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Organophosphate Pesticides Use and Contamination in Groundwater of Pakistan: A Review

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ABSTRACT

Water pollution and contamination is a grave risk to the human as well as environment in Pakistan augmented by the disposal of industrial waste, fertilizers and pesticides into the water sources. The objective of this review paper is to sum-up the use and evaluating the studies of organophosphate pesticides contamination in groundwater of Pakistan. This review paper also pinpoints the detrimental effects of these pesticides on to the human health and environment. It also considers the present state of familiarity to fix the future action plan in research on pesticides in Pakistan. It is manifested that pesticides have a long history of use against insects and other pests. Pesticides are used to enhance agricultural productivity as well as for indoor applications, however, their side effects include damaging the useful insects, wildlife losses, ruins the crops and food chain and health danger to the human and animals etc. It is also evident that in Pakistan, the groundwater is being contaminated at higher levels with the excessive use of pesticides especially organophosphates. It is also noted that a little work has been done on residues analyses of these organophosphates in groundwater of Pakistan especially in Punjab province. Therefore, in order to make sustainable use of pesticides and decrease their harmful impacts, the strong implementation of legislation is required and the utilization of pesticides should be reduced. Furthermore, favoring the biological control and integrated pest management (IPM) should be the main focus of the quarters concerned.

Keywords: *Organophosphate Pesticides, Groundwater, Environment, Human Health, Pakistan*

1. Introduction

Pesticides are referred to as chemicals to control and regulate a diversity of pests that can destroy crops and livestock and lessen the productivity of farmlands. Organophosphates (OP) are a set of pesticides compounds including some of the highly poisonous chemicals employed in agriculture. Organophosphate poisonousness is because of the capacity of the chemicals to constrain an enzyme, acetylcholinesterase (Figure 2) at cholinergic junctions of the nervous system [1]. Water pollution and contamination are amongst the important issues in Pakistan caused by poor monitoring and management of drinking water quality. Many of the parameters of potable water quality agreed by the WHO are often violated in many developing countries like Pakistan etc. [2-4]. Additionally, the drinking water sources are being contaminated with the disposal of industrial waste, fertilizers and pesticides into the water sources throughout the country [5]. Applications of pesticides are the major contributing aspects to the decline of quality of water [6]. The pesticides are the chemical compounds that are utilized to switch, destroy, alleviate, prevent, or resist many insects, rodents, wild plants, fungi or other organisms that can impends human health and the area's economy [7]. The pesticides are used to protect crop, preserve food, materials and protect from vector-borne diseases (malaria, dengue, leishmaniasis and Japanese encephalitis) which executes up to one million children each year. Pesticides save energy and labor, and increase crop production in agriculture [8]. The increasing intensification of agricultural practices in developing countries (e.g. Pakistan) enhances the occurrence and risk of pest attacks [9].

Pesticides are toxic by design, their manner of action is by marking systems or enzymes in the pests which may be alike or very same to systems or enzymes in humans and thus, they put dangers to the environment and the health of humans. Mishandlings and over use of pesticides cause deposition of pesticides to inner part of vegetable, soil and water in the residual form [10, 11]. The objective of this review paper is to sum-up the use and evaluating the studies of organophosphate pesticides contamination in groundwater of Pakistan. It also pinpoints the detrimental effects of these pesticides on to the human health and environment. Further, this paper also considered the present status of pesticide knowledge in Pakistan to formulate and direct the future action plan in pesticide research.

2. Pesticides Consumption in Pakistan

Agriculture is the largest sector of Pakistani's economy with 21% contribution to GDP and employing about 44% of the workforce [12]. Agrochemicals use in Pakistan had come into practice in the year of 1954 with the volume of 254 metric tons. For meeting its domestic needs, Pakistan has extremely trusted on imported pesticides and insecticides. By the mid-1960s, Pakistan made great progress in domestic pesticides manufacturing by founding two manufacturing units viz. DDT-Nowshera and BHC and DDT-Kala Shah Kaku and pesticides consumption has reached over 7,000 tons per annum [13]. During 1970s, no further progress have been made and these plants became out of dated and were

