Current Trends in Biotechnology and Pharmacy
Vol. 18 (Supplementry Issue 4A) 138 - 151, November 2024, ISSN 0973-8916 (Print), 2230-7303 (Online)
10.5530/ctbp.2024.4s.11

A Study on Toxicity Mechanisms of Xenobiotics Using Network Pharmacology Approach

Shreenidhi K S, Vigneshwar R, Sai Rahul Sv, Jothi Murugan S, Maline M, Sujata Roy*, and Vijaya Geetha*

Department of Biotechnology, Rajalakshmi Engineering College (Autonomous), Thandalam, Chennai 602105, Tamil Nadu, India

*Corresponding author: sujataroy@rajalakshmi.edu.in

Abstract

In recent years, modern medicine has grown exponentially. Many drugs are being developed and reused for different diseases. Although these drugs help cure these diseases, there are some side effects on the human body. The most affected organ in the human body. Is the liver these side effects in the liver were studied using marine toxicity studies using several species of marine organisms. This study aimed to investigate the toxicity mechanisms of xenobiotics using a network pharmacological approach. Xenobiotics are chemicals that are foreign to an organism and exposure to them can cause adverse health effects. Network pharmacology is a systems-level approach that integrates information about interactions between drugs, proteins, and biological pathways. The study involved using publicly available data to construct a human xenobiotic-protein interaction network using sites such as PubChem, PharmMapper, the KEGG/PANTHER pathway, and the Cytoscape software. The network was analysed to identify key proteins and pathways involved in xenobiotic toxicity. The study also explores the potential for repurposing existing drugs to minimize xenobiotic toxicity. Study results reveal several key targets and pathways involved in xenobiotic toxicity, including oxidative stress, inflammation, and apoptosis. The study also identified several existing drugs that could potentially be repurposed to minimize xenobiotic toxicity. Taken together, this study provides insight into the mechanisms underlying xenobiotictoxicity and highlights the potential for using network pharmacological approaches toidentify novel therapies for the treatment of xenobiotic diseases.

Keywords: Xenobiotics, Network pharmacology, PubChem, PANTHER pathway, PharmMapper

Introduction

Xenobiotics are foreign chemical substances that the body doesn't naturally produce. The liver is the vital organ responsible for the metabolism and excretion of xenobiotics. Some xenobiotics can damage liver cells and become toxic (1-5),but others go through a process called biotransformation in the liver that makes them more readily excretable (6). The effects of xenobiotics are influenced by various factors, including dosage, duration of exposure, chemical properties of the xenobiotic, and individual variations in liver function (7-9). Hepatotoxicity, steatosis, inflammation, poor drug metabolism, and carcinogenicity are typical effects (10 - 11) hang. The effects of xenobiotics are very critical (12). It is true that knowledge of xenobiotic mechanisms is essential for remedial research. While many of the proteins impacted by xenobiotics are well-known, there might be some that are still unknown or poorly understood. Numerous enzymes, receptors, and transporters, including cytochrome P_{450} enzymes, nuclear receptors like PXR and CAR, and drug transporters like P-glycoprotein, have been found to be involved in the metabolism and response to xenobiotics (13-15). Ongoing research attempts to identify additional

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proteins and pathways involved in xenobiotic-induced toxicity and therapeutic responses (16). Nevertheless, the complete scope of protein targets impacted by xenobiotics is still being clarified. This information is crucial for creating safer medications, focusing on treating specific diseases, and lessening the negative consequences of xenobiotic exposure (17-18).

Different studies have been reported on xenobiotics pathways (19). As CP450 is the main metabolising enzyme, it interacts with it. It also affects different detoxification pathways differently as the body eliminates it and its metabolites by these pathways. Many transporter pathways and signalling pathways are also affected by xenobiotics. Many xenobiotics may have harmful toxic effects that could be fatal if they are not completely removed and are not properly metabolized by xenobiotic metabolizing enzymes (20). That is why the spectrum of targets which get affected by xenobiotics should be studied. All xenobiotics are different, but as a foreign entity they have some similarity also (11). Here we have studied a few xenobiotics and their effects using bioinformatics tools (21). Also, their remedial methods were investigated. There are a number of xenobiotics present in the environment, but in this study, we have selected a few, these studies can be extended for other molecules using similar ways (20). The name of the compounds which we have chosen here are Acetaminophen, Amoxapine, Alfacalcidol, Atorvastatin, Bisphenol, Clomiphene, Dichlorvos, Diclofenac, Erythromycin and Lovastatin (22-25).

