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Looking at Neonicotinoid Insecticides: Environmental Perspective

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Abstract

The recent "Global report on Food Crises" published by Food Security Information Network (FSIN, 2017) calls for intervention in methods and technologies to improve the quality and timeliness of food security and tackle the present food crises. India has a huge challenge to feed 1.32 billion and it is a daunting task. Droughts and other meteorological phenomena including, climate change, increase in pollution levels and spread of plant diseases and pests are some of the most common problems that continue to have an impact on food production. In order to manage crop diseases and reduce crop losses, low cost broad-spectrum insecticides have been synthesized. Farmers are using these both in situ and ex situ to save the crops and minimize the losses. However, all major pesticides have been found to have detrimental effects on social insects, and insects develop resistance to these after consistent and rampant use. Prolonged residence time of these in the environment also have harmful health implications and sometimes cause irreversible damage to human health. Therefore, time and again scientists are at look out for novel products and chemicals that can help in managing pests. The use and discovery of neonicotinoids proved to be a novel innovative method in diseases management of major crops. The newly discovered family of pesticides is attributed with various properties that are inherently different from other pesticides, and have the potential to kill a bouquet of crop pests including those that affect fruits, vegetables, fish and veterinary without conferring any resistance to them. However, the rampant use of neonicotinoids for crop protection has resulted in many unforeseen environmental problems. It is important to look for alternatives for the existing ones to tackle the human health problems. Scientists are also looking at decreasing the doses and treatment methods to reduce the impact on agro-ecosystems. A paradigm shift is required in crop management practices and indiscriminate use has to be stopped. Discovery of new generation neonicotinoids with interdisciplinary approach is one of the ways to tackle the present problems and meet the future challenges. Though, there are evidences that these novel formulations show developmental neurotoxicity, the dosage and frequency of applications show variable response. Research in this field is further required to substantiate the evidences of these insecticides to be safe to environment.

1. Introduction

The population in India is growing at a fast pace and the projections state that India may surpass China in population in the next few decades. The increase in population suggests that the production of food resources should also increase substantially to meet the growing demands (FAO: Global agriculture towards 2050). However, the potential to raise crop yields with the existing technologies does not seem to be possible. Therefore, focus should be on some other domains such as saving of crop losses on and off field from pests.Management of crop losses on account of spread of diseases caused by insect pests both in the field and post-harvest interests scientists all across the globe.

Agrochemical industries are witnessing spur in investments as well as profits via increased outreach and job markets (Jeschke *et al*., 2011). India is now the second largest producer of pesticides in Asia (Nollet *et al*., 2016). We also stand third in terms of pesticide use and are one of the largest global pesticide consumer nations of the world (Nollet *et al*., 2016). Some of these pesticides have also found a huge market base in many parts of South East Asia, especially neighbouring countries of Bangladesh, Pakistan, Nepal and Sri Lanka. However, there are lots of negative implications of excessive use of these on environment, biodiversity and human health. This aspect has been neglected and ignored for a long time, and is of great concern.

Among the most popular pesticides, are the insecticides which have seen many transitions from the first plant based nicotine insecticides in 1690 to synthetic organic forms like organophosphates, methylcarbamates, organochlorines and pyrethroids from 1940s-1970s (Tomizawa and Casida, 2011). Resistance in the pests to these widely used insecticides in the late 1980s gave a head start to the newly introduced neonicotinoid insecticides that recorded unique success in turnover in the 1990s. The use of these has increased and these have captured markets reaching a share of 24% in many countries. Though, these new generation pesticides could overcome the draw backs of conventional agrochemicals that were being used all over the world, some of the concerns are raised

regarding their long persistence period. The present paper reviews the usage of neonicotinoids and the environmental and human concerns such as teratogenic impacts about these in India, especially when diseases like cancer and in-born errors of metabolism are being diagnosed on a large scale. Besides, these new generation pesticides are also now being implicated for loss of many invertebrate species especially useful insects and earthworms that are of enormous ecological and economic value.

