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Insilico Toxicological Assessment and Molecular Docking Investigations of Pesticides Employed used in Sokoto State, Nigeria

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ABSTRACT

Many pesticides are associated with severe health implications, and end users are at risk. *In silico* studies make it easier to quickly perform toxicity *for* chemicals. The present work was aimed at conducting a survey in Sokoto, Sokoto State Nigeria, to determine the types of pesticides used, and attitudes towards their safe handling. 242 respondents from Sokoto, Sokoto State, were interviewed to collect the information using an indept field survey. Chemical library of pesticides in the study area were developed and the pesticides from the survey were investigated *in-silico* for absorption, distribution, metabolism, excretion and toxicity (ADMET), drug likeness and toxicity prediction using SwissADME webserver, the target proteins were also predicted using Swiss Target prediction. Molecular docking of the pesticide against their predicted target proteins was done using PyRx and PyMol. Acetylcholinesterase and MAP kinase was selected as target protein for dichlorvos and cypermethrin. The results obtained showed that atrazine, bifenthrin, cypermethrin, dichlorvos, glyphosate, lindane, paraquat and pendimethaline were the pesticides used in Sokoto, Sokoto State. The docking studies show that dichlorvos have lower binding affinity to acetylcholinesterase compared to galantamine a known potent (Alzheimer's disease) cholinesterase inhibitor drug. The study revealed that all the selected pesticides have good oral bioavailability as they did not violate the Lipinski Rule of five. In conclusion, all the pesticides used in Sokoto were classified as highly toxic to human health.

Keywords: ADMET screening, molecular docking, pesticides, toxicology

1.0 INTRODUCTION

Pesticides are a class of chemicals that are used world wide as weed killers, insecticides, fungicides, rodenticides, molluscides, nematicides and plant growth regulators to control weeds, pests and diseases in crops and animals (Ma Laura *et al.,* 2013). Records show that there is an increase in global pesticides production of about 11% every year. Interestingly, only 1% of those are employed to effective in the control of insect pests on target plants (Tang *et al*., 2021). Pesticides contamination has subsequently produced environmental pollution and adverse effects on human and animal health (Tudi *et al.*, 2021).The use of pesticide causes severe health consequences because of their bio magnification and persistence in nature (Anket *et al.,* 2019). In developed countries, pesticides are largely used as chemical tool to manage weeds due to high labour cost in these areas (Anket *et al.,* 2019). Similarly, in Nigeria, not only does it reduce labour costs but pesticides have been established as necessary tools in preventing production losses and increasing crop yield (Isah *et al*., 2020). Pesticides are also necessary in agricultural production, many farmers have utilized them to manage weeds and insect in agricultural production and there have been notable increases in food production (Tudi *et al*., 2021)**.** Pesticides disrupt activities of the nervous and reproductive system of the target pests as well as non-targets. In animals and humans, the three major route of exposure to pesticide are skin, oral ingestion, and inhalation. The resultant effect from exposure may be acute or chronic (Tang *et al*.,2021). In humans and animals, the body system is designed to eliminate toxic substances. But if ingestion of pesticides overwhelms the detoxification capacity and excretion system then it may be absorbed by the circulatory system and can undergo various chemical ligand interaction in the body. Thus, it can be linked with various deadliest diseases, including cancer, hormone disruption, respiratory diseases like asthma, allergies, and hypersensitivity (Ritika *et al*., 2021). Recently concerns have been raised about knowledge, handling practices, and associated health impacts of pesticides in Nigeria. Predicting the *in silico* pharmacokinetics and toxicity of commonly used pesticides in the area would further shed more light on the dangers associated with the use of these pesticides. Limited understanding hampers targeted interventions and policy formulations. Additionally, molecular interactions between common pesticides and target proteins remain largely unexplored (Tang *et al*., 2021). With a survey of Sokoto State, Nigeria, this study was aimed at determining the knowledge, attitude and practices towards the use of pesticides in Sokoto and the *in silico* prediction of toxicokinetics of most commonly used pesticides in this area.

2.0 MATERIALS AND METHODS

Information regarding the pesticides was gotten with the aid of a cross sectional survey using a total of 242 questionnaire. The questionnaire was targeted at pesticide vendors, agricultural workers, farmers and also agricultural professors and students in Sokoto, Sokoto state. The questionnaire included questions concerning demography: age, educational qualification, occupation and sex, information about the pesticides used, prohibited pesticides and the health implication of exposure to pesticides (self-reported toxicity symptoms associated with pesticides use, including the Knowledge of the acute and chronic toxicity of pesticides. Knowledge on the use of protective during preparation and application of pesticides was also ascertained.

Study Area

Sokoto is one of the seven states that form the North West geographical zone in Nigeria. It is bordered to the North by the Niger republic, Zamfara state to the east, Kebbi state to the south and west. It is situated in the savannah on the temperature of 44ºC annually (Kpeama *et al.,* 2019). Most of the Sokoto farmers used pesticides for weed control, they also use selective herbicide to control weed species, leaving the desired crop relatively unharmed (Kpeama *et al.,* 2019).

