

Evaluation Of Pesticides Practices and In Silico Toxicity Profiling Of Pesticides Used In Tsafe Zamfara State, Nigeria

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Received on: August, 2025 Revised and Accepted on: September, 2025

Published on: October, 2025

ABSTRACT

some of the major difficulties such as time and cost in evaluating pesticides through traditional techniques (*in vitro* and *In vivo*). This study aims to identify the type of pesticides being used and to access attitudes towards pesticide use and safe handling and analyze using computational methods the toxicity and pharmacokinetic properties of commonly used pesticides in Tsafe. Data was gathered through interview of 206 respondents. Chemical library of chemicals from Tsafe was created and then screened using for ADMET, drug likeness and toxicity prediction was done using *insilico* methods (SwissADME). Using PyRx and PyMol, molecular docking was performed on the predicted target proteins acetylcholinesterase and MAP kinase for two of the pesticides in Tsafe. The results indicated that the pesticides used in Tsafe were chlorpyrifos, cypermethrin, deltamethrin, dichlorvos, paraquat, and glyphosate. According to the prediction analysis's results, all selected pesticides exhibited good human intestinal absorption. Dichlorvos and paraquat were able to cross the blood-brain barrier, and all of the pesticides were found to be highly toxic. The docking studies indicate that chlorpyrifos has a lower binding energy to acetylcholinesterase compared to donepezil, a strong cholinesterase inhibitor drug. Cypermethrin exhibits a higher binding energy for MAP kinase compared to methotrexate, a well-established anticancer agent. Six highly toxic pesticides were identified, with some capable of crossing the blood-brain barrier. Docking analysis showed strong protein interactions, indicating potential health risks.

Keywords: acetylcholinesterase, chlorpyrifos, cypermethrin, MAP kinase, PyRx, PyMol

1.0 INTRODUCTION

Pesticides are a group of chemicals applied to eliminate, repel, or control unwanted organisms (Garud *et al.*, 2024). Their purpose is to prevent, control, kill, or destroy insects, unwanted plants, rodents, fungi, or other harmful pests that damage crops. These compounds can be either naturally occurring or synthetically produced (Bilalo *et al.*, 2025). Pesticide development and use escalated during World War II (1939–1945). Widespread pesticide use in the 1940s led to increased food production (Khan *et al.*, 2025). From 1950 to 2000, global pesticide production grew at an approximate rate of 11% annually (Khan *et al.*, 2025). Some organochlorines like DDT, dieldrin and hexachlorobenzene have been used worldwide. These pesticides are known to cause harmful effects on both humans and the environment (Gawali *et al.*, 2023). Owing to their importance, almost all countries of the world use pesticides in one way or the other (Rajput *et al.*, 2022). The success of Africa's economy is to a large extent determined by agriculture, and it contributes greatly to the economy (Yami *et al.*, 2025). As a result, Africa contributes 2-4% of global market share of pesticides. It is expected that with increasing population in Africa, the food requirement will increase in a swift

pace over the coming 30 years, hence, the need for pesticides, will also increase (Simane *et al.*, 2024). The use of pesticide to improve the agricultural good yield by farmers has brought a great relief and availability of various foodstuff (Keleb *et al.*, 2024). Pesticide residues are toxic to both human and animals with serious short and long time effects such as immune and reproductive system damage, mutation and carcinogenic effect. (Onwudiegwu *et al.*, 2025). Despite known health risks and international bans, Nigerian farmers continue to use hazardous pesticides with little regard for safe handling practices or PPE (Bamiwuye *et al.*, 2023). These unsafe practices persist due to inadequate regulation, poor enforcement, and limited education, creating a pressing need to investigate pesticide usage patterns, safety awareness, and health implications among farming communities (Yami, 2025). There is a lack of comprehensive, up-to-date data on the types of pesticides currently in use across Nigeria, especially those banned by international bodies like the WHO. Additionally, limited research exists on farmers' awareness, attitudes, and practices regarding pesticide safety and the use of personal protective equipment (PPE), particularly in both urban and rural settings (Yami, 2025). Apart from been

exposed to agrochemicals in the farms and agrochemical shops, research indicates that about 30% of farm households repurpose agrochemical containers for other storage uses, including storing food items like seasonings and palm oil (Okafoagu, 2017; Akinneye *et al.*, 2023; Omohwovo *et al.*, 2024). The pesticides that are most typically used in Nigeria include, those in the class of organophosphates, organochlorines, bipyridium and pyrethroids (Raimi, 2021). Pesticide contamination resulting from the overuse of these classes of pesticides poses harm to both animals and human health (Zhang *et al.*, 2025). The present study thus, aims to evaluate pesticide usage and safety practices among farmers in Tsafe, Zamfara state, Nigeria. Also, it seeks to identify the types of pesticides currently in use and understand farmers' attitudes toward safe handling and personal protective equipment. Furthermore, computational methods was used to predict the toxicity, drug-likeness, and ADMET properties of these pesticides. Additionally, molecular docking was performed to assess the interaction of selected pesticides with key human proteins, highlighting potential health risks.