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shut downs. Later on about 20 formulation plants were installed in Pakistan, the pesticide manufacturing, importing, selling, and monitoring rules and regulations were quantified according to the Agricultural Pesticide Ordinance 1971 and Agriculture Pesticide Rules 1973 [14, 15]. By the installation of pesticides plants, the level of consumption of pesticides was increased to 16,226 metric tons in 1980s. In 1989, the pesticides distribution and sale were transferred to the private sector from the public sector, which carried out a five-fold surge in the consumption of pesticide in one year and has increased by 1,169% during the last 20 years [16, 17]. During the financial year of 2019-20, Pakistan has imported the pesticides of the worth of 220 million US dollars that increased to 484 million US dollars in financial year of 2021-22 [18, 19].

Empirical analysis of pesticide import trend and marketing price index showed that the total expense on the buying of pesticides is increasing annually in Pakistan. Local companies offered incentive schemes and great profit margins of up to 30% to the brokers to fetch full share of market as compared to the transnationals of up to 15% in Pakistan [20]. Among the top active transnationals' of pesticide trade in Pakistan were Bayers, Burma Shell, Ciba-Giegy, FMC, Dow Chemicals, ICI, Hoechest, Sandoz and Pacific. Now at present time, over 108 types of insecticides, 39 types of weedicides, 30 types of fungicides, 6 types of rodenticides and 5 types of acaricides are being utilized in Pakistan. Among the province wise share of pesticide market, the Punjab is on top with 90% share, Sindh for 8% and both KPK and Balochistan hold 2% respectively [21]. In the Punjab province, before 1983 to 1997 only 5-10% of the crop cultivating area has been handled with pesticides which are now enhanced to 100% [17].

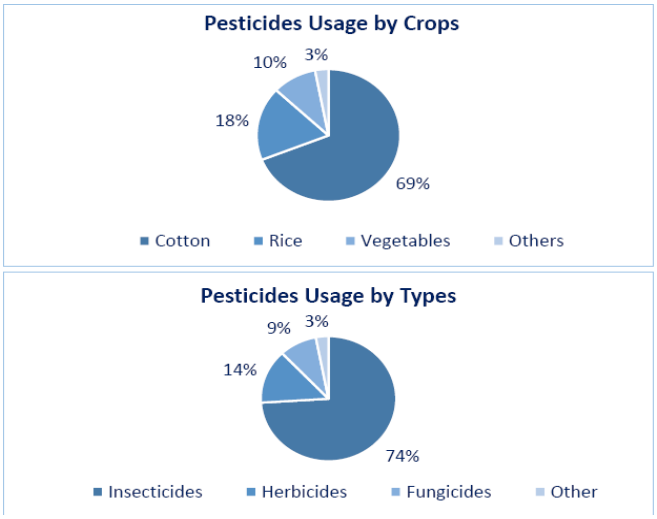

Fig. 1: Pesticides Usage by Crops and Types in Pakistan [19]

In Pakistan, the usage of pesticides is ever increasing to control pests and for better output of agricultural crops [22]. A study conducted at Multan shows that the highest share of cultivators (79.4%) dependent on the pesticides for management of pests [23]. Presently, there are about 170 registered pesticide products and 272 registered importers of these pesticides in the country that are being regulated by the Department of Plant Protection (Ministry of National Food Security and Research). Majority of the pesticides are utilized in cotton crop which are chiefly insecticides (Figure 1) [19].