2.1 Pesticide Library

The information generated from the questionnaire study was used to prepare a list of pesticides. Data mining, literature surveys were conducted using Pub-Chem Database as described by (Kim *et al*., 2019).

2.2 *In silico* Pesticide Screening

The pesticides gotten from the survey were evaluated for toxicokinetic parameters such as bioavailability, brain penetration, oral absorption, carcinogenicity, and human intestinal absorption properties of the active compounds were determined using swissaddme webserver (http://www.swissadme.ch/).For each of these pesticide from the compound library generated, 3D SDF format was downloaded from the PubChem database (Kim et al., 2019) and was imported into "Swiss Target Prediction" webserver (Xiaoying *et al*., 2023).

2.3 **Selection of Ligand**

Dichlorvos (pubchem ID: 3039) and cypermethrin (pubchemID: 2912) were recognized as acetylcholinesterase inhibitors and MAP kinase activator, respectively, based on Swiss Target Prediction" webserver. The structure of these pesticides were downloaded from PubChem (http://pubchem.ncbi.nlm.nih.gov). The control drug galantamine (PubChem CID: 9651) and methotrexate (PubChem CID: 126941) were also downloaded.

2.4 Selection of Target Protein (acetylcholinesterase and MAP kinase)

The crystal structure of the target protein acetylcholinesterase (PDB ID: 5hfa) database https://doi.org/10.2210/pdb5HFA/pdb and MAP kinase (PDB ID:1leW)https://doi.org/10.2210/pdb1LEW/pdb were downloaded from RSCB PDB and saved as PDB format.

2.5 Preparation of Ligands (Dichlorvos and Cypermethrin) and Target Protein (Acetylcholinesterase and MAP kinase)

The ligands were prepared by converting them to PDBQT file format using PyRx. Energy of the acetylcholinesterase and MAP kinase was minimized based on the optimization algorithm at force field set at mmff94 on PyRx, water was removed and Polar hydrogens were added to acetylcholinesterase and MAP Kinase.Molecular docking studies was conducted using PYPx Autodock Vina based on scoring functions. Exhaustive search docking was done and the grid box resolution was centered at 3.2604X, 9.5875X-13.7981 along the x, y, and z axes, respectively at grid dimensions of 25 × 25 × 25 A to define the binding site (George *et al*., 2018). The docking diagram were obtained using PyMOL Molecular Graphics System, Version 1.2r3pre, Schrodinger, LLC. The best docked results were interpreted.

2.6 Statistical Analysis

The data were analyzed using Graph pad prism version 8.0. Descriptive analysis was used to analyze the socio demographic data of the respondents, health symptoms, the percentage and scores of correct answers in knowledge, attitude and practice on pesticide exposure.

3.0 RESULTS

3.1 Socio Demographic Characteristics of Respondents

The questionnaire revealed that majority of the respondents 50(20.7%) had primary education, 102(42.1%) completed secondary school having only secondary school certificate, while 16(6.6%) had post graduate education, 30(12.4%) were university graduate, while 44(18.2%) had no formal education (Figure 1).

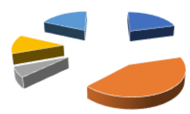

Figure 1: Educational background of the respondents

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Statistical interpretation revealed that most of the respondents154 (63.6%) were within the age group of 21-30 years. The distribution of age of respondents is as shown in Figure 2

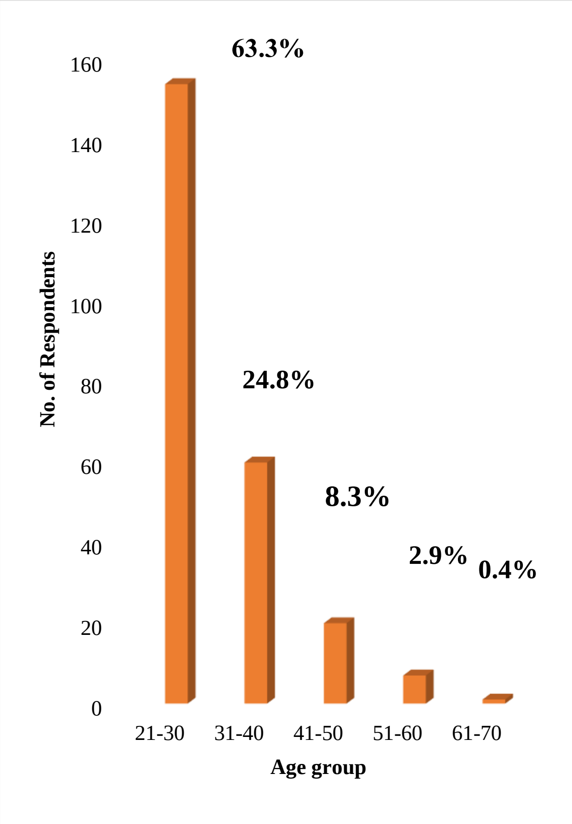

Figure 2: Age group of respondents

Analysis of the questionnaire revealed that 146 of the total242were males and the remaining 96 respondents were females (Figure 3)