2.0 MATERIALS AND METHODS

Study area

Tsafe, is a local government in Zamfara State, Nigeria (11.9586° N, 6.9219° E), is a predominantly agrarian community where pesticide use is common among farmers. Data concerning the pesticides were gathered using a cross-sectional study using a total of two hundred and six (206) survey forms. The forms were targeted at pesticide sellers, farm workers, farmers, as well as agricultural professors and students in Tsafe, Zamfara State, Nigeria. The survey included questions on demographic details (age, education level, occupation, sex), pesticide usage info, banned pesticides, and health impacts of pesticide exposure Knowledge of protective equipment use in pesticide handling was also assessed.

2.1 Pesticide Information Repository

A list of pesticide used in Tsafe was developed using data generated from the survey. Additional data mining and literature surveys were done via PubChem Database as described by Kim *et al.* (2019).

2.2 *In silico* assessment of pesticides

Pesticides from the survey were assessed for toxicokinetic properties using the SwissADME webserver (<http://www.swissadme.ch/>). 3D SDF files for each pesticide from the information repository in section 2.1 above were downloaded from PubChem following the method of Kim *et al.* (2019). These files were also imported for analysis in Swiss Target Prediction webserver (Gfeller *et al.*, 2014).

2.3 Ligand selection/ structure retrieval from Pubchem ID

The Swiss Target Prediction webserver identified MAP kinase activator and acetylcholinesterase inhibitor as cypermethrin (pubchemID: 2912) and chlorpyrifos (pubchem ID: 2730) inhibitors respectively. The structure of these pesticides was retrieved from PubChem (<http://pubchem.ncbi.nlm.nih.gov>), also the control drug donepezil (PubChem CID: 3152) and methotrexate (PubChem CID: 126941) were also downloaded.

2.4 Acetylcholinesterase and MAP kinase as target proteins

The structure of target proteins: acetylcholinesterase (PDB ID: 5hfa) and MAP kinase (PDB ID:1leW) were downloaded from RSCB PDB as a PDB file. (<https://doi.org/10.2210/pdb5HFA/pdb> and <https://doi.org/10.2210/pdb1LEW/pdb>).

2.5 Preparation of Ligands (chlorpyrifos and cypermethrin) and Target Protein (acetylcholinesterase and MAP kinase)

Ligands were formatted to PDBQT using PyRx. Minimization of acetylcholinesterase and MAP kinase energies was performed in PyRx with mmff94 force field.. Water was deleted and polar hydrogens added to acetylcholinesterase and MAP kinase proteins. PyRx's Autodock Vina was used for molecular docking based on scoring functions. Exhaustive docking was conducted with a grid box centered at x=3.2604, y=9.5875, z=-13.7981. Grid size was 25 × 25 × 25 Å to define the binding area (George *et al.*, 2018). Docking diagrams were generated with PyMOL Molecular Graphics System (Version 1.2r3pre, Schrodinger, LLC). The top docking results were then analysed (Ritika *et al.*, 2021).

2.6 Data Analysis

Data analysis was performed using GraphPad Prism version 8.0. Descriptive methods were used to analyze respondents' socio-demographics and health symptoms. The percentage and scores of correct answers were used to assess the knowledge, attitude and practice of pesticide exposure.

3.0 RESULTS

3.1 Socio-demographic profile of study participants

Table 1 shows that 66 (32.04%) of the study participants had no formal schooling, 37 (17.96%) of the study participants had basic education, 51 (24.76%) had secondary school leaving certificate (SSCE), 35(16.99%) were university graduates and only17 (8.25%) of the study participants had Master's or doctoral level education (Figure 1) The age of respondents ranged from

21 – 70 years. 72(34.95%) were in the age range of 21-30 years, 74(35.92%) fell between the ages of 31-40 years, 32(15.53%) were aged between 41-50 years, 14(6.79%) had of ages 51-60 years while the remaining 14(6.79%) of the study participants were between the ages 61-70 years (Figure 2). Majority of the respondents 125 (60.68%) were males, and 81 (39.32%) were females (Figure 3). majority of the respondents 69 (33.49) were farmers and 65(31.55) were traders (Figure 4).