Artemisinin is an antimalarial drug derived from the sweet wormwood plant, *Artemisia annua*. Artemisinin-based combination therapies (ACT) are currently generally considered the best treatment for uncomplicated falciparum malaria (26-27). They are fast and reliably effective (28). The derivatives of artemisinin such as artemether, artesunate and dihydroartemisinic, have played a crucial role in the prevention and treatment of human schistosomiasis. They are also shown to be beneficial for many other conditions, against new viruses (e.g., HIV, Ebola virus, chikungunya virus, etc.) or classic infections caused by drug-resistant viral strains (e.g., human viruses, cytomegalovirus) (29). The fatal effects of diclofenac on marine life have been investigated. The hypothesis that the drug causes oxidative stress and metabolic disturbances in fish was supported by histopathological and cortisol studies. The toxic effects were reduced when *Artemisia pallens*, the remediator, was introduced, indicating the potential of the plant for natural regeneration and promoting environmental sustainability in fish models (30). Consequently, in order to prevent the long-term adverse effects, it is necessary to decrease the rate of use of painkillers like diclofenac (31). Here we have explored the possible remedial effects of xenobiotics and its mechanism through Bioinformatics lenses. First, we predicted the possible targets of these compounds and then studied and compared those using different bioinformatics tools (32-33).

Methodology

PubChem

PubChem is a large collection of freely accessible chemical information. The PubChem (pubchem.ncbi.nlm.nih.gov) is the world's largest collection of freely accessible chemical information. PubChem contains nucleotides, carbohydrates, lipids, peptides, chemically-modified macromolecules and other molecules. We collect information on chemical structures, identifiers, chemical and physical properties, biological activities, patents, health, safety, toxicity data, and many others. One of PubChem's key features is its ability to link chemicals to biological activity data. This allows researchers to explore the potential use of chemical compounds in drug discovery and other applications. This was accessed and the following drugs (Acetaminophen, Amoxapine, Alfacalcidol, Atorvastatin, Bisphenol, Clomiphene, Dichlorvos, Diclofenac,

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Erythromycin and Lovastatin were searched for their structural information. These major drugs were chosen randomly for the study. Artemisinin also was searched and retrieved from the same website. The 3D conformers of the given xenobiotics were downloaded in .sdf format (34-37).

PharmMapper

The PharmMapper Server is a user-friendly online tool freely accessible designed to help find potential targets for specific small molecule probes using pharmacophore mapping. With its efficient mapping technique, PharmMapper can quickly identify potential target candidates from its database within hours(38). The server utilizes a comprehensive pharmacophore database that contains data on more than 7,000 protein structures and their related ligands (7). They have their own in-house repertoire of pharmacophore databases and annotations from different target databases like Binding DB, Target Bank. Drug Bank etc. This server is used for *in-silico* target identification using a pharmacophore model. The 3D conformer file was uploaded to the PharmMapper website (http://www.lilab-ecust.cn/pharmmapper/) and target count was set to 500. The default settings were used for other parameters. The results were downloaded in .csv file format (39).

PANTHER Pathway

PANTHER Pathway is a comprehensive online tool developed by the University of Pittsburgh to help students explore and plan their academic and career paths. This tool is available to current and prospective students, as well as alumni. There are over 177 pathways in the Panther pathway including metabolic and signalling pathways which can be explored. The targets from the PharmMapper results are used as input for the PANTHER pathway for pathway analysis. Various pathways for the involved targets and their molecular function can be accessed (40).The diagram can also be exported as SBGN Pathway and they are interactive and include tools for visualizing gene expression data.

Cytoscape

Cytoscape is an open source software platform for the visualization and analysis of complex networks. It is widely used in bioinformatics and systems biology, but can also be used in other fields that are related to network analysis, such as social network analysis, traffic network analysis, etc. (3).Cytoscape allows users to import network data from various sources, such as Excel spreadsheets, text files, or databases. Users can then manipulate the data, add properties to nodes and edges, and apply different algorithms to analyze and visualize the network. The PharmMapper results are used for drug interaction network analysis by cytoscape (41). The PDB ID is converted to Gene ID for accurate results (42). The drug name is given as source node and the target as target node. Using layout functions, the targets are displayed in a network (43). The intersection function is used to merge multiple networks and find all possible targets which are present in all xenobiotic drugs. All the networks of 10 xenobiotics were merged to get the common targets of all 10 compounds. The targets of artemisinin were compared with all the targets and found HSP90B1 is common (pdb 1d: 1tbw) with HSP90AA1 (1ihg) with diclofenac (44)

Homology Modelling, Docking and visualisation

From the PharmMapper and Cytoscape analysis we have come to know that HSP90 is the common target for all xenobiotics including diclofenac and artemisinin (45). Thus, we investigated the binding site and binding mode of diclofenac and Artemisinin with HSP90. As the experimental studies have been conducted with fish models, we have modelled the structure of HSP90 protein from "*Pangasianodon hypophthalmus*".

