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Pesticides' role enhancement through use of synergists: a worthy approach

Namita Kumar and Nikhil Kumar
Department of Zoology, Mahatma Gandhi Post Graduate College, Gorakhpur (U.P.) India

Summary: ***Synergism is a term used in pharmacology which refers to the conditions where a s e t o f c h e m i c a l s p r o d u c e synergistic effects, and enhance their efficacy. The combined effects of at least two substances make significant impact as compared to both of them as an individual. Toxicity of certain insecticides like pyrethrin (from chrysanthemums) and synthetic pyrethrins (pyrethroids) had been increased several times by the addition of compounds that themselves are not insecticides. These synergists are Sesame, Sesamolin, Piperonyl Butoxide (P B) a n d M G K - 2 6 4 (b i - cycloheptene dicarboximide). Piperonyl butoxide had perhaps been the most widely used synergist to synthetic pyrethroids. Synergy refers to the interaction of biological structures or entities so that the overall impact will be greater that the overall impact is so great that it cannot be reproduced singly.***

Sahay et. al. (1991) demonstrated that 1.1 mg/l of Fenvalerate, a pyrethroid, could kill 50% of the snail Lymanea acuminata after 96 hours of exposure. However, when it was used in combination with PB (5X), its toxicity increased nearly 10 folds. Similarly, the pesticide Phorate, in its synergistic studies showed surprising results. When used in a concentration of 15.0 mg/l, it killed 50% of the snail population to which it was administered after an exposure period of 96 hours. When this concentration was further reduced and mixed with five times its concentration of Piperonyl Butoxide (PB), a mixed function oxidase (MFO) inhibitor, just 0.74 mg/l killed the same percentage of snails after 96 hours (Singh and Agarwal, 1983a). These examples of synergism are demonstrative of, but only one type of joint action, where addition of a non-toxic compound to a toxic compound increases the toxicity of the latter. Even after for past two decades, much is u n d e r s t o o d a b o u t s u c h synergism, comparatively little work has been done on the joint action of mixtures where both compounds are independently toxic to the target animal. Sahay et. al. (1994) found that a binary m i x t u r e o f t h e p y r e t h r o i d Deltamethrin and a carbonate Sevin, showed high synergism when given in 1:9 ratio. It has also been stated that the lowering of doses at longer exposure periods say from 24 hours to 96 hours, is perhaps because of the increase in the titer of the pesticide and its effect at the active site (Singh, 1990).

DISCUSSION: The toxicity of the mixture containing Fenvalerate and Phorate cannot be explained by the separate toxicities of its constituents on the assumption that they acted independently. When two toxic substances act independently, they affect different physiological systems in a pest and the action of one toxicant upon an individual neither augments nor interferes with that of the other (Bliss, 1939). If two toxicants act simultaneously but independently upon a pest, it would die only if it receives lethal dose of either toxicant, but not if it receives sublethal doses of the two toxicants (Hewlett, 1969). In the experiments of Sahay and Agarwal (1996), the mixture of Fenvalerate and Phorate killed snails at sublethal doses of the two pesticides. The hypothesis of independent uncorrelated action thus, was rejected. When the slope values of the doseresponse regression lines of the mixture of the two pesticides were compared with those values of each of the pesticides, it was found that the slope value of the former were lower. Thus, it was concluded that while the mixtures caused higher mortality at lower doses, the tolerance of the individuals in the population was distributed over a wide range. It was also explained that the mode of action of the mixture was different from its two components since the log-dose probation (ld-p) lines had a lower value and was not parallel to the ld-p lines of the components (Finney, 1971).

The natural pyrethroids, the esters of two different alcohols with two different acids. In synthesising most pyrethroids, various substitutions in the alcohol moiety were made. In case of Fenvalerate, however, even the cyclopropane ring of the acid side, regarded as an essential moiety for insecticidal activity of pyrethroids, had been substituted. Despite this, Fenvalerate like other pyrethroids, was found susceptible to hydrolytic degradation with the help of esterases found in the snails (Matsumura, 1985). Phorate on the other hand, whose cholinesterase inhibiting action had been used for pest control, was also found to be a general inhibitor of esterases (Casida and Ruzo, 1980). Hopefully, the nonspecific esterase inhibiting property of Phorate was responsible for delaying the hydrolysis of Fenvalerate so that higher concentrations of the latter were accumulated at the site of action. Thus, those low doses of Phorate which couldn't produce sufficient enough inhibition of acetylcholinesterase to cause death, were adequate to prevent the degradation of Fenvalerate so that it accumulated at the site of action and acted more strongly. This seemed to be a reasonable explanation for the joint action of the two pesticides. This had long been established that the mixture of Fenvalerate and Phorate could be successfully used for the purpose of pest control. The obvious advantage would be less environmental pollution and lower cost of pesticides.

