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Gambierol, a marine dinoflagellate toxin, potently increases evoked quantal transmitter release and reverses pre- and post-synaptic neuromuscular block at vertebrate junctions

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Gambierol is a marine polycyclic ether toxin that was first isolated together with ciguatoxins from cultured *Gambierdiscus toxicus* dinoflagellates collected in French Polynesia. The chemical synthesis of gambierol permitted the analyses of its mode of action, which includes the selective inhibition of voltage-gated K⁺ (KV) channels in various cells and tissues expressing such channels. In the present study, we investigated the action of synthetic gambierol at vertebrate skeletal neuromuscular junctions using conventional techniques. Nanomolar concentrations of gambierol inhibited the fast K⁺ current and prolonged the duration of the presynaptic action potential in motor nerve terminals, as revealed by presynaptic focal current recordings, and increased stimulus-evoked quantal transmitter release in neuromuscular junctions blocked either by a high Mg²⁺-low Ca²⁺ medium, or by botulinum neurotoxin type-A. Also, gambierol reversed the postsynaptic block produced by d-tubocurarine. In motor nerve terminals loaded with fluo-3/AM, gambierol increased the transient Ca²⁺-signals in response to nerve-stimulation at 1-10 Hz. The results suggest that gambierol, which on equimolar basis is more potent than 3,4-diaminopyridine, can have potential application in pathologies in which it is necessary to antagonize pre- or post-synaptic neuromuscular block, or both.