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Commentary

Spinosad: A biorational mosquito larvicide for vector control

Vector-borne diseases are among the extensive causes of illness throughout the tropics and to some extent in subtropics. Globally, vector-borne diseases account for >17 per cent of all infectious diseases that cause >1 million deaths annually and >2.5 billion people are at risk of vector-borne diseases[1]. Vector control is one of the essential components for vector-borne disease management. Currently, there are four classes of insecticides recommended by the WHO for indoor residual spray for vector control, namely, organochlorines, organophosphates, carbamates and pyrethroids; and larvicides include bacterial pesticides, benzoylureas, juvenile hormone mimics, organophosphates and spinosyns while only one class *i.e.* synthetic pyrethroids is recommended for insecticide treated nets (ITNs).

Global efforts over the last decade and increased availability of synthetic insecticides mainly for adult vector control have dramatically reduced the incidence of vector-borne diseases. Also with the concomitant increase in insecticide resistance retarded the progress challenged sustenance of the gains achieved so far. Since 2010 based on the available data, a total of 61 countries have reported resistance to at least one class of insecticide and 50 of those countries reported resistance to two or more classes[2]. However, use of synthetic chemical insecticides is still an important component for vector control and use of insecticide class (*e.g*. neonicotinoids, pyrrole and butenolides) having novel mode of action (MoA) is gaining importance and many co-formulated insecticide compounds with variable MoA are being tested for efficacy. In addition, combination intervention, for example, combination ITNs with insecticide-insecticide and insecticide-synergist are being evaluated. It is known that continued use of synthetic insecticides will develop resistance in disease vector sooner or later except to insect growth regulator (IGR) compounds that are reported to have relatively longer shelf-life for use. Another major concern has always been contamination of environment and the resultant impact on flora and fauna. Since, the last few decades, efforts are being made to develop non-chemical insecticides from plants being eco-friendly products with limited success. However, bacterial pesticides, namely, *Bacillus thuringiensis* serotype *israelensis* (*Bti*) and *B. sphaericus* have been found to be highly effective larvicides and are being used since many decades[3]. Another promising bacterial origin larvicide for vector control, spinosad has gained importance in the last decade and is being used in several countries[3].

Spinosad is highly active in numerous insect species in agriculture, veterinary and public health importance. Spinosad shows variable efficacy among the species and stages and acts both by contact and ingestion. Spinosad was recommended as mosquito larvicide by the United States Environmental Protection Agency and World Health Organization's Pesticide Evaluation Scheme (WHOPES) during 2007 following which 120 suspension concentrate (SC) formulations were registered in Morocco followed by many countries namely, Turkey, Tunisia and Spain with more countries to follow[3]. Spinosad has been registered and approved for use for crop protection by Central Insecticides Board, India[4].

Spinosad is a natural pesticide with bacterial origin. It was first isolated from the soil from *Saccharopolyspora spinosa* (Actinomycetales) from an abandoned rum distillery in 1982[5]. Spinosad contains a mix of two complex organic compounds, spinosyn A, the major component and spinosyn D, the minor component, roughly in 85:15 ratio[3]. It is a white crystalline solid with a unique tetracyclic ring system attached to an amino sugar (D-forosamine) and a neutral sugar (tri-O-methyl-L-rhamnose). Spinosyns are non-volatile, have low water solubility, resistant to hydrolysis up to *p*H 5

that increases slowly beyond this *p*H and show rapid aqueous photolysis at *p*H 7.0 and have a half-life of less than one day[6]. These characteristics make it ideal for usage as larvicide.

As per WHO, spinosad as a mosquito larvicide does not pose any threat to the health of users and to the environment. As per WHO Hazard Classification, spinosad is classified as class III compound as slightly hazardous with oral and dermal toxicity (LD_{50} for rat of over 2000 mg/kg body weight)[7]. Spinosad does not cause dermal sensitization, faintly irritates eyes, not mutagenic, does not induce tumours and causes no teratogenicity, neurotoxicity and reproductive impairment. Spinosad is highly toxic to honeybees, moderately to fish and none to birds[6]. However, in laboratory studies, spinosad has not shown any deleterious impact on the larvivorous fish *Gambusia*[3] and *Poecilia reticulata* (guppy)[8].

The MoA of spinosad is unique and novel. It primarily attacks nicotinic acetylcholine receptor and then the gamma-aminobutyric acid receptors[9]. It kills insects by hyper-excitation of the insect nervous system. As per MoA Classification Scheme of Insecticide Resistance Action Committee, it is classified to Group 5 based on primary site of action[10]. No cross-resistance was exhibited to existing insecticides in use, organophosphates, carbamates and pyrethroids that confer metabolic resistance mechanism and also exhibited absence of synergism to synergists of esterases (s,s,s-tributyl phosphorotrithioate) and monooxygenases (piperonyl butoxide)[3]. Further, spinosad can also be used in rotation with chemical insecticides in insecticide resistance management (IRM) with other biorational larviciding agents such as *Bti* and with IGR compounds such as diflubenzuron, methoprene, pyriproxyfen and novaluron[11].

WHOPES has reviewed the use of different formulations of spinosad namely, granular formulation (0.5% GR)[6], suspension concentrate (12% SC)[6], emulsifiable concentrate (20.6% EC)[12], dispersible tablets (83.3 monolayer DT)[13] and spinosad 25 extended release granular[13] formulation for the treatment of polluted and non-polluted open water bodies. Other formulations, a bilayer tablet (7.48% DT - two layer) with effervescence for longer persistence is being evaluated. Thus, various formulations for container breeding to polluted and non-polluted water bodies are available (for information on dosages; *http://www.who.int/whopes/Mosquito_larvicides_March_2016.pdf*). The expected persistence with different formulations in different breeding habitats varied from about 2-4 wk that depends on the formulation and content of organic matter in the target habitats[6].