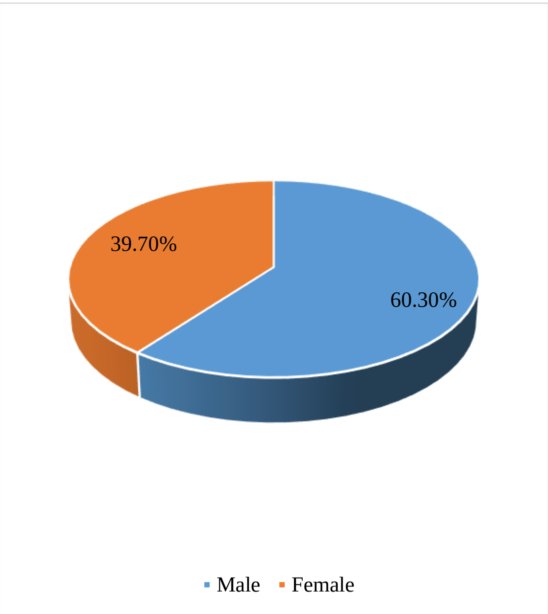

Figure 3: Sex of respondents

Figure 4 shows that 151 (62.4%) of the respondents were students, 21(8.7%), farmers, 58(24%) agrochemical users and 22(9.1%) agrochemical shop owners.

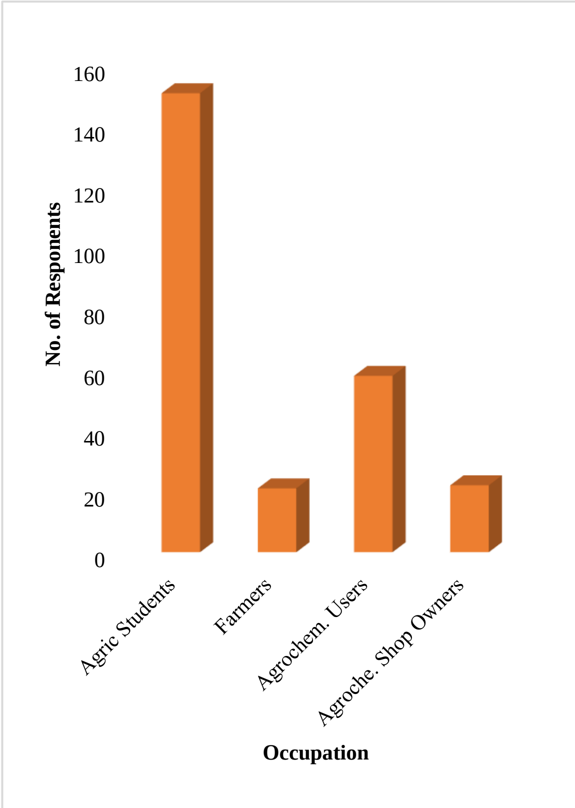

Figure 4: Occupation of Respondents

3.2 Awareness about Pesticides

Table 1 shows the level of awareness about pesticide. A good proportion of the respondents 163(67.4%) had awareness on different pesticides and knew their different names while 79(32.6%) did not have any knowledge about pesticides and their toxicity. Most of the respondents 56(23.1%) use dichlorvos while atrazine and aluminum phosphate, 3(1.2%) and 3(1.2%) were the least used, respectively. 110(45.5%) of the respondents use agrochemicals while 132(54.5%) of the respondents did not use them. Most of the respondents 155 (64%) were aware of harmful toxic effect of agrochemicals. Respiratory distress 28 (1.6%) and skin irritation 25(10.3%), respectively, were the signs mentioned by most of the respondents (Table 1).

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Table 1: Awareness On The Use Of Pesticides

Awareness of Pesticide Toxicity	Description	Percentage
Are you aware of any Pesticide	Yes	163 (67.4%)
	No	79 (32.6%)
If yes, which	Blank	71(29.3%)
	Dichlorvos	56(23.1%)
	Lindane	8(3.3%)
	Atrazine	3(1.2%)
	Paraquate	15(6.2%)
	Zinc phosphate	10(4.1%)
	Bifenthrin	16(6.6%)
	Aluminium phosphate	3(1.2%)
	Cypermethrin	33(13.6%)
	Glyphosate	8(3.3%)
Do you use them?	Pendimethaline	5(2.1%)
	Yes	110(45.5%)
Are you aware of any harmful health effects	No	132(54.5%)
	Yes	155(64.0%)
If yes, which	No	87(36 %)
	Poisoning	15(6.2%)
	Asthma	2(0.8%)
	Carcinogenic effect	1(0.4%)
	Damage immune system	4(1.7%)
	Stomach ache	11(4.5%)
	Diarrhea	4(1.7%)
	Nausea	8(3.3%)
	Respiratory distress	28(1.6%)
	Skin irritation	25(10.3%)
	Coughing	13(5.4%)
	Eye irritation	7(2.9%)
	Dizziness	10(4.1%)
	Headache	5(2.1%)
	Painful urination	7(2.9%)
	Hand swelling	6(4.1%)
	Sneezing	10(4.1%)
	Neurological Disorder	4(1.7%)
Are these effects noticed		5(2.1%)
immediately?	Yes	98(40.5%)
	No	144(59.5%)
If yes, when		
	1-2hours	10(4.1%)
	Few days	14(5.8%)
	Old age	12(5%)
	1-3years	20(8.3%)

