatal cases were the result of a neriifolin intoxication, this toxin having been transmitted through the coconut crab.

1. Introduction

Coconut crab *Birgus latro* (Linné, 1767) poisoning has been occasionally described in Japan and French Polynesia (Hashimoto et al., 1968; Bagnis, 1970). Although it is said to be potentially lethal, no fatality has been previously fully described. *B. latro* L., family Coenobitidae, is the largest land arthropod ever known (Fig. 1). It geographically spreads in oceanic islands, atolls, and coastal islets of the Indo-Pacific area (El Karidi-Ja, 1995). As its flesh is much appreciated, *B. latro* L. populations nowadays tend to decrease under human pressure (El Karidi-Ja, 1995). In New Caledonia, the coconut crab is mainly found in the Loyalty Islands where the local people consume it despite the fact it is known to be sometimes toxic.

2. Clinical cases

No. 1. On the 12th of April 2008, at 11:00 pm, Mr. K., 41 years old, was admitted at the Emergency Department of the Territorial Hospital of New Caledonia. He complained of diarrhoea, felt exhausted and had been vomiting for a few hours. He had a previous history of insulin-dependent *diabetes mellitus* and mild kidney insufficiency (creatinine clearance = 48 mL/min). His blood pressure was 80/40 mmHg, his pulse rate was around 25, electrocardiogram

* Corresponding author. Tel.: +687 81 91 91.
E-mail address: claudemaillaud@yahoo.com.au (C. Maillaud).

0041-0101/$ – see front matter © 2009 Published by Elsevier Ltd.
doi:10.1016/j.toxicon.2009.06.034

showed complete atrio-ventricular block. Soon after admission, the patient turned to asystolia, and resuscitation (including chest compressions, oral intubation and intravenous adrenaline) was immediately attempted. A temporary pacemaker was set up by the cardiologist on night duty.

Blood examination revealed major hyperkaliemia (9.4 mmol/L). Thus, his cardiac arrest was interpreted as the consequence of an acute renal failure. The patient was treated for both hyperkaliemia and asystolia (salbutamol, sodium bicarbonate, glucose solution, insulin, furosemide, adrenaline, calcium gluconate) and a hemodialysis was also performed, since he was still under chest compressions. Although the treatment was successful in reducing kaliemia to 5.5 mmol/L, no spontaneous cardiac activity was obtained, and the patient's death was called at 01:40 am.

No. 2. On the 13th of April, at 07:45 am, Mr. S., 75 years old, arrived at the same Emergency Department presenting the same symptoms as Mr K. (exhaustion, diarrhoea, vomiting). He told the medical team that he had been to Mare (Loyalty Islands) with Mr. K., where they together bought coconut crabs they then ate separately. Mr. S. ate the crab 12 h after Mr. K. did. Meanwhile, Mr. S. had heard about Mr. K.'s death and was very anxious as he learnt the coconut crabs they both had been eating could be deadly toxic. Like Mr. K., he was from Futuna Island (Wallis & Futuna), but his French was very poor, so it was difficult to know precisely his previous history. Nevertheless, the medical team was able to understand that he was treated with furosemide, digoxin, perindopril and ascarbose.

On admission, Mr. S. was fully conscious but adynamic, with greyish complexion and oxygen saturation at 90% on pulse oxymeter. His blood pressure was 87/61, his pulse rate was 25, his electrocardiogram showed complete atrio-ventricular block. His kaliemia, immediately checked, was raising 7.7 mmol/L. Although he was given atropine with sodium bicarbonate intravenously, he soon went into cardiopulmonary arrest (08:40 am). Resuscitation was attempted (including chest compressions, oral intubation, adrenaline, electric shocks), since hyperkaliemia was treated (with hypertonic glucose solution, insulin and calcium gluconate). No spontaneous cardiac activity was obtained, and the patient died at 09:25 am. The results of a full blood examination, received after his death, showed metabolic acidosis and creatinine serum level at 279 μmol/L, even though no previous history of kidney insufficiency was known, and confirmed the high potassium serum level (8 mmol/L). Digoxin serum level (immunoassay dosages) was found within therapeutic range (1.9 ng/mL). The same dosage was performed *a posteriori* on patient no. 1 serum, showing a serum level at 2.7 ng/mL, although this patient did not take any digitalic treatment.