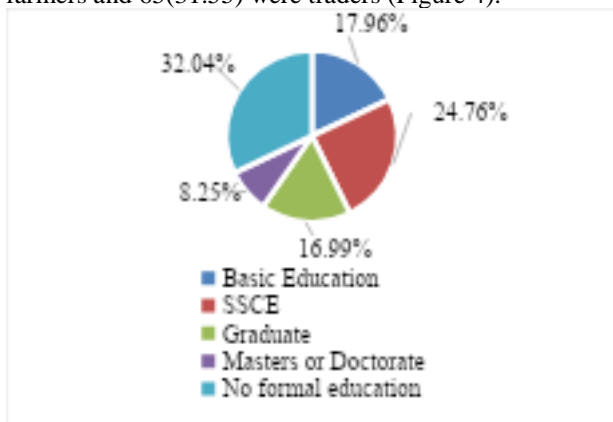


Figure 1: Educational Background of Respondents

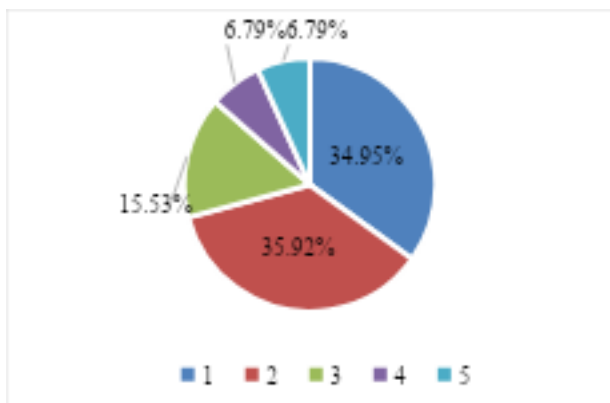


Figure 2: Age range of respondents

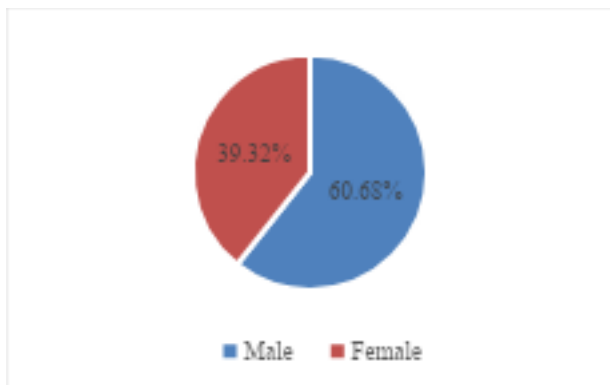


Figure 3: Gender of Respondents

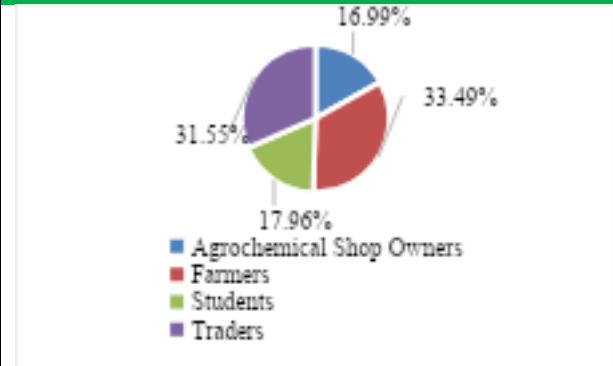


Figure 4: Occupation of Respondents

3.2 Awareness of toxic agricultural chemicals

Some of the respondents 97 (47.09%) were aware of the agrochemicals and were aware of different names or labels of the pesticide used. However, most of them 109(52.91%) were not aware of agrochemicals (Figure 5). High proportion of respondents 55(26.69%) used dichlorvos. Other respondents used paraquat 5(2.43%), cypermethrin 7(3.39%), glyphosate 6(2.91%), deltamethrin 4(1.94%), chlorpyrifos 4(1.94%) and sulfuric acid 16(7.77%) (Figure 6).

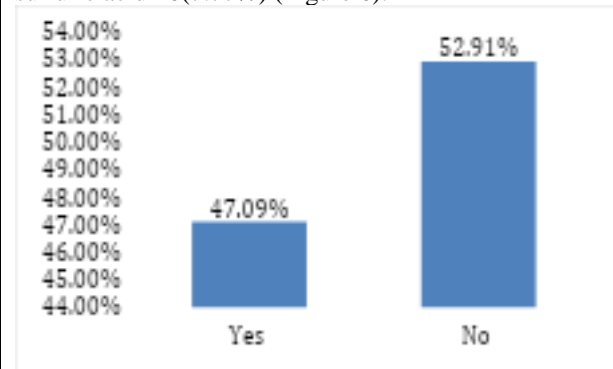


Figure 5: Awareness on the use of pesticides

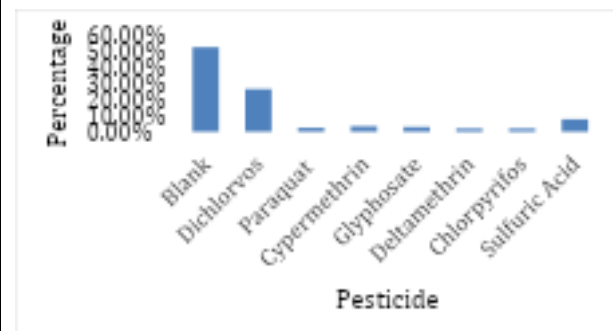


Figure 6: Awareness on the name pesticides used.