3. Organophosphate Pesticide in Pakistan

Organophosphate (OP) chemicals are the organic compounds of phosphoric acid derived that are most commonly used as pesticides and nerve agents with highly poisonous nature [24]. They also used in cropping areas and having massive efficiency, wide coverage of numerous species and low diligence. Moreover, the OP pesticides and nerve agents have a mutual mechanism of work [25, 73]. In Pakistan, OPs and CMs (Carbamates) are used because of their availability and rapid decay in the environment instead of organochlorine (OC) pesticides [26, 27]. Tetraethyl pyrophosphate was the first OP synthesized in 1854. During the years of 1934-1944, a German chemist named Gerhard Schrader and his coworkers synthesized about 2,000 OP compounds at I.G. Farben industries including parathion (as a pesticide) and sarin, soman and tabun, as chemical warfare nerve agents [28]. Today, more than 100 kinds of OP pesticides are available in the market for the check of numerous pests and insects, each having different toxicity levels and a variety of pest control applications including insecticides, nematicides, acaricides, and fungicides [29, 30]. Nowadays, OP pesticides are extensively manufactured and utilized in Pakistan. A survey of Southern parts of Punjab, Pakistan, was conducted to evaluate the extent of wide-ranging used pesticides and demonstrated that many OP pesticides were used in different districts of Pakistan, i.e. Layyah, Muzaffargarh, Multan, Khanewal and Faisalabad [31]. Among Organophosphorus pesticides, Malathion, Profenofos, Chlorpyrifos and Triazophos were extensively used and the top ten insecticides in Pakistan [32]. Sale of endosulfan, chlorpyrifose, profenophose and monocrotophos was 117.9, 44.9, 36.7 and 22.3 metric tons respectively [33]. These pesticides are used to control bollworms, aphids, fruit borers, red spiders, cutworms and leaf hoppers on a wide range of crops such as wheat, cotton, maize, cereals, fruits and vegetables. These are generally efficient in the control of plant roundworms [34, 35].

4. Fate of Organophosphate Pesticides

The knowledge on chemical, physical and biological processes that governs the transportation, distribution and fate of pesticides and their transformation products in the groundwater is important to assess the pesticides residues. Pesticide contamination in the groundwater is due the certain reasons like occurrence and distribution in relation to their use. In the environment, these OP chemicals do not persist however; their larger usage and decaying rates can cause these compounds to deposit in soils, and from where they ultimately enter into groundwater and rivers [36]. The pesticide contamination in groundwater may be from non-point sources and from point sources [37]. Like the

Diazinon, an OP, often exists in point sources (e.g. wastewater treatment plant effluents) and non-point sources (e.g. storm water runoff) in agricultural and urban areas and is extremely toxic [38]. In last few years, attention of political, public and scientific concerns have shifted toward non-point sources. Groundwater contamination from nonpoint sources (NPSs) is a bigger environmental concern because non-point sources are comparatively not easy to recognize [39]. Furthermore, the use of agricultural pesticides is one of the key problems in urban and rural cultivated areas, with the dispersion of common pollutants through polluted air, water and other physical ways [40]. It is observed that hydrophobicity and persistence are two key properties of the pesticides. If these are water solvable or have fewer octanol–water partition co-efficient and low soil half-life then the contamination of groundwater will be higher [41, 42, 17]. Also, the rate of pesticides degradation is affected by soil type, pH, soil moisture, organic contents and the concentration of pesticides in the soil. However, the mobility of pesticides and their transfer to water bodies depend on total organic contents in soil, pesticide half-life, soil texture, depth to water table, mechanisms and kinetics of sorption and desorption from soil particles [43]. Sandy loam soil facilitates the mobility of pesticides and they may get distributed in the soil up to a depth of 35 cm [44]. Especially, the main concerns are the timings and application amounts, and the usage of larger quantities of these pesticides during irrigation to crops rainfall aids the chemicals to reach groundwater [45]. Therefore, the organophosphates (OPs) are more readily infiltrated in the groundwater as compared to other types of pesticide [46].

