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## Gambierol effects on k<sup>+</sup> currents and catecholamine release in single rat fetal adrenomedullary cultured chromaffin cells

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The purpose of this work was to study the action of the polycyclic ether gambierol on K<sup>+</sup> currents and catecholamine secretion in single rat fetal adrenomedullary cultured chromaffin (AMC) cells using perforated whole-cell voltage-clamp recordings, and current-clamp and electrochemical recordings. From the several types of voltage-gated K<sup>+</sup> channels (KV) contributing to the total outward current of rat fetal AMC cells, gambierol only partly inhibited the total K<sup>+</sup> current, when added after or before K<sub>Ca</sub> and K<sub>ATP</sub> blockers, and affected neither K<sub>Ca</sub> nor K<sub>ATP</sub> channels. After blocking of Nav and K<sub>ATP</sub> channels, and preventing the activation of K<sub>Ca</sub> channels, gambierol blocked 50% of the maximal K<sup>+</sup> current fraction with an inhibitory concentration (IC<sub>50</sub>) of  $5.8 \pm 1.56$  nM (n = 9). In marked contrast to ciguatoxins, gambierol slowed the kinetics of K<sup>+</sup>-current activation by  $75.4 \pm 10.1\%$  (n = 4) with respect to controls (p = 0.031). Hence, before and after gambierol the activation time constants of K<sup>+</sup> current were  $3.82 \pm 0.39$  ms (n = 4) and  $6.80 \pm 1.02$  ms (n = 4), respectively. Simultaneous current-clamp and single-cell amperometry recordings revealed that gambierol did not modify the membrane potential following 11-seconds depolarizing current-steps, in both quiescent and active cells displaying repetitive firing of action potentials, and it did not increase the number of exocytotic catecholamine release events, with respect to controls. The subsequent block of K<sub>Ca</sub> channels, both depolarized the membrane and enhanced by 2.7 and 3.5-fold the exocytotic event frequency in quiescent and active cells respectively, highlighting the key modulatory role played by K<sub>Ca</sub> channels in the control of exocytosis from rat fetal AMC cells

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Mots-Clés : gambierol ; potassium currents ; calcium ; activated K<sup>+</sup> channels ; ATP ; sensitive K<sup>+</sup> channels ; catecholamine release

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