3.3 Attitude of Respondents Towards the use of Pesticides

Majority of the respondents 100(41.3%) take protective measures when using pesticides, while 142(54.5%) of the respondents did not use any protective measures (Table 2).

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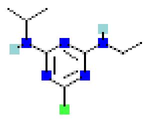
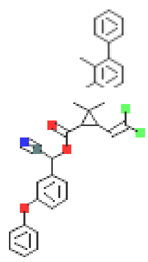
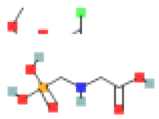
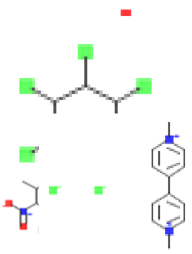
Table 2: Attitude of respondents towards the use of pesticides

Variable	Description	Percentage
Do you take any protective measure?	Yes No	100(41.3%) 142(54.5%)

3.4 Chemical Library of Pesticides

The chemical library of the pesticides from the survey in Sokoto showed that most of the pesticides under chemical safety constitute health and environmental hazard. Aluminium phosphate and glyphosate were classified as corrosive (Table 3).

Table 3: Chemical Library Of Pesticides From The Survey

Chemical name	PubChem CID	Types	Chemical Safety	Chemical Structure of drug	Oral LD50
Atrazine	2256	Herbicide	Health hazard, environmental hazard.		3090mg/kg
Bifenthrin	64442842	Insecticide, ascariside	Acute toxic, health hazard, environmental hazard.		54mg/kg in male rat. 70mg/kg in female rats.
Cypermethrin	2912	Insecticide	Environmental hazard, irritant.		250mg/kg
Dichlovors	3039	Insecticide, pesticide	Environmental hazard, irritant, acute toxicity.		70.4-250mg/kg
Glyphosate	3496	Herbicide	Environmental hazard, corrosive		5600mg/kg
Aluminium phosphate	64655	Pesticide	Irritant, corrosive		2000mg/kg
Lindane	727	Insecticide	Acute toxic, health hazard, environmental hazard.		60-250mg/kg
Paraquat	15939	Herbicide	Acute toxic, health hazard, environmental hazard.		110-150mg|Kg
Zinc Phosphate	24519	Rodenticide	Environmental hazard.		12-35mg/kg
Pendimethaline	38479	Herbicide	Health hazard, environmental hazard.		1050mg/kg in females 1250 mg/kg in male.

3.5 ADMET Properties of Pesticides from Swiss Target Prediction

All the pesticides gotten from the survey were evaluated for toxicokinetic parameters such as absorption, distribution, metabolism, excretion, and toxicity (Table 4). Atrazine and paraquat had high HIA (≥ 30%), dichlorvos had the highest blood brain barrier penetration. All the pesticides were predicted to be non CYP3A inhibitors except cypermethrin. Atrazine, dichlorvos and pendimethaline bifenthrin were predicted to be hepatotoxic. Also, atrazine, dichlorvos and paraquat were predicted to be carcinogenic (Table 4).

Table 4: ADMET properties of pesticide from the questionnaire study HIA Human intestinal absorption, HHT Human hepatotoxicity, CL High > 15ml/min/kg , Moderate 5-15 ml/min/kg, Low < 5ml/min/kgBBB – no BBB penetration, BBB+ low BBB penetration, BBB ++ moderate BBB penatration, BBB +++ high BBB penetration.