3.3 Farmers' attitudes on pesticide use and awareness of poisoning symptoms

Most of the study participants 158(76.69%) don't take safety measures with pesticide use while 48(23.30%)

took protective measures. Most of the study participants 64(31.07) were familiar with the harmful effects of agrochemicals but the remaining 142(68.93%) were not aware of harmful effect of toxic agrochemicals. The signs noticed by respondents after using pesticides are:

respiratory distress 10(4.85%), skin irritation 8(3.88%), headache 7(3.39%), coughing 8(3.88%), diarrhea 5(2.43%), vomiting 7(3.39%), dizziness 5(2.43%), abdominal pain 2(0.97%), eye bruising 3(1.45%) and death 2(0.97%) (Table 1)

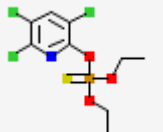
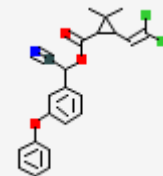
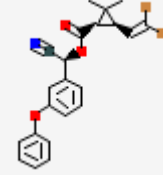
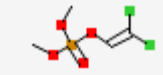
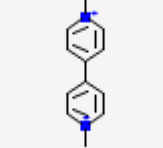
Table 1: Participants Knowledge and Attitude Towards Pesticides Use



Characteristic	Summary	Percentage
Do you employ any personal safety measures when using pesticides?	Yes	48(23.30%)
	No	158(76.69%)
Are you aware of any adverse health impacts	Yes	64(31.07%)
	No	142(68.93%)
Which one? If answer above is yes	Respiratory distress	10(4.854%)
	skin irritation	8(3.883%)
	Headache	7(3.398%)
	Coughing	8(3.883%)
	Diarrhoea	5(2.427%)
	Vomiting	7(3.398%)
	Dizziness	5(2.427%)
	abdominal pain	2(0.970%)
	eye bruising	3(1.456%)
	Death	2(0.970%)
	Poison	3(1.456%)
	Blank	146(70.874%)
Are these effect seen immediately.	Yes	92(44.66%)
	No	114(55.34%)
If yes, when	Within 24hours	10(4.85%)
	Few day	5(2.43%)
	Month	2(0.97%)
	Week after	2(0.97%)
	Few minute	1(0.49%)
	Blank	187(90.78%)

3.4 Chemical catalogue of pesticides from survey data in Tsafe, Zamfara State

The chemical catalogue (library) of pesticides from Tsafe, Zamfara state revealed that chlorpyrifos (Pub chem ID 2730) is an insecticide which is acutely toxic and constitutes environmental hazard. Cypermethrin (Pub chem ID of 2912) is an irritant which constitutes health and environmental hazard. Other pesticides in Tsafe are acutely toxic and poses environmental hazard. (Table 2).

Table 2: Chemical Catalogue of Pesticides From Survey Data in Tsafe, Zamfara State

Chemical identifier	Pub chem CID	Types	Chemical safety	Structure	Oral LD ₅₀
Chlorpyrifos	2730	Insecticide	Acute toxic Environmental Hazard		95 to 270 mg/ kg in rats
Cypermethrin	2912	Acaricide	Irritant Health Environmental Hazard		Doses of 250 mg/kg with corn oil or 4123 mg/kg with water in rat experiments
Deltamethrin	40585	Insecticide	Acute toxic Environmental Hazard		Toxicity in rats varies from 30 mg/kg with oil to above 5000 mg/kg with water vehicle
Dichlorvos	3039	Insecticide	Acute toxic Environmental Hazard		50 to 150 mg kg ⁻¹ in rats
Paraquat	15938	Herbicide	Acute toxic Environmental Hazard		110-150 mg/kg dosage range in rats

Glyphosate	3496	Herbicide	Acute toxic Hazard	Environmental		4320 mg/kg daily dose in rat experiment
Sulfuric Acid	1118	Fertilizer	Acute toxic Hazard	Environmental		5000 mg/kg in rats

3.5 ADMET properties of pesticides from Tsafe, Zamfara State

Pesticides from the survey were analysed for toxicokinetic parameters: absorption, distribution, metabolism, excretion (Table 3). SwissADME revealed that glyphosate and paraquat had high intestinal absorption of > 30%. Of all the pesticides from the survey in Tsafe, dichlorvos had the highest blood brain barrier penetration. Chlorpyrifos, dichlorvos, paraquat and glyphosate were predicted to be non CYP3A inhibitors while cypermethrin and deltamethrin were estimated to be inhibitors. Dichlorvos and paraquat were projected to be carcinogenic.

