Original Article

Recent Trends In The Analysis Of Organophosphate Posing

Nikhil Sidhu[1]

[1] M.Sc., Department of Forensic Science, Chandigarh University, Punjab, India.
Email: [1] nikhilsidhu95@yahoo.com
DOI: 10.47750/pnr.2023.14.02.184

Abstract

Organophosphates (OPs) are a class of chemical compounds that have been widely used in agriculture and industry as pesticides, herbicides, and fungicides. These compounds are known to be toxic to humans and animals, and exposure to high levels of OPs can cause a range of health problems, including neurological damage and cancer. As a result, there has been a growing interest in the analysis of OPs in food, water, and air.

Recent trends in the analysis of OPs have focused on developing new and more sensitive analytical methods that can detect low levels of these compounds in complex matrices. One of the most widely used methods for the analysis of OPs is gas chromatography-mass spectrometry (GC-MS). This technique has been used to detect and quantify a wide range of OPs in various matrices, including food, water, and air.

Another trend in the analysis of OPs is the use of advanced analytical techniques, such as liquid chromatography-mass spectrometry (LC-MS) and inductively coupled plasma-mass spectrometry (ICP-MS). These techniques offer higher sensitivity and specificity than traditional methods and are able to detect even trace levels of OPs in complex matrices.

In recent years, there has also been an increase in the use of sample preparation techniques, such as solid-phase extraction (SPE) and solid-phase microextraction (SPME), to isolate and concentrate OPs from complex matrices. These techniques help to improve the sensitivity and specificity of the analysis and are often used in conjunction with GC-MS, LC-MS, or ICP-MS.

Overall, the recent trends in the analysis of OPs have been focused on developing new and more sensitive analytical methods that can detect low levels of these compounds in complex matrices. These methods are playing a crucial role in monitoring and controlling the exposure of humans and animals to OPs and in protecting public health. In India, organophosphates (OPs) have been widely used in agriculture as pesticides and herbicides. The use of these compounds has led to concerns about the potential health effects of exposure, particularly in rural areas where agriculture is a major source of income.

Key words: Organophosphates, pesticides, herbicides, and fungicides.

INTRODUCTION

Organophosphorus pesticides (OPPs) are commonly used to protect crops from pests. Because the use of OPPs in various agricultural activities has increased substantially, careful monitoring of their concentration levels has become a key concern for protecting ecological systems and food security. The World Health Organization (WHO) has, however, classified them as extremely hazardous chemical compounds. Given their widespread usage and toxicity, the development of simple, quick, and highly sensitive procedures is required. Despite the fact that there are many traditional methods for detecting OPPs, the development of portable sensors is necessary to make routine analysis much more practical. Colorimetric sensors, fluorescence sensors, molecular imprinted polymer-based sensors, and surface plasmon resonance-based sensors are examples of sophisticated approaches.

The Organophosphate pesticides (OP) poisoning and its forensic significance is very important to find out the actual cause of the death among the population. Since at least 1958, when 100 people died after consuming flour contaminated with the Organophosphorus (OP) insecticide parathion, after that pesticide poisoning has been a serious issue in India (1). In India, there are thought to be 230,000 suicides every year of which 70,000 (or 30%) involve pesticides (2).

Organophosphorus (OP) pesticide poisoning is a serious issue for world health, and it is the main cause of suicide in India. The National Crime Records Bureau in India estimates that every five minutes, one person commits suicide and seven others make an attempt, totaling roughly 100,000 fatalities annually. The majority of victims were between the ages of 14 and 34, and the most often employed agent in suicide attempts is an organophosphorus chemical (OPC) consumer for the cause of the death (3).

One class of pesticides known as organophosphate insecticides (including diazinon) function by harming the body's acetylcholinesterase enzyme (1). The body's ability to regulate nerve messages depends on this enzyme. Pests are killed by the damage to this enzyme, but exposed people may experience unfavourable side effects. What items are treated with organophosphate pesticides (4). Acephate, bensulide, chlorpyrifos, diazinon, dimethoate, ethoprophos, malathion, naled, phorate, and phosmet are some of the pesticides with this classification that are approved for use on "agricultural crops (2)."

To protect the plants, those who work in agriculture consume orgnophosphate insecticides. The concentration of the necessary pesticides is recommended by the relevant authorities for the purposes because different grains or other seedlings are susceptible to insect attack (2).

