



# Gambierol blocks a K(+) current component affecting action potential duration in fetal adrenomedullary chromaffin cells. Is this action sufficient to modulate catecholamine release?

Jordi Molgó, Roland Bournaud, Sébastien Schlumberger, Makoto Sasaki, Haruhiko Fuwa, Denis Servent, Evelyne Benoit

## ► To cite this version:

Jordi Molgó, Roland Bournaud, Sébastien Schlumberger, Makoto Sasaki, Haruhiko Fuwa, et al.. Gambierol blocks a K(+) current component affecting action potential duration in fetal adrenomedullary chromaffin cells. Is this action sufficient to modulate catecholamine release?. ICHA 2021 - 19th International conference on Harmful algae, Oct 2021, La Paz (Virtual), Mexico. hal-04471073v2

**HAL Id: hal-04471073**

**<https://hal.science/hal-04471073v2>**

Submitted on 21 Feb 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

## Gambierol blocks a K<sup>+</sup> current component affecting action potential duration in fetal adrenomedullary chromaffin cells. Is this action sufficient to modulate catecholamine release?

Jordi Molgo<sup>1</sup>, Roland Bournaud<sup>2</sup>, Sébastien Schlumberger<sup>2</sup>, Makoto Sasaki<sup>3</sup>, Haruhiko Fuwa<sup>4</sup>, Denis Servent<sup>5</sup>, Evelyne Benoit<sup>5</sup>

<sup>1</sup> Université Paris-Saclay, CEA, INRAE, Institut des sciences du vivant Frédéric Joliot, Département - Bâtiment 152, Gif sur Yvette, F-91191, France. <sup>2</sup> Laboratoire de Neurobiologie Cellulaire et Moléculaire, Gif-sur-Yvette, France. <sup>3</sup> Tohoku University, Graduate School of Life Sciences, Rm E516, 468-1, Aramaki Aza-Aoba, Aoba-ku Sendai 980-8572, Japan. <sup>4</sup> Chuo University, Faculty of Science and Engineering, Department of Applied Chemistry, 1-13-27, Kasuga, Bunkyo-ku, Tokyo 112-8551, Japan. <sup>5</sup> Université Paris-Saclay, CEA, INRAE, Institut des sciences du vivant Frédéric Joliot, Département Médicaments et Technologies pour la Santé (DMTS), Service d'Ingénierie Moléculaire pour la Santé (SI).

[jordi.molgo@cea.fr](mailto:jordi.molgo@cea.fr)

The genera *Gambierdiscus* and *Fukuyoa* produce numerous ladder polycyclic ether compounds including gambierol, characterized by a transfused octacyclic polyether core, and the identified ciguatoxins, responsible for ciguatera poisoning. Gambierol inhibits voltage-gated K<sup>+</sup> (K<sub>v</sub>) channels in various cells, and motor nerve terminals and enhances acetylcholine release. The purpose of this work was to study the effects of gambierol on cultured rat fetal adrenomedullary chromaffin cells. These excitable cells have different types of K<sub>v</sub> channels and release catecholamines. Perforated patch-clamp current-recordings revealed that gambierol (100 nM) only blocked a small component of the total outward K<sup>+</sup> current, and did not affect calcium-activated K<sup>+</sup> channels (K<sub>Ca</sub>) and ATP-sensitive K<sup>+</sup> (K<sub>ATP</sub>) channels. When K<sub>ATP</sub> and K<sub>Ca</sub> channel activation were blocked, the gambierol concentration inhibiting 50 % of the K<sup>+</sup> current-component (IC<sub>50</sub>) was 7.6 ± 1.10 nM (n = 9). Gambierol also slowed the kinetics of K<sup>+</sup> current activation. The recording of all-or-none action potentials in chromaffin cells disclosed that gambierol (50 nM) prolonged by 33 % their repolarizing phase. Gambierol did not modify the membrane potential following 15-second depolarizing current-steps, and did not increase the number of exocytotic catecholamine release events, as determined by simultaneous patch-clamp and single-cell amperometry recordings. Under the same conditions gambierol enhanced catecholamine secretion provided K<sub>Ca</sub> and K<sub>ATP</sub> channels were blocked. In conclusion, the specific inhibition of K<sub>v</sub> channels by gambierol is not enough to modulate catecholamine-secretion, emphasizing the key role played by K<sub>Ca</sub> and K<sub>ATP</sub> channels.