Fig. 1. *Birgus latro* L. (credit P. BACCHET).

Fig. 2. *Cerbera manghas* L. (credit M. RALIJOANA).

Out of three other people who had been eating different parts of the same coconut crabs (legs and claws), two experienced diarrhoea, and one (a child who consumed a very small amount of flesh) remained unscathed. Another patient, who ate coconut crabs he had bought at the same place and at the same time than Mr. K. and Mr. S., was admitted in Mare Medical Centre with diarrhoea and vomiting.

Cardenolides assays using high performance liquid chromatography/ion trap tandem mass spectrometry (LC–IT-MS/MS) in patients' plasma samples, powdered dry kernel of *Cerbera manghas* L. and guts of a coconut crab *B. latro* L. collected at the same time and at the same place than the supposed toxic ones, and since kept frozen in order to undergo analysis, have been performed by one of the authors (MC) in May 2009. Significant levels of neriifolin were found in the three tested materials (Table 1). Cerberin and cerberigenin were present in both powdered dry kernel of *C. manghas* L. (Fig. 3) and guts of the coconut crab (Fig. 4), but were not clearly detected in the patient's serum (Fig. 5). Neriifolin wasn't detected in the serum of the two patients who only experienced diarrhoea, and the unscathed one was not tested.

Table 1
Cardenolides levels found in patients' plasma samples, powdered dry kernel of *Cerbera manghas* L. and guts of the coconut crab *Birgus latro* L.

	Neriifolin	Cerberigenin	Cerberin
Plasma sample, patient case no. 1	<1 ng/mL	nd*	nd*
Plasma sample, patient case no. 2	7 ng/mL	nd*	nd*
Cerbera manghas powdered dry kernel (150 mg)	70 μg/g	6.8 μg/g	0.71 μg/g
Coconut crab *Birgus latro* guts (821.4 mg)	2.7 μg/g	6.3 μg/g	0.014 μg/g

* Not detected.

3. Discussion

We describe two fatal outcomes following coconut crab *B. latro* L. consumption, in two patients having eaten crustaceans caught at the same time and at the same place in Mare, Loyalty Islands, New Caledonia.

The coconut crab, *B. latro* L., is traditionally eaten by native islanders in the Indo-Pacific area. Claws, legs, fleshy parts of the cephalothorax and the oily abdominal sack (the latter prized as "foie gras" in New Caledonia, "Paumotu caviar" in Tuamotu Islands, or "délices de big ball" in Vanuatu), are considered edible parts of the crustacean (Hashimoto et al., 1968).

B. latro L. poisoning has been first described by Hashimoto et al. in Ryukyu and Amami Island (Japan) and soon after by Bagnis in Tuamotu Islands (French Polynesia) (Hashimoto et al., 1968; Bagnis, 1970). According to Hashimoto et al., main clinical features were asthenia, diarrhoea and vomiting (Hashimoto et al., 1968). Bagnis described one clinical case with complete adynamia, anuria and ileus lasting more than 48 h, followed by the onset of blackish vomit and profuse diarrhoea, preceding general improvement (Bagnis, 1970). Both authors stated that fatalities had occurred, but no details were given. The toxicity of coconut crab was linked to parts of *Diospyros maritima* Blume, *Hernandia nymphaeifolia* Kubitzki and *Pisonia coronata* Florence, included in the crab's diet, but this remains unproven.

