



# How does calcium-dependent intracellular regulation of voltage-dependent sodium current increase the sensitivity to the oxadiazine insecticide indoxacarb metabolite decarbomethoxylated JW062 (DCJW) in insect pacemaker neurons

Submitted by Emmanuel Lemoine on Thu, 02/05/2015 - 14:28

Titre	How does calcium-dependent intracellular regulation of voltage-dependent sodium current increase the sensitivity to the oxadiazine insecticide indoxacarb metabolite decarbomethoxylated JW062 (DCJW) in insect pacemaker neurons
Type de publication	Article de revue
Auteur	Lavialle-Defaix, Céline [1], Moignot, Bénédicte [2], Legros, Christian [3], Lapied, Bruno [4]
Editeur	American Society for Pharmacology and Experimental Therapeutics
Type	Article scientifique dans une revue à comité de lecture
Année	2010
Langue	Anglais
Date	2010/04
Numéro	1
Pagination	264 - 272
Volume	333
Titre de la revue	The Journal of pharmacology and experimental therapeutics
ISSN	1521-0103
Mots-clés	Animals [5], Calcium-Calmodulin-Dependent Protein Kinase Type 2/physiology [6], Ganglia, Invertebrate/cytology/drug effects/physiology [7], In Vitro Techniques [8], Insecticides/pharmacology [9], Ion Channel Gating [10], Male [11], Neurons/drug effects/physiology [12], Oxazines/pharmacology [13], Patch-Clamp Techniques [14], Periplaneta [15], Phosphorylation [16], Signal Transduction [17], Sodium Channels/physiology [18]

Résumé en  
anglais

Decarbomethoxylated JW062 (DCJW), the active component of the oxadiazine insecticide (S)-methyl 7-chloro-2,5-dihydro-2-[[methoxycarbonyl]4-(trifluoromethoxy)phenyl] amino]carbonyl] indeno[1,2-e][1,3,4]oxadiazine-4a(3H)-carboxylate (DPX-JW062) (indoxacarb), was tested on 2 inward voltage-dependent sodium currents (named INa1 and INa2) expressed in short-term cultured dorsal unpaired median neurons of the cockroach *Periplaneta americana*. Under whole-cell voltage-clamp conditions, application of DCJW resulted in a biphasic dose-dependent inhibition of the global sodium current amplitude illustrating the differing sensitivity of sodium channels to DCJW. INa2 was less sensitive to DCJW [half-maximal inhibitory concentration (IC(50)) = 1.6 µM] compared with INa1 (IC(50) = 1.7 nM). Although a previous study demonstrated that INa1 was regulated by the cAMP/protein kinase A cascade, we showed that INa2 was mainly regulated in an opposite way by the activation of calcium-calmodulin-dependent protein phosphatase 2B (PP2B) and calcium-calmodulin-dependent protein kinase II (CaM-kinase II). Furthermore, we demonstrated that activation of CaM-kinase II by intracellular calcium via the calcium-calmodulin complex affected the sensitivity of INa2 channels to DCJW. By increasing the intracellular calcium concentration and/or using 1,2-bis(o-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid (BAPTA) (a calcium chelator), N-(6-aminohexyl)-5-chloro-1-naphthalenesulfonamide hydrochloride (W7) (a calmodulin inhibitor), cyclosporine A (a PP2B inhibitor), and 1-[N,O-bis(5-isoquinolinesulfonyl)-N-methyl-L-tyrosyl]-4-phenylpiperazine (KN-62) (a CaM-kinase II inhibitor), we revealed that activation of CaM-kinase II was involved in the modulation of the voltage dependence of steady-state inactivation and that the CaM-kinase II pathway activated by elevation of the intracellular calcium concentration might render INa2 channels approximately 3000-fold more sensitive to DCJW. These results indicated that manipulating specific intracellular signaling pathways involved in the regulation of sodium channels might have fundamental consequences for the sensitivity of insects to insecticides. This finding reveals an exciting research area that could lead to improvement in the efficiency of insecticides.

URL de la notice <http://okina.univ-angers.fr/publications/ua7541> [19]  
DOI 10.1124/jpet.109.163519 [20]  
Lien vers le document <http://dx.doi.org/10.1124/jpet.109.163519> [20]  
Titre abrégé J Pharmacol Exp Ther

---

## Liens

- [1] [http://okina.univ-angers.fr/publications?f\[author\]=11340](http://okina.univ-angers.fr/publications?f[author]=11340)
- [2] [http://okina.univ-angers.fr/publications?f\[author\]=7706](http://okina.univ-angers.fr/publications?f[author]=7706)
- [3] <http://okina.univ-angers.fr/christian.legros/publications>
- [4] <http://okina.univ-angers.fr/bruno.lapied/publications>
- [5] [http://okina.univ-angers.fr/publications?f\[keyword\]=964](http://okina.univ-angers.fr/publications?f[keyword]=964)
- [6] [http://okina.univ-angers.fr/publications?f\[keyword\]=11319](http://okina.univ-angers.fr/publications?f[keyword]=11319)
- [7] [http://okina.univ-angers.fr/publications?f\[keyword\]=11320](http://okina.univ-angers.fr/publications?f[keyword]=11320)
- [8] [http://okina.univ-angers.fr/publications?f\[keyword\]=11214](http://okina.univ-angers.fr/publications?f[keyword]=11214)
- [9] [http://okina.univ-angers.fr/publications?f\[keyword\]=11201](http://okina.univ-angers.fr/publications?f[keyword]=11201)
- [10] [http://okina.univ-angers.fr/publications?f\[keyword\]=11321](http://okina.univ-angers.fr/publications?f[keyword]=11321)
- [11] [http://okina.univ-angers.fr/publications?f\[keyword\]=968](http://okina.univ-angers.fr/publications?f[keyword]=968)
- [12] [http://okina.univ-angers.fr/publications?f\[keyword\]=11215](http://okina.univ-angers.fr/publications?f[keyword]=11215)
- [13] [http://okina.univ-angers.fr/publications?f\[keyword\]=11322](http://okina.univ-angers.fr/publications?f[keyword]=11322)
- [14] [http://okina.univ-angers.fr/publications?f\[keyword\]=9184](http://okina.univ-angers.fr/publications?f[keyword]=9184)

- [15] [http://okina.univ-angers.fr/publications?f\[keyword\]=9153](http://okina.univ-angers.fr/publications?f[keyword]=9153)
- [16] [http://okina.univ-angers.fr/publications?f\[keyword\]=1711](http://okina.univ-angers.fr/publications?f[keyword]=1711)
- [17] [http://okina.univ-angers.fr/publications?f\[keyword\]=6050](http://okina.univ-angers.fr/publications?f[keyword]=6050)
- [18] [http://okina.univ-angers.fr/publications?f\[keyword\]=11323](http://okina.univ-angers.fr/publications?f[keyword]=11323)
- [19] <http://okina.univ-angers.fr/publications/ua7541>
- [20] <http://dx.doi.org/10.1124/jpet.109.163519>

Publié sur *Okina* (<http://okina.univ-angers.fr>)