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Advancement in integrated pest management strategies: a review

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Abstract: With the recent developments in agricultural technology, modern communication tools, changing consumer trends, increased awareness for sustainably produced food systems, and globalization of trade and travel, there seems to be a need to revisit the IPM paradigm as appropriate for modern times. Global pesticide use has, however, largely continued unabated, with negative implications for farmer livelihoods, biodiversity conservation, and the human right to food. In this review, we examine how IPM has developed over time and assess whether this concept remains suited to present-day challenges. Accordingly, various plant protection technologies have been deployed with the trend of focusing on the use modern biotechnological tools that are proven to be most effective and mandatory. The review covers a wide array of pest management methods ranging from the conventional biological control methods up to molecular breeding techniques. IPM is a sustainable, science-based, decision-making process that combines biological, cultural, physical, and chemical tools to identify, manage, and reduce risk from pests and pest management tools and strategies in a way that minimizes overall economic, health, and environmental risks.

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Introduction:

Plants are exposed to a vast range of pathogens and pests. In natural ecosystems, the coevolution during millions of years between genetically diverse plant and pathogen populations has resulted in disease being relatively rare and geographically restricted (Razzaq et al., 2022; Haroon et al., 2022; Zafar et al., 2022; Sahar et al., 2021; Farooq et al., 2021). In contrast, agricultural environments with monoculture cropping systems often provide an environment for the selection of virulent pathogen races, which can result in considerable pre-harvest crop losses, threatening food security (Razzaq et al., 2021; Zafar et al., 2021; Zafar et al., 2022). The concept of integrated pest management (IPM), a sustainable strategy for managing pests, has been in practice for a long time (Schneider et al., 2022; Zafar et al., 2022; Zafar et al., 2021; Zafar et al., 2020). Although multiple sources define IPM in different ways, previous models primarily focused on the ecological, and to some extent on the evolutionary, aspects of pest management (Peterson et al. 2018; Zafar et al., 2022). A recent IPM pyramid presented by Stenberg (2017) identified a lack of a holistic IPM approach that uses both traditional and modern tools. However, his conceptual framework mainly dealt with the ecological aspects of pest management with an emphasis on interdisciplinary research approach. Several reports indicated that IPM implementation depends on numerous factors including the level of education, economic and social conditions, environmental awareness, rational thinking, moral values, regulatory aspects, government policies, availability of IPM tools, extension education, consumer preference, and retail marketing. However, there is no IPM model that encompasses all these factors and provides a comprehensive description.

The interpretation of IPM also varies among those who develop, promote, or practice IPM strategies (Zafar et al., 2022). IPM is a sustainable, science-based, decision-making process that combines biological, cultural, physical, and chemical tools to identify, manage, and reduce risk from pests and pest management tools and strategies in a way that minimizes overall economic, health, and environmental risks. Several other definitions also focus on minimizing or eliminating the reliance on chemical control options, adopting a number of other options with the emphasis on environmental and human health. However, some practitioners interpret IPM as rotating chemicals from different mode of action groups to maintain pest control efficacy and reduce pesticide resistance with an emphasis on reducing pest damage. These definitions and interpretations represent a variety of objectives and strategies for managing pests including vertebrate and invertebrate pests, diseases, and weeds. IPM is not a principle that strictly and uniformly applies to every situation, but a philosophy that can guide the practitioner to use it as appropriate for their situation. For example, host plant resistance is effectively used in some crops with pest and disease resistant or tolerant varieties, but not in other crops. Pheromones are widely used for mating disruption, mass trapping, or monitoring of certain lepidopteran and coleopteran pests, but not for several hemipteran pests (Razzaq et al., 2021; Rasheed et al., 2022). Biological control is commonly used for greenhouse pests, but not to the same extent in the field. Mechanical tools such as bug vacuums are used in high-value crops such as strawberry, but they are not an economical option in non-specialty crops and are not carbon efficient because of fossil fuel consumption. While chemical pesticides should be used as the last resort, in principle, sometimes they are the first line of defense to prevent the area-wide spread of certain endemic or invasive pests and diseases or to protect the seed and transplants from common and persistent pest problems. Seed treatment with chemical pesticides, e.g., has become a popular prophylactic measure in many crops in recent years.