The protein sequence of 'heat shock protein 90, alpha (cytosolic), class A member 1, tandem duplicate 2' (Accession no.: XP_026779203) (46) of *Pangasianodon*

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hypophthalmus was obtained from NCBI GenBank. The template 'Chain A, HEAT SHOCK PROTEIN HSP 90 BETA' (PDB Id: 5FWK) (10) with 86.52% identity and 'Chain A, kDa heat shock protein, mitochondrial' (PDB Id: 4PJ1) (47) with 87.71% identity obtained from the PDB site was modelled using the template 'Chain A, HEAT SHOCK PROTEIN HSP 90 BETA' and 'Chain A, kDa heat shock protein, mitochondrial' respectively. The Modeller 10.1 tool was used in modelling to obtain the 3D structures of heat shock protein and then optimized. The protein model was validated using Ramachandran plot through PRO-CHECK analyses.

The ligands Artemisinin and Diclofenac were obtained from PubChem Artemisinin_Conformer3D_CID_68827 and Diclofenac_Conformer3D_CID_3033 (48) respectively. The 3D structures were docked into the docking grid of the 3D structures of heat shock protein: HSP90 by Autodock vina v1.2.0 (49). The identification of hydrogen and hydrophobic interactions in the protein-ligand complexes were analysed using BIOVIA Discovery Studio Visualizer (50). III. Visualization of Molecular Docking: The docking positions were validated through the best DOPE scores.

Results and Discussion

Cytoscape software was utilized to explore the xenobiotic and target interaction. Here we have shown only for AMOXAPINE (Figure 1) (51). Same procedure was followed for all 10 xenobiotics and then merged to get the common targets (Figure 2). (Other pictures can be provided as Supplementary materials)

Cytoscape Network of the targets obtained from the PharmMapper for the xenobiotic Amoxapine

Total 9 proteins are found to be the same in all the 10 xenobiotics. Beta-lactamase, Heat shock protein HSP90-alpha, Tyrosine-protein phosphatase non-receptor type I, CAMP –specific, 3,5 cyclic phosphodiesterase 4D, Stromelysin-1, CDK2, Glycogen phosphorylase, carbonic anhydrase 2, Mitogen-activated protein kinase 14.

Panther Pathway analysis

Panther pathway analysis of the gene list from the predicted targets of Acetaminophen shows that the most predominant path is unknown or uncharacterised. The second most predominant pathway is angiogenesis. Most of the other xenobiotics showed the same pattern (Figure 3).

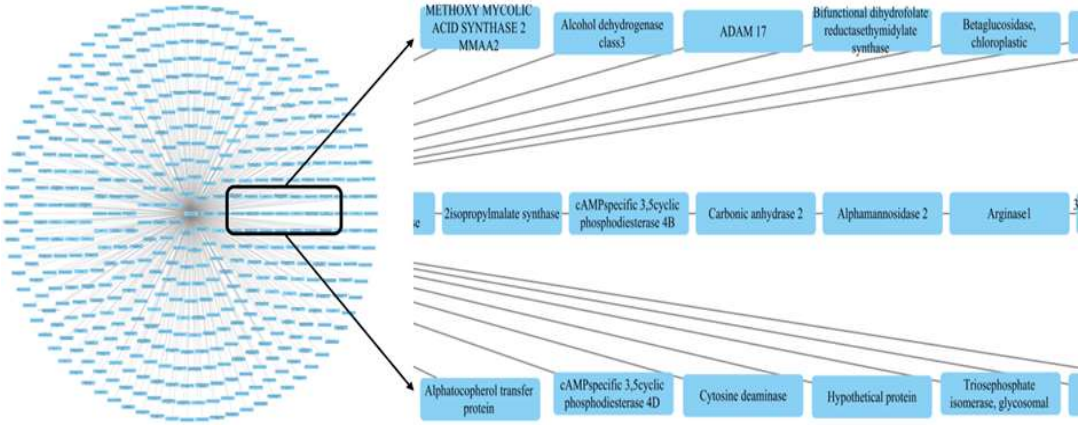

Figure 1: Cytoscape network for Amoxapine

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Diclofenac and Artemisinin:

Our aim is to find the common pathways of these xenobiotics and whether artemisinin can act as a remedy (Figure 4) (52). To understand that we compared the targets of diclofenac (53) and targets of artemisinin using a Venn diagram. The uniport IDs of the targets from the output of PharmMapper of diclofenac and all the targets of artemisinin were taken and performed the Venn diagram analysis using (Draw Venn Diagram (ugent.be)). The common targets are listed below in Table 1. Most of the proteins are involved in enzymatic reaction, catalysis, metabolic process, cellular process and biological regulation. The network of genes which are affected by both diclofenac and artemisinin is shown in Figure 5. With these proteins Artemisinin and Diclofenac both may have competitive binding effects. ALB protein is a very crucial (high degree) protein in this network.

Comparison of data with Artemisinin

It has been observed that ALB gene, serum albumin binds with Artemisinin. Recent docked structure shows the atomic level interaction of Serum albumin and Artemisinin. Similarly, structural studies of the diclofenac, binding to human serum albumin has been resolved (54). In both the cases the residue R218 plays a crucial role. Both the compounds bind with the same cavity. The drug pharmacokinetics varies because of this competitive binding (55).

Detailed investigation of binding of artemisinin and diclofenac shows that artemisinin binds with HSP90B1 and Diclofenac binds with chaperon protein HSP90AA1 (not shown in the network). So, there must be a mechanistic role of HSP90 protein with both of these molecules so we did homology modelling studies of HSP90 protein using a fish model Figure 6.

The interaction of protein-ligand complexes indicates that the Artemisinin and Diclofenac binds to the same site and

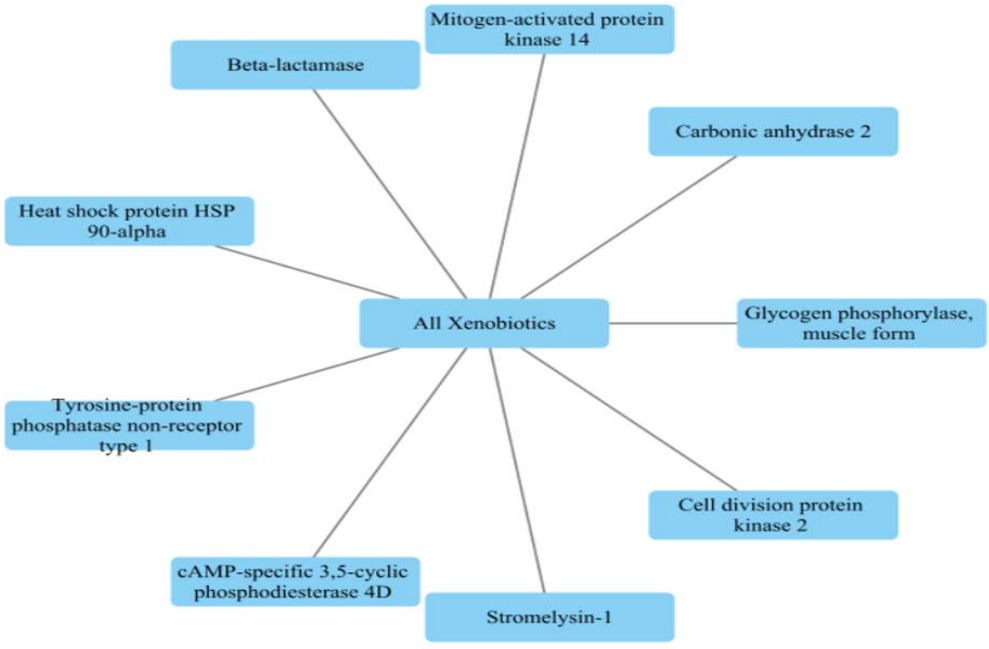

Figure 2: Cytoscape network of multiple xenobiotics

Toxicity Mechanisms of Xenobiotics

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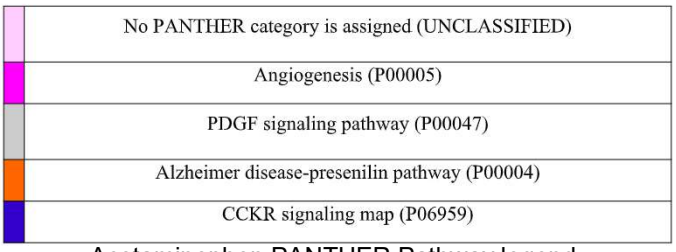