5. Pesticide Contamination of Groundwater in Pakistan

The extensive pesticides use has regulated the pests in Pakistan, but it has originating many environmental issues same as other developing countries. It is estimated that annually, over half million people in Pakistan are unluckily suffered from pesticides and other agro-compounds [47]. Pesticide contamination of groundwater is an extensive pollution problem. As a consequence of widespread and repeated use, pesticide residues have been detected in high concentrations in groundwater serving as drinking water resources. Pesticide concentration may cross the limits in drinking water ($0.1 \mu g L^{-1}$) for individual pesticides [48]. Ali and Jabbar [49] carried out a research in Faisalabad (Punjab, Pakistan) and disclosed that the groundwater fetched from a depth of 30 to 40 feet is polluted with remains of pesticide namely cyalothrin (traces to 0.0002 ppm), monocrotophos (0.04-0.06 ppm) and endrin (0.0001-0.0002 ppm). In some areas of Sindh and Punjab, groundwater has been established toxic and is continuously being polluted due to excessive use of pesticides [50].The residues of pesticides are found in shallow drinking water wells of Punjab close to the areas where a large amount of pesticides are being used [51]. In addition, a fish slaying tragedy in the Rawal Lake was become a headline news in Pakistan and at international level. The said lake supplies the drinking water to a population of 1.5 million of Rawalpindi City. Numerous research institutions reported high elevated percentage of pyrethroids pesticide in this lake [52]. Similar investigation of pesticide contamination in groundwater was conducted in the tobacco growing area of Mardan (KPK) where methyl parathion, chlorpyrifos, endosulfan and profenophos were found. The water table of this area was 3.6 to 5 feet [53]. In Pakistan, it is reported in a study that out of 107 collected samples of groundwater, 31 were contaminated with pesticides and were exceeding the safe potable water limit as per the WHO and FAO [5]. This influence the groundwater utilized as potable water by the human and marks them susceptible to the detrimental effects of these pesticides [55]. Ahad et al., [51] reported that diazinon, methyl parathion, fenitrothion, endosulfan and azinophos methyl with residual level of 0.003, 0.01,0.00,0.13 and 0.001ug/L respectively in cotton-growing area of Multan with water table of 5.0 to 18 feet.

In continuation with the above facts of the studies, the pesticides pollution of groundwater in four concentrated districts of cotton growing had also been elevated. Water samples were collected from wells in the areas of Dera Ghazi Khan, Bahawalnagar, Rajanpur and Muzaffargarh, districts of Punjab. The pesticides which are mostly applied in these districts were analyzed. The percentage of detection of endosulfan, methyl parathion and monocrotophos was 8%, 5.4% and 35.1% in July; 24.3%, 8% and N.D. (not detected) respectively in October [41]. A bulk of pesticides with 5,000 and 3,000 tons are distributed in the Punjab and Sindh provinces respectively. In addition, 46,500 liters of liquid pesticides and 366 tons of solid were used in Karachi, the biggest city of Pakistan and a major share of these pesticides has seeped down to groundwater and polluted it. Moreover, it was found that about 70 tons of pesticides were vanished because of low quality packing material and caused groundwater contamination in Sahiwal [56]. Furthermore, WWF-Pakistan [57] revealed that about 3,800 tons of expired pesticides could not be abolished in Pakistan because of lack of budget and necessary technology. As well as a considerable amount of outdate pesticides and obsolete were testified in majority of the districts of Punjab province, which in result, mounting the risk of environmental degradation.

6. Pesticides Exposure and Poisoning

The consumption and varieties of pesticides have been enhancing significantly as crop production and population numbers are geared up. In this regard, pesticide mishandling turns into more serious and this has outcome in great environmental pollution and danger for human health. It is established that consumption patterns of pesticides has passed notable variations since 1960s. In 1962, the American biologist Rachal Carson was amongst the first to mention the problems associated with the overuse of the pesticides in her seminal book ‘Silent Spring’. This publication raised the huge concerns about the influences of the pesticides on the human health and environment [45]. The excessive pesticide

use is dangerous for not only environment but also for human health [58, 59]. Likewise, contamination of water bodies and deaths due to pesticides has been serious in past years [60]. Policy formulators, farmers and other shareholders should be search for devices to evaluate the dangers of pesticide for minimizing pesticide effects on human health and surrounding ecosystem. In this regard, the new decision support system of Pesticide Use Risk Evaluation (PURE) developed by California Environmental Protection Agency (CEPA) is being used to evaluate specific pesticide risks to soil and groundwater. In PURE, the risk score is calculated by the corresponding share of the Predicted Environmental Concentrations (PEC) to the poisonous score for chosen endpoint organisms. The risk scores in PURE is ranging between 0-100, (where 0 represents negligible risk while 100 for the highest risk) [61].