2. Neonicotinoids

Neonicotinoids (novel insecticides resembling nicotine) are synthetic insecticides but are similar in action to nicotine, an alkaloid derived from Solanaceae, such as *Nicotiana* sps. These are primarily analogues of natural organic compound nicotine and also act in the similar manner on nervous tissues of insects and neuro-receptors. Due to their role in incapacitating insects and potential use as novel natural compounds in insect control, these are an in huge demand. Neonicotinoids have broad spectrum use and help in containing variety of insect pests and can be used for many crop species. The pharmacore moiety containing nitromine, nitromethylene, or cyanimide determines the insecticidal potency and selectivity of neonicotinoids (Matsuda *et al*., 2005). Presently, neonicotinoids are represented by many commercial compounds such asacetamiprid, clothianidin, imidacloprid, nitenpyram, nithiazine, thiacloprid and thiamethoxam and are available in the market and sold all over the world. Dinotefuran and sulfoxaflor are some new neonicotinoids which are synthesized on commercial scale in many parts of South East Asia especially, China (Shao *et al*., 2013). Another reason for their huge success is the versatile method of application on plants and the flexible nature of applications. Neonicotinoids can be put to use in various ways, for example in many places, these are mixed with water used for irrigation of vegetables. Their application in float system for tobaccos, seedling box application for rice, soil drenching method for citrus plants, application on trunks of apple trees, drench and drip application for coffee and grapevines, soil injections, bud injection for bananas are some other ways in which these are used. Application as seed treatments and soil injectionare the most common methodsof application and account for 60% of usage (Jescke *et al*., 2011). The method has high success rate for various crop species used in food industry. In USA from 2000 to 2012, virtually all neonicotinoids applied to maize, soybeans, and wheat were applied as seed treatments (Douglas and Tooker, 2015). Experimental analysis of effect of neonicotinoids on the leaf hopper (*Empoasca kerri*), a sucking pest on cowpea plants revealed that when seeds are treated in combination with foliar sprays, the plants acquire more resistance to the pests and combining the methods of treatment is more effective than either of the applications alone (Antu *et al*., 2017).

Moreover, they also have higher persistence and long residence time in the environment hence longer crop protection potential. Bonmatin *et al*. (2015) have comprehensively summarised the environmental fate and half-life of these insecticides in abiotic and biotic environments. Similarly, Jones *et al*. (2014) demonstrated that post application these stay in soil residues and may persist for several years, making them cost effective.

3. Mode of Action

Neonicotinoids are systemic in nature i.e. they are taken up by the plants through roots or leaves and then translocated to other plant parts. Thus, are among the most effective insecticides against sucking insect pests such as aphids, whiteflies, thrips, leaf and plant hoppers, some Lepidoptera and Coleopteran pests (Simon-Delso *et al*., 2015). In an inclusive summary, Elbert *et al*. (2008) have mentioned the use of the seven neonicotinoid insecticides (excluding sulfoxaflor) on the number of plants along with their specific pest target spectrum and the quantity of application as either foliar, soil or seed treatments. Some of the key crops mentioned are vegetables, pome and stone fruits, citrus, rice, cotton, corn, potato, sugar beet, oilseed rape, and soybean and many more.

Neonicotinoids target Acetylcholine receptors in the central nervous system of insects. Acetylcholine is a neurotransmitter, and the blockage of its receptors leads to overstimulation and paralytic condition in the insects. Thus, there is no cross-resistance to conventional insecticides such as organophosphates, pyrethroids, etc. (Vastrad, 2003). Unlike other insecticides, they are selectively toxic to the Insecta and reported to be relatively harmless to other mammals due to differences in properties and structure of subunits of nicotinic acetyl choline receptors (Tomizawa and Casida, 2003). This protects crops from an array of sap feeding insects (Nauen *et al*., 2008; Magalhaes *et al*., 2009; Bonmatin *et al*., 2015) and other agriculturally important crop pests (Elbert *et al*., 2008; Jeschke *et al*., 2011). Insects are exposed to multiple interacting environmental parameters and factors. There is also immense amount of diversity in the insects at populations, species and individual level. Social insects, such as bees, have been studied for their response to neonicotinoids but the studies are confined to lab experiments and the responses vary with the size of the bee, foraging behaviour and amount of the insecticide used. In many species, the foraging activity of individual bees was reduced. However, most of the social bees work in coordination in groups and studies have not been carried out at population level in the field. Studies are required that look at the research or cases at population level that link individual effects and reflect upon the synergism as well. However, a study conducted by Woodcock *et al.* (2017) on honey bees at multiple sites at Hungry, United Kingdom and Germany on oilseed rape crops suggested a varied effect on bee populations. There was a colony collapse observed in UK during the winter season and these persisted in environment for longer durations.