Acetaminophen PANTHER Pathway legend

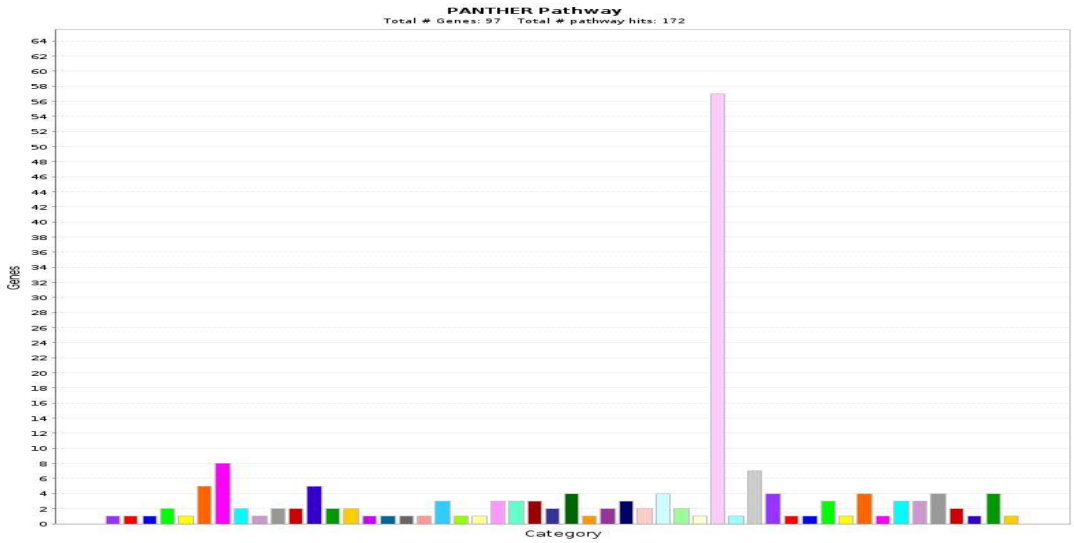

Figure 3: Panther pathway analysis of Acetaminophen

Artemisinin and the Diclofenac molecules tends to bind in different positions as the primary docking site is occupied. The amino acid associated with the interaction of HSP90 and Artemisinin are Phenylalanine (Phe134), Glycine (Gly133), and Serine (Ser109); HSP90 and Diclofenac are Glycine (Gly131 and Gly133), Phenylalanine (Phe134), Asparagine (Asn47); Diclofenac HSP90 complex and Artemisinin is Tyrosine (Tyr460); and Artemisinin HSP90 complex and Diclofenac are Threonine (Thr489), and Serine (Ser499).

The use of network pharmacology in investigating the toxicity mechanisms of xenobiotics offers a unique opportunity to explore the complex interactions between xenobiotics and the human body. The

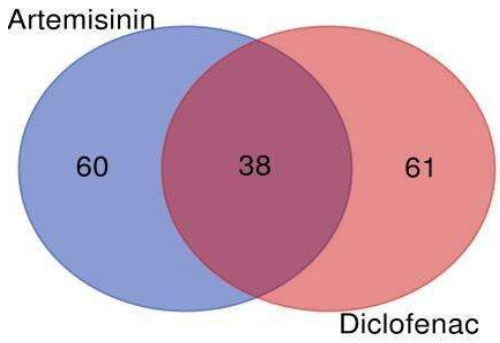

Figure 4: Common pathways between diclofenac and artemisinin

approach allows the recognition of key proteins and pathways involved in xenobiotic toxicity, which can inform the development of

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Table 1: Common targets of diclofenac and artemisinin

