EFFECTS OF PESTICIDE EXPOSURE ON CHRONIC DISEASES IN SOUTH AFRICA: ADVANCING GOOD AGRICULTURAL PRACTICES FOR FOOD SAFETY

MOTSHABI, N. – MALEBO, N. J. – KHETSHA, Z. P.*

Centre for Applied Food Security and Biotechnology & Department of Agriculture, Central University of Technology, Free State, Private Bag X20539, Bloemfontein 9301, South Africa

**Corresponding author*
e-mail: zkhetsha@cut.ac.za; phone: +27-51-507-3130

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Abstract. Pesticides are essential for agricultural production, protecting crops from pests and diseases. However, their widespread use poses significant health and environmental risks. This review analyzes academic literature from 2004 to 2024, identifying pesticide residues, exposure pathways, and their impacts on human health and food safety. The findings reveal that health impacts vary by pesticide type, with certain chemicals linked to neurological disorders, skin and eye irritation, carcinogenicity, and endocrine disruption. Even at low exposure levels, cumulative risks underscore the necessity of comprehensive assessments of pesticide toxicity and exposure likelihood. This review highlights the importance of strategies to minimize human exposure and protect public health, advocating for improved pesticide management and regulation in South Africa.
Keywords: *fertilizers act, health risk assessment, human exposure, organochlorine, organophosphates*

Introduction

Pesticides refer to substances or mixtures designed to prevent, destroy, repel, or mitigate pests or to function as plant regulators, defoliants, or desiccants (da Silva and Chan, 2014; Joint FAO/WHO meeting, 2017). Pesticides play a leading role in food agriculture and are an essential contributor to the protection of crops against disease and pests (Akan et al., 2013; Macharia, 2016). While pesticides benefit agriculture and public health, they also lead to environmental contamination (Motshabi et al., 2021; Mohapi et al., 2024a) Mohapi et al., 2024b) and adverse public health effects.

Pesticide exposure can lead to severe health effects. Pesticides can cause adverse health effects in humans, ranging from acute impacts, such as nausea, headaches, and skin and eye irritation, to chronic effects, such as cancer, neurological and development defects, diabetes, reproductive disorders, congenital disabilities, and cardiovascular disease (Mostafalou and Abdollahi, 2013). Furthermore, pesticide exposure is linked with various diseases, including cancer, hormone disruption, asthma, allergies, and hypersensitivity (Van Maele-Fabry et al., 2010; Dabrowski et al., 2014).

The application of pesticides is often not very precise, and unintended exposures occur to other organisms. Even low levels of exposure during development can result in adverse health effects. It is, therefore, essential to identify critical areas where specific pesticides may result in a high risk of exposure to humans or the environment. The World Health Organization (WHO) has estimated the deaths of 355,000 people globally each year due to pesticide poisoning. In developing countries, two-thirds of these deaths occur from poisonings associated with excessive exposure to and inappropriate use of pesticides (WHO, 2018).

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There is circumstantial evidence of the relationship between pesticide exposure and the elevated rate of chronic diseases observed in farmers and consumers (Lehmann et al., 2017; Njoku et al., 2017). A line of evidence also exists for the negative impacts of pesticide exposure leading to cancers (Alavanja and Bonner, 2012; Lerro et al., 2014), leukemia (Malagodi et al., 2016; Gunier et al., 2017), asthma (Ranaan et al., 2015), Parkinson disease (Tanner et al., 2011; Mostafalou and Abdollahi, 2013; Macharia, 2016; Gerage et al., 2017) and diabetes (Lee et al., 2011; Taylor et al., 2013).

Based on scientific evidence, pesticides' actual, predicted, and perceived risks to human health and the environment are fully justified. In light of the environmental significance of pesticide contamination and its impact, this review has been organized to describe the general aspects of pesticides concerning classification, the status of contamination and the effects on human health. The objective of this review is to conduct a systematic review of published studies from 2004 to 2024 concerning the use of pesticides and their harmful impacts on human health.

Methodology

The authors conducted a comprehensive desktop and academic literature analysis from 2004 to 2024, investigating common pesticide residues, exposure pathways, and their deleterious effects on human health and food safety (Holcombe, 2023). This analysis includes research articles, reviews, book chapters, theses, and communications, analyzing their relevance to the study's primary objective.

Common pesticide residues in South Africa

Residue means any specified substances in or on food, agricultural and other commodities or animal feed, as well as in environmental media, including soil, air and water resulting from pesticide use (Pandya et al., 2014). The term "*pesticide residue*" includes residues from unknown or unavoidable sources and known, authorized pesticide uses (da Silva and Chan, 2014). Due to a large number of chemicals and pesticides, combinations of compounds have been classified for use in insecticides, algicides, miticides, herbicides, nematicides, fungicides, biocides, molluscicides and rodenticides (Garcia et al., 2012). Pesticides are also grouped according to their chemical properties, and these include organophosphates, organochlorines (chlorinated hydrocarbons), carbamates and thiocarbamates, and pyrethroids (Adewumni and Fapohunda, 2018). *Table 1* summarizes the commonly used pesticides in South Africa and their effects on human health in South Africa.

Routes of exposure to pesticides

Pesticides can enter the human body through the skin (dermal), the lungs (inhalation), and the mouth (ingestion).

Dermal exposure

The dermal route of exposure is also called absorption, which occurs through the skin. Pesticides enter the body through the pores that release sweat. Humans can be exposed when a worker mixes or sprays pesticides or becomes exposed without wearing

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suitable personal protective clothing. Skin contact can occur when equipment is touched, protective clothing is worn, or a surface has pesticide residue (Sarwar, 2015).