Crop production is an art, a science, and an enterprise, and by adding environmental (Zafar et al., 2022; Zafar et al., 2021; Farooq et al., 2020; Manan et al., 2022) and social factors, IPM—an approach used in crop production—is also influenced by a number of factors. Each grower has their own strategy for producing crops, minimizing losses, and making a profit in a manner that is acceptable to the retailer, safe for the consumers, and less disruptive to the environment. In other words, IPM is an approach to manage pests in an economically viable, socially acceptable, and environmentally safe manner.

Release of sterile insect pests

There are many successful examples of the integration of the SIT in AW-IPM programs against Lepidoptera. These include operational programmes for containment (pink bollworm Pectinophora gossypiella (Saunders) (USA)), suppression [codling moth Cydia pomonella (L.) (Canada) and false codling moth Thaumatotibia leucotreta (Meyrick) (South Africa)], or eradication [cactus moth Cactoblastis cactorum (Berg) (USA, Mexico), painted apple moth Teia anartoides Walker (New Zealand)] (Shahan Aziz 2022, Vreysen et al. 2006). In addition, several pilot field projects have demonstrated the feasibility of using the SIT against the gypsy moth Lymantria dispar (L.), the tobacco budworm Heliothis virescens (F.), the corn earworm Helicoverpa zea (Boddie), the oriental fruit moth Grapholita molesta (Busck), the carob moth Ectomyelois ceratoniae (Zeller), and the Asian corn borer Ostrinia furnacalis (Guene´e). As with other insects, the SIT/IS can be applied against Lepidoptera using different strategic approaches, e.g., suppression, local eradication, and containment strategies (Hendrichs et al., 2009).

The OKSIR program is the longest-running, most successful, area-wide integrated pest program for the suppression of codling moth in the world, and its implementation is accompanied by continuing extensive research (Thistlewood et al., 2019). The SIT is integrated with orchard sanitation, surveillance, tree banding, and mating disruption. After more than 20 years of operation, the codling moth populations in the valley have been drastically reduced, and as a result, the growers, the industry, and the local community have significantly reduced fruit damage and costs associated with codling moth control. The program has achieved less than 0.2% damage in more than 90% of all commercial pome fruit acreage and reduced insecticide use to control codling moth by over 95% in the valley (from 50,000 kg of chemicals in 1991 to <3000 kg in 2015). In addition, the number of chemical sprays targeting codling moth has been reduced from 1.5–2.7 sprays/acre in the early 1990s to <0.3 sprays/acre in 2013 in the southern part of the valley. A recent cost–benefit analysis showed the economic efficiency of the program, i.e., a benefit to the producers from insecticide cost savings, monitoring cost savings and reduction in codling moth injury amounting to CAN $395/acre (versus CAN $377/acre for mating disruption). The economic benefits per acre of orchard were much higher using the OKSIR strategy as compared to using conventional insecticides: the overall cost–benefit ratio of the SIT program was 1.19 for the producer and 2.51 in total. The use of sterile moths against pink bollworm started as a containment program in 1968 to protect the cotton fields in the San Joaquin Valley of California. For more than 20 years, sterile moths were released every season, covering 0.4 million hectares of cotton that prevented the establishment of the pest (Bouyer et al., 2014).

The success of area-wide pink bollworm management is highly dependent on participation by all segments of the agricultural community in the planning, site selection, implementation, and assessment phases of the programme. A highly effective extension-education communication programme is an essential component. The outstanding performance of *Bt*-cotton and pheromone behavioural control for pink bollworm, and the availability of historically-proven effective pink bollworm population suppression technologies (cultural controls, crop residue destruction, water management, planting dates, and sterile moth release), encouraged formulation of a multi-agency and transboundary pink bollworm eradication plan. The eradication programme was initiated in 2001-2002 in the El Paso/Trans Pecos area of Texas, in South Central New Mexico and in Chihuahua, Mexico. The results of area-wide suppression have been exceptionally encouraging and provide promising expectations for the other infested areas of the south-western USA and north-western Mexico. The pink bollworm population has been reduced to levels that can be targeted for sterile pink bollworm releases to pursue the goal of eradication (Bouyer et al., 2007).