Pesticides are used to slay the certain organisms on crops, houses, gardens and parasites in medicines but low awareness caused environmental and health risks. Therefore, the pesticides are being extensively abused in the farms in Pakistan. In a study, it is found that very few (less than 2%) farm participants were aware the names of the pesticides they were utilizing and one-third of the workers were not aware the pesticides to be used in crops. Few workers (29%) used protective clothing and majority of the participants (96%) had contributed in immixing pesticides together before use. A considerable number of participants (18%) had no information about the health related risks of pesticides. It is noted that at least one pesticide metabolite was found in every field worker. Hence, pesticide contamination is not source-dependent but hostile in human metabolism system [62]. The pesticides, particularly organophosphate (OP) pesticides like chlorpyrifos, have been often utilized for excessive time to maintain product quality, protect agricultural crops from various pests and to increase yield. Lappharat et al. [63] evaluated the dermal exposure to chlorpyrifos in rice farmers. The concentrations of chlorpyrifos were higher and ranging 526.34 ± 478.84 mg/kg in males than the females (500.75 ± 595.15 mg/kg). Average daily intake collected from seven study sites on male and female farmers were as 31.72 × 10(-4), 193.32 × 10(-4), 5.38 × 10(-4), 190.48 × 10(-4), 170.47 × 10(-4), 465.91 × 10(-4) and 43.04 × 10(-4) mg/kg/day respectively. The mean hazard quotient (HQ) and 95th percentile level was noticed to be higher than permissible limit of HQ>1. Especially the paddy farmers in paddy fields were at great danger for antagonistic health effects due to constant dermal exposure to chlorpyrifos. Shakerkhatibi et al. [64] assessed the contamination of pesticides in rural groundwater of northwest Iran. The pesticides residual of the 78 collected water samples was found 26.9% of the total samples with accumulations of over 0.5 μg/L and amongst diazinon, profenofos and malathion were traced as the most recurrently detected pesticides with the determined accumulations of 0.614, 0.542 and 0.456 μg/L respectively.

However, the bioavailability of pesticides in humans can become severe dysfunctions, metabolic and even absolute disease states. A study showed that pesticide spray-workers (n=140) and controls (n=110) have the substantial impact on serum enzyme point ($p<0.001$) by analytical means. Monocrotophos was the major cholinesterase inhibitor among all the pesticides used there. The finding of deposit absorptions in blood serum samples of spray-workers for monocrotophos was determined as 0.005 mg/kg body weight [65]. The notable rise in enzyme level of glutamate oxaloacetate transaminase (GOT), alkaline phosphatase (ALP) and glutamate pyruvate transaminase (GPT) was also reported in farm-station workers, Gadap, Karachi due to the diazinon and monocrotophos [66]. The dolphin (*Platanista gangetica minor*) found in Indus River (Pakistan) is one of the world's highly threatened cetacean mammals. The largest population of this dolphin is found between Sukkur and Guddu barrages, officially declared as the Reserve of Indus dolphin. The habitat of this species is compact to one fifth of its historic distribution range. The major threat to the Indus dolphin is water contamination due to usage of toxic pesticides to exploit fish catch [67, 68]. The toxicity of pesticides has the potential to enter in aquatic system and the possible consequences of pesticide bioaccumulation of the food chain. The organophosphates were also detected in Rawal and Simly lakes [69]. Therefore, because of the extensive applications of pesticides, there has been a turn in the new algal biocoenosis that subsidize to water blooms [70].

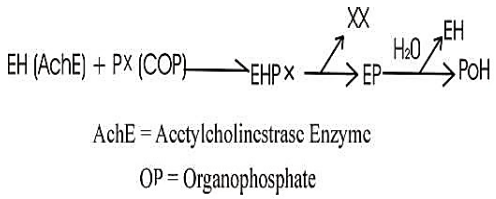

Fig. 2: Organophosphates binding to the enzyme acetylcholinesterase [24]

Diazinon, a poisonous OP, prevents the enzyme acetylcholinesterase, which hydrolyzes the neurotransmitter acetylcholine and driven to a suite of intermediary syndromes (Figure 2) including respirational, myocardial and neuromuscular transmission impairment [71]. Further, it also causes diarrhea, generalized weakness, depression, abnormal posturing and anorexia [72, 73]. Acetylcholinesterase (AChE) has an ability to measure the inhibitory strength of certain nerve agents and may offer an early estimation on the toxic level. A wide range of nerve agents are there having more strength of *k*i values (Table 1) than many pesticides except few ones. For instance, chlorpyrifos-oxon, a vigorous substance of pesticide chlorpyrifos is much stronger than tabun, a nerve agent [74]. These values give the information of early raw approximation of the potential in vitro poisonousness. Nevertheless, different intervening factors are considered vital for the determination of real in vitro poisonousness of OPs i.e. volatility, biological and chemical steadiness, lipophilicity and the way of contact [75, 76].