Table 3: ADMET Properties of Pesticides from Tsafe, Zamfara State.

Pesticide	Absorption	Distribution	Metabolism	Excretion	Toxicity
Chlorpyrifos	HIA ---	BBB	CYP1A2 inhibitor CYP3A4 Non inhibitor	4.259	High rat oral toxicity Eye irritation, Respiratory toxicity, Skin sensitization.
Cypermethrin	HIA ---	BBB -	CYP1A2 inhibitor CYP3A4 inhibitor	3.950	High rat oral acute toxicity, Respiratory toxicity.
Deltamethrin	HIA --	BBB-	CYP1A2 inhibitor CYP3A4 inhibitor	0.904	High Rat oral acute toxicity, Respiratory toxicity.
Dichlorvos	HIA ---	BBB +++	CYP1A2 non inhibitor CYP3A4 non inhibitor	3.324	Carcinogenicity, Respiratory toxicity, HHT,
Paraquat	HIA +++	BBB+	CYP1A2 non inhibitor CYP3A4 non inhibitor	12.583	Eye irritation, High rat oral acute toxicity, Carcinogenicity, Eye irritation High rat oral acute toxicity, Respiratory toxicity
Glyphosate	HIA +++	BBB-	CYP1A2 non inhibitor CYP3A4 non inhibitor	1.897	Eye irritation Corrosiveness,

Key: HIA Human intestinal absorption; HHT Human hepatotoxicity; CL-Clearance CL High > 15ml/min/kg Moderate 5-15 ml/min/kg Low < 5ml/min/kg. BBB-blood brain barrier.: BBB – no BBB penetration, BBB+ low BBB penetration, BBB +++ high, BBB ++ Moderate

3.6 Proteins targeted by pesticides according to Swiss Target Prediction

Target proteins of pesticides as revealed by Swiss target prediction showed that chlorpyrifos and cypermethrin targeted acetylcholinesterase enzyme. cypermethrin targeted MAPkinase P38 alpha while deltamethrin targeted serine/threonine-protein kinase PIMI. There was no target protein predicted for paraquat (Table 4).

Table 4: Proteins Targeted By Pesticides According To Swiss Target Prediction

PESTICIDE	TARGET PROTEIN	UNIPROT ID	CHEMBL ID
Chlorpyrifos	Acetylcholinesterase	P22303	CHEMBL220
Cypermethrin	MAP kinase p38 alpha	Q16539	CHEMBL260
Deltamethrin	Serine/threonine-protein kinase PIMI	P11309	CHEMBL2147
Dichlorvos	Acetylcholinesterase	P22303	CHEMBL220
Paraquat	No target predicted		
Glyphosate	Matrix metalloproteinase 3	P08254	CHEMBL283

4.7 Drug-likeness and physicochemical characteristics

Only deltamethrin violated the Lipinski's rule. Of all the pesticides, paraquat had the lowest number rotatable bonds with no hydrogen bond acceptors. Furthermore, the number of hydrogen bond acceptors and donors was highest for glyphosate. (Table 5).

Table 5: Drug likeness and physicochemical characteristics of pesticides from repository

Drug likeness/physicochemical properties	Chlorpyrifos	Cypermethrin	Deltamethrin	Dichlorvos	Paraquat	Glyphosate
Lipinski	Yes; 0 violation	Yes; 0 violation	Yes; violation: MW>500	1	Yes; 0 violation	Yes; 0 violation
Number of rotatable bonds	6	7	7	4	1	4
Number of hydrogen bond acceptors	4	4	4	4	0	6
Number hydrogen bond donors	0	0	0	0	0	4

3.8 Molecular Docking

The binding energy of chlorpyrifos to acetylcholinesterase is lower (-6.8kcal/mol) compared to binding energy of donepezil-acetylcholinesterase (-8.5kcal/mol). Also, Cypermethrin binds to MAPkinase with a binding energy of -8.4 kcal/mol. This binding energy is lower (more favorable) compared to methotrexate binding to MAPkinase (Table 6).

Table 6: Molecular Docking Scores of Chlorpyrifos and Cypermethrin with Their Binding Energy

Complex	Binding energy (kcal/mol)	rmsd/ub	rmsd/lb
Chlorpyrifos-Acetylcholinesterase	-6.8	3.899	1.923
Donepezil-acetylcholinesterase	-8.5	4.600	1.873
Cypermethrin-Mapkinase	-8.4	5.327	3.416
Methotrexate-Mapkinase	-7.8	2.423	1.681

Chlorpyrifos-acetylcholinesterase binding (in 2D/3D representations) showed significant interplay of van der Waals, attractive charge, and conventional hydrogen bond interactions Carbon Hydrogen Bond, Pi-sigma, Pi-Pi stacked, Alkyl, Pi-Alkyl interaction compared to the binding modes of donepezil to acetylcholinesterase (Figures 7,8, 9, and 10).

