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Title Structure-activity relationship of indole alkaloids okaramines on insect glutamate-gated chloride channels
[Objective] Indole alkaloids okaramines produced by *Penicillium simplicissimum* AK-40 show insecticidal activities against silkworm larvae. Their unique structures inspired total synthesis, yet its target remained unknown. We have studied the mode of action of okaramines and found that they target L-glutamate-gated chloride channels (GluCl) to paralyzing the larvae. However, it is still unknown what structural factors of okaramines contribute to the GluCl-activating actions. Hence, the structural factors of okaramines underlying the potency on silkworm GluCl were investigated.
[Materials and Methods] Okaramines, A, B, G, N and Q were obtained by purifying them with silica gel column chromatography from the products in okara of wild-type *P. simplicissimum* AK-40, whereas okaramine H and 2-hydroxy-3-demethoxy okaramine B were isolated from the products of biosynthesis-gene-knockout strains of the fungus. The action of the okaramines on the silkworm GluCl expressed in *Xenopus laevis* oocytes were investigated by two-electrodes voltage-clamp electrophysiology.
[Results] It was found that the double bonds in the azocine ring and 3-methoxy group are critical for the activity and that the azetidene ring also contributes to the activity. Also, the N-prenylation was important for the activity. However, elimination of 2-hydroxy group hardly affect the activity. All these findings would help design new okaramine analogs to control pest insect species.
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