Table 1. *Commonly used pesticides in South Africa and their effects on human health*

Type of pesticide	Definition	Cases in South Africa
Organochlorine	Organochlorine pesticides are used to control pests and diseases in agriculture. They primarily contain organochlorinated insecticides, which include 1,1,1-Trichloro-2,2′bis(*p*-chlorophenyl) ethane (also known as DDT), chlordane, aldrin, dieldrin, heptachlor, endrin, toxaphene, and hexachlorocyclohexane (Rodrigues et al., 2010; Van den Berg et al., 2017; Samsidar et al., 2018)	Madjar et al. (2024) conducted a study on water containing organochlorine pesticide residues, and it was reported that the quality of the water had organochlorine ranging between 0.01 to 0.81 μg/L, higher as prescribed by the international drinking water standards set by the WHO. In this study, which highlights some key pesticide contaminants, the levels of DDT, dieldrin, paraquat, aldrin, metribuzin, butachlor, alachlor, atrazine, phenol, endrin, and benzene were recorded as higher. Interestingly, the variation of these compounds differed across the two study seasons, which showed no monitoring and evaluation of compliance by the Fertilisers, Farm Feeds, Seeds and Remedies Act No. 36 of 1947 In another study, Yahaya et al. (2017) reported that organochlorine pesticide detection varied between seasons, from 4403 to 313 ng/L in summer and autumn. As with the international limit (100 ng/L), the organochlorine pesticide was recorded to be significantly higher; thus, as reported by the author, there are chronic disease risks such as cancer, leukemia, diabetes, and asthma. This study recommended the regulation of agrochemical storage, use, and disposal in South Africa, subsequently addressing the compliance by the Fertilisers, Farm Feeds, Seeds and Remedies Act No. 36 of 1947 A study conducted in the Eastern Cape Province, South Africa, on the different water sources, showed that persistent DDT and its metabolites, chlordane and hexachlorobenzene, were prevalent. This study recorded findings similar to those of recently reported studies by Madjar et al. (2024) and Yahaya et al. (2017). Fatoki and Awofolu (2004), the authors of this research, reported that the range of DDT increased exponentially from 71.03 to 101.25, a range above the limit as per the WHO
Carbamates	Carbamates are used as insecticides, herbicides, fungicides, and nematicides, primarily in agricultural settings, to safeguard crops from pests, as well as in household pest control (Fothergill and Abdelghani, 2013). The mode of action of carbamates is similar to that of organophosphates, although they exhibit less persistence than organochlorines and organophosphates (Garcia et al., 2012). Additionally, carbamates may function as stomach and contact poisons and can be used as fumigants (Yadav and Devi, 2017). Notable insecticides within this group include the propoxur metabolite 2-isopropoxyphenol (2-IPP) and carbofuranphenol (Samsidar et al., 2018)	
Organophosphates	Organophosphate pesticides are widely utilized in agricultural practices, particularly in cultivating vegetable crops, fruit trees, grains, cotton, and sugarcane. Key organophosphorus insecticides include disulfoton, azinphosmethyl, parathion, methyl parathion, chlorfenvinphos, dichlorvos, diazinon, dimethoate, trichlorfon, and malathion. The application of Organophosphate pesticides has been linked to an elevated risk of breast cancer. At the same time, malathion has been associated with an increased risk of thyroid cancer and a decreased risk of non-Hodgkin lymphoma. Additionally, diazinon exposure has been correlated with ovarian cancer in humans (Lerro et al., 2014; Samsidar et al., 2018). Furthermore, organophosphates have detrimental effects on the immune system in rodent models and have been shown to disrupt reproductive processes in fish (Rehman et al., 2010; Díaz-Resendiz et al., 2015)	

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		In a study by Botha et al. (2015), 135 confirmed organophosphorus and carbamate pesticide poisonings in wildlife, including avian species, were documented at the Toxicology Laboratory (ARC-OVI) in South Africa. These incidents were recorded between 2009 and 2014, with vultures and eagles being the most frequently affected birds. Additionally, Balme et al. (2010) reported pesticide exposure incidents involving 306 patients, with at least 311 cases attributed to acute pesticide poisoning. The predominant classes of pesticides involved in these exposures were organophosphates and carbamates In a recent study by Veludo et al. (2024), pesticide spraying has been reported to affect children raised near farming areas. In their study conducted in 2018, it was reported that, at most, children raised in agricultural areas are exposed to the prevalent organophosphate and pyrethroid. This study showed a higher risk associated with organophosphate than pyrethroid; however, the two pesticides remain at risk, which may lead to chronic diseases As it has been banned in South Africa, methamidophos is known to be a highly hazardous type of organophosphate. In the recent study reported by de Villiers et al. (2024), any exposure, particularly to children, to methamidophos leads to protracted cholinergic toxidrome lasting ten days, with a period of near-full recovery during this time. This study shows that exposure to this chemical is detrimental; however, this depends on the level of exposure The level of pesticides in the soil has been reported to be detrimental to soil microbes. Reinecke and Reinecke (2007) reported that organophosphate pesticide application, particularly chlorpyrifos, before the commencement of various production systems, affected the soil microbes and the earthworm population. In addition, depending on the concentration level, it was also reported that due to the drifting of pesticide residues reaching untargeted areas, the pesticide residues were transported as debris to a wide area, subsequently
Pyrethroids	Pyrethrum is a natural insecticide extracted from the flowers of *Chrysanthemum cinerariaefolium* and *C. cineum* (Schleier and Peterson, 2011). Pyrethroids are synthetic analogues of pyrethrins utilized for pest control in various crops (Fothergill and Abdelghani, 2013; Sarwar, 2015). The primary commercially available pyrethroids include allethrin, bifenthrin, cyfluthrin, lambda-cyhalothrin, cypermethrin, deltamethrin, permethrin, d-phenothrin, resmethrin, and tetramethrin (Sainllenfait et al., 2012). Compared to other insecticides, pyrethroids demonstrate lower toxicity to mammals and birds, enhanced selectivity for target species relative to organophosphate pesticides, and reduced persistence compared to organochlorine insecticides (Palmquist et al., 2012). Both pyrethrins and pyrethroids are critical insecticides due to their rapid action in paralyzing flying insects, relatively low toxicity to mammals, and swift environmental degradation (Schleier and Peterson, 2011)	

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		leading to reduced soil biota. Their study reported that the chlorpyrifos' effects on earthworms were measured by measuring biomass change and cholinesterase inhibition As with the Fertilisers, Farm Feeds, Seeds and Remedies Act No. 36 of 1947, all pesticides are classified according to their toxicology. In the study by Davies et al. (2023), compliance with the use and access to these chemicals has been further shown to be detrimental. In their toxicological study, it was revealed that at least 26% of adolescents committed suicide using the organophosphate pesticides terbufos, methamidophos and diazinon. In addition, these chemicals also led to at least 18.5% of the accidental child deaths in South Africa In a recent study conducted in Limpopo, South Africa, by Elsiwi et al. (2024), pyrethroid metabolites (cis-DBCA, cis-DCCA, trans-DCCA, and 3-PBA) were reported to be most prevalent, subsequently being reported to the risk associated with asthma, and the wheezing or whistling in the chest. In addition, it was also observed that pyrethroid metabolites also have the potential to lead to a risk associated with the risk of asthma and other respiratory allergy symptoms among preschool children from an indoor residual spraying area pyrethroid insecticides Intent to commit suicide is common in using pesticides; another case was reported recently by Scheepers et al. (2023) in the Eastern Cape, where an adult used cypermethrin to attempt suicide. Authors in this study argue the ease of access to these toxic chemicals, especially for people not farming. With the Fertilisers, Farm Feeds, Seeds and Remedies Act No. 36 of 1947, it should be regulated that access should be restricted, and this goes back to the years when chlorpyrifos was banned due to high cases related to suicide using organophosphate poisoning

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Inhalation exposure

The inhalation route of exposure occurs through breathing in pesticides. The pesticides enter the body through the lungs. Humans can be exposed when a worker breathes in pesticides or becomes exposed without wearing suitable personal protective equipment. Skin contact can occur when a piece of equipment, protective clothing, or a surface with pesticide residue is touched. Pesticides with a high inhalation hazard should be labelled with directions for respirators (Sarwar, 2015).