Fusetani et al., in experiments on mice, showed that the toxic parts of *B. latro* L. are the hepatopancreas and the

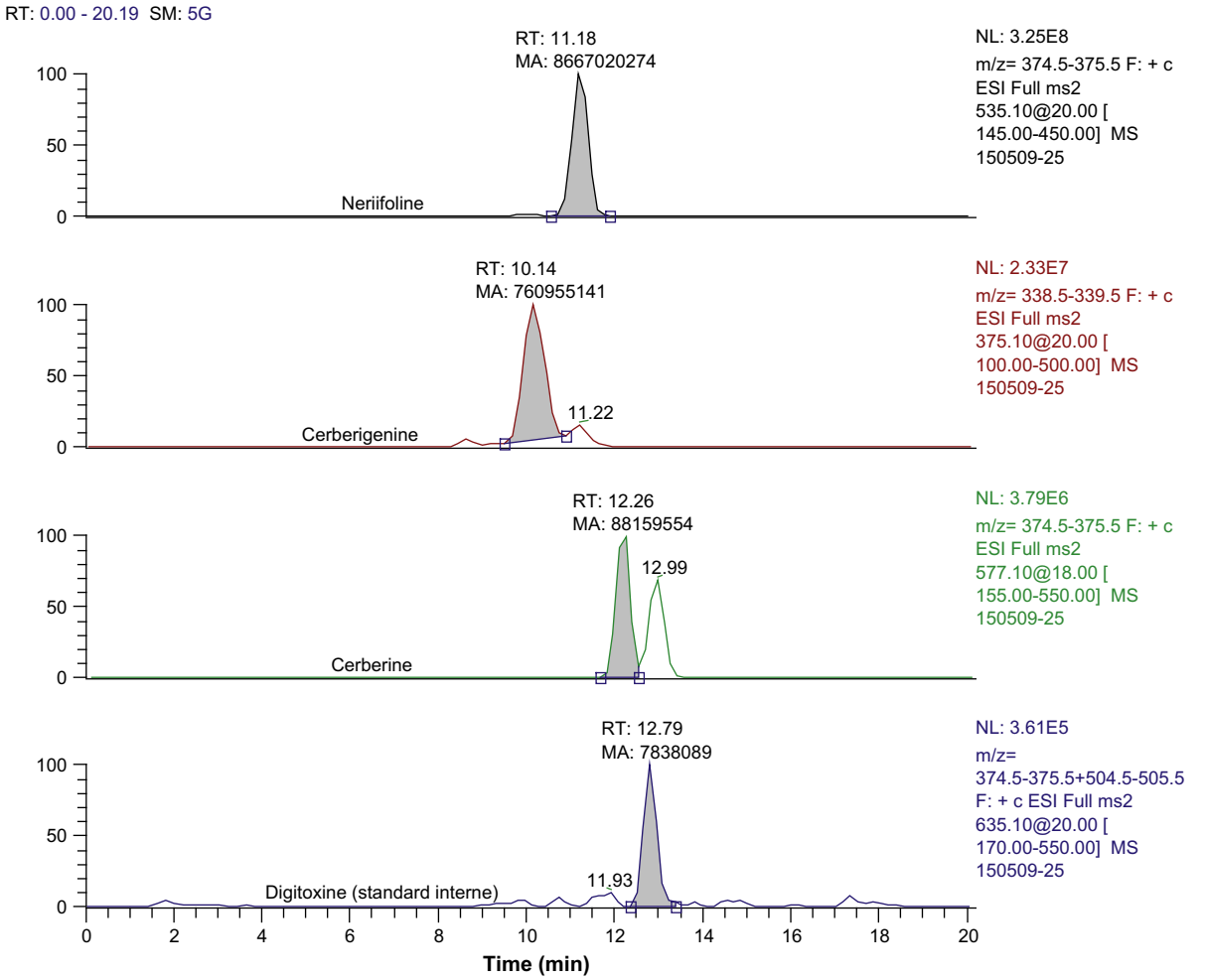

Fig. 3. Chromatogram of the extract of a powdered dry kernel of *Cerbera manghas* L., spiked with 50 ng digitoxin as internal standard.