Tuta absoluta is one of the most devastating pests of Solanaceae crops in Africa. We previously demonstrated the efficacy of *Metarhizium anisopliae* isolates ICIPE 18, ICIPE 20 and ICIPE 665 against adult *T. absoluta*. However, adequate strain selection and accurate spatial prediction are fundamental to optimize their efficacy and formulations before field deployment. This study therefore assessed the thermotolerance, conidial yield and virulence (between 15 and 35 °C) of these potent isolates. Over 90% of conidia germinated at 20, 25 and 30 °C while no germination occurred at 15 °C. Growth of the three isolates occurred at all temperatures, but was slower at 15, 33 and 35 °C as compared to 20, 25 and 30 °C. Optimum temperatures for mycelial growth and spore production were 30 and 25 °C, respectively. Furthermore, ICIPE 18 produced higher amount of spores than ICIPE 20 and ICIPE 665. The highest mortality occurred at 30 °C for all the three isolates, while the LT_{50} values of ICIPE 18 and ICIPE 20 were significantly lower at 25 and 30 °C compared to those of ICIPE 665. Subsequently, several nonlinear equations were fitted to the mortality data to model the virulence of ICIPE 18 and ICIPE 20 against adult *T. absoluta* using the Entomopathogenic Fungi Application (EPFA) software. Spatial prediction revealed suitable locations for ICIPE 18 and ICIPE 20 deployment against *T. absoluta* in Kenya, Tanzania and Uganda. Our findings suggest that ICIPE 18 and ICIPE 20 could be considered as effective candidate biopesticides for an improved *T. absoluta* management based on temperature and location-specific approach (Hendrichs et al., 2021).

There have also been a number of successful studies combining SIT and biological control for lepidopteran targets. The combined use of inheritedly sterile (sterile F1 adults) potato tuber moth, Phthorimaea operculella (Zeller) and Trichogramma spp. (oophagous parasitoids) in a laboratory trial was more effective in reducing fertile F1 P. operculella progeny than either technique used alone. Furthermore, the level of suppression attained by the combined releases was thought to be additive in effect (Saour, 2004). The authors predicted that because this reflected a single release, when multiple releases of sterile insects and Trichogramma occur, that synergism of treatment effects may be obtained and concluded that further work on the integration of these two control strategies was warranted. Field cage studies of sterile adult codling moth, Cydia pomonella (L.) along with the parasitoid Trichogramma platneri led to less apple damage than when either tactic was used alone (Bloem et al., 1998). In an earlier study, T. platneri were released in apple orchards using SIT against codling moth in British Columbia, Canada (Cossentine and Jensen, 2000). Combined use of parasitoids and SIT led to significantly lower codling moth damage compared with plots where T. platneri was not released. A further benefit of this integrated strategy was that the non-viable codling moth eggs produced by released steriles were suitable hosts for T. platneri and so contributed to persistence of the parasitoid population

Kumano et al. (2010), evaluated the effect of irradiation dose intensity on fertility, mating propensity, and mating competitiveness in sweetpotato weevil, Cylas formicarius elegantulus (Summers) (Coleoptera: Curculionidae), for 16 d after irradiation. Although the mating propensity of males irradiated with 200 Gy, the dose currently used to induce complete sterility of C. f. elegantulus in the SIT program in Okinawa Prefecture, was equal to that of nonirradiated weevils for the first 6 d, the mating propensity of males irradiated with doses between of 75 and 150 Gy was maintained for the first 12 d. The potential fertilization ability of weevils was highly depressed compared with the control weevils, even in those treated with 75 Gy. Mating performance was severely compromised in weevils that were irradiated with a dose of 100 Gy or more.

Role of biopesticides in IPM

Crop protection has relied basically on synthetic chemical pesticides in past, but their availability is now declining as a result of new laws and legislations and the evolution in the process of insect resistance. Therefore, it is necessary to replace the pest management strategy. Biopesticide is the best alternative to synthetic chemical pesticides based on living micro-organisms or natural products. Biopesticides include a broad array of microbial pesticides, biochemicals derived from microorganisms and other natural sources, and processes involving the genetic modification of plants to express genes encoding insecticidal toxins (**Chandler** et al., 2011). Biopesticides have demonstrated the potential of pest management and used worldwide. In the European Union, there are new opportunities for development of biological pesticides in combination with integrated pest management, ecological science and post genomic technologies. In this regard, the use of biopesticides and bio-agents has assumed significance as an important component of IPM due to their economic viability and eco-friendly nature instead of chemical synthetic pesticides (Zafar et al., 2020). Biopesticide application as a component of IPM programs can play important role in overcoming disadvantage of chemical insecticides that have some important characteristics such as biodegradable and self- perpetuating, less harmful on beneficial pests, mostly host specific and less shelf life. Baculovirus biopesticides are an alternative to chemical pesticides in integrated pest management; however, they have a wide range of difficulties for commercial uses such as slow killing, short life time, high production costs and current laws and regulations of biological control agents. To overcome many problems of wild-type baculoviruses, many strategies have been developed to improve their killing action by recombinant DNA technology, including the insertion of genes encoding insect hormones or enzymes, or insect-specific toxins (**Samada et al., 2020)**.