S. No	Gene name	PANTHER Family/ Subfamily	PANTHER protein class
1.	Aldo-keto reductase	ALDO-KETO REDUCTASE FAMILY 1 MEMBER B1 (PTHR11732:SF294)	reductase
2.	Delta-aminolaevulinic acid dehydratase	DELTA-AMINOLEVULINIC ACID DEHYDRATASE (PTHR11458:SF0)	dehydratase
3.	Albumin	ALBUMIN (PTHR11385:SF15)	transfer/carrier protein
4.	Lysozyme	LYSOZYME C (PTHR11407:SF28)	glycosidase
5.	Kinesin-like protein	KINESIN-LIKE PROTEIN KIF11 (PTHR47970:SF26)	microtubule binding motor protein
6.	Serine threonine-protein kinase pim-1	SERINE_THREONINE-PROTEIN KINASE PIM-1 (PTHR22984:SF29)	non-receptor serine/threonine protein kinase
7.	Serine threonine-protein kinase Chk1	SERINE_THREONINE-PROTEIN KINASE CHK1 (PTHR24343:SF564)	non-receptor serine/threonine protein kinase
8.	Ribosyldihydronicotinamide dehydrogenase [quinone]	RIBOSYLDIHYDRONICOTINAMIDE DEHYDROGENASE [QUINONE] (PTHR10204:SF33)	oxidoreductase
9.	Mitogen-activated protein kinase 1	MITOGEN-ACTIVATED PROTEIN KINASE 1 (PTHR24055:SF599)	non-receptor serine/threonine protein kinase
10.	Nck-associated protein 1	NCK-ASSOCIATED PROTEIN 1 (PTHR12093:SF11)	-
11.	Fas-binding factor 1 FBF1	FAS-BINDING FACTOR 1 (PTHR33689:SF1)	-
12.	Protein farnesyltransferase_geranylgeranyltransferase type-1 subunit alpha	PROTEIN FARNESYLTRANSFERASE_GERANYLGERANYLTRANSFERASE TYPE-1 SUBUNIT ALPHA (PTHR11129:SF5)	acyltransferase
13.	Ephrin type-B receptor 4	EPHRIN TYPE-B RECEPTOR 4 (PTHR24416:SF296)	transmembrane signal receptor
14.	Glutathione S-transferase P	GLUTATHIONE S-TRANSFERASE P (PTHR11571:SF141)	transferase
15.	Caspase-7	CASPASE-7 (PTHR10454:SF31)	protease

(*Contd.*)

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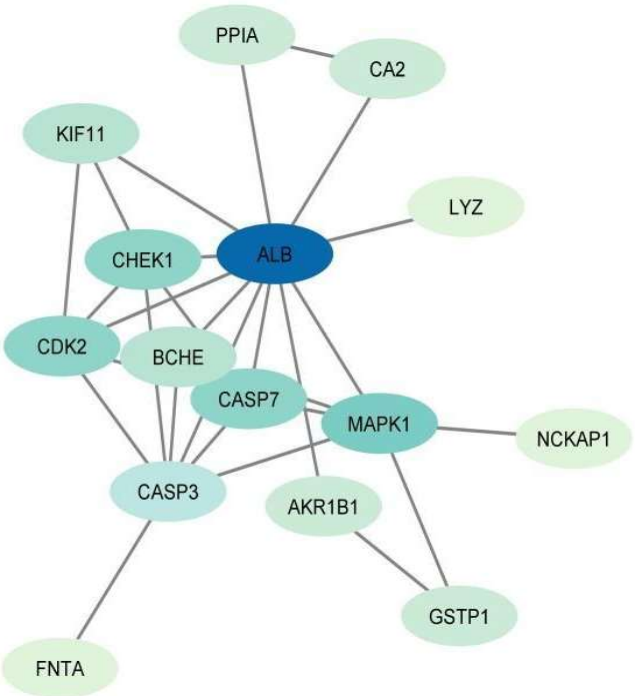
Table 1: Common targets of diclofenac and artemisinin (*Contd.*)			
S. No	Gene name	PANTHER Family/ Subfamily	PANTHER protein class
16.	Cholinesterase	CHOLINESTERASE (PTHR43918:SF5)	esterase
17.	Carbonic anhydrase 2	CARBONIC ANHYDRASE 2 (PTHR18952:SF120)	dehydratase
18.	Caspase-3	CASPASE-3 (PTHR10454:SF198)	protease
19.	Peptidyl-prolyl cis-trans isomerase A	PEPTIDYL-PROLYL CIS-TRANS ISOMERASE A (PTHR11071:SF490)	chaperone
20.	Cyclin-dependent kinase 2	CYCLIN-DEPENDENT KINASE 2 (PTHR24056:SF521)	non-receptor serine/threonine protein kinase
21.	Oxysterols receptor LXR-beta	OXYSTEROLS RECEPTOR LXR-BETA (PTHR24082:SF316)	C4 zinc finger nuclear receptor



The colour of the nodes has been given according to the degree.
Dark colour denotes the high degree value.