Pesticide	Absorption	Distribution	Metabolism	Excretion	Toxicity
Atrazine	HIA +++	BBB ++	CYP1A2 non inhibitor CYP3A4 non inhibitor	8.851	Skin sensitization, Carcinogenicity Respiratory HHT[
Bifenthrin	HIA---	BBB +	CYP1A2 non inhibitor CYP3A4 non inhibitor	Cl 8.006	HHT High rat acute oral toxicity
Cypermethr in	HIA ---	BBB -	CYP1A2 inhibitor CYP3A4 inhibitor	3.950	High Rat Oral Acute Toxicity Respiratory Toxicity
Dichlorvos	HIA ---	BBB +++	CYP1A2 non inhibitor CYP3A4 non inhibitor	3.324	Carcinogenicity Respiratory Toxicity HHT Eye Irritation High Rat Oral Acute Toxicity
Glyphosate	HIA +++	BBB-	CYP1A2 non inhibitor CYP3A4 non inhibitor	1.897	High Eye Irritation High Eye Corrosiveness Respiratory Toxicity Low Rat Oral Acute toxicity
Lindane	HIA ---	BBB-	CYP1A2 non inhibitor CYP3A4 non inhibitor	5.340	Eye Irritation Resp. Toxicity
Paraquat	HIA +++	BBB+	CYP1A2 non inhibitor CYP3A4 non inhibitor	12.583	Carcinogenicity, Eye irritation High Rat oral acute toxicity Respiratory toxicity
Pendimetha line	HIA--	BBB++	CYP1A2 inhibitor CYP3A4 non inhibitor	4.090	Skin Sensitization, Carcinogenicity, Respiratory toxicity HHT+

3.6 Target Proteins of Pesticides by Swiss Target Prediction

Target proteins of pesticide based on Swiss target prediction showed that most of the pesticide had different target proteins as shown in Table 5. Only paraquat had no target predicted (Table 5)

Table 5: Target proteins of pesticides based on Swiss target prediction

PESTICIDE	TARGET PROTEIN	UNIPROT ID	CHENBL ID
Atrazine	Phosphodiesterase 4A	P27815	CHEMBL254
Bifenthrin	Cannabinoid receptor 1	P21554	CHEMBL218
Cypermethrin	MAP kinase p38 alpha	Q16539	CHEMBL260
Dichlorvos	Acetylcholinesterase	P22303	CHEMBL220
Glyphosate	Matrix metalloproteinase 3	P08254	CHEMBL283
Lindane	GABA receptor beta-3 subunit	P28472	CHEMBL1847
Paraquat	No target predicted		
Pendimethaline	Nitric oxide synthase, inducible	P35228	CHEMBL4481

3.7 Drug Likeness and Physicochemical Properties of the Pesticides

Drug likeness and physicochemical properties of the pesticides from Swiss addme showed that none of the pesticides violated Lipinskis rule.Bifenthrin and cypermethrin had the highest number of rotatable bonds. Glyphosate had the highest number of hydrogen bond acceptors and donors (Table 6).

Table 6: Drug likeness and physicochemical properties of pesticides from compound library.

Drug likeness/physicochemical properties	Atrazine	Bifenthrin	Cypermethrin	Dichlorvos	Glyphosate	Lindane	Paraquat	Pendimethaline
Lipinski	Yes No violation	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Number of rotatable bonds	4	7	7	4	4	0	1	6
Number of hydrogen bond acceptors	3	5	4	4	6	0	0	4
Number of hydrogen bond donors	2	0	0	0	4	0	0	1

3.8 Molecular Docking

Docking scores of dichlorvos to acetylcholinesterase interaction revealed a lower binding energy compared to galantamine to acetylcholinesterase. However, cypermethrin to Mapkinase shows a higher binding energy compared to methotrexate to Mapkinase (Table 7)

Table 7: Docking scores of dichlorvos and cypermethrine with their RMSD values

Complex	Binding energy	rmsd/ub	rmsd/lb
Dichlorvos- Acetylcholinesterase	-5.2	3.455	2.738
Galantamine-Acetylcholinesterase	-9.2	5.689	2.882
Cypermethrin- Mapkinase	-8.4	5.327	3.416
Methotrexate-Mapkinase	-8.0	-7.8	2.423

Two- and three-dimensional representations of dichlorvos to acetylcholinesterase showed significant interactions such as Vander Waals, conventional hydrogen bond, carbon hydrogen bond, alkyl, and pi-alkyl compared to galantamine- acetylcholinesterase (Figures 5, 6, 7 and 8).

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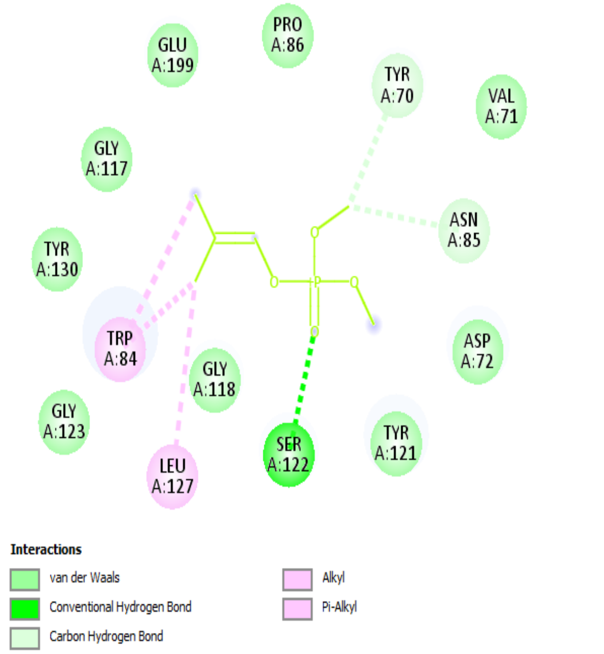

Figure 5: Two-dimensional representation of the binding modes of dichlorvos to acetylcholinesterase (PDB ID:3039).