Deviations in metabolism among species and exposed levels have a fundamental part in diazinon's bioaccumulation among various organisms in a wide variety of efficiencies and concentrating ratios [83]. In Pakistan, malathion is one of the greatly used pesticides in agriculture. The recurrence exposure to malathion at the groundwater pollution degrees exerts unsympathetic effects on the hepatic drug-metabolizing system. Malathion exposure affects the body or weight of liver and the different biochemical parameters [84].

Table 1. In vitro potential strength of selected OPs (pesticides, nerve agents) toward human Acetylcholinesterase.

OP	*ki*	OP	*ki*
Fenamiphos	0.002	TEPP	59.7
Propophos	0.03	Methylsarin	105
Tetrachlorvinphos	0.03	Dimethyl-VE	125
Methamidophos	0.05	Leptophos	134
Monocrotophos	0.06	Tabun	182
Trichlorfon	0.07	Dimethyl-VX	222
Dicrotophos	0.15	Chlorpyrifos-oxon	269
Omethoat	0.16	Ethylsarin	327
Ethoprophos	0.23	Diisopropyl-VE	368
Heptenophos	1.38	Naled	377
Bromfenvinphos	1.43	Sarin	398
Chlorfenvinphos	1.72	VE	433
Pirimiphos-methyl-oxon	2.81	Diethyl-VX	551
Dichlorvos	3.55	VX	1150
Profenofos	4.08	n-Propylsarin	1260
Malaoxon	4.74	Soman	1930
Mevinphos	6.64	n-Butylsarin	2790
N-Diethyltabun	7.77	Chinese VX	3210
Dimethyl-amiton	8.57	neo-Pentylsarin	3240
Paraoxon-methyl	11.3	Cyclosarin	4390
N-n-Propyltabun	11.8	Russian VX	4580
Amiton	18.9	sec-Pentylsarin	4870
Diisopropyl-amiton	27.4	iso-Butylsarin	5330
O-Methyltabun	32.1	iso-Pentylsarin	5460
Paraoxon-ethyl	33.0	n-Pentylsarin	9500

Source: [77, 78, 79, 80, 81, 82]

Note: ki is the bi-molecular inhibition rate constant assumed as 105 M^{-1} min^{-1}

However, the adverse impacts of malathion on the health of human and ecosystem are of mounting apprehension. The narrative malathion haptens are synthesized to develop an enzyme linked immunosorbent assay (ELISA) screening method and this ELISA is utilized to assess malathion in the samples of groundwater and surface water. On this basis, the satisfactory results were obtained by the GC-MS reference method for malathion environmental monitoring in natural waters [85]. Likewise, methyl parathion, ethyl parathion were also found to be acutely toxic [86]. Similarly, profenofos, a type of organophosphate is a potential acetylcholinesterase inhibitor [87]. Generally, the organophosphates impede acetylcholinesterase in the nervous system of pests and are splits into six sub-types as; phosphates, phosphorothioates, phosphorodithioates, phosphorothiolates, phosphonates and phosphoramidates (Figure 3) [24]. The toxicity and metabolism levels of OPs are depends on the structural variations of these compounds. For instance, the pesticides i.e. paration, diazinon and malathion [88].