Semiochemicals:

A semiochemical by definition is a chemical signal produced by one organism, usually insects which caused a behavioural change in an individual of the same or different species. For crop protection, the most widely used semiochemicals are the insect pheromones which serve as a signal to communicate with others in their species for a number of reasons and synthesized for pest control by mating disruption, Lure-and-Kill systems and mass trapping. Insects produce chemicals called pheromones to stimulate a certain behavioral reaction from other individuals. These pheromones have numerous effects and are named according to their evoked response, for example, sex pheromones, aggregation pheromones, alarm pheromones, etc. A few pheromones function as sex attractants, permitting individuals to detect and locate mates, whereas others induce trail following, oviposition, and aggregation in other congeners. Pheromones have become essential tools for monitoring and controlling agricultural pest populations, and as such, a huge collection of over 1,600 pheromones and sex attractants has been reported (**Fenibo et al., 2022)**. Nowadays, pheromones and other semiochemicals are applied to monitor and control pests in millions of hectares. There are several advantages of utilizing pheromones for monitoring pests, including lower costs, specificity, ease of use, and high sensitivity. Insect pest monitoring by using pheromone lures can profit management conclusions such as insecticide application timing (**Sharma & Gaur, 2021)**. Pheromones produced by insects are highly species specific. Virgin female insects are developing sex pheromones when expecting for a mate and males along the concentration slope for the female producer. Aggregation pheromones are released by insects such as wood-invading beetles to show to others the presence of a good food source.

Plant-Based Extracts and Essential Oils

More than 2400 different plants have been documented for their pesticidal activities. Botanical insecticides can be crude plant extracts or dried and grounded plant materials, or essential oils isolated from the plants which are used for pest management in plants (Zhang et al., 2022). This protective action against pests is due to secondary metabolites produced by plants. These secondary metabolites include alkaloids, steroids, phenols, flavonoids, non-protein amino acids, quinones, tanins, terpenoids, glycosides, glucosinolates etc. Different parts of the plants such as leaves, stems, barks, flowers, fruits, seeds, cloves, rhizomes are used to prepare botanical pesticides. The mode of action of most of the plants, their extracts and essential oils are by repelling, oviposition deterrence, feeding deterrence as well as interfering with physiological activities of pests and can be toxic and lethal as well to them (**Mondédji** et al., 2021).

Essential oils extracted from many medicinal plants have great potential to be insecticidal. Essential oils and their components extracted from plant source cause toxic effects in insects via contact, ingestion, or fumigation. Various studies have shown the insecticidal activities of the essential oils extracted from the plants belonging to Apiaceae, Asteraceae, Lamiaceae, Laureaceae, Myrtaceae and Rutaceae families. Essential oils from different plants can destroy and kill insect's species at their egg and larvae stage or at an adult stage as well as they can be antifeedant and repellent to them. Essential oils can change the feeding behavior of insects thus causing mortality and also it alters insect's behavior during oviposition and mating (**Peace et al.**, 2022).