ANALYSIS OF ORGANOPHOSPHATE PESTICIDE BY VARIOUS CHROMATOGRAPHIC TECH:

Pesticides containing organophosphorus, pyrethroids, carbamates, and phenylureas continue to be important chemical classes that require chemical analysis using gas chromatography-mass spectrometry (GC-MS), gas chromatography-tandem mass spectrometry (GC-MS/MS), or liquid chromatography-tandem mass spectrometry (LC-MS/MS) (2). These are the most popular methods used by most labs and research operations to confirm the precise quantity of Organophosphates in soils, food, and other biological materials. Organophosphates may be detected using LCMS, GC, and TLC, which can be used to identify Organophosphates in soil samples (5).

2.1 Organophosphate pesticide detection by HPLC:

High-performance liquid chromatography, also known as high-pressure liquid chromatography, is an analytical chemistry technique used to separate, identify, and quantify each component of a mixture. Pumps are used to move a pressured liquid solvent containing the sample combination through a column containing a solid adsorbent material. Each component in the sample interacts somewhat differently with the adsorbent material, resulting in varying flow rates for the various components and component separation as they flow out of the column (6).

2.2 Organophosphate pesticide detection by LCMS:

To determine organophosphorus pesticide residues, a simple and specific analytical method based on solid phase extraction (SPE) and liquid chromatography-electrospray ionization-tandem mass spectrometry (LC-ESI-MS/MS) in multipule reaction monitoring (MRM) mode with dynamic time segment acquisition windows was developed (7).

2.3 Organophosphate pesticide detection by the GC:

Parathion, malathion, chlorpyrifos, diazinon, and other organophosphorus pesticides specified by the client are included in the procedure. Methodology - A water sample was extracted with a liquid/liquid solvent, and organophosphorus pesticides were determined using gas chromatography and mass spectrometric detection (GC-MS) (7).

2.4 Organophosphate pesticide detection by the TLC:

The researchers investigated the multi-residue analysis of organophosphorus pesticides (OPs) in rice (8). The extracts were cleaned using semi-automatic gel permeation chromatography. TLC-cholinesterase inhibition and GC-FPD procedures were used to examine the organophosphorus insecticides. TLC was used to assess pesticides' minimal detectable amounts (MDQ), Rf, and RRf values. The average recoveries of organophosphorus pesticides from fortified rice samples were 75-88% by TLC and 82-93% by GC at three different doses (9). When compared to GC, the TLC approach was less sensitive, but it might be utilised by monitoring laboratories to do preliminary screening of materials to support instrumental tests (3).

After analysing data on mortality from pesticide exposure for 19 years, researchers in Tunisia came to a conclusion in one study. They reported the results of the autopsy of those who had died as a result of pesticides(10). Both houses and agriculture routinely use pesticides. These goods are potentially fatal due of their accessibility and availability (5). Numerous studies have underlined the seriousness of acute pesticide exposure, but very few have discussed the autopsy results. No further indications of pesticide toxicity were found during the autopsy, except from the pesticide being found in the stomach contents (11). We must emphasise that because many cases are mistakenly classified as natural deaths, the frequency of pesticide poisoning is significantly underreported. As a result, general practitioners, especially paediatrics, need to pay more attention and demand an autopsy anytime they suspect intoxication (3). This study demonstrates that a significant number of pesticide poisoning fatalities can be avoided. On the one hand, prevention involves limiting pesticide availability, and on the other, it involves enacting stricter regulations governing the production, promotion, and use of these chemicals (1).

This particular review is a summary of case studies involving deaths from poisoning or exposure to the aforementioned organophosphate pesticides, as reported by the world (3,12,13).

Health Organization classification for pesticides toxicity according the WHO guidelines.

Table 2: Quantitative results of phorate in analyzed biological samples

WHO Class		**LD50 for the Rat (mg/kg Body Weight)**	
		Oral	**Dermal**
	Extremely hazardous	<5	<5
	Highly hazardous	5-50	5-50
	Moderately hazardous	50-2000	50-2000
	Slightly hazardous	Over 2000	Over 2000
	Unlikely to present acute hazard	5000 or Higher	

Medical management is challenging:

The case mortality rate is often greater than 15%. We still don't know the ideal way to administer the three main treatments—atropine, oximes, and diazepam—more than 50 years after they were first used (4). In the present study we focused on the case studies as well as the real data from the different sources. The case studies mostly noted as well as the confirmed cases. This is really the great contribution to stop or check these kinds of deaths in India due to the use of OP in the agriculture practices (3).