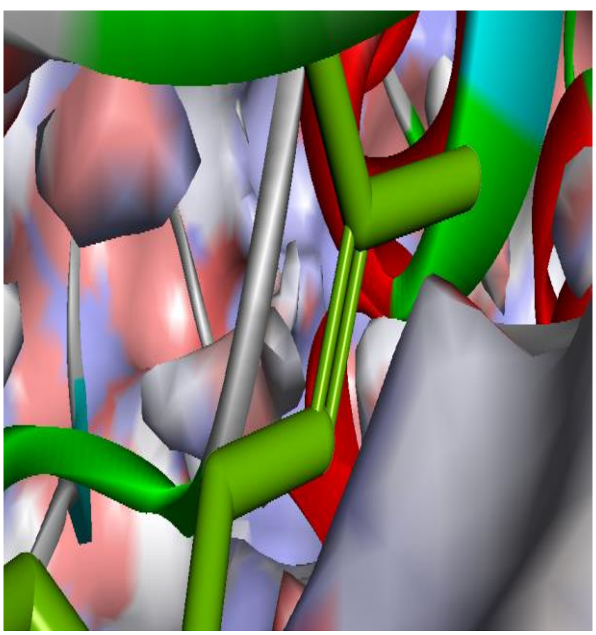

Figure 6: Three-dimensional representation of the binding modes of dichlorvos to acetylcholinesterase (PDB ID: 3039).

Two- and three-dimensional representation of the binding modes of galantamine to acetylcholinesterase showed the following interactions of Vander Waals, conventional hydrogen bond, pi- pi stacked, and pi-alkyl.

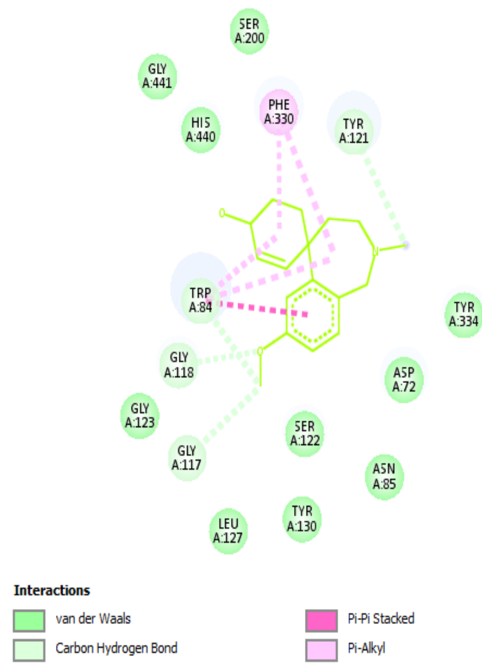

Figure 7: Two-dimensional representation of the binding modes of galantamine to acetylcholinesterase (PDBID: 9651)

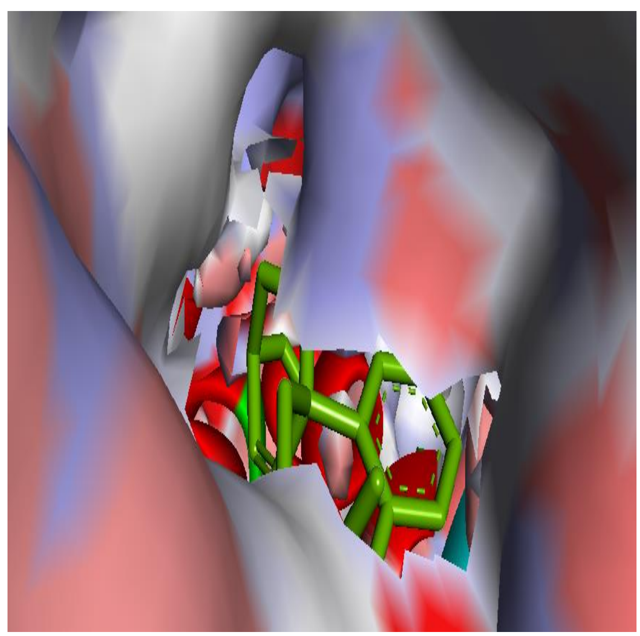

Figure 8: Three-dimensional representation of the binding modes of galantamine to acetylcholinesterase (PDB ID: 9651)

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Two and three-dimensional representation of the binding modes of cypermethrin to Map kinase showed interactions with Vander Waals, conventional hydrogen bond, carbon hydrogen bond, pi-cation, pi- anion, alkyl and pi –alkyl (Figures 9 and 10).