An elaborate review by Hertlein *et al*[3] suggested susceptibility ranking of public health disease vectors based on the LC_{50} values derived from the field usage of spinosad formulations from databases of 101 studies sourced from published and unpublished reports and was *Anopheles gambiae* (Giles) = *Anopheles pseudopunctipennis* (Theobald) >*Culex pipiens* (Linnaeus) = *Aedes albopictus* (Skuse) > *Aedes vigilax* (Skuse) = *Anopheles sinensis* (Wied.) > *Culex quinquefasciatus* (Say) > *Aedes aegypti* (Linnaeus) > *Anopheles albimanus* (Wied.) *Anopheles stephensi* (Liston) > *Ae*. *albopictus* (Skuse). *Ae. albopictus* appeared twice in this list because of two conflicting sets of data[3].

The study by Sadanandane *et al*[14] in this issue is an important contribution for employing two formulations (20% EC and 12% SC) as biorational insecticide for effective larval control with persistence of about two weeks in different polluted breeding habitats of *Culex quinquefasciatus*. The 20 per cent EC formulation was found more effective than 12 per cent SC and 0.5 per cent GR in providing protection. However, this molecule as evidenced from this study and other previous studies has shown promise for vector control because of its variant MoA which is non-metabolic and absence of cross-resistance with the existing insecticide classes. At present, more formulations are available and a few are in use in some countries and others are in efficacy trials. The product has gained importance in view of its availability in diverse formulations and its effectiveness to all the public health disease vectors. The tablet formulations will be more effective for containing the arboviral disease vectors that are presently showing an upward trend in different countries. Importantly spinosad having a novel MoA can be used in rotation for IRM and also as a component of integrated vector management. Many countries are intending for vector-borne disease elimination in near future and are also experiencing rise in emerging and re-emerging diseases, thus, more such compounds like spinosad are needed.

***Conflicts of Interest*:** None.

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References

1. Vector-Borne Diseases; 2016. Available from: *http://www.who.int/mediacentre/factsheets/fs387/en/*, accessed on September 9, 2016.
2. Insecticide Resistance; 2015. Available from: *http://www.who.int/malaria/areas/vector_control/insecticide_resistance/en/*, accessed on January 16, 2018.
3. Hertlein MB, Mavrotas C, Jousseaume C, Lysandrou M, Thompson GD, Jany W, *et al.* A review of spinosad as a natural product for larval mosquito control. *J Am Mosq Control Assoc* 2010; *26* : 67-87.
4. Central Insecticides Board & Registration Committee. Insecticides Registered under/section 9 (3) of the Insecticide Act, 1968, as on 17/06/2011, Available from: *http://www.cibrc.nic.in/reg_products.htm*, accessed on January 16, 2018.
5. Mertz F, Yao RC. *Saccharopolyspora spinosa* sp. nov. Isolated from soil collected in a sugar mill rum still. *Int J Syst Evol Microbiol* 1990; *40* : 34-9.
6. World Health Organization. *Report of the Tenth WHOPES Working Group Meeting*. WHO/CDS/NTD/WHOPES/2007.1. Geneva: WHO; 2007. Available from: *http://www.who.int/whopes/recommendations/WHO_CDS_NTD_WHOPES_2007_1.pdf*, accessed on July 1, 2016.
7. The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 2009. Available from: *http://www.who.int/ipcs/publications/pesticides_hazard_2009.pdf*, accessed on July 1, 2016.
8. Anogwih JA, Saliu JK, Linton EW, Makanjuola WA, Chukwu LO. The compatibility of spindor dust with *Poecilia reticulata* for integrated mosquito larviciding. *J Clin Res Bioeth* 2013; *4* : 4.
9. Scott JG. Unraveling the mystery of spinosad resistance in insects. *J Pestic Sci* 2008; *33* : 221-7.
10. Insectcide Resistance Action Committee. Mode of Action Classification Scheme; 2016. Available from: *http://www.irac-online.org/documents/moa-classification/*, accessed on June 1, 2016.
11. Su T. Resistance and its management to microbial and insect growth regulator larvicides in mosquitoes. In: Trdan S, editor. *Mosquitoes, insecticides resistance*. Rijeka: InTech; 2016. Available from: *http://www.intechopen.com/books/insecticides-resistance/resistance-and-its-management-to-microbial-and-insect-growth-regulator-larvicides-in-mosquitoes,* accessed on July 1, 2016.
12. World Health Organization. *Report of the Fourteenth WHOPES Working Group Meeting*. WHO/HTM/NTD/WHOPES/2011.7. Geneva: WHO; 2011. Available from: *http://www.apps.who.int/iris/bitstream/10665/44669/1/9789241502160_eng.pdf,* accessed on July 1, 2016.
13. World Health Organization. *Report of the Sixteenth WHOPES Working Group Meeting*. WHO/HTM/NTD/WHOPES/2013.6. Geneva: WHO; 2013. Available from: *http://www.apps.who.int/iris/bitstream/10665/90976/1/9789241506304_eng.pdf,* accessed on July 1, 2016.
14. Sadanandane C, Gunasekaran K, Boopathi Doss PS, Jambulingam P. Field evaluation of the biolarvicide, spinosad 20 per cent emulsifiable concentrate in comparison to its 12 per cent suspension concentrate formulation against *Culex quinquefasciatus*, the vector of bancroftian filariasis in India. *India J Med Res* 2018; *147* ; 32-40.