Ingestion exposure

The oral route of pesticide exposure is also called ingestion, which occurs through mouth swallowing. Pesticides enter the body when eating contaminated food and drinks or when handling pesticides and eating without washing their hands. Therefore, the risk of illness increases as the pesticide concentration and exposure duration increase. The likelihood of becoming ill from exposure to pesticides depends on several factors, including the type of pesticide, amount of pesticide to which a person is exposed to concentration or strength, length of exposure, route of entry into the body and other carriers or chemicals in the pesticide products (Sarwar, 2015).

Impact of pesticide residues on human

The WHO has estimated the death of 355,000 people globally each year due to pesticide poisoning. In developing countries, two-thirds of these deaths occur from poisonings associated with excessive exposure to and inappropriate use of pesticides (WHO, 2018). Pesticides are stored in the colon, where they take time to slowly poison the body. Human exposure to pesticides can occur through ingesting contaminated foods, drinking water, and animal products because of bioaccumulation, inhalation, or skin contact (Bakirci et al., 2014). Pesticide exposure can lead to severe human health effects. Pesticides can cause adverse health effects in humans, ranging from acute impacts, such as nausea, headaches, and skin and eye irritation, to chronic effects, such as cancer, neurological and development defects, diabetes, reproductive disorders, congenital disabilities, and cardiovascular disease (Mostafalou and Abdollahi, 2013).

There is circumstantial evidence of the relationship between pesticide exposure and the elevated rate of chronic diseases observed in farmers and consumers (Lehmann et al., 2017). Pesticides may be related to various diseases, including cancer risk, Parkinson’s disease, leukemia, and asthma. *Table 2* displays the general types of health impacts caused by pesticide exposure.

Table 2. *Common chronic disease cases are caused by pesticide exposure globally*

Chronic diseases	Exposure risks	Cases of pesticides exposure globally	Citation
Cancer	The identification of whether specific compounds are responsible for specific human cancer risks is a significant	A Canadian study estimated a total lifetime cancer risk of 3.3×10^{-4}, highlighting increased prostate cancer risk among private and commercial applicators in Iowa, as well as elevated risks for lip cancer and multiple myeloma. The evidence suggests that pesticide exposure is carcinogenic to both direct users and those indirectly exposed, with risks potentially heightened in developing countries with limited regulations	Panis and Lemos (2024) Mhlongo et al. (2024) Martinek et al. (2024) Pluth et al. (2019)

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	challenge for epidemiology. However, many studies have reported the link between cancer and pesticides. Nowadays, chronic low-dose exposure to pesticides is considered one of the critical risk factors for cancer expansion	In a study across 10 health districts in Andalusia, Spain, cancer prevalence rates were significantly higher in areas with greater pesticide use than those with lower use. Conditional logistic regression analyses indicated an increased cancer risk at various organ sites, except for Hodgkin's disease and non-Hodgkin lymphoma. These findings support previous occupational studies, suggesting that environmental pesticide exposure may be a risk factor for cancer in the general population A literature review found that 64 studies reported significant associations between pesticides and cancer, identifying 53 pesticide types linked to at least one cancer type among 19 cancers. While a few studies had contradictory results, being a farmer or residing near agricultural areas was associated with increased cancer risk. The literature notably highlights associations with prostate, bladder, and colon cancer Colon cancer mortality in Brazilian states was reported to steadily increasing in colon cancer mortality over more than a decade, correlating with pesticide sales, particularly in the Southern and Southeast regions. Despite the methodological limitations of ecological studies, the data suggest that pesticide exposure may be a risk factor for colon cancer A case-control study in Rondonópolis, Mato Grosso, involved 85 women with confirmed breast cancer and 266 controls from primary healthcare users. Multiple logistic regression identified significant risk factors: living near cropland with pesticides and women over 50 with early menarche. The study underscores the role of pesticide exposure as an environmental risk factor for breast cancer in women Pesticide exposure among women involved in rural activities such as field spraying, unprotected handling, and washing contaminated clothes raises concerns due to potential links between specific pesticides and breast cancer risk. Evidence suggests significant differences in exposure levels, particularly in populations chronically exposed to higher doses. Educational initiatives are essential to mitigate breast cancer risk in farm women, especially those directly handling pesticides. The risks posed by widely used pesticides like glyphosate and atrazine are not well understood, nor is the impact of lifelong exposure to pesticide mixtures. Thus, biomonitoring pesticide levels in vulnerable populations and examining how exposure affects different breast cancer subtypes are critical for understanding and addressing these risks The whole genome sequencing of TK6 human lymphoblastoid cell clones exposed to subtoxic concentrations for 30 days revealed that captafol and malathion induced specific mutational signatures;	Silva et al. (2019) Martin et al. (2018) Damalas and Parrón et al. (2014) Alavanja (2013) Damalas and Eleftherohorinos (2011) Koutros et al. (2010) (Alavanja and Bonner, 2012)