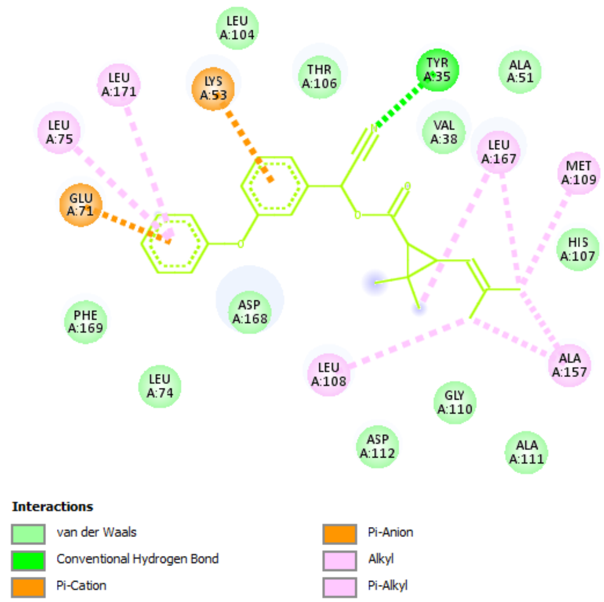

Figure 9: Two-dimensional representation of the binding modes of cypermethrin to Map kinase (PDB ID: 2912)

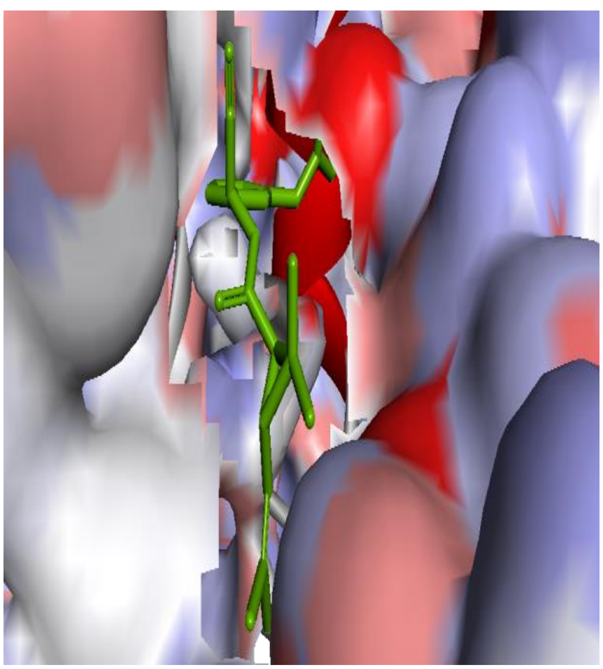

Figure 10: Three-dimensional representation of the binding modes of cypermethrin to Map kinase (PDB ID:2912).

4.0 DISCUSSION

The present work was conducted in Sokoto, Sokoto State Nigeria to evaluate the knowledge attitude and practices of respondents towards pesticides. On the level of education, majority of the respondents were illiterates, accounting for 42.10% of the sampled population. It is logical to say formal education makes it easier for better understanding of the effects of pesticides on health and environment (Khan et al., 2023, Jun *et al*., 2023, Constantine *et al*., 2023). Most of the respondents were males and students studying agriculture. This may be because of the intensive nature of farming hence we have more males than females. This agrees with the research by Ayanlade *et al*. (2023), that Fadama farming in Nigeria is dominated by males. On the awareness of towards the types of pesticides used, most of the respondents (67.4%) were aware that pesticides were toxic and knew the names of the pesticides they used while majority of them did not. This shows the level of awareness on pesticide usage in the study area is high. Implying that with proper awareness on pesticide toxicity on the part of the respondents they were more likely to properly dispose empty pesticide containers on the ground outside the farm and will be very careful on their reuse for domestic purposes. The re-use of pesticide containers represents a route of serious non-occupational human exposure, as several traces of pesticides could still be found in the containers even after washing and rinsing (Okoffo *et al*., 2016). Furthermore, many of the farmers reported signs of acetylcholinesterase inhibition which is one of the mechanisms of toxicity of some organophosphate pesticides. This shows that organophosphates is the most used pesticide in the study area.

The use of appropriate protective gear and safe protective practices during when using pesticides are necessary to reduce occupational exposure to pesticides. Majority of the respondents (54.5% did not take protective measures when using pesticides. With the high record of improper handling of pesticides by both pesticide sellers and users there is need for training/continuing education (Rostami *et al*., 2019). Many pesticides are associated with severe health implications, and end users are at risk. All the chemicals screened in Sokoto, Sokoto state, Nigeria had high LD_{50} and are considered hazardous (Table 3). This may pose a problem because it increases the probability of adverse effects caused by these pesticide (Ritika *et al.*, 2021). In developed countries alternative to toxic pesticides such as bio pesticides are currently been marketed for use. This problem may be solved by educating the farmers an alternative pest management and control strategy, such as integrated pest management (IPM), which may be helpful in minimizing the number and volume of pesticide applications by combing several control measures against pest (Khan *et al*., 2023). Due to