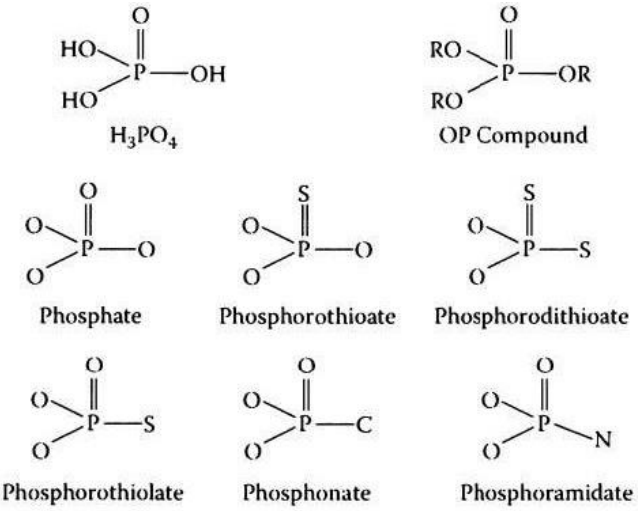

Fig. 3: The structure of Organophosphates by chemical arrangement [24]

Endocrine glands have unique importance in human body as they accomplish certain tasks and characteristics but they disrupted by many chemical compounds [89]. Endocrine disrupting chemicals (EDCs) are chemicals that change the humans' usual working of the endocrine system. Pesticides are the compounds that have been recognized as endocrine disruptors [90]. The extreme contact to regular and synthetic environmental compounds and poisons can have negative impacts on the endocrine system and reproductive health [91]. An assessment of susceptibility to a composite mix-up of pesticides resulted in a substantial rise of DNA decay in farmers, who were persistently disclosed to pesticides in crop fields. The Leukocytes exposed to pesticides from 47 agriculture workers were assessed with comet assay. The significant variation ($P<0.001$) in DNA decay of disclosed individuals ($14.80 \pm 3.04\mu m$) was noticed when compared with control group ($6.54 \pm 1.73\mu m$) in cotton grown areas of Pakistan [92].

Pesticides have negative impact on environment and human health. Intensive pesticide use in Bolivia has reported increasing problems of acute pesticide poisonings and chronic effects like neurological problems, cancers, teratogenicity, sterility and environmental pollutions [93]. Apart, the excessive misuse and overuse of pesticides by

Table 2. Brief of the physicochemical properties and phase of the intoxication of Organophosphates.

Pesticides	Physical and Chemical Properties	Exposition	Toxicokinetics	Toxicodynamics	Signs and Symptoms	Treatment
Organophosphorus	Organic compounds containing phosphorus. The properties vary with the size and structure. In general are more soluble in organic solvents	Skin, conjunctiva, gastrointestinal tract and lungs	Rapidly absorbed and metabolized by P450 isozymes in oxom form, more toxic than the parent compounds	Covalent bonds with the serine residue in the active site of acetyl cholinesterase (reversibly or irreversibly)	Muscarinic syndrome and nicotine syndrome, resulting of excess acetylcholine in the synaptic cleft	Maintenance of vital functions and cholinesterase levels. It is important to avoid the use of parasympathomimetic agents

Source: [88, 102, 103, 104, 105, 106]

naive growers enhanced the health and environmental danger particularly in the vital cotton growing districts of Pakistan [94]. In Pakistan, cotton picking is mainly accomplished by women who are at a great risk to pesticide remains due to their low fiscal freedom and wide use of pesticides during the picking season [95].

Abbas et al. [96] published findings from their investigation in Bahawalnagar, Sahiwal and Vehari districts of Punjab that most of the women respondents (91.3%) were unaware of the health risks of the pesticides. Therefore, the peripheral blood was collected from 69 unexposed females and 69 cotton pickers and employed to evaluate the impact of pesticide vulnerability on inherited decay as well as on serum cholinesterase and hepatic enzymes. Rates of alkaline aspartate, aminotransferase and phosphatase were higher; the levels of serum cholinesterase were lower in the vulnerable workers as compared with the control group (P<0.001). The vulnerable group shown greatly enhanced occurrences of total number of micronuclei in binucleated lymphocytes was (16.51 ± 4.27 vs. 5.86 ± 3.09, P<0.001 and binucleated cells with micronuclei were (12.72 ± 3.48 vs. 4.35 ± 2.44, P<0.001) in comparison with the control group [97]. Similar study was done in Multan district of Punjab and Khairpur district of Sindh and found impact of pesticides on reproductive hormones (LH and FSH) of females [98, 99]. A broad range of terrestrial and aqua ecosystems have been long known as polluted with OP pesticides. These pesticides have great mammalian poisonousness and it is absolutely vital to eliminate them from the environment. About 200,000 metric tons of nerve agents have to be cracked worldwide due to this group of pesticide [100]. However, specific OPs such as triorthocresyl phosphate inhibits neurotoxic esterase and results in a delayed type of axonal pathology. Hexane pathology has been found in screen printers and these circumstances highlighted the demand for improved precautionary and work-related measures [101]. The selected physiochemical properties and intoxication of organophosphates is summarized in table 2.