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		captafol primarily caused C to A mutations, while malathion resulted in C to T mutations. In addition, captafol also led to chromosomal instability and DNA damage markers. The findings suggest that captafol induces DNA adducts bypassed by translesion synthesis, indicating potential mechanisms of action. Mutational signatures could aid in detecting past exposures in tumor samples	
Leukemia	The association between residential and childhood pesticide exposure may be a contributing risk factor for childhood leukemia. There are different types of leukemia, the most common being chronic lymphocytic leukemia	A study found that paternal occupational pesticide exposure from the year before pregnancy to the child’s third year increased the risk of acute lymphoblastic leukemia, particularly during the perinatal period. This suggests a heightened leukemia risk for children living near agricultural areas, thus highlighting the need for preventive measures, including education to reduce pesticide use and exposure. In a similar PubMed literature review study, reported under the cancer section, cases associated with leukemia were also extensively documented The risk of non-Hodgkin lymphoma and its subtypes, including B-cell lymphoma, follicular lymphoma, and T-cell lymphoma, was found to be elevated among individuals exposed to solvents, hydrocarbon solvents, pesticides, meat products, and sunlight, with risks increasing with more prolonged exposure duration. This was reported from socio-demographics, clinical history, and occupational exposure data. In this study, significant trends were observed for solvents (non-Hodgkin lymphoma and B-cell lymphoma), pesticides (non-Hodgkin lymphoma and T-cell lymphoma), meat products (non-Hodgkin lymphoma) and sunlight (B-cell lymphoma), with strong correlations In another study, join-point model analysis of childhood and adolescent leukemia incidence, mortality, and disability-adjusted life years from 1990 to 2019 revealed that countries with a middle socio-demographic index experienced the most significant decrease in incidence, with an average annual per cent change of -2.8%. Global disability-adjusted life years for male childhood leukemia were estimated at 155.98, while for females, it was 117.65. Despite the decline in incidence, mortality, and disability-adjusted life years over the past three decades, the burden of leukemia remains significant, especially in lower socio-demographic index regions Using a database of hematological malignancies from 1974 to 2003, authors in another study analyzed the incidence of acute lymphoblastic leukemia in Sardinia, Italy, and considered sex and age. Findings showed that the age- and sex-standardized incidence rate was 2 per 100,000, with an overall annual percent change of -1.4% over the study period. A downward trend was observed from 1974 to 1996, followed by an increase from 1996 to 2003, particularly in females, while male	Sarpa et al. (2024) Ciu et al. (2024) Broccia et al. (2024) Ciesielska et al. (2024) Rafeeinia et al. (2022) Karalexi et al. (2021) Pluth et al. (2019) Gunier et al. (2017) Malagodi et al. (2016) Bailey et al. (2014) Parrón et al. (2014)

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		incidence remained stable. In this study, the spatial analysis revealed clustering of acute lymphoblastic leukemia cases in the southwestern region among females, with urban residence posing a risk for younger individuals and proximity to industrial areas for those aged 25 and older. These findings indicate age-related differences in the etiology of acute lymphoblastic leukemia WHO reported that acute leukemia is the most common childhood cancer in 2020. Thus, the incidence is expected to remain stable globally, influenced by biological factors such as age, gender, and race. In this study, the peak incidence occurs in children aged 1-4 and 9-19 years, with boys more frequently diagnosed. This report reiterates that understanding risk factors associated with acute leukemia is crucial for reducing harmful exposures and disease risk Despite substantial epidemiological evidence linking pesticide exposure to adverse health outcomes like acute childhood leukemia, conclusions remain inconclusive due to varied exposure assessments and statistical challenges. A meta-analysis of 55 studies from over 30 countries involving 160,924 participants found that maternal environmental pesticide exposure during pregnancy is associated with increased leukemia risk, with a higher risk for acute lymphoblastic leukemia. Specific maternal exposures to herbicides and insecticides also showed significant associations. Notably, the risks for acute childhood leukemia were more considerable, especially for acute lymphoblastic leukemia and acute myeloid leukemia. Additionally, paternal pesticide exposure was linked to increased acute childhood leukemia risk. The findings indicate that maternal pesticide exposure during pregnancy heightens the risk of childhood leukemia This research examined the relationship between organochlorine pesticides and oxidative stress biomarkers in 109 leukemia patients and 109 healthy controls. The study found significantly higher serum concentrations of seven organochlorine derivatives in leukemia patients than controls. Additionally, malondialdehyde, nitric oxide, and protein carbonyl levels were higher. These findings suggest that organochlorine pesticides may contribute to leukemia development by disrupting the oxidant/antioxidant balance	
Parkinson's disease	Parkinson's disease is a progressive movement disorder characterized by progressive bradykinesia,	Parkinson's disease is a neurodegenerative disorder linked to the aggregation of misfolded proteins, including α-synuclein and parkin, and the formation of Lewy bodies. The authors of this review focused on how pesticides contribute to Parkinson's disease pathogenesis. It details the mechanistic pathways pesticides induce Parkinson's disease, such as mitochondrial dysfunction, oxidative stress, protein	Dorsey and Bloem (2024) Polaka et al. (2024) Urasa et al. (2024) Dorsey et al. (2024)

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	rigidity, rest tremor, and postural disturbances. Parkinson's disease is associated with pesticides and other environmental toxins, and chronic exposure to a common pesticide can reproduce Parkinson's disease's anatomical, neurochemical, behavioral and neuropathological features	aggregation, disrupted calcium homeostasis, altered dopamine levels, and genetic changes. Additionally, the review discusses specific classes of pesticides- fungicides, herbicides, organophosphates, organochlorides, and pyrethrins- along with their mechanisms of action in causing Parkinson's disease, supported by various case studies In this study, the authors investigated the relationship between pesticides and Parkinson's disease, emphasizing the roles of environmental factors and genetic predisposition. They helped identify specific pesticides that inhibit mitochondrial complex I and cause oxidative stress, linked to increased Parkinson's disease risk, with notable odds ratios for rotenone and paraquat. Their article also discussed other unsatisfactory explanations for the rise in Parkinson's disease cases, such as improved diagnostics and ageing populations, and highlights three major environmental toxicants-certain pesticides, trichloroethylene, and air pollution as significant contributors to Parkinson's disease. These toxicants are widespread and affect mitochondrial function. Ultimately, the authors suggest that much of Parkinson's disease is preventable, advocating for efforts to reduce exposure and make Parkinson's disease increasingly rare Long-term pesticide exposure is increasingly recognized as a risk factor for developing Parkinson's disease, especially in agricultural communities of Sub-Saharan Africa, where ageing populations face chronic exposure to neurotoxic pesticides that are restricted elsewhere. Interestingly, some semi-nomadic populations in Tanzania have a low prevalence of Parkinson's disease, potentially due to limited pesticide exposure. While pesticides have helped control famine and infectious diseases in the region, this presents a complex risk-benefit scenario that calls for affordable, non-neurotoxic alternatives. Additionally, the review proposes that inhaled environmental toxicants may trigger pathological changes in alpha-synuclein within the olfactory system, leading to a "*brain-first*" subtype of Lewy body disease. Conversely, ingested toxicants could contribute to a "*body-first*" subtype through the gut and autonomic pathways. These mechanisms could be tracked through symptoms, clinical assessments, and imaging. However, the proposed links have limitations, including unanswered questions about the role of the skin, microbiome, and ongoing exposures. Despite these gaps, the interaction between external factors and the body's systems may help unravel some of the mysteries surrounding Parkinson's disease and contribute to prevention strategies In another study, the authors evaluated the association between pesticide use and incidents of Parkinson's disease among 38,274 pesticide applicators and 27,836 of their spouses over 20 years within the Agricultural	Perrin et al. (2021) Shrestha et al. (2020) Cagac (2020) Baltazar et al. (2014) Tanner et al. (2011)