Figure 5: Network of genes affected by both diclofenac and artemisinin using cytoscape

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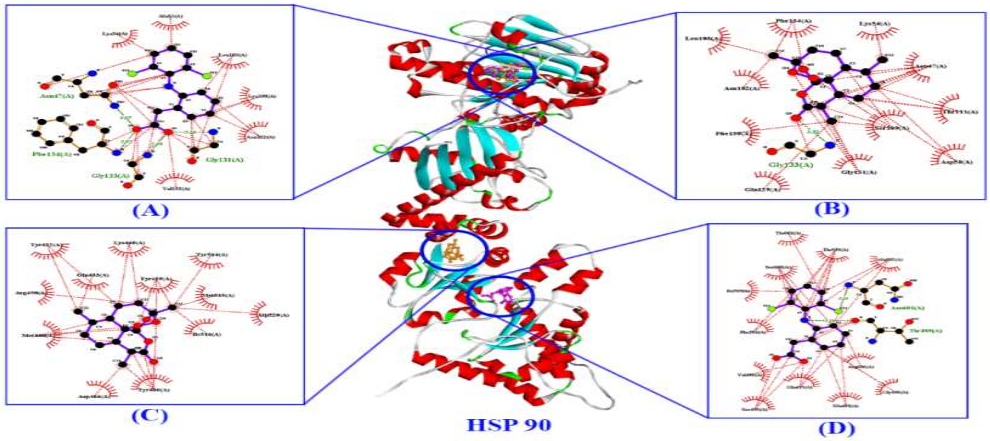

Figure 6 The identification of hydrogen and hydrophobic interactions of HSP90. A and D: Artemisinin. B and C: Diclofenac

new remedial strategies for mitigating the adverse effects of xenobiotics.

By leveraging the power of network pharmacology, we can embark on an exciting journey touncover the mysteries of xenobiotic toxicity. This innovative approach enables us to map the intricate dance between xenobiotics and the human body, pinpointing the critical proteins and pathways that are implicated in harmful interactions. The knowledge gleaned from this endeavour has the potential to transform the approach with which we combat the adverse effects of xenobiotics, paving the way for the development of novel therapeutic strategies that promote human health and well-being.

The study identified several key pathways involved in xenobiotic toxicity, including oxidative stress, inflammation, and apoptosis. These pathways have been previously implicated in the pathogenesis for many diseases, including cancer, cardiovascular disease, and neurodegenerative disorders. Therefore, the identification of these pathways as being involved in xenobiotic toxicity suggests that the effects of xenobiotics on human health may cause many problems than previously thought. Beta-lactamase enzymes has a pivotal role in the detoxification of harmful substances in environment. They have the remarkable ability to break down certain beta-lactam-containing compounds found in drugs and chemicals, effectively rendering them harmless. Insome cases, beta-lactamase activity can even convert xenobiotics into less toxic forms,making them less harmful to living organisms.

While the effectiveness of beta-lactamases on xenobiotics may vary based on factors such as the specific enzyme, the type of xenobiotic, and the context in which it is encountered, the potential benefits of these enzymes cannot be ignored. By leveraging the power of beta-lactamases, we may be able to develop new strategies for neutralizing harmful pollutants and promoting environmental health.

Moreover, the versatility of beta-lactamases suggests that they could be used to address a range of environmental challenges. For example, they could be employed to clean up contaminated soil and water, or to break down harmful chemicals in industrial settings. The possibilities are vast, and the potential impact of beta-lactamases on our planet's ecosystems could be significant.

Tyrosine protein phosphatase non-receptor type 1 (PTPN1), also known as

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protein tyrosine phosphatase 1B (PTP1B), is an enzyme involved in the regulation of many cellular processes, including xenobiotic metabolism. PTPN1 is primarily expressed in the liver and plays a crucial role in xenobiotic metabolism in this organ (56). Specifically, PTPN1 dephosphorylates and inactivates several key enzymes involved in drug metabolism, which includes cytochrome P_{450} enzymes, UDP-glucuronosyltransferase, and sulfotransferase. Although they can have both beneficial and adverse effects on drug efficacy and toxicity, they remain important targets for the development of new therapeutic strategies for various diseases.