Literature survey suggests that the dosage of treatments is crop dependent. Concentrations in plant tissues and sap between 5 and 10 ppb (parts per billion) were sufficient to provide protection against pest insects (Castle *et al*., 2005; Byrne and Toscano, 2006). Toxicity studies carried out in 1,800 lab rats resulted in NOEL (No Observable Effect Level) of 100 ppm; hence neonicotinoids are very less toxic to mammals and can exit the body within 48 hours of ingestion (Fishel, 2005). Despite the immense potential of neonicotinoid insecticides

against plant pests, agricultural yield in the developed countries have been modest in the past 20 years (Goulson, 2013). There is need for more studies comparing the effectiveness of neonicotinoids with other available crop protection measures like Integrated Pest Management (IPM) (Goulson, 2013).

4. Concerns

4.1. Human health

The studies on effect of neonicotinoids are largely carried out on insects. Sheets (2002) has summarized in his book that animals exposed to the neonicotinoid and imidacloprid results in tremors, hypothermia and impaired papillary function similar to that of exposure to nicotine. Reports published recently in leading journals suggest that these pesticides can affect the respiratory and nervous system. In a recent research Seltenrich (2017) reviewed the effect of neonicotinoids on humans and concluded that these compounds have shown an ability to bind to the most common receptor in nerve cells, cholinesterases nACRs in mammals. Change in the density of this neuroreceptor causes several central nervous system disorders such as Alzheimer's, Parkinson's, schizophrenia, and depression. The studies in laboratory animals suggest that these pesticides can affect hormones and their functioning thus affecting various metabolic processes in them. Therefore, the focus on effect of low dosage on endocrine effect of the chemical pesticides has now become crucial field of studies for scientists. Investigations are also on to study the effect on various enzymatic and metabolic pathways to decipher the role of these on humans.

4.2. Environment and biodiversity

Ecosystem services are gaining importance through economic valuation. In the year 2011, the total global ecosystem services were estimated to be $125 trillion/year (Costanza *et al*., 2014). This concept is now being widely used in decision making especially in cases of ecological risk assessment of the plethora of chemicals being developed every day. Due to their unique properties, neonicotinoids have entered and retained themselves in every sphere of the Earth. Their presence in soil, air and water has been documented even at places where their use is irrelevant.

Soil ecosystem services are largely driven by biological interactions. Neonicotinoid insecticides in the form of soil injections and release from seed coatings; pose a risk of harm to earthworms and other soil invertebrates as well as on microbes (Pisa *et al*., 2015) and are equally up taken by plants (Mullins, 1993). Their long persistence poses a relevant threat to soil ecosystem services (Chagnon *et al*., 2014). The effect thus can be detrimental as earthworms help in churning and aeration of soil that is important for the growth of plants.

Contamination of ground water is another negative consequence of application of pesticides on soil; depending on type of soil and concentration of pesticides in soil (Gupta *et al*., 2002; Huseth and Groves, 2014). Runoff from agricultural land, urban and semi-urban regions also contaminate the surface water causing negative impacts on aquatic organisms (Armbrust and Peeler, 2002).

A literature review conducted by Sánchez-Bayo *et al*. (2016) revealed that 22 studies have focussed on the effect of neonicotinoids (especially imidacloprid, thiacloprid and acetamiprid) and that there is no detailed study conducted to assess their impact on the entire ecosystem. The consequences of widespread water residues cause decline in the population of invertebrates and in turn starvation of insectivores. Thus, an impact on food chain can be detrimental to entire structure and functioning of the aquatic ecosystem.

Moreover, seed coating of insecticides which used to be considered as a safer option has shown increased release of insecticides in the air, which in turn affects non-target organisms. Greatti *et al*. (2003) stated that abraded insecticides settle on nearby flowering plants and are responsible for direct exposure to the pollinators. Therefore, the purpose for which they were introduced can fail and the pollinator loss will have to be addressed with some novel strategy.

High toxicity towards insect pests has increased the production and usage of neonicotinoids to many folds; however, their so called selective mode of action has not spared other non-target organisms. There have been constant debates between their effectiveness and consequent harm on non-target organisms. The massive loss of bee population is now linked to the presence of insecticides in pollen and bee bread (Bonmatin *et al*., 2015).