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		Health Study cohort. Researchers used self-reported data on using 50 specific pesticides and analyzed intensity-weighted lifetime days for applicators. A total of 373 applicators and 118 spouses reported being diagnosed with Parkinson's disease. Key findings included elevated Parkinson's disease risks associated with specific pesticides: Terbufos, Trifluralin, 2,4,5-T. Conversely, Diazinon and 2,4,5-TP were linked to reduced Parkinson's disease risk. The study found heterogeneity in associations based on history of head injury and the use of chemical-resistant gloves, with increased risk for those with a head injury and those not using gloves. Applicators in the highest intensity-weighted lifetime days category for Dichlorvos, Permethrin, and Benomyl also showed elevated Parkinson's disease risk. Overall, the study indicated increased Parkinson's disease risk associated with specific pesticides and suggests that individuals with a history of head injury may be more susceptible. At the same time, gloves could offer some protection The authors of this study aimed to identify potential risk factors for Parkinson's disease among elderly individuals living in rural Turkey. It included 72 consecutive Parkinson's disease patients referred to the Neurology Clinic at Iğdır State Hospital. Among the 72 patients, 68.1% consumed healthy water, with an average consumption duration of 20 years. The study found that levels of nitrates, sulphates, and heavy metals were significantly higher in healthy water compared to city network water. The findings suggest that consuming healthy water containing heavy metals and nitrates during early life may contribute to the development of Parkinson's disease in the elderly population of Iğdır province, Turkey In another study, which utilized the French National Health Insurance database to identify incident Parkinson's disease cases among farmers from 2010 to 2015, authors combined pesticide expenditure data with the agricultural census, and researchers computed pesticide expenditures for nine farming types across 3,571 French cantons in 2000. A total of 10,282 incident Parkinson's disease cases were identified. The analysis revealed that cantons with the highest pesticide expenditures for vineyards without designation of origin had a 16% higher Parkinson's disease incidence. This finding was statistically significant, particularly among men and older farmers. The incidence of Parkinson's disease increased notably with higher pesticide expenditures in these vineyards, especially those using high levels of fungicides. These results suggest that agricultural practices and pesticide usage in vineyards may contribute to Parkinson's disease risk, emphasizing the need for preventive measures to reduce exposure among farmers. The study also highlights the importance of considering farming type in pesticide and Parkinson's disease research and the	

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		potential of using pesticide expenditure data for exposure assessment	
Diabetes	Diabetes classification has primarily distinguished between type 1 diabetes, marked by near-complete insulin deficiency due to autoimmune destruction of pancreatic beta cells, and type 2 diabetes, characterized by insulin resistance. Diagnostic criteria rely on vague phenotypic traits and biomarkers with limited sensitivity, failing to address the diverse and complex nature of diabetes today. The global diabetes epidemic affects 1 in 11 adults, with type 2 diabetes rising due to lifestyle changes and obesity, while type 1 diabetes results from pancreatic cell destruction	Diabetes poses a significant global health burden, with cases projected to rise from 171 million in 2000 to at least 366 million by 2030. Exposure to organochlorine pesticides in food and soil may impact human health, and research suggests that simultaneous exposure to various persistent organic pollutants could contribute to common precursors of type 2 diabetes in the general population Epidemiological studies indicate that pesticide exposure is linked to an increased risk of diabetes, yet few have focused on mixed pesticide exposure, particularly in the elderly. This study quantified levels of 39 pesticides in a Chinese elderly population using gas chromatography-tandem mass spectrometry and explored their association with type 2 diabetes mellitus through various statistical models. Results revealed a significant association between pesticide exposure and type 2 diabetes mellitus, with *β*-Hexachlorocyclohexane and oxadiazon identified as major contributors, especially among older adults. The linear relationship underscores the urgent need for measures to control these harmful pesticides This cross-sectional study investigated the adverse effects of pesticide use on human health, focusing on non-communicable diseases through acetylcholinesterase and pesticide concentrations in blood samples from 353 participants with over 20 years of agricultural pesticide exposure. The study detected 26 pesticides, including 16 insecticides, three fungicides, and seven herbicides, with concentrations significantly differing between exposed and control groups. Acetylcholinesterase levels were significantly lower in case samples compared to controls, indicating a correlation with symptoms of non-communicable diseases such as Alzheimer’s, Parkinson’s, obesity, and diabetes. The findings suggest chronic pesticide exposure and reduced acetylcholinesterase levels are associated with increased health risks While pesticides have enhanced grain productivity and controlled vector-borne diseases, their widespread use has led to environmental residues that pose health risks to humans. This article reviews the presence of pesticides in the environment and their links to diabetes and glucose dysregulation based on epidemiological studies, alongside in vivo and in vitro evidence of their diabetogenic effects. Potential mechanisms include lipotoxicity, oxidative stress, inflammation, acetylcholine accumulation, and gut microbiota dysbiosis. It highlights significant gaps between laboratory research and epidemiological findings, calling for urgent studies on the effects of herbicides, current-use insecticides, low-dose pesticide exposure,	Chen et al. (2024) Kumar et al. (2023) Wei et al. (2023) Kampouraki et al. (2023) Balasubramanyam (2021) Tyagi et al. (2021) Velmurugan et al. (2020) Gounder and Ameer (2018) Rowley et al. (2017) Li et al. (2014) Sharf et al. (2013) Taylor et al. (2013)

