Effects of Synergists on the Insecticidal Activity of Chloronicotinyl-related Benzyl Compounds against Houseflies

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INTRODUCTION

Chloronicotinyl compounds including imidacloprid, acetamiprid, and nitenpyram have a larger market share than many other insecticides. Insecticidal effects of this class of compounds are primarily due to their binding to the nicotinic acetylcholine receptor (nAChR). Following application, the insecticidal activity of these compounds is affected by several factors including metabolism and transportation. We used the inhibitors piperonyl butoxide (PB) and propargyl propyl phenylphosphonate (NIA 16388; NIA) to eliminate the oxidative and hydrolytic metabolism of pyrethroids in insecticidal tests against the American cockroach, Periplaneta americana, and the housefly, Musca domestica.

PB is an oxidative metabolic inhibitor of P450s and NIA is a hydrolytic metabolic inhibitor, particularly for the pyrethroid tetramethrin. Even for non-ester chloronicotinyl compounds, we have observed a much greater effect of NIA on the insecticidal activity than that of PB.

For a number of substituted-benzyl compounds related to chloronicotinyl insecticides, we have measured their insecticidal activity against the housefly under the conditions using NIA as a metabolic inhibitor and their binding activity to nAChR of housefly heads, which is evaluated by measuring the inhibition of the [125I] α-bungarotoxin binding. These two activities were linearly correlated at a certain level. To examine the correlation more precisely, we measured the insecticidal activity of some compounds using both PB and NIA. We confirmed a certain role of PB to inhibit a metabolic mechanism even for this class of compounds.

RESULTS AND DISCUSSION

Based upon the standard deviation, the difference between the pEC50 values needs to be greater than 0.4 (2.5-fold) to compare them at a significant level. Among the compounds tested, activities of compounds 2, 4, 7–10, 13, 14, and 17 measured with NIA were enhanced by 0.5-1.6 log units (3-40 folds) by using a mixture of NIA and PB. PB did not actually increase the activities of compounds 3, 5, 6, 11, 15, 16, and 19 (acetamiprid). For other compounds 1, 12, and 18 (imidacloprid), the enhancing effect was small. We previously found that the pEC50 (NIA) values of this class of compounds were correlated with the binding activity (pK_a) (n=15, s=0.43, r=0.91), excluding compounds 11, 17, imidacloprid (18) and acetamiprid (19). Compounds 11 and 17 have a common substituent, methyl group at the para position of the benzene ring (compound 11) and at the corresponding position of the pyridine ring (compound 17).

As shown in Fig. 1, the pEC50 (NIA + PB) values were almost linearly correlated with the binding activity that we have reported for the compounds 1–17 (n=17, s=0.58, r=0.85). The insecticidal activities of imidacloprid (18) and acetamiprid (19) were still higher than those expected from the correlation. The nitroimine substructure of compounds such as imidacloprid and an open structure of acetamiprid might be favorable to enhance the insecticidal activity. Among the compounds 1–17, compound 17 still seemed to be an outlier, with its insecticidal activity being higher than that expected from the correlation. Excluding this compound, the correlation was improved (n=16, s=0.44, r=0.89). Although NIA might be a metabolic inhibitor for a certain

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oxidase system, the enhancing effect of PB over NIA was not uniform (Table 1). Moreover, since the correlation analysis of the pEC50 (NIA) and pK1 for the same compound set gave a poorer result (n=16, s=0.50, r=0.86), the present finding indicated that it is better to additionally use PB as a synergist for the analysis of these two activities of this class of compounds. At present the metabolic study of these chloronicotinyl compounds is in progress using housefly enzymes to make clear the roles of synergists.

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