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### ► 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

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## 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?

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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  $7.6 \pm 1.10$  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.