Genome editing through CRISPR/Cas9 technology

Genome editing allow plant breeders to manipulate crop genomes at the nucleotide level with high precision. In particular, the advent of prokaryotic-derived Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)/CRISPR associated protein (Cas) systems and its use in plant genome editing has been a crucial turning point towards a new era of crop breeding. Cas9 and Cas12a, are two popular RNA guided engineered nucleases (RGENs) which mediate genome editing, directed by the sequence-specific pairing of a guide RNA (gRNA) to the target DNA (Jinek et al., 2012). The pace of discovery, both of essential insect traits and of reagents to perturb these traits, has increased dramatically through molecular biology and genomics, and opportunities for interventions are continuing to expand as technologies (e.g., sustained expression of multiple stacked transgenes in plants) are optimized and as new technologies (e.g., editing of plant genomes by CRISPR) are introduced. It is now routine to address crop resistance to insect pests in molecular terms. Specifically, the insect trait is defined in terms of one or multiple gene targets, and plant resistance is defined as a gene or suite of genes with a product or products that inactivate or otherwise disable the product or products of the target insect gene or genes. A second consequence of the genomic revolution has been the development of molecular methods to investigate the composition and function of microbial communities, including unculturable forms, leading to the recognition that the sustained vigor and fitness of both plants and insects are dependent on interactions with resident microorganisms, collectively known as the microbiome (Douglas, 2015). Briefly, the Cas9 protein is a DNA-specific nuclease that makes a double-stranded break in DNA at a site guided by the binding of a synthetic guide RNA. Multiple CRISPR protocols are available, including those with the capacity to generate site-specific indels (often yielding frameshift mutations), to replace or insert specific sequences, and (by using a deactivated Cas9) to suppress gene expression. In relation to insect pests, the first applications of CRISPR in crops confer resistance to insect-vectored viruses, especially the geminiviruses, which have DNA genomes (Fondong, 2017). CRISPR is also the technology of choice to produce new crop varieties in response to insect pest genotypes that break plant resistance mechanisms. This is because resistant and susceptible alleles of plant resistance loci generally differ by just one or a few nucleotides. Specifically, CRISPR can be used to edit the susceptible allele to the resistance allele, thereby eliminating the need for extensive crosses and back crosses by conventional methods. The relative ease with which CRISPR can be applied to edit all copies of a gene makes CRISPR the technology of choice for polyploid crops. It is becoming increasingly evident that members of the microbiome can influence insect-plant interactions and can contribute to strategies for enhanced crop resistance to insect pests.

RNA interference (RNAi)

Alternatively, other strategies like RNA interference (RNAi) aimed at silencing of selected genes involved in insect feeding. Either as an alternative or a complement to Bt toxins, RNA interference (RNAi) has great promise for insect pest control (Ren et al., 2019). RNA Interference RNA interference (RNAi) offers the opportunity to design insecticides that have even greater flexibility than protein toxins with regard to both mode of action and specificity. Double-stranded RNA (dsRNA) specific to an essential gene of an insect pest is internalized into cells, where it is processed by Dicer enzymes to small interfering RNA (siRNA) molecules that guide the Argonaute protein of the RNA-induced silencing complex (RISC) to degrade complementary mRNAs and, in some instances, to interfere with translation of the target mRNA (Scott et al., 2013). RNAi can therefore be exploited to suppress gene expression through highly specific depletion of target transcripts. The functional RNAi machinery has two major components, (1) the core component inside the cells, which is comprised of Dicer enzymes, RNA-binding factors, and Argonaute protein, and (2) systemic component that amplifies the dsRNA signal and allows it to spread to other tissues within the animal (Siomi & Siomi, 2009). dsRNA is most commonly delivered by genetic modification of the plant (Price and Gatehouse, 2008), but topical application of dsRNA by sprays or drenches has also been reported to control lepidopteran and hemipteran pests (Li et al., 2015). Orally delivered RNAi is particularly effective against many coleopteran insects, routinely mediating >80% reduction in expression of target genes and conferring significant crop protection, e.g., in corn against the western corn rootworm (Baum et al., 2006), and in potato against the Colorado potato beetle Leptinotarsa decemlineata (Zhang et al., 2015). Besides oral delivery, dsRNA constructs can be administered in insects topically, through soaking and with microinjections into hemolymph (Yu et al., 2013). Microinjections can bypass the midgut, thereby inducing a systemic response. There are several microinjection techniques available, but the majority of them are time consuming and require equipment ranging from in-house produced devices to sophisticated microprocessor-controlled injectors (Dzitoyeva et al., 2001). Thus, microinjection procedures are not practical as means of pest control, but they are useful to investigate optimal dsRNA candidates and to demonstrate proof of concept. Topical administration is defined as direct dsRNA administration via the exoskeleton. It can be achieved by uniform spraying of dsRNA in the whole insect body (Wang et al., 2011) or through ventral micro-application. Relative to injections, this would be labor-saving and can allow for high-throughput gene screening. However, only a few publications have shown promising results using this approach (Killiny et al., 2014). One of the few examples includes studies conducted in adult *Diaphorina citri,* in which dsRNA solutions targeting five *cytochrome P450* genes was applied topically into the thoracic region. Mortality was significantly higher in adults treated with dsRNA than untreated controls. A similar method has also been described for *Ostrinia nubilalis* larvae, in which topically applied fluorescent dsRNA confirmed that dsRNA did penetrate the body wall and circulate in the body cavity (Wang et al., 2011). RNAi against lepidopteran and hemipteran pests is used widely in research but can be less reliable than in the Coleoptera (Scott et al., 2013). Strategies to enhance the efficacy of in planta RNAi against insect pests include expression of long hairpin RNA (hpRNA) in the chloroplast to minimize processing by the plant RNAi machinery (Bally et al., 2016) and stacking the hpRNA against the gene of interest with hpRNA against nonspecific nucleases expressed in the gut of the target insect (Song et al., 2017).