7. Pesticide Management and Control

Information concerning mobility of pesticide is vital for the estimation of pesticide management practices. In recent times, there has been a great rise in the use of pesticide for numerous purposes like: to control plant insects, weeds and other plant disease [107]. However, in spite of their effectiveness, it is estimated that just 0.1% of OPs are reached their wished goal [108]. But still the population is threatening by the nerve agents and OP pesticides and their treatment is a continuing challenge for medical field [74]. Thus, lysimetric studies have been undertaken to expand evaluation schemes to save groundwater from deleterious impacts reasoned by the use of pesticide. By using lysimetric studies, particular observing tasks and deterrence ways for the safety of waters can be examined. The obtained findings can offer to the local agencies and the decision makers with recognition of a device for delimitating hazard areas. Pesticide remnants form found at the bottom of lysimeters were 1.52 > 2.1 > 2.74 m which could be a sign of an 'Index of Risk' for groundwater contamination [109]. A recent study detected the chief pesticide groups' chemical residues of OPs, i.e. profenofos, chlorpyrifos and triazophos in collected water samples of 15 districts of the Punjab province, where the maximum concentration in water sources of core areas during winters exhibited by profenofos at 5,665 ng L^{-1} [110]. Notwithstanding, the continued efforts made on national and international level to ban greatly noxious OP pesticides self-poisoning with pesticides residues remains a key medical issue particularly in developing countries, initiating over 100,000 causalities every year [111]. Therefore, the Integrated Pest Management (IPM) suggests different pest control ways to minimize the artificial pesticide application [112]. Pesticides are vital element of an IPM that plays a key role in rising agrarian production. Biopesticides are safer alternatives to conventional pesticides. The synthetic insecticides (imidacloprid, endosulfan and profenofos) and biopesticides (spinosad and biosal) were analyzed and measured their half-lives. The average half-life of biopesticides, was 3.47 and 1.66 days for spinosad and biosal respectively whereas, conventional pesticides were persistent with average half-life of 3.14, 2.57 and 2.11 days for endosulfan, imidacloprid, and profenofos respectively [113]. Bioremediation can propose a competent and cheap way for sanitization of contaminated ecosystems and obliteration of nerve agents. The first microorganism identified that could damage OP chemicals was *Flavobacterium sp*. Since, a number of bacterial and fungal species were isolated and cultured which can damage a variety of OP chemicals in liquid cultures [114]. The

agriculture ministries of less developed countries must focus on the enhanced and monitored use of OP compounds as pesticides. They should also encouraged growers to utilize natural pesticides and organic agriculture rather than compound pesticides [1]. It is also necessary to educate the public about the various forms of natural pest control and select unbleached paper products like paper (for office or home use), coffee filters, toilet tissues and napkins [91].

8. Conclusion

Pesticides are widely used since long ago against insects and other pests in Pakistan. Pesticides especially the OPs are used to enhance agricultural productivity are inevitable in agriculture and other uses but they are proven to be highly toxic and harmful for wildlife, positive insects, remnants in crops and food chain. They are also posing risk to human health, animals and surrounding environment due to fatal chemicals and toxins. It is therefore, strong implementation of legislation is required and the usage of pesticides should be minimizing and strongly dispirited. While the focus should be on biological controlling measures usage and encouraging the IPM. It is also evident that the groundwater resources in Pakistan have been contaminated particularly with OPs pesticides. A little work has been done on residues analyses of these pesticides in groundwater of Pakistan exclusively in Punjab Province. Therefore, this study will be supportive for future research and policy formulation regarding to monitor the nature and adverse impacts of these pesticides in groundwater, on humans health and environment.

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