Since their water solubility is relatively higher than other pesticides, they are easily taken up by the plants and get translocated through both xylem and phloem to all plant parts. This systemic property which is very advantageous in controlling sap sucking pests, is equally harmful for pollinators like honey bees which depend on nectar and pollen from the crop plants. The lethal dose (LD50) value for oral/contact toxicity of neonicotinoid insecticides based on laboratory estimates show that imidacloprid, dinotefuran, clothianidin and thiamethoxam are considered highly toxic to honey bees while acetamiprid and thiacloprid are moderately toxic (Hopwood *et al*., 2016). The risk of exposure to non-target organisms, however also depends on crop type, method of application and the time period following the treatment.

Residues and high concentrations of neonicotinoids are also found in guttation droplets (Tapparo *et al*., 2011). Similarly, bees using resins for their hives are exposed to pesticides used on sunflower plants (Pareja *et al*., 2011). Thus, pollen, nectar, guttation droplets, resins and fruits are direct contacts for a pollinator to get exposed to insecticides. This can lead to toxic deposits in honey used for pharmaceutical preparations or as food in the human diet.

A toxicity analysis of nine insecticides carried out in rice fields in Tamil Nadu, India revealed that thiamethoxam showed highest toxicity to *Trichogramma chilonis* (polyphagous wasps) which is a natural enemy to important rice pests and often used in Ecological Pest Management, an approach that uses intrinsic strength of natural processes to reinforce the biological control of pests (Preetha *et al*., 2009). Similarly, thiacloprid was found to be inappropriate and ineffective for application on eggplants as well as for human consumption (Saimandir *et al.*, 2009). Another laboratory analysis deciphered the impact of imidacloprid on development of chick embryos. The dosage ranged from 5 to 50µg and resulted in

growth retardation leading to failure in retraction of yolk sacs, defective limbs and neural tube (Hussein *et al*., 2014).

Recently cases of resistance towards neonicotinoids have also come in the limelight more specifically to the use of imidacloprid. Pests including *Amrasca biguttula biguttula* (cotton leaf hopper) and *Aphis gossypii* (cotton aphid) have shown resistance to imidacloprid (Wang *et al*., 2001; Kshirsagar *et al*., 2012). Gorman *et al*. (2008) illustrated how rice brown planthopper collected from India, China, Indonesia, Malaysia, Thailand and Vietnam showed reduced efficacy to imidacloprid. Continuous use of neonicotinoids has resulted in their resistance among pests belonging to various insect classes.

A study conducted in Netherlands has shown a decreasing trend in insectivorous bird population with the increase in use of imidacloprid insecticides (Hallmann *et al*., 2014). Pisa *et al*. (2015) documented extensively about the effect of neonicotinoids on non-target organisms including both terrestrial and aquatic invertebrates. They also comprehend the fact that although the plethora of literature has focussed on the negative impacts of neonicotinoids on a few organisms, it is enough to support their polluting potential and adverse biological and ecological impacts on organisms in terrestrial, aquatic, marine and benthic habitats.

6. Conclusions

Neonicotinoids are systemic insecticides which have proven to be very effective against many crop pests and have gained huge market success. However, as has happened with all insecticides, neonicotinoids also have harmful effects on non-target organisms. While in the developed countries a tremendous amount of literature is available about their sectorial usage, applications, and effect on non-target organisms like honey bees and on ecosystem services; there is a dearth of informationon their usage in countries like India. Only a few selected studies have focussed on the persistence of particular neonicotinoids in soil. Thiamethoxam and imidacloprid are two such insecticides of which effect on particular pests; and development of resistance has been studied.

There are some knowledge gaps that exist in neonicotinoid research in India. Assessment of state wise utilisation of insecticides and evaluation of persistence of neonicotinoids in all environmental media with special emphasis on aquatic ecosystems is something that needs immediate attention. Field related studies to understand the effect of metabolites and residues on non-target organisms, and finally to understand the effect of all insecticides acting together in the environment is much desired.

Furthermore, experiments need to be carried out in field conditions with substitutes or fortified neonicotinoids so that the latest strategy of Ecological Pest Management and development ofsafe pest control measure is the adopted in large scale farm holdings so that the natural forces and processes of pest regulation come into play. This can be reinforced by conserving the biological diversity of the regions. Usage of safe control measures, dosage and frequency at which these should be applied has to be standardized for various crop species.

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