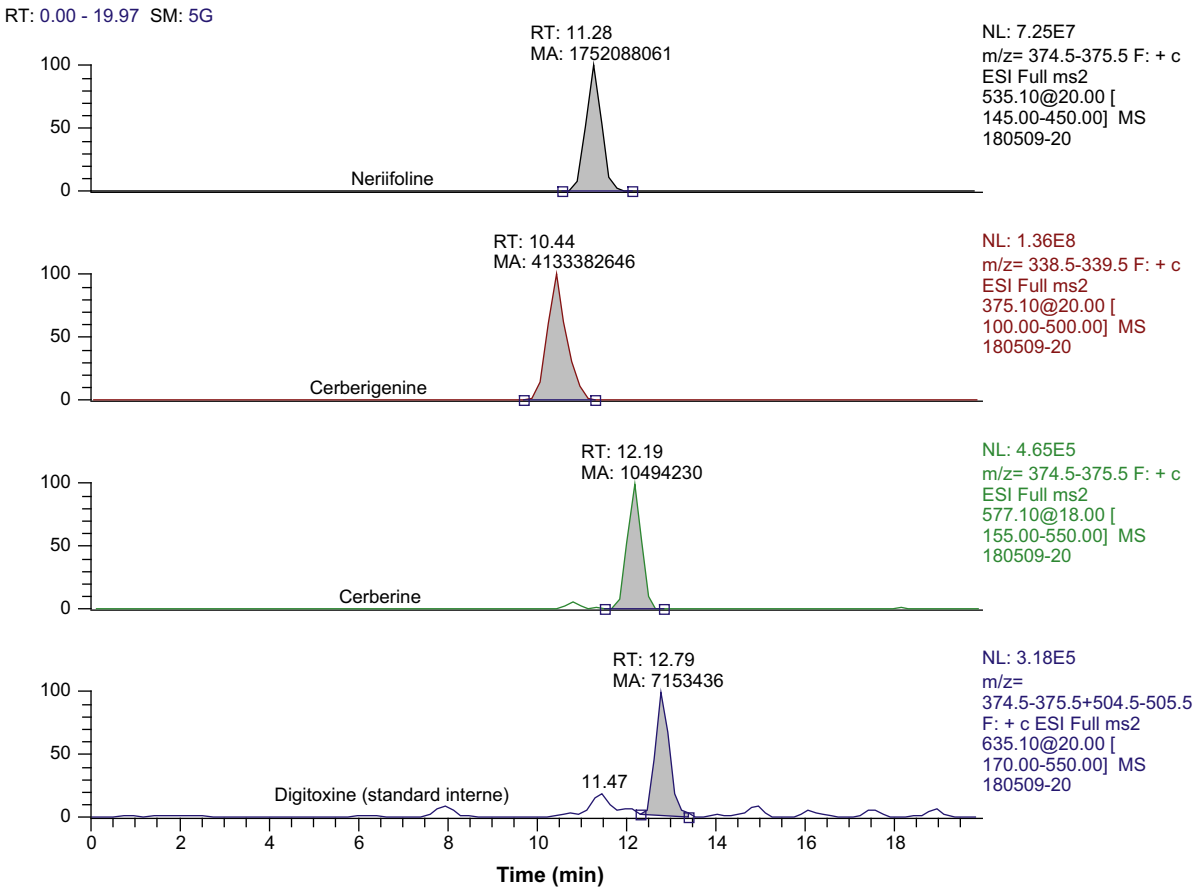

Fig. 4. Chromatogram of the extract of guts of the coconut crab, spiked with 50 ng digitoxin as internal standard.

intestine – the latter containing much less toxin than the former does, suggesting that "the toxin is derived from the diet and accumulated in the hepatopancreas" (Fusetani et al., 1980).

Studies on *B. latro* L. diet showed that it feeds on seeds, fleshy fruits, prey animals and carrion, which are rich in proteins, storage polysaccharides or fat. The digestion of this species is remarkably slow, very likely to enable abdominal sack fat storage (Wilde et al., 2004). Traditionally in Oceania, coconut crabs are starved before they are consumed, in order to empty their guts.

According to traditional knowledge in the Loyalty Islands (New Caledonia) as stated by two of the authors (PC, EH), the coconut crab is considered to be toxic after eating the fruit of the red-eye-sea mango tree, *C. manghas* L. (often called *faux manguier* in New Caledonia), also falsely named "*Cerbera odollam*", following a common misapplication of that name in the Pacific (not *C. odollam* Gaertner). This species is known under different common names in English and French: *native frangipani* in Townsville, Australia, *bois de lait rouge, faux tiaré, faux manguier rose, boulé, manguier cerbera* in New Caledonian French, also by vernacular names in the Pacific islands: *reva*, *hutureva* in Tahitian, *eva* in Marquisian, *'leva* in Samoan, *so/so madra* in Drehu (Lifou), *co/co dridri* in Nengone (Mare), *thö* in Iaai (Ouvea), *leva* in Fagauvea (Ouvea), this list being non-exhaustive.

