Nitric oxide production in Pacific ciguatoxin-1B-stimulated RAW 264.7 cells: evidence for the role of NO pathway in the pathophysiology of Ciguatera Fish Poisoning in a mouse model

Serge Paulliac\(^a\), Shilpa Kumar-Roiné\(^b\), Mariko Matsui\(^c\), Karine Reybier\(^d\), Taiana Darius\(^e\), Mireille Chinain\(^e\) and Dominique Laurent\(^f\)

\(^a\) Institut Pasteur de Nouvelle-Calédonie, Laboratoire des Biotoxines, 9-11 avenue Paul Doumer, BP 61, 98845 Noumea, New Caledonia
\(^b\) Institut de Recherche pour le Développement, UMR152, IRD centre de Nouméa, BPA5, 98848 Noumea, New Caledonia
\(^c\) Institut Pasteur IPNC / Institut de Recherche pour le Développement IRD, UMR152, IRD centre de Nouméa, BPA5, 98848 Noumea, New Caledonia
\(^d\) Institut de Recherche pour le Développement, UMR 152 IRD - Pharmacochimie des Substances Naturelles et Pharmacophore Redox, Université Paul Sabatier Toulouse III, 31062 Toulouse Cedex 9, 31062 Toulouse, France, Metropolitan
\(^e\) Institut Louis Malardé, Laboratoire des Microalgues Toxiques, BP30, 98713 Papeete, Tahiti, 98713 Papeete, French Polynesia
\(^f\) Institut de Recherche pour le Développement, UMR152 IRD - Pharmacochimie des Substances Naturelles et Pharmacophore Redox, Université Paul Sabatier Toulouse III, Cedex 9, 31062 Toulouse, France, Metropolitan

Ciguatera Fish Poisoning (CFP), characterized by gastrointestinal, neurological and cardiovascular disorders, is caused by the ingestion of a variety of tropical reef fish which have bioaccumulated ciguatoxins (CTXs) in their tissues. These potent compounds, produced by benthic dinoflagellate Gambierdiscus spp are transferred from benthic feeding herbivorous fish to carnivorous coral reef fish via marine food chain. The primary target of CTXs is the voltage-gated sodium channel and the resulting depolarization of nerve cells is believed to cause the array of neurological and cardiovascular signs. Later on other pharmacological studies revealed a more complex action of CTXs on other voltage-gated ion channels (K+ and Ca2+); however certain unexplained phenomena such as symptoms recurrence could be related to immunologically mediated sensitization to CTXs after initial exposure. Therefore, the multifaceted clinical feature of CFP and its resemblance to the Chronic Fatigue Syndrome (CFS) prompted us to investigate the potential role of nitric oxide radical (NO), a pleiotropic regulator of neuronal, vascular and immune functions, in this pathology. The in vitro effects of the main Pacific ciguatoxin (P-CTX-1B) and bacterial lipopolysaccharide (LPS) were first comparatively studied in macrophage RAW 264.7 cell lines then experiments were conducted on 6-8-week-old OF1 mice of either sex. The overexpression of the high NO output inducible nitric oxide synthase (iNOS) enzyme, was evidenced at the mRNA and protein levels by quantitative PCR (qPCR) and ELISA or western-blot techniques, respectively. These results were confirmed by the measurement of nitrite (a stable metabolite of NO) in the cell culture supernatant by Griess reagent. The implication of NO in CFP paves the way for further exploration of the inflammatory host response against CTXs in order to help the development of targeted drug therapy retrieve from the western or traditional medical knowledge.

Number of words in abstract: 290
Keywords: Ciguatera - ciguatoxins - inducible nitric oxide synthase - Lipopolysaccharide
Technical area: Health Challenges in the Pacific: Infectious Disease, Non-Communicable Disease and the Health Workforce
Special session: Not specified
Presentation: Oral presentation preferred
Special equipment: No special equipment