Insecticides called organophosphorus (OP) chemicals are commonly used in agriculture to manage pests, weeds, and plant diseases. These OP compounds are beneficial for crop protection and pest control because of their unique effect and control the pests but the sometime the people consumed them for personal misused (1,2,11,14–16).

Acute poisoning cases (%) due to organophosphorus pesticides in India:

Symptoms	**Cases**
Vomiting	96
Nausea	82
Miosis	64
Excessive salivation	61
Blurred vision	54
Giddiness	93
Headache	84
Disturbances in consciousness	44
Sinus tachycardia	25
Sinus bradycardia	6
Depression of ST segment	6

Organophosphates are less bioaccumulative and persistent in nature, but pesticide residues have also been discovered in human blood, urine, breast milk, semen, adipose tissue, amniotic fluid, and umbilical cord blood all around the world. Numerous findings in India point to the existence of OP residues in both human and animal components. Pesticides can be ingested by food, drink, air, dust, soil, etc. Organophosphorus insecticides are persistent in the body for a considerable amount of time since they are found in blood (1,3,11,14–17).

Monocrotophos, chlorpyrifos, malathion, and phosphamidon were found in human blood samples taken at random from four separate Punjabi villages, according to a CSE study from March 2005. These pesticides made up the majority of the pesticides found (2).

In addition, methyl parathion, malathion, and chlorpyrifos residues were found in breast milk from Bhopal, Madhya Pradesh. Bovine milk from the Allahabad region has also been found to be tainted with methyl parathion residues, which is a hazardous group according to WHO class 1a(11).

There have also been reports of organophosphate residue accumulation in fish due to their ease of movement in aquatic ecosystems. Rita rita fish from the river Gomti in northern India had blood that had bioaccumulated chlorpyrifos while being a bottom feeder, according to research on fish.

In the Kolavai lake of Chengalpet, Tamil Nadu, Cirrhinus mrigala was discovered to be chlorpyriphos-contaminated. The contamination of two fish species, Channa striata and Catla catla, with malathion and chlorpyrifos by Amaraneni and Pillala was discovered through comparable investigation on tissue samples of the two fish species (1,3,14).

Indian scenario:

Particularly in the developing world, pesticides are now widely acknowledged as a substantial cause of sickness and mortality. Particularly noteworthy consideration has been given to India's intentional self-harm caused by the use of pesticides. In India, intentional poisoning—of which pesticides account for the lion's share—is the cause of almost 50% of suicides (3). Young children are frequently poisoned through unintended cutaneous or inhalational exposure, accidental ingestion, or self-harm attempts; teenagers are more seriously poisoned. The goal of this essay is to draw attention to the pesticide poisoning issue affecting India's paediatric population and to provide governmental solutions to deal with this widespread issue (18). A more comprehensive approach to addressing these life-threatening poisonings in children can include restricting access to pesticides, teaching farmers and the public on the correct storage and use of pesticides, and expanding poison control facilities in India (1).

Poisoning from organophosphates (OP) is widespread in India. There are not many case reports of parenteral OP poisoning. We describe a case of methyl parathion poisoning caused by self-injection that presented four days later with seizure, altered sensorium, and respiratory distress. This case presented diagnostic and therapeutic challenges (2). He was treated based on suspicion even though there was no history of OP poisoning; he responded well clinically to the atropine and pralidoxime treatment trial and made a full recovery (1).

Following parenteral injection of OP poison, atypical presentations may be observed, and even a remote suspicion of this necessitates appropriate research and care for a successful outcome. A persistently low plasma cholinesterase level is a helpful diagnostic sign. In India during the past few years, both pesticide production and consumption have increased in lockstep (7). Organophosphorus pesticides are currently the most significant and frequently utilised class of pesticides being used in India. *(Parma MedicalSchool, Parma, Italy, 2008)*. Despite being frequently employed as an alternative to organochlorides, organophosphate compounds pose a serious threat to both living things and our environment due to their vast and uncontrolled use (15). Monorotophos, phorate, methyl parathion, malathion, chlorpyrifos, diazinon, phorate, quinalphos, ethion, and other organophosphates that have been widely used in India are primarily extremely to moderately harmful, according to WHO. It's interesting to note that many of the organophosphates registered for use in India under Section 9 (3) of the Insecticides Act, 1968 are prohibited or subject to rigorous regulations.