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
DOI: http://dx.doi.org/10.15666/aeer/2302_32033229

		and combined exposures to multiple pesticides and other chemicals, particularly in children This study investigates the potential link between exposure to sulfonylureas, commonly used herbicides in agriculture, and the risk of developing type 2 diabetes. It presents three unrelated cases of agronomists who had used sulfonylureas for over three decades and subsequently developed type 2 diabetes. The research explores the association between occupational dermal and inhalation exposure to these herbicides and type 2 diabetes. The authors call for further studies with larger sample sizes to clarify this association and aid in developing prevention strategies Organochlorine pesticides are widely used synthetic pesticides known for their high toxicity, slow degradation, and potential for bioaccumulation, leading to increased contamination of drinking water. This study assessed the levels of organochlorine pesticides in drinking water and blood samples from the North Indian population, investigating their association with glucose intolerance, lipid metabolism, and insulin resistance risk factors for type 2 diabetes mellitus. A case-control study involved 390 participants who had consumed water from the same source for at least ten years. Results showed significantly higher levels of α-HCH, β-HCH, γ-HCH, p,p'-DDE, and o,p'-DDT in groundwater than tap water. Among participants consuming contaminated groundwater, 42% had type 2 diabetes, 38% were pre-diabetic, and 20% were normal. Higher organochlorine pesticide levels correlated with increased type 2 diabetes risk, suggesting that long-term exposure to contaminated groundwater may contribute to the development of type 2 diabetes This study investigates the association between co-accumulation of arsenic and organophosphate insecticides with the prevalence of diabetes and atherosclerosis in a rural Indian population. Analyzing data from a cross-sectional study involving 865 participants, researchers assessed clinical parameters, including HbA1c and carotid intima-media thickness, alongside urinary heavy metals and serum organophosphate residues. Multivariate regression analyses revealed that higher levels of both arsenic and total organophosphates were associated with increased prevalence of diabetes and atherosclerosis	
Asthma	Asthma is a common chronic inflammatory airway disease characterized by variable and recurring respiratory symptoms	Several studies indicate that pesticide exposure is linked to respiratory symptoms and potential asthma diagnoses, particularly in children. A meta-analysis of 38 studies involving 118,303 children found that pesticide exposure significantly increases the risk of asthma by 24%, wheezing by 34%, and lower respiratory tract infections by 79%. The analysis utilized various statistical models to assess effect sizes and heterogeneity among studies. These findings	Keleb et al. (2024) Veludo et al. (2024) Hughes et al. (2024) Van Horne et al. (2024) Ranaan et al.

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
DOI: http://dx.doi.org/10.15666/aeer/2302_32033229

	(wheezing, breathlessness, chest tightness and dry cough), airflow obstruction, and increased bronchial responsiveness	highlight the negative impact of pesticide exposure on respiratory health in children, emphasizing the need for preventive strategies and public health interventions Another study of 38 children in agricultural areas of South Africa investigated their exposure to organophosphate and pyrethroid insecticides during the 2018 spraying season. Urine, wristband, and dust samples were collected weekly to assess exposure variability. While chlorpyrifos showed strong temporal agreement in dust and moderate agreement in urine, correlations among the exposure matrices were generally weak. Notably, 21% of urine samples exceeded health-risk thresholds for organophosphate exposure, indicating significant short-term variability and the need for further investigation into exposure pathways and health risks In this study, the authors examined the combined effects of air pollution and pesticide exposure on respiratory health in 75 participants from Central California. It assessed associations between urinary leukotriene E4, a biomarker of respiratory inflammation, and various pollutants, including delicate particulate matter, ozone, nitrogen dioxide, and metabolites of organophosphate pesticides. Multiple regression models showed that increases in total pesticide metabolites were linked to higher urinary leukotriene E4 levels, particularly in winter. However, the analysis found no significant interactions with air pollutants, highlighting the need for further research on the health impacts of exposure mixtures The authors analyzed the impact of pesticide exposure on respiratory health in 708 children aged 5–12 in the Imperial Valley, near the US–Mexico border. Researchers categorized pesticide use near homes into none, low, and high exposure groups based on applications from 2016 to 2020. About 62% of children lived within 400 m of pesticide applications. Findings indicated high exposure was associated with a 10% higher prevalence of wheezing than those not exposed, with significant associations for specific pesticides like chlorpyrifos and glyphosate. The results suggest that proximity to pesticide applications may increase respiratory symptoms in children	(2015) Amaral (2014) Lötvall et al. (2011)

Accumulation of pesticides on food plants

Pesticide application may harm other non-target organisms, including earthworms, predators, pollinators, humans, fishes, amphibians, and birds, cause environmental damage through contaminating soil, water, and other plants, and increase resistance in the target pest organisms (Gill and Garg, 2014) (*Fig. 1*). The increased exposure includes incorrect application techniques and poorly maintained or inappropriate spraying equipment (Damalas and Eleftherohorinos, 2011).

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
DOI: http://dx.doi.org/10.15666/aeer/2302_32033229

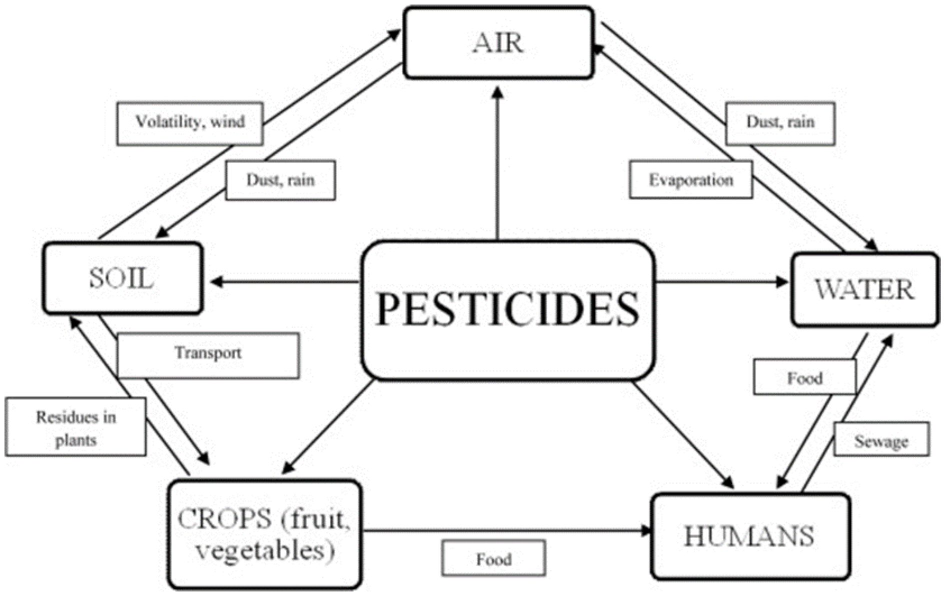

Figure 1. *The circulation of pesticides in nature (including crops) (Fenik et al., 2011)*

The widespread use of pesticides by farmers provides many possible sources of pesticides in the environment. Pesticides may reach the soil, water, and air during crop application because they do not always stay in the location where they are applied and cause contamination (Mwanja et al., 2017; Okoffo et al., 2017). Irresponsible handling, storage, and transport can also lead to contamination of the environment, and *Figure 1* shows the circulation of pesticides in nature.

After pesticides are applied to the crops, they interact with the plant surfaces, are exposed to environmental factors such as wind and sun and may be washed off during rainfall. The pesticide may be absorbed by the plant surface and enter the plant transport system or stay on the plant's surface. While still on the surface of the crop, the pesticide can undergo wash-off, volatilization, and photolysis, as well as chemical and microbial degradation (Keikotlhaile, 2011; Akan et al., 2013).