The toxin is said to be concentrated in the "blackish part" (i.e. hepatopancreas and intestine) of the cephalothorax. It is to be mentioned that both poisoning victims we reported on, being native of a non-Melanesian archipelago, were unaware of this.

C. manghas L., sometimes miscalled "*C. odollam*" in the Pacific, belongs to the notoriously poisonous Apocynaceae family (Fig. 2). Gaillard et al. states that this tree produces fruits whose kernel contains the active glycosides cerberin, cerberoside and odollin (cerberin being a mono-acetyl neriifolin) (Gaillard et al., 2004), while Cheenpracha et al. isolated several cardenolides from the seeds of *C. manghas* : 2′-*o*-acetyl-cerleaside A, 17β-neriifolin, cerberin, cerleaside A, 17α-neriifolin, deacethyltanghinin, tanghinin and 7,8-dehydrocerberin (Cheenpracha et al., 2004). Those cardenolides are closely related to digoxin and digitoxin. Poisoning by the "true" *C. odollam* Gaertner is common in India where it has been involved in hundreds of fatalities (by suicide or homicide), whilst the close species *Cerbera venenifera* Steud killed thousands in Madagascar during collective ordeals (it is still uncertain whether *C. venenifera* Steud is actually a close species or the same species). It features both gastro-intestinal symptoms and effects of suppression of the impulse-producing and conducting tissues of the heart, such as sinus bradycardia, wandering pacemaker, second-degree atrio-ventricular block and