In some nations, such as those in Europe and the USA. Although they are not as permanent in the environment, several researchers have found remnants from them in soil, water, vegetables, and other food products (5). Additionally, remnants of several organophosphates have been discovered in human blood, urine, breast milk, etc., indicating that they do stay in the body for a considerable amount of time (15).

There are guidelines for applying particular organophosphates to particular plants; however some instances in this study demonstrated their utter disregard (1). Due to their accessibility, these substances are frequently used in India by individuals who attempt suicide; when early diagnosis and targeted therapy were provided, several of these individuals had successful recoveries (3). There are rules for their use, sale, and specificity to crops, but they must be properly implemented and made people aware of them (14). To reduce the causalities and mortality from these potentially fatal chemicals, early identification and appropriate treatment of particularly acute poisoning are imperative. Although they naturally degrade, improved degradation procedures are still required to reduce the likelihood of their accumulation and the associated health risks (17).

Status over the Globe:

The history of ingestion or muco-cutaneous exposure, clinical signs, and plasma cholinesterase levels are used to make the diagnosis of OP poisoning. The diagnosis of OP poisoning is confirmed by the reduced plasma cholinesterase levels, which persist for 4 to 7 weeks (16). More precise estimations are made of red blood cell cholinesterase. Gastric lavage is performed and a sample is obtained in cases of OP substance consumption for analytical and medicolegal purposes (2,5,14). Atropine counteracts muscarinic receptor-mediated effects and functions as a physiological antidote. A 2- to 5-mg loading dose of

atropine is given Only a few examples of parenteral OP poisoning were found in the literature. IV monocrotophos poisoning resulting in intermediate state requiring ventilator support was documented by Badhe and Sudhakar (15,17).

Two cases of dichlorvos poisoning treated with atropine and pralidoxime were described by Raina et al. in their study. Nishioka reported two cases, one of which had a local reaction without any systemic toxicity and one of which had a death due to respiratory failure. Guven et alaccount .'s of an IV methamidophos poisoning that within 30 minutes exhibited symptoms of an acute cholinergic crisis (16). According to Zoppellari et al, an intramuscular injection of isofenphos resulted in cholinergic crisis 5 hours later, with symptoms persisting for 3 weeks. He had injected a substance that is marketed as metacid-methyl parathion. Methyl parathion is an aryl phosphate, and they are phosphoric acid esters (2,14). In south Asian nations, metacid is the OP chemical that is both most utilised and most hazardous. The lethal dose of this substance is 175 mg orally or 80 mg intramuscularly, followed by doses every 5 to 10 minutes, until atropinization is seen (1).

The dose is then modified based on the clinical response and is then injected at a rate of 0.02 to 0.08 mg/kg/min. Both the application and dose of oximes are in question(1). The usual dosage of pralidoxime is 1 gm every 6 to 8 hours, however recent studies have shown that high-dose infusions of 18 to 24 gm/day provide superior effects. Diazepam is used to treat seizures brought on by OP. Legal issues arise when handling these kinds of cases (1). When dealing with suspected poisoning scenarios, stomach wash, excreta, and other materials like empty pill or drink bottles should be collected and stored. The police were informed of our filing a medical legal registration entry for this incident (1).

The speed at which OP toxin enters systemic circulation determines how lethal it is. If the OP chemical is delivered parenterally, the plane of delivery affects absorption and systemic symptoms. The onset of an acute cholinergic crisis within 30 minutes of IV treatment has only been described by a few writers (1,3,4,11). When self-injecting, symptoms take a little while to manifest, and if less is given, there may simply be a local abscess. The situation we discussed manifested four days after the injection. He experienced an abscess in his arm, which might have been caused by using contaminated material (1).

Prognosis of OP:

Pesticides are enormously used to control the pests in agriculture, industry and human premises. Agricultural production has been significantly increased with the help of pesticides but their uncontrolled and excessive use is polluting the environment, food, water and agricultural products. Presence of pesticides residues in food products and human milk is the alarming sign to set up stringent monitoring system and eradication remedies. Many advancements have been happened in recent years for the detection and quantification different pesticides in the various matrices. The present review article specifically focuses on the detection techniques for the organophosphorus pesticides. Organophosphorus pesticides are now a days hugely applied in agriculture after ban on many organochlorine pesticides and hence creating health complications. Visual or colorimetric detection of the pesticides using different nanostructures is considerably exploited for the onsite monitoring of organophosphorus pesticides. These advancements in pesticides detection are presented in detail along with brief overview of pesticides removal methodologies.