Insect growth regulator

A new approach to insect pest control is the use of substances that adversely affect insect growth and development. These substances are classified as "insect hormone mimics'' or "insect growth regulators'' (IGRs) owing to their effects on certain physiological regulatory processes essential to the normal development of insects or their progeny. They are quite selective in their mode of action and potentially act only on target species. The action of IGRs, however, should not be confused with other synthetic insecticides, such as organophosphates and carbamates, since these chemicals interfere with other physiological processes but do not regulate the development of normal insects. Insect growth regulators (IGRs) primarily target the immature stages of insect pests. Because IGRs elicit limited effects on nontargets, especially mammals, they are considered reduced-risk insecticides (Graf 1993). Compared with the conventional insecticides, IGRs do not exhibit quick knock-down in insects or cause mortality, but the long-term exposure to these compounds largely stops the population growth, as a result of the effects mentioned in both the parents and progeny (Mondal et al., 2000).

Gene pyramiding

Resistance developed through a single gene can be overcome by pests after a few years (Esse et al., 2020), so it is necessary to develop unique and efficient strategies to enhance crop resistance against stresses to improve yield and quality on a sustainable basis (Zafar et al., 2020a). Gene pyramiding may be one of the superior techniques to accomplish durable resistance against various stresses in crop production (Razzaq et al., 2021). Sustainable improvement of crops by integrating multiple resistance genes is essential to ensure agricultural production across a range of climatic conditions (Ren et al., 2019; Zafar et al., 2020a). In most cases, more than one gene controls a specific trait, so it is necessary to manipulate multiple genes for evolving resistance against biological and non-biological agents, such as chemicals, diseases, pests, and weeds (Razzaq et al., 2021). For long-term and durable resistance development, the pyramiding of diverse resistance genes against a single pathogen or pest in a single genotype can help for long-term resistance development (Nelson et al., 2018). Marker-assisted breeding could make it possible to effectively combine resistant genes into a single genetic background in the shortest possible time (Dixit et al., 2020).

Multiple Gene Pyramiding and Silencing (MGPS)

Insect pests can acquire resistance against single Bt toxins; therefore, pyramided Bt crops and efficacy of refuge for regulating the evolution of resistance against Bt-crops were introduced to overcome this resistance (Carrière et al. 2019). Recently, studies have suggested that insect pests (i.e., *P. gossypiella, H. zea, S. frugiperda*) have developed tolerance against dual gene pyramided cotton, and refuge also lost its efficacy in case of non-recessive resistance, i.e., cotton bollworm (Jin et al. 2015). Presently, new strategies are needed to be developed to delay the evolution of resistance in agricultural pests. Plant-mediated RNAi of essential pest genes involved in defense, detoxification, digestion and development is being utilized for enhancing tolerance against insects and pests. In recent years, new types of insect resistant transgenic crops have been developed using RNAi technology or RNAi pyramided with Bt genes (Ni et al. 2017; Zafar et al., 2020a). Ni et al. (2017) developed a pyramid of cotton containing Bt and RNAi, and found excellent results against cotton bollworm, but also substantially delayed resistance as compare with using Bt alone. Pyramiding of multiple RNAi expression cassettes against various essential genes involved in defense, detoxification, digestion and development of agricultural pests will successfully obtain favorable agronomic characters for crop protection and production. The MGPS involves the construction of transformable synthetic chromosomes, that have multiple distinct Bt toxins and RNAi to knockdown various essential target genes of pest (Ren et al. 2019). The evolution of resistance in agricultural pests will be delayed or blocked due to synergistic action of high dose of Bt toxins and RNAi(s) as well as compliance of ample refuge. The transgenic crops based on MGPS coupled with refuge can be an effective and smart way to control pests.

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