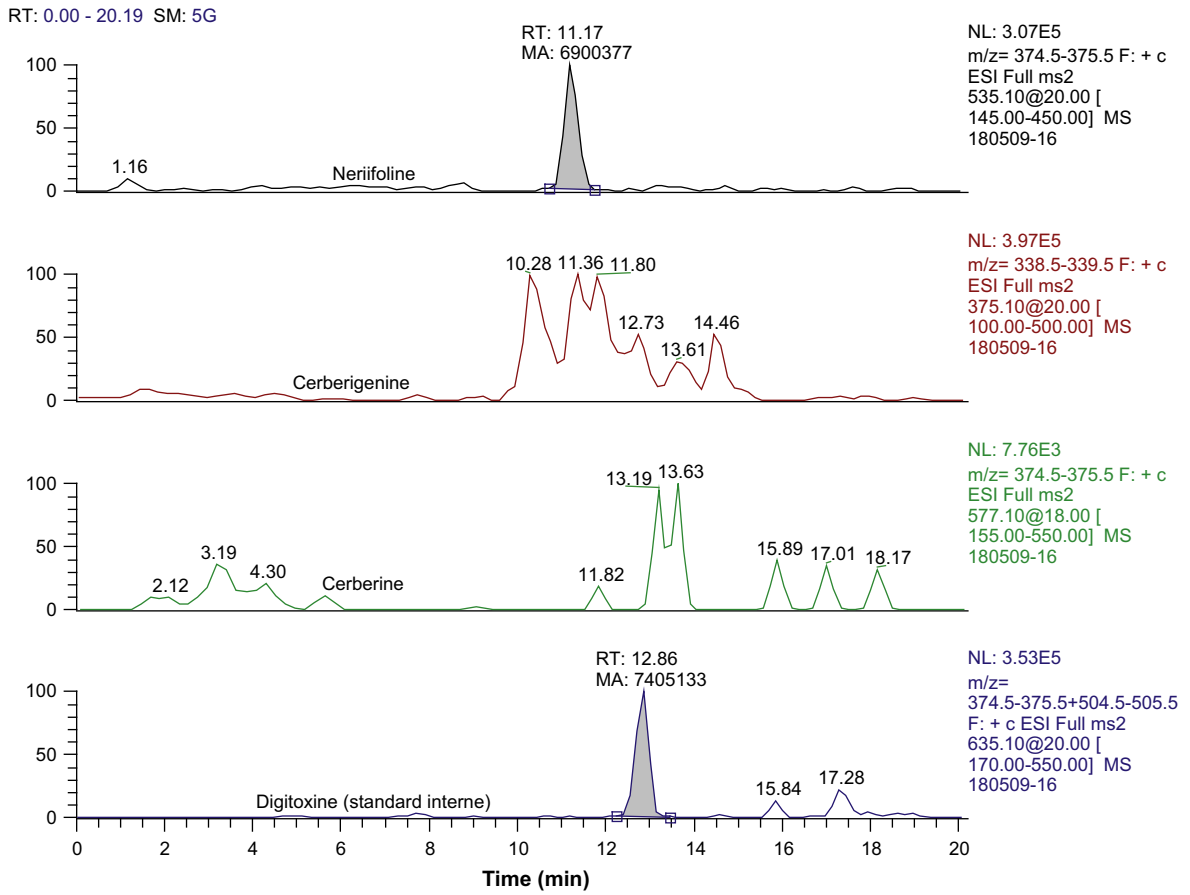

Fig. 5. Chromatogram of the extract of Mr S.'s plasma, spiked with 50 ng digitoxin as internal standard.

nodal rhythm. Hyperkaliemia is commonly observed, and high plasma potassium level clearly linked to toxicity ("out of 12 patients with plasma potassium above 8 mmol/L, eight people died") (Gaillard et al., 2004).

The depressant action of *C. odollam* Gaertner cardenolides on myocardic cells accounts for the lack of atropine to effectively abolish the vagotonic action of the toxin (Gaillard et al., 2004). In our patient no. 2, atropine was ineffective in avoiding cardiac conduction worsening.

Cardiovascular outcomes of these poisoning cases do not strongly differ from those of acute digitalic intoxication, although in this latter plasma potassium levels, considered to affect prognosis, do not happen to be as high as in *C. odollam* Gaertner poisoning, and acute renal failure is unusual in acute digitalic intoxication (Lapostolle, 2000; Lapostolle et al., 2008). Differences between acute digitalic intoxication and acute yellow oleander cardenolides poisoning, including higher plasma potassium levels, have elsewhere been shown (Eddleston and Warrell, 1999; Rajapakse, 2009).

Nevertheless, in our cases, digoxin was found in both patients' serum; in case no. 2 probably due to the patient's previous medical treatment, but as patient no. 1 had no previous history of digitalic treatment this tends to suggest a digitalic-like substance intoxication.

Confirmation of the involvement of *C. manghas* L. toxins in those two fatalities has been provided by one of the authors' (MC) assays using high performance liquid chromatography/ion trap tandem mass spectrometry (LC–IT-MS/MS) in patients' plasma samples, powdered dry kernel of *C. manghas* L. and guts of the coconut crab *B. latro* L. Neriifolin is the main substance found in the three tested materials, and has been found only in the serum of both the patients Mr K. and Mr S., who are supposed to have experienced its myocardic toxicity, leading to death. This suggests that neriifolin should be involved in those two fatalities. Neriifolin serum level under 1 ng/mL found in case no. 1, appears enough to be related to a fatal event.

Digoxin-specific antibody fragments are considered as effective in the management of life-threatening cardiac glycoside poisoning, including those resulting from ingestion of parts of Apocynaceae such as seeds of the yellow oleander *Cascabela thevetia* (L.) Lippold – formerly known as *Thevetia peruviana* (Pers.) K. Schum – which contain thevetins A and B and neriifolin (Eddleston and Warrell, 1999; Rajapakse, 2009), and leaves of the pink oleander *Nerium oleander* L., which contain oleandrin (Bourgeois et al., 2005). This suggests that the use of digoxin-specific Fab antibody fragments should be considered in the future

management of *B. latro* L. poisoning with severe cardiac outcomes.