DISCUSSION

India is a heavily rural nation with an agrarian economy. Pesticides with OP are frequently used for suicide purposes. Although intentional consumption with the intention of harming oneself is a frequent mode of poisoning, occupational exposure while spraying in fields is a significant modality (17). The pesticide used, the dosage, the method of administration, and the interval between the time of poisoning and the beginning of treatment all have an impact on the clinical manifestations and result of OP poisoning. The following list includes the clinical signs of OP poising (11). There are two types of cholinergic crises: I acute cholinergic crisis, which appears within 24 to 72 hours due to acetylcholine accumulation at muscarinic and nicotinic sites and accumulation in the CNS, resulting in headache, giddiness, seizures, and altered sensorium; and (ii) intermediate syndrome, which appears after 24 to 96 hours due to prolonged activity of acetyl choline at nicotinic receptors resulting in weakness of ocular, neck,limb, and respiratory muscles.

The possibility of infection was taken into consideration, but it was challenging to explain his flaccid quadriperesis and pulmonary edoema only on the basis of sepsis, and he responded well to atropine treatment. Nishioka also reports the establishment of local site abscesses (15). In cases where insecticides have been injected subcutaneously or intramuscularly, local inflammatory signs are to be anticipated. These wounds could serve as entry points for a variety of species. Local debridement is necessary for abscess drainage and, if done promptly, may help with pesticide clearance (17). The history of the compound's injection was known in every case of parenteral OP poisoning that has been previously published. Due to the lack of a history of compound injection at the start of treatment, the case we described presented a substantial diagnostic challenge (1). Because of his altered sensory state, the patient was unable to provide a history. It is uncommon for OP poisoning to cause seizures, and there haven't been any reports of seizures developing after parenteral injection (2).

In India during the past few years, both pesticide production and consumption have increased in lockstep. Organophosphorus pesticides are currently the most significant and frequently utilised class of pesticides being used in India. (*Parma MedicalSchool, Parma, Italy*, 2008). Despite being frequently employed as an alternative to organochlorides, organophosphate compounds pose a serious threat to both living things and our environment due to their vast and uncontrolled use (15). Monorotophos, phorate, methyl parathion, malathion, chlorpyrifos, diazinon, phorate, quinalphos, ethion, and other organophosphates that have been widely used in India are primarily extremely to moderately harmful, according to WHO. It's interesting to note that many of the organophosphates registered for use in India under Section 9 (3) of the Insecticides Act, 1968 are prohibited or subject to rigorous regulations.

In some nations, such as those in Europe and the USA. Although they are not as permanent in the environment, several researchers have found remnants from them in soil, water, vegetables, and other food products (5). Additionally, remnants of several organophosphates have been discovered in human blood, urine, breast milk, etc., indicating that they do stay in the body for a considerable amount of time (15).

There are guidelines for applying particular organophosphates to particular plants; however some instances in this study demonstrated their utter disregard (1). Due to their accessibility, these substances are frequently used in India by individuals who attempt suicide; when early diagnosis and targeted therapy were provided, several of these individuals had successful recoveries (3). There are rules for their use, sale, and specificity to crops, but they must be properly implemented and made people aware of them (14). To reduce the causalities and mortality from these potentially fatal chemicals, early identification and appropriate treatment of particularly acute poisoning are imperative. Although they naturally degrade, improved degradation procedures are still required to reduce the likelihood of their accumulation and the associated health risks (17).

CONCLUSION

The diagnosis of parenteral OP compound poisoning is difficult. The onset of symptoms may be delayed, and they may show differently than usual. Even though the symptoms are initially minor, closer monitoring is needed. Because there are no protective precautions in place, even a tiny injection might be lethal. In the event that an OP poisoning is suspected, the treating physicians must be on the lookout and offer the proper care.

AUTHOR CONTRIBUTIONS

All the authors contribute equally for the preparation and the editing of current review and this may be helpful for further to check the organophosphate poisoning in the population. So that the toxicity by the OP can be reduced by following such guidelines should be prepared or made.

Funding

No funding source for the current work.

Institutional Review Board Statement

The study topic has been approved by the Institutional Ethical committee for the partial fulfilment of the Master Course in the field of forensic sciences. This study has been carried out in the Chandigarh University. This work has not been produced anywhere for the academic purpose.