Pesticides move through the air during application and end up in other parts of the environment, such as soil or water, when sprayed on crops (Kim et al., 2017). When pesticides are applied to bodies of water for weed control, leaching from boat paint or runoff from soil may lead to the build-up of pesticides in water and contribute to air levels through evaporation (Khatri and Tyagi, 2015). The heavy use of pesticides may result in environmental problems like disturbance of the natural balance, widespread pest resistance and environmental pollution.

Pesticides may be broken down or degraded by the action of sunlight, water, other chemicals, or microorganisms, such as bacteria. This degradation process usually leads to the formation of less harmful breakdown products but, in some instances, can produce more toxic products (Tiryaki and Temur, 2010). The pesticide will resist degradation by any means and thus remain unchanged in the environment for long periods. The ones that are most rapidly broken down have the shortest time to move or have adverse effects on humans (Pandya et al., 2014).

Many substances that play important roles in modern society are persistent, organic, and halogenated and cause problems associated with bioaccumulation (Rodrigues et al., 2018). Many synthetic pesticides are difficult to break down. Persistent pesticides can

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
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move over long distances and build up in the environment, creating a more significant potential for adverse effects (Pandya et al., 2014). Persistence is affected by photodegradation, chemical degradation and microbial degradation. All three processes may contribute to the breakdown of a single pesticide (Tiryaki and Temur, 2010).

With the problem associated with bioaccumulation, many synthetic pesticides are difficult to break down (Gerber et al., 2016; Kim et al., 2017; Rodrigues et al., 2018). Once they enter the body of an organism, they are permanently stored in the body tissue (Gerber et al., 2016; Abubakar et al., 2015); they are transferred and subsequently integrated into the tissue of an organism when consumed by a predator. Organisms that are mostly consumed, like fish, will have increased concentrations of pesticides in the body of their prey because of pesticides stored in the ingested organisms (Deribe et al., 2013), which becomes the same issue with the vegetables that are mostly consumed.

Persistent organic pollutants (POPs) have been used in various agricultural and industrial commodities, resulting in vigorous deterioration of the environment and human health. POPs confirm their presence in various environmental compartments and the human body. India has prepared the National Implementation Plan (NIP) of the Stockholm Convention to address this global concern. Examined the distribution pattern of POPs in multi-compartment environments and human samples, meta-analysis of time trends in exposure levels to environment and humans, and cross-country comparison of POP contamination with China. The comparative meta-analysis showed similar high DDT and HCH exposure levels for humans and the environment in India and China. It was concluded that the Indian climate and human population are highly contaminated by DDTs and HCHs (Sharma et al., 2014).

The United Nations Environment Program’s (UNEP) governing council established an international negotiating committee that led to a global agreement to phase out the production, use, and release of POPs. The Stockholm Convention on POPs aims to protect human health and the environment from POPs by eliminating and reducing the worldwide production, use, and emission of POPs (FAO/WHO, 2015).

Resistance of pests is commonly managed through pesticide rotation, which involves alternating among pesticide classes with different modes of action to mitigate existing pest resistance. Degradation and sorption influence the persistence of pesticides in the soil. Depending on the chemical nature of pesticide, such processes directly control the transportation from soil to water and, in turn, to air and food. Breaking down organic substances, degradation involves interactions among microorganisms in the soil. Sorption affects the bioaccumulation of pesticides, which depend on soil organic matter. Weak organic acids are weakly sorbed by soil because of pH and mostly acidic structure. Sorbed chemicals are less accessible to microorganisms (Sparks and Nauen, 2015).

Pesticide use practices of vegetable farmers were investigated in major vegetable production zones of the humid tropics of Cameroon. It was found that weekly spray of pesticides was the most common practice; 40% of farmers sprayed insecticides and 28% sprayed fungicides. Farmers applied 0.5-9 L of pesticide per year, 10-49 kg, and 10 to 49 packets of chemicals depending on farm size. Ninety per cent of farmers used a knapsack sprayer, and 20% of farmers noticed that their health was affected by pesticides. About 25% of farmers store chemicals at home. Seventy-five per cent receive information about agricultural production from other farmers and have never received any training on pesticide use practices and health effects (Abang et al., 2013).

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
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Pesticides should be controlled at an optimum level due to their relative toxicity to human health (Łozowicka et al., 2013). The use of pesticides on vegetables must be documented by farmers and regulated by several government agencies worldwide. Farmers use pesticides during agricultural production to repel pests and diseases and produce high-quality vegetables quickly and with greater yields. The chemicals used in pesticides are regulated by the Environmental Protection Agency (EPA), the United States Department of Agriculture (USDA), and the Food and Drug Administration (FDA). These agencies monitor the types and amount of pesticides used on vegetable crops. Based on scientific evidence, these agencies have deemed the use of pesticides to be safe, and the residues that remain on food, if any, do not cause adverse health effects.

Minimizing health risks from pesticide-contaminated food: future research on trends and mitigation strategies

There are relatively few pesticides excess reduction tactics that have been proposed as safe and have a reasonable chance of success under various circumstances. These include monitoring pesticide residues in food after pesticide application, considering proper pesticide applications and restricting certain pesticides, the most difficult challenge in managing pesticide reduction in food.

In the current scenario, optimized use of pesticides is essential to reduce human impact on consuming contaminated food while reducing their effect on humans. This will minimize pesticide excess use and human health risk problems. This requires considering the rational use of pesticides and public knowledge about the risk of pesticides in food.

Humans should reduce their pesticide exposure because of their links to severe illnesses. This study found consistent evidence of serious health risks such as cancer, nervous system diseases, and reproductive problems in humans exposed to pesticides. Similarly, this study has linked exposure to pesticides to increased presence of neurological disorders, Parkinson’s disease, leukemia, cancer, asthma, and many more (Kim et al., 2017).

Guidelines for recommended application dosage and training

Recommended usages of pesticides, referred to as Good Agricultural Practices (GAPs), differ between Member States and are published by EFSA. GAPs include the recommended application dosage (mass per hectare) applied with a specific method on a crop or crop class together with other information, such as minimum pre-harvest intervals and application counts per season (Steingrimsdóttir et al., 2018). The pesticide manufacturer sets the dose to ensure an acceptable level of control, producing acceptable residue levels and maximizing returns per unit of formulated insecticide (Gill and Garg, 2014). Proper pesticide application through various production systems in vegetables (Khetsha et al., 2024; Moyo et al., 2024), including correct selection, accurate use of pesticides on agricultural commodities, and harvesting crops after the residues have washed off after application, can lead to reduced residues on produce consumers eat (Chen et al., 2011).