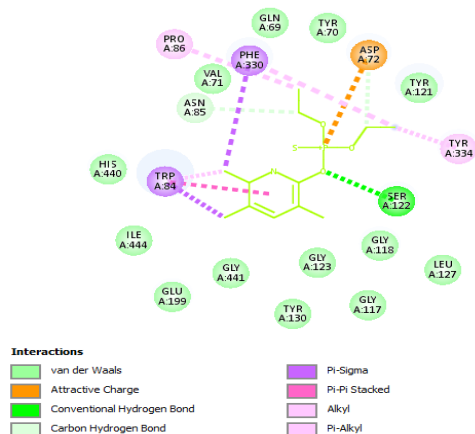


Figure 7: Chlorpyrifos-acetylcholinesterase binding (PDB ID: 2730) (2D representation)

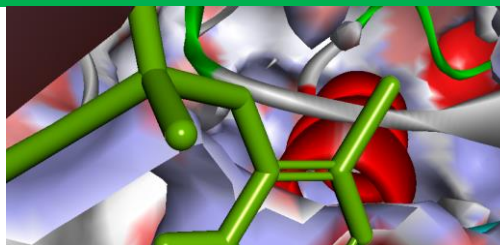


Figure 8: Chlorpyrifos-acetylcholinesterase binding (PDB ID: 2730) (3D representation) (PDB ID: 2730)

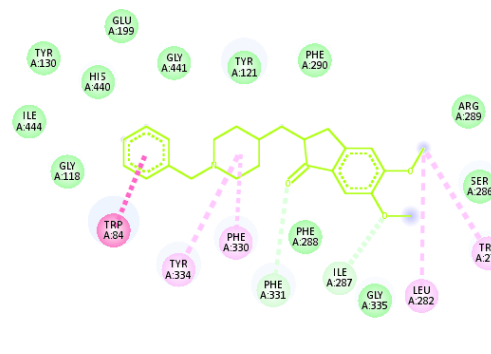


Figure 9: Donepezil-acetylcholinesterase binding (PDB ID: 3152) (2D representation)

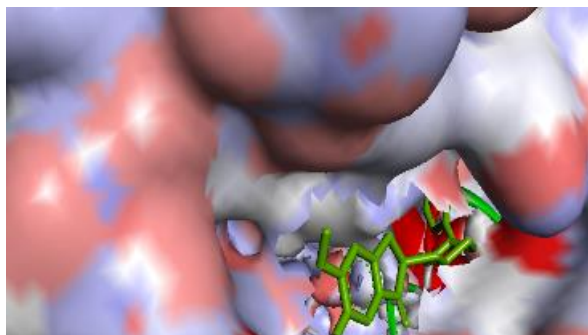


Figure 10: Donepezil-acetylcholinesterase binding (PDB ID: 3152) (3D representation)

Cypermethrin-Mapkinase binding (in 2D/3D representations) showed substantial interactions including van der Waals, hydrogen bonds, and several Pi-based (Pi-cation, Pi-anion, Pi-alkyl) and alkyl interactions (Figures 11 and 12).

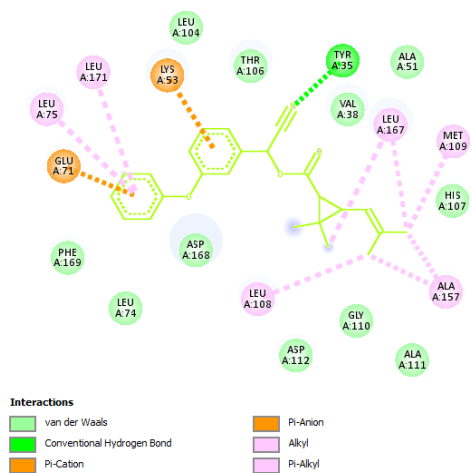


Figure 11: Cypermethrin-MAPkinase binding (PDB ID: 2912) (2D representation)

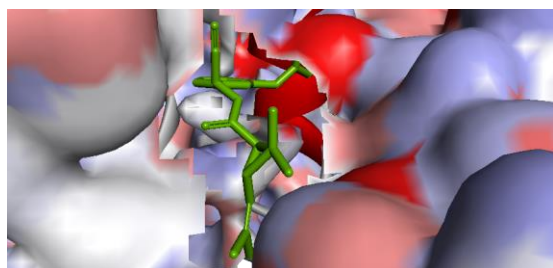


Figure 12: Cypermethrin-MAPkinase binding (PDB ID: 2912) (3D representation)