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the high cost of *in vivo* toxicity tests, an increasing number of *in silico* models have been designed to estimate the toxicity of pesticides to various organisms (Yang *et al.*, 2024). These models follow a data-driven approach, which necessitates sizable datasets and effective descriptors due to the intricate physicochemical and structural properties of pesticides, complex organism systems, agricultural practices, and varying climatic conditions (Yang *et al*., 2024). Human intestinal absorption (HIA), blood-brain barrier (BBB) permeability, identification of the sites of cytochrome P450 enzyme metabolism, acting as a substrate or receptor of P-gp, drug-induced liver damage, cardiotoxicity, and cytotoxicity are datasets that help drug-likeness research. *In silico* analysis reduce cost, time and aid *in vivo* correlations (Tharik & Meyyanatha, 2022). Absorption was predicted using intestinal human absorption (HIA). Paraquat, atrazine and glyphosate were predicted to have high intestinal absorption > 30%. Distribution was predicted using blood–brain barrier (BBB) permeability. In the present study, only cypermethrin, glyphosate and lindane were not predicted to cross the BBB. The BBB is an important structure that separates the central nervous system (CNS) from the peripheral tissue. In order to maintain homeostasis in the CNS, the BBB controls the transfer of material, nutrients and cells from the blood to the brain and from the brain to the blood (Małkiewicz *et al.*, 2019).

In silico metabolism was predicted using SwissADME according to inhibition of the main cytochromes (CYP) of the P450 superfamily. These enzymes include: CYP1A2, CYP2C19, CYP2C9, CYP2D6 and CYP3A4 (Domínguez-Villa *et al*., 2021). Cytochrome P450 (CYP450) enzymes are a family of heme proteins that participate in phase I metabolism reactions (oxidation, reduction, and hydrolysis). These enzymes are mainly expressed in the liver, and they underlie the metabolism of various endogenous and exogenous compounds, including drugs and pesticides. In the present study, cypermethrin, paraquat and pendimethaline are inhibitors of CYP1A2. Exposure to any of these three pesticides, may cause undesirable CYP450 pesticide-drug interactions in humans and animals (Nayara *et al*., 2020). Excretion of xenobiotics is due to hepatic and renal clearance is related to bioavailability (Domínguez-Villa, *et al*., 2021). Cypermethrin, dichlorvos, glyphosate and pendimethaline had low clearance of less than 5ml/min/kg based on Swiss addme prediction. The toxicity levels of the pesticides from the questionnaire study in this work were predicted using human hepatotocity (HHT) and oral rat acute toxicity (LD_{50}).

The liver plays a critical role in detoxification and the metabolism of pesticides and drugs. Liver suffering from damage always disrupts normal metabolism and could even lead to liver failure (Benić, *et al*., 2022). Swiss ADME predicted that atrazine, bifenthrin, dichlorvos and pendimethaline could cause hepatotoxicity. Computational tools can be used to estimate most probable targets of drugs or pesticides (Domínguez-Villa *et al*., 2021). Ligand-based target prediction has shown high-quality performance and the ability to perfectly predict the right protein targets of compounds. This is important as this proteins can be targeted for molecular docking in drug discovery and new antidote production. Out of the eight pesticides, none of them violated Lipinski's rule of five for oral availability (Table 6), demonstrating that the pesticides have drug-like molecular nature It is important to note that Lipinski's rule of five is essential 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. Since none of these pesticides violated the rule most of them will be highly toxic as they would have high intestinal absorption and permeability. The absence of violations of Lipinskis rules, suggests that these pesticides would display well-behaved absorption or permeability. In the present study, the target protein acetylcholinesterase was docked against dichlorvos and compared with galantamine (an Alzheimer drug) which is a potent inhibitor of acetylcholinesterase. Galantamine-acetylcholinesterase showed a better binding affinity when compared with dichlorvos-acetylcholinesterase Also, the target protein MAPkinase was docked against cypermethrin and compared with methotrexate an anticancer agent. Cypermethrin showed a better binding affinity when compared with methotrexate-MAPkinase.

5.0 CONCLUSION

The investigation conducted in Sokoto State revealed the use of several pesticides including atrazine, bifenthrin, cypermethrin, dichlorvos, glyphosate, lindane, paraquat, and pendimethaline. Notably, docking studies indicated that dichlorvos exhibited a lower binding affinity to acetylcholinesterase in comparison to galantamine, a well-known potent cholinesterase inhibitor drug. Additionally, cypermethrin demonstrated a higher binding affinity compared to Methotrexate, a recognized anticancer agent. These findings underscore the need for further research to explore antioxidants, compounds, or agents targeting proteins identified by the Swiss Target database. Such investigations are essential for developing novel and cost-effective methods to mitigate pesticide toxicity, necessitating subsequent *in vitro* and *in vivo* experiments for validation.

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