Another pesticide Deltamethrin had been shown to have highest toxicity amongst pyrethroids of its generation against molluscans. This was clear from steep slopes of the regression lines of dose response curves obtained against its administration against fresh water snail Lymnaea acuminata. This was supposed to be due to its high lipophilic nature. Narahashi (1983) had stated that pyrethroids of high lipophilic nature can move rapidly to the nerve membrane, the site of their action, and are, therefore, more toxic. Moreover, Singh et. al. (1993) showed that sublethal doses of Cypermethrin, yet another synthetic pyrethroid, increased the lipid peroxidation and caused reduction in the levels of phospholipids in the nervous tissue of the snail Lymnaea acuminata. They were of the opinion that this is the mechanism by which pyrethroids change the permeability of the nerve membrane.

The synergistic effect of Piperonyl butoxide (PB) on the toxicity of Deltamethrin, had shown in its statistical analysis that there was increase in the intercept and decrease in slope of the regression lines as compared to these values of Deltamethrin alone. This clearly indicated an increase in dose range of the mixture. Toxicity data of Deltamethrin with Piperonyl Butoxide (PB) demonstrated that there was a nearly four to eight fold increase in the toxicity of Deltamethrin when the LC50 was compared. PB, however, had no independent toxic effect on the snails. Singh and Agarwal, (1986) had reported that the synergistic ratio of Cypermethrin was 97 to 60 times and that of Permethrin 34-38 times when used along with PB in a 1:5 ratio. These observations indicated that while the major pathway for the breakdown of Permethrin and Cypermethrin might be oxidative, in case of Deltamethrin, oxidation might be playing a minor role.
Another chemical which was used as a putative synergist along with Deltamethrin and Fenvalerate was

MGK-264 (MGK). This compound is an esterase inhibitor (Wilkinson, 1976) and prevents hydrolysis of pesticides where esteratic hydrolysis is their normal way of catabolism. When MGK was given in a 1:5 ratio with Deltamethrin, the slope values were lower as compared to Deltamethrin + PB or Deltamethrin alone. Since MGK is an inhibitor of esterase, it also synergized other pesticides which are rendered inactive by esterase hydrolysis. Thus, it mildly synergised Aminocarb against a resistant strain of Spodoptera littoralis (El Guindy et.al. 1979; Riskillah, 1984) and Lannate against the Bollworms, Heliothis armigera (El Guindy et. al. 1980). MGK when administered singly, though exhibited a slight toxicity against certain insects, however, it did not do so in the case of Lymnaea acuminata.

It needs to be pointed out that when two toxic substances act independently, they affect different physiological systems in a pest and the action of the toxicant upon an individual, neither augments nor interferes with that of the other. If two toxicants act simultaneously but independently upon a pest, it would die only if it receives lethal dose of any one, or, both of the two toxicants, making it doubtful which toxicant killed the pest. The combined action of two pesticides resulting in a substantially increased level of toxicity than either of the two compounds used alone, represents a form of joint action defined as potentiation (Hewlett, 1969). The experiments carried out on pyrethroids and anticholinesterase pesticides is indeed a case of potentiation. A model developed by Corbett (1974) indicated that potentiation occurred when one chemical (synergist) interferes with the microsomal detoxification of the principal toxicant thereby potentiating the toxicity of the latter. These studies also showed that the synergistic ratio increased with increase in exposure period. This was further proof of the fact that the Carbamate and OP compounds, by preventing the degradation of the pyrethroids, over a period of time, allowed these to accumulate at the site of their action.

The importance and impact of the insecticides under field conditions cannot be denied, both, in terms of the usefulness and residual effects. Similarly, they form a major part of the agriculture industry, since the pesticides available are expensive, environmentally undesirable, and have problem of developing resistance towards them. Synergists have contributed significantly to improve the efficacy of insecticides which increase the effectiveness of insecticides. These natural or synthetic chemicals, which increase the lethality of the insecticides, are usually non toxic by themselves. It will be beneficial in true sense if they are exploited in pest management programs for intention of resistance management in pests. The need should be to further examine the potential role of synergists in pesticide resistance management, mode of their action, natural occurrence and their significance. This information should be explored and then exploited in pest management program which most likely will lead to a new perspective on the nature and significance of synergism.

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