4.0 DISCUSSION

The present study was done on respondents of Tsafe local government of Zamfara State located in northwest of Nigeria. Despite Tsafe been an agrarian community the present study is the first study that was undertaken to assess understanding, attitudes toward, and practices of pesticide usage. Because pesticide use and farming is not limited to farmers alone in this community other members of the community were included in this study. Majority of the study participants had no formal education which agrees with the result of similar studies in the third world (Samuel *et al.*, 2015; Desye *et al.*, 2024). Most of the study participants fall within the category of 21 to 40 years. This implies that post primary school certificate most of them find means of livelihood as they may not be able to further their education. How much education farmers have can affect their understanding and ability to grasp some critical operations and basic understanding of safe pesticide use. This means that education enhances farmers' ability to comprehend critical operations, such as proper pesticide handling, understanding toxicity levels, and using personal protective equipment. The lack of formal education, as seen in many rural farming communities, often correlates with poor safety practices,

increasing health and environmental risks. (Desye *et al.*, 2024). Furthermore, from the demographic characteristics most of the respondents were males. This is expected because been an area located in the northern part of Nigeria, more males will be available to respond to the questionnaire than females due to religious and cultural beliefs. Most of the respondents were farmers, this may be because Tsafe is an agrarian community. The timing of symptom onset, with 44.66% of respondents experiencing symptoms within 24 hours (Table 1), supports the computational prediction of rapid absorption and systemic impact, since all pesticides demonstrated good human intestinal absorption in ADMET analysis (Table 3). The understanding or awareness of study participants towards the types of pesticides used was also evaluated during the survey Most of them (52.1%) did not know that pesticides were toxic. A few of the study participants knew the pesticide names they used, whereas the did not. This reveals a low level of awareness regarding pesticide use in the study area. This lack of awareness and poor protective behavior towards pesticide use directly correlates with the *in silico* findings, which showed that all identified pesticides: chlorpyrifos, cypermethrin, deltamethrin, dichlorvos, paraquat, and glyphosate were highly toxic, with some capable of crossing the blood-brain barrier (e.g., dichlorvos and paraquat). Mengistu *et al.* (2024) in their study revealed that that 18–26% of farmers in African regions used basic protective equipment like masks, gloves, or boots when handling pesticides. Alarmingly, 51% stored pesticides in their living rooms, and 26% reused empty containers for other purposes, reflecting widespread unsafe practices and limited knowledge of pesticide toxicity. In the present study, with limited awareness of pesticide toxicity on the part of participants they are more likely to throw empty pesticide containers on the ground outside the farm, reuse or burn used pesticide containers. Re-using pesticide containers is a pathway for serious non-workplace human exposure as residues persist after washing. Other researchers have found widespread reuse of pesticide containers for various household activities (Desye *et al.*, 2024). Most of the participants in this study do not wear personal protective equipment while handling pesticides, this may be responsible for reported signs of toxicity related to acetylcholinesterase inhibition by some of them. This agrees with the work of Rostami *et al.* (2019). This lack of awareness has also been reported by Yami (2025) in a study involving 1,556 tomato farmers from Northern Nigeria. They found that participant in their study reused pesticide containers, and violated pesticide safety guidelines. The study emphasized that training and market regulation significantly improved safe pesticide handling, yet such interventions remain scarce

Most of the chemicals screened in Tsafe, Zamfara state had Low rat oral LD₅₀ and are considered hazardous (Table 2). This increases the probability of toxicity signs of these pesticides in humans and animals (Ritika *et al.*, 2021). Furthermore, the symptoms such as respiratory distress, skin irritation, headache, and dizziness reported by respondents in this study correlates with the predicted toxicological profiles of these chemicals. For instance, chlorpyrifos showed strong binding to acetylcholinesterase, a key enzyme in the nervous system, suggesting potential for neurotoxicity, which matches the neurological symptoms observed in the field.

In Nigeria, pesticides banned by NAFDAC are still found in markets. In developed countries, bio-pesticides and other less toxic alternatives to chemical pesticides are being sold for use. Other means of pest control such as like cultural control, the use of resistant genotypes, and physico-mechanical control along with chemical control should be encouraged (Khan *et al.*, 2023). Anticipating mammalian toxicity of agrochemical pesticides or their metabolites is a key part of agrochemical development (Ball *et al.*, 2025). *In silico* tests for toxicity rely on data-driven methods needing large datasets and effective descriptors given the complexity of pesticide chemistry, organisms, agriculture, and climate factors (Yang *et al.*, 2024). Absorption, distribution, metabolism, excretion and metabolism are toxicokinetic parameters necessary to understand how a compound behaves *in vivo*. In this work, pesticides data generated from the survey were evaluated for their physicochemical, toxicokinetics and drug-likeness using the SwissADME. *In silico* analysis is cheaper, less time consuming and gives relevant preliminary information before *in vitro* and *in vivo* tests (Tharik and Meyyanatha, 2022).