4. Conclusion

In this case of a double lethal poisoning, the coconut crab *B. latro* L. toxicity appears to be related to the consumption of the red-eye-sea mango tree *C. manghas* L. fruit kernel by the crustacean. This hypothesis relies on traditional knowledge about *B. latro* L. in the Loyalty Islands, New Caledonia. Both patients' symptoms appeared closely similar to *C. odollam* Gaertner poisoning as previously described in India. Cardenolides, active glycosides supposed to have been involved in those fatalities, have been measured in patients' plasma samples, powdered dry kernel of *C. manghas* L. and guts of the coconut crab *B. latro* L., leading to consider neriifolin to be the main toxic agent in our cases. The use of digoxin-specific antibody fragments in such life-threatening intoxications should be considered.

Acknowledgments

We acknowledge P. BACCHET and M. RALIJOANA for providing us with the photographs of *Birgus latro* L. and of *Cerbera manghas* L. and for kindly allowing us to reproduce them.

We are grateful to Ms Anne GIBERT, Assistant Librarian at SPC – Secretariat of the Pacific Community, BP D5 – 98848 Noumea Cedex, New Caledonia, for her precious help in our bibliographical research, and to the AMUNC – Association des Médecins Urgentistes de Nouvelle-Calédonie (Association of Emergency Physicians of New Caledonia) – for its contribution in funding the English edition and the biochemical assays.

Conflict of interest

The authors declare that there are no conflict of interest regarding this paper.

References

Bagnis, R.A., 1970. Case of coconut crab poisoning. Clin. Toxicol 3, 585–588.

Bourgeois, B., Incagnoli, P., Hanna, J., Tirard, V., 2005. Nerium oleander self poisoning treated with digoxin-specific antibodies. Ann. Fr. Anesth. Reanim. 24, 640–642 (in French).

Cheenpracha, S., Karalai, C., Tat-A-Pa, Y., Ponglimanont, C., Chantrapromma, K., 2004. New cytotoxic cardenolide glycoside from the seeds of *Cerbera manghas*. Chem. Pharm. Bull. 52, 1023–1025.

Eddleston, M., Warrell, D.A., 1999. Management of acute yellow oleander poisoning. Q. J. Med. 92, 483–485.

El Karidi-Ja, N. Biologie des populations de crabes de cocotiers, *Birgus latro* (L.), dans trois îles du Pacifique: Lifou et Vauvilliers: archipel des Loyauté, Nouvelle-Calédonie; Taiaro: archipel des Tuamotu, Polynésie française. [thèse] Nouméa; 1995 (in French).

Fusetani, N., Hashimoto, K., Mizukami, I., Kamiya, H., Yonabaru, S., 1980. Lethality in mice of the coconut crab *Birgus latro*. Toxicon 18, 694–698.

Gaillard, Y., Krishnamoorthy, A., Bevalot, F., 2004. *Cerbera odollam*: a "suicide tree" and cause of death in the state of Kerala, India. J Ethnopharmacol. 95, 123–126.

Hashimoto, Y., Konosu, S., Yasumoto, T., 16–22 August, 1968. Ciguatera in the Ruykyu and Amami Islands [WP 7]. South Pacific Commission, Noumea, New Caledonia, Seminar on Ichtyosarcotoxism, Rangiroa, French Polynesia. 4 p.

Lapostolle, F., Borron, S.W., Verdier, C., Arnaud, F., Couvreur, J., Megarbanne, B., Baud, F., Adnet, F., 2008. Assessment of digoxin antibody use in patients with elevated serum digoxin following chronic or acute exposure. Intensive Care Med. 34, 1448–1453.

Lapostolle, F., 2000. Intoxication digitalique aigue. In: Bismuth, C., Baud, F., Conso, F., Dally, S., Frejaville, J.P., Garnier, R., Jaeger, A. (Eds.), Toxicologie Clinique, 5ème édition. Flammarion, Paris, pp. 254–265 (in French).

Rajapakse, S., 2009. Management of yellow oleander poisoning. Clin. Toxicol. 47, 206–212.

Wilde, J.E., Linton, S.M., Greenaway, P., 2004. Dietary assimilation and the digestive strategy of the omnivorous anomuran land crab *Birgus latro* (Coenobitidae). J. Comp. Physiol. B 174, 299–308.