Informed Consent Statement:

This study does not require the human consent to perform the intervention this study is not related to the involvement of the direct human exposure. This study is only to collect the data and from the previous studies.

Conflicts of Interest:

None Declare

REFERENCE:

1. Eddleston M. Novel clinical toxicology and pharmacology of organophosphorus insecticide self-poisoning. Annu Rev Pharmacol Toxicol. 2019;59:341–60.
2. Karunarathne A, Bhalla A, Sethi A, Perera U, Eddleston M. Importance of pesticides for lethal poisoning in India during 1999 to 2018: a systematic review. BMC Public Health. 2021;21(1):1–13.
3. Kumar S, Kaushik G, Villarreal-Chiu JF. Scenario of organophosphate pollution and toxicity in India: A review. Environ Sci Pollut Res. 2016;23(10):9480–91.
4. Rao CS, Venkateswarlu V, Surender T, Eddleston M, Buckley NA. Pesticide poisoning in south India: Opportunities for prevention and improved medical management. Trop Med Int Heal. 2005;10(6):581–8.
5. Mlayeh S, Annabi K, Daly A Ben, Jedidi M, Dhiab M Ben. Pesticide poisoning deaths: a 19-year retrospective study of medicolegal autopsies in center Tunisia. Egypt J Forensic Sci. 2020;10(1).

6. Mukherjee B, Mahapatra S, Das S, Roy G, Dey S. HPLC detection of plasma concentrations of diclofenac in human volunteers administered with povidone-ethylcellulose-based experimental transdermal matrix-type patches. Methods Find Exp Clin Pharmacol. 2006;
7. Deme P, Azmeera T, Kanjilal S, Jonnalagadda P, Upadhyayula VS. LC-MS/MS Determination of Organophosphorus Pesticide Residues in Coconut Water. Food Anal Methods. 2013;6(4):1162–9.
8. Li SL, Li ZH, Wang YF, Xiao R, Pan C De, Wang Q. Preliminary study for the allelopathic effect of water extracts from Solidago canadensis leaves. In: Advanced Materials Research. 2013.
9. Corrales DC, Carlos Corrales J, Figueroa-Casas A. Hacia la detección de plagas y enfermedades en cultivos a través de aprendizaje supervisado. Ing y Univ [Internet]. 2015;19(1):207–28. Available from: http://dx.doi.org/10.11144/Javeriana.iyu19-1.tdcd
10. Gil De Los Santos D, Gil Turnes C, Rochedo Conceição F. Bioremediation of parboiled rice effluent supplemented with biodiesel-derived glycerol using pichia pastoris X-33. Sci World J. 2012;
11. A. Karbelkar A, E. Reynolds E, Ahlmark R, L. Furst A. A Microbial Electrochemical Technology to Detect and Degrade Organophosphate Pesticides. ACS Cent Sci. 2021 Sep;7(10):1718–27.
12. Robb EL, Baker MB. Organophosphate Toxicity [Internet]. StatPearls Publishing, Treasure Island (FL); 2021. Available from: http://europepmc.org/books/NBK470430
13. Deye, N., Vincent, F., Michel, P., Ehrmann, S., Da Silva, D., Piagnerelli, M., … Laterre, P.-F. (2016). Changes in cardiac arrest patientsâ€TM temperature management after the 2013 â€œTTMâ€• trial: Results from an international survey. Annals of Intensive 6(1). http://doi.org/10.1186/s13613-015-0104-6, Al-Hussaini, M., & Mustafa, S. (2016).
14. Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. Lancet. 2008;371(9612):597–607.
15. Jing Z, W FW, Takami T, Takanashi H, Fukada F, Kawano Y, et al. OPEN NB - LRR - encoding genes conferring susceptibility to organophosphate pesticides in sorghum. Sci Rep. 2021;(0123456789):1–14.
16. Liu H, Maria A, Wang Y, Kannan K, Liu M, Zhu H, et al. Organophosphate pesticide exposure : Demographic and dietary predictors in an urban pregnancy cohort *. Environ Pollut. 2021;283:116920.
17. London L, Mergler D, Kromhout H. Suicide and Exposure to Organophosphate Insecticides : Cause or Effect ? 2005;321:308–21.
18. Donahoe. 基因的改变 NIH Public Access. Mol Cell Biochem. 2012;23(1):1–7.
19. Dept. of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA, USA, 2 Dept. of Human Anatomy, Pharmacology, and Forensic Sciences, University of Parma Medical School, Parma, Italy. 2008;1240–9.