Human intestinal absorption (HIA), was employed to determine absorption (Table 3). The predicted HIA data of the pesticides from the questionnaire which showed that paraquat and glyphosate have high HIA ($\geq 30\%$) whereas the others were low implying predicted HIA below 30% (Table 3). Blood Brain Barrier (BBB) permeability was employed to evaluate the distribution of the pesticides. paraquat had the highest BBB penetration. The BBB is an important structure in the nervous system. The BBB controls the movement of drugs, pesticides, nutrients, and cells into and out of the brain from the blood. (Malkiewicz *et al.*, 2019). It also participates in the

transport of cellular waste and toxins out of the brain to the bloodstream. Of all the pesticides in Tsafe, Zamfara, only dichlorvos and paraquat had high BBB penetration. Metabolism simulation using computational methods was predicted using Swiss ADME according to the inhibition of primary CYP enzymes of the P450 superfamily. This enzymes include: CYP1A2, CYP2C19, CYP2C9, CYP2D6 and CYP3A4 (Domínguez-Villa *et al.*, 2021). All the pesticides used in Tsafe, Zamfara state were modelled to be non-inhibitors of CYP1A2 except cypermethrin, deltamethrin and chlorpyrifos (Table 5). CYP1A2 enzymes are important determinants in the therapeutic efficacy and toxicity of chemicals/drugs. The interactions at the CYP1A2 level are often the cause of pronounced drug-drug interactions it is well known that the inhibition and induction of the CYP enzymes are a probable major cause of interactions involving drugs and pesticides (Klomp *et al.*, 2020). Contact with any of these three pesticides may result in adverse CYP450 pesticide-drug interactions in both humans and animals. (Nayara *et al.*, 2020). The predicted toxicological end points of the pesticides are organ toxicity (hepatotoxicity), carcinogenicity, irritation, respiratory toxicity, skin sensitization and eye irritation and skin sensitization. Dichlorvos was anticipated to be harmful to the liver. Also, paraquat and dichlorvos were predicted to have carcinogenic effects. Acute toxicity predictions showed that all the pesticides are fetal except for glyphosate with low oral acute toxicity (LD₅₀), there for are categorized as harmful toxic pesticides. Two important pharmacological indicators in renal drug excretion of drugs or chemicals are fraction of drug excreted unchanged in the urine and renal clearance (Domínguez-Villa *et al.*, 2021). All the pesticide from the questionnaire survey had a low clearance threshold of less than 5 ml/min/kg based on SwissADME projection except paraquat. Low clearance means they are not readily cleared from the system hence are very toxic. In this work, pesticide toxicity levels from the questionnaire study were predicted based on human hepato toxicity (HHT) and oral rat acute toxicity (LD₅₀). The pesticides with high oral rat acute toxicity meaning are less toxic compared to those with low oral acute toxicity. The liver has a major role in detoxification and metabolism of pesticides and drugs. Liver damage disrupts normal metabolic processes and can lead to liver failure. (Triakha and Ray, 2025). Dichlorvos was predicted to potentially cause hepatotoxicity by Swiss ADME. Computational analysis can identify probable targets of drugs/pesticides. (Domínguez-Villa *et al.*, 2021). Ligand-based methods predict protein targets of compounds effectively. This is useful for drug discovery and antidote production via molecular docking. Deltamethrin was the only pesticide of eight violating Lipinski's oral bioavailability rule. (Table 5), This shows that pesticides

have drug-like molecular properties. Lipinski's rule is important in *in silico* studies this is because low permeability or poor absorption for a given compounds results when it violates one of Lipinski's rule of five. Deltamethrin was predicted mildly toxic with low HIA from drug likeness analysis. The other pesticides that did not violate Lipinski's rule will be extremely toxic because they are predicted to have a high HIA.

Chlorpyrifos acts by inhibiting acetylcholinesterase same as the target protein predicted by Swiss target prediction. Molecular docking was performed with acetylcholinesterase against chlorpyrifos and compared with donepezil, a drug for Alzheimer's, strongly inhibits acetylcholinesterase the binding affinity of donepezil to acetylcholinesterase was greater than that of dichlorvos. The highest binding energy (-8.2kcal/mol) attributed to chemical interactions of donepezil at the receptor's active site are thought to cause this effect (Figure 3). Also, the target protein MAPkinase (A protein that couples extracellular signals to intracellular processes governing growth, proliferation, migration, and apoptosis) Cypermethrin-MAPkinase interaction had greater binding affinity than methotrexate-MAPkinase. Cypermethrin's strong binding energy (-8.4kcal/mol) is thought to be due to its chemical interactions in the receptor's active site.

5.0 CONCLUSION

The study reveals a disconnect between pesticide toxicity and farmer awareness in Tsafe, where unsafe practices and banned chemicals remain prevalent. *In silico* analysis shows the high toxicity and health risks of commonly used pesticides, reinforcing the urgency for policy reform, farmer education, and safer pest control strategies. Addressing these gaps is essential to protect both human health and environmental sustainability in Nigeria's agricultural communities

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