However, insufficient farmers’ training on pesticide use could increase the danger of using pesticides and the cost to human health. Accuracy and proper pesticide use, including continuous monitoring of food by markets, can help reduce environmental and human health hazards through improved training for farmers and awareness

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
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regarding the hazards of mishandling pesticides, farmers, markets and consumers linkage to improve farmers' knowledge on the use of pesticides to protect consumers from pesticide risks.

Monitoring

The information on pesticide residues in food commodities is essential and can be obtained through regular monitoring procedures. To protect consumers, most countries, especially those in the developed world, have established regulatory frameworks, effective inspection bodies, and analytical laboratories with International Organization for Standardization International Electrotechnical Commission accreditation (ISO/IEC 17025, 2017) to monitor pesticide residue levels in food (Mutengwe et al., 2016b; Jallow et al., 2017).

Pesticide residue analysis is tremendously important in determining the safety of certain pesticides. The evaluation of pesticide safety, scientific data, policy guidelines, and professional judgment must be incorporated and estimate whether a pesticide can be used beneficially within acceptable risk limits (Damalas and Eleftherohorinos, 2011). Pesticide residues in food do not exceed the maximum residue limits (MRLs) in order not to violate legislation (Mebdoua et al., 2017). The appropriate practices and application of pesticides, such as suitable spraying equipment, prevent the risks of pesticides (Damalas and Eleftherohorinos, 2011).

The EPA guideline brings together the requirements that regulate the responsible use of pesticides. For setting the tolerance process, EPA requires the submission of the following:

1. Pesticide residue chemistry data
2. Toxicity data
3. An analytical method to detect pesticides and their toxic metabolization in foods for which a tolerance is to be set

The EPA uses the first two sets of data to determine the likely level of dietary exposure to pesticide, the level of dietary exposure acceptable for human health, and the tolerance level of each food (EPA, 2017). The EPA considers the toxicity of pesticides and their breakdown products, how much pesticides are used, how often pesticides are applied, and how much pesticide residue remains in food when they are marketed. It ensures safe tolerance to food grown in the U.S. and imported food (EPA, 2017).

Annual reports have been prepared to summarize the results of the FDA pesticide residue monitoring program since 1987. The annual reports and data published from 1993 to the present. Each report is available in the format used when it was written (FDA, 2019). Without monitoring programs, they may encounter violative shipments of foods containing banned or restricted substances or residues exceeding legal limits, and they may be exported to countries with inadequate sampling programs and lower inspection rates, increasing risks to food safety (Sola et al., 2014).

The national monitoring programs create a database to help assess the levels of pesticide residue and foods containing banned or restricted substances or residues exceeding legal limits, and they may be exported to countries with inadequate sampling program levels of residue intake. In addition, it assesses human exposure to pesticide residues and ensures compliance with regulations (Jardim and Caldas, 2012). The pesticide residue monitoring program is a compliance program used by the FDA to

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monitor the level of pesticide chemical residues in domestic and imported foods. The FDA monitors a broad range of foods (almost 7,000 in fiscal year 2016) using a multi-residue method that analyses approximately 700 pesticide chemical residues in a single analysis (FDA, 2019).

Furthermore, monitoring pesticide residues also ensures compliance with good agricultural practices (GAP) in the use of pesticides. The farm must apply GAP practices to ensure food safety during the pre-production, production, harvest and post-harvest stages. Therefore, pesticides facilitate disease prevention and reduction beyond food and agricultural uses. Safety considerations on the use of pesticides for vegetable production and human health require adherence to proper application practices. In many cases, such practices also help protect the workers' environment and safety (FAO, 2016).

Markets that sell fresh produce to the public must adhere to pesticide tolerance limits, defined as the amount that may legally remain on food post-production. Department of Health agencies in South Africa perform relatively low testing on these vegetables. However, information remains limited on how these vegetables may expose SA consumers to elevated pesticide residues relative to domestically grown produce (Makhafola, 2010). The risk of pesticides on health can also be minimized with commercial processing operations applied on food, such as washing, peeling (Yang et al., 2017), frying and freezing (Keikotlhaile, 2011; Syed et al., 2014; Wanwimolruk et al., 2015).

Moreover, treating vegetables with acidic and alkaline solutions can effectively minimize pesticide residues (Ahmed et al., 2011). Surface pesticide residues were most effectively removed by sodium bicarbonate (baking soda; $NaHCO_3$) solution compared to tap water or Clorox bleach. Moreover, the negative impacts of pesticides can also be reduced by adequately educating farmers regarding pesticide usage, handling, and training (Syed et al., 2014). Pesticide-related laws should also be implemented strictly and amended to reduce the number of pesticide residues in food.

Proper pesticide use decreases these associated risks to a level deemed acceptable by pesticide regulatory agencies such as the Department of Agriculture Forestry and Fisheries and the WHO of South Africa. Considering registration, application costs, resistance, and toxicity-related impacts consistently. Hence, to align farmers' practices with sustainability goals, a screening framework is required that aids farmers and other relevant stakeholders in identifying the most sustainable pesticides under specific conditions. Such a framework must apply to various pesticide-crop combinations and settings (Steingrímsdorrír et al., 2018).

Conclusion

Although pesticides were manufactured to benefit humans through increased agricultural productivity by controlling pests and diseases, their adverse effects contradicted the benefits associated with their use. The risk caused by pesticides used in agriculture is associated with those applying pesticides and the consumers. The study highlights the adverse health effects of pesticide use on humans. The adverse effects not only affect humans but include persistent pesticides that cause a decline in untargeted organisms such as predators, pollinators, and earthworms, as well as water, soil, and air contamination. Pesticides have entered into food chains and humans. Some acute and chronic human illnesses have emerged due to polluted food, water, and air. Hence, the

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study suggests using pesticides to protect humans and the environment and reduce associated health risks. Continuous monitoring of pesticide residues in food, commercial methods to reduce excess residues in food, and rational use of pesticides could minimize pesticide applications. Further, public development and various extension programs that could educate and encourage farmers to adopt Good Agricultural Practices hold the key to reducing the harmful impact of pesticides on the environment and eventually to human health. In addition, the findings include reducing health risks from pesticide-contaminated food, promoting adherence to Good Agricultural Practices, and addressing limitations in the Fertilisers, Farm Feeds, Seeds and Remedies Act No. 36 of 1947 regarding pesticide safety in vegetable cultivation.

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