MAPK14 is involved in a several cellular processes including inflammation, apoptosis (programmed cell death), and cell differentiation. Its activation is involved in regulating cell survival and death in response to various stimuli such as oxidative stress, cytokines and xenobiotics (57). In response to exposure to xenobiotics, MAPK14 may be activated, triggering cellular stress responses that ultimately lead to cell death. The activation of MAPK14 has been shown to promote survival of hepatocytes (hepatocytes) exposed to various xenobiotics such as alcohol and acetaminophen. On the other hand, activation of MAPK14 is also involved in the induction of cell death in response to certain xenobiotics such as arsenic and benzene. Carbonic anhydrase 2 (CA2) is a vital enzyme which plays a central role in maintaining the delicate balance of acid and base levels in our bodies. Found in diverse tissues such as the kidneys, lungs, and liver, CA2 facilitates the conversion of carbon dioxide into bicarbonate ions and protons, a process essential for proper respiration and ion transport (58). Moreover, recent research has revealed that CA2 also supports the growth and survival of certain cancer cells, making it an attractive target for the development of innovative cancer therapies. By inhibiting CA2, scientists have successfully reduced the viability and proliferation of cancer cells, raising hopes for a new generation of cancer treatments. Although the precise manner in which CA2 promotes cell survival remains unclear, researchers are making steady progress towards unravelling its mysteries. As we deepen our understanding of CA2's role in cellular processes, we may uncover novel opportunities to exploit its potential for the betterment of human health. Glycogen phosphorylase is a key enzyme in glycogen metabolism. This increase in glycogen phosphorylase activity may help provide an energy source to stressed cells and promote cell survival. Cell division protein kinase 2 (CDK2) is a key cell cycle regulator that controls the transition of cells from G1 to S phase. In addition to its role in cell cycle regulation, CDK2 has also been shown to play a role in DNA repair and apoptosis, processes critical in maintaining genomic stability and cell viability. The role of CDK2 in xenobiotic-induced cell survival is complex and context-dependent, and further studies are needed to fully understand the role of CDK2 in xenobiotic toxicity and carcinogenesis (59). Stromelysin 1 is a member of the matrix metalloproteinase (MMP) family and plays an important role in the degradation of extracellular matrix (ECM) proteins during tissue remodelling and repair processes. Overall, the precise role of stromelysin-1 in xenobiotic metabolism and cell viability are complex and context dependent. Further studies are needed to fully elucidate these functions and their potential impact on human health and disease. Cyclic AMP-specific 3',5'-cyclic phosphodiesterase 4D, also known as PDE4D, is an enzyme that catalyses the hydrolysis of cAMP (cyclic adenosine monophosphate) to inactive 5'-AMP. PDE4D has been found to play an important role in regulating the cAMP signalling pathway in various cellular processes including cell proliferation and differentiation.

Overall, PDE4Ds play an important role in regulating cellular responses to xenobiotic stress and cell survival (60). Modulation of PDE4D activity may be a promising target for the development of new therapeutic strategies for xenotoxicity and cancer therapy. HSP90 (Heat Shock Protein

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90) is a powerful molecular chaperone that plays a vital role in safeguarding the integrity and functionality of numerous client proteins. These proteins are involved in a variety of cellular processes, including cell proliferation, differentiation, and survival. Remarkably, HSP90 has been shown to play a dual role in responding to xenobiotics, such as chemotherapy drugs, environmental toxins, and drugs of abuse. On one hand, it acts as a protective shield, preventing the denaturation and degradation of client proteins in the presence of these harmful compounds. On the other hand, it promotes cell survival by conferring resistance to chemotherapeutic agents and fostering cell resilience. The intricate mechanisms underlying HSP90-mediated regulation of xenobiotic responses are currently under intense scrutiny, with researchers eager to uncover new ways to leverage this knowledge for the development of innovative therapeutics. By understanding how HSP90 influences cellular responses to xenobiotics, scientists may be able to devise novel strategies to boost the effectiveness of cancer treatments while minimizing harmful side effects(61).

Additionally, this research may shed light on how to overcome chemoresistance, a major obstacle in the fight against cancer. It is important to note that this study has several limitations. Firstly, the study relied on publicly available data to construct the xenobiotic-protein interaction network, which may be incomplete or contain errors. Secondly, the study did not investigate the effects of specific xenobiotics on human health, instead focusing on the general mechanisms of xenobiotic toxicity. Therefore, further studies are necessary to determine the specific effects of different xenobiotics on human health and the mechanisms underlying these effects. In conclusion, the use of network pharmacology in investigating the toxicity mechanisms of xenobiotics are a promising approach that offers new insights into the complex interactions between xenobiotics and the human body. The findings of this study provide a basis for future research in this area, which has the potential to lead to the development of new therapeutic strategies for mitigating the adverse effects of xenobiotics on human health.

Conclusion

In summary, the application of network pharmacology in studying the toxicity mechanisms of xenobiotics has proven to be a game-changer. By illuminating the intricate connections between xenobiotics and the human body, this innovative approach has opened up new avenues for exploration and discovery. The insights gained from this research have laid the groundwork for future investigations that could lead to the creation of novel therapies designed to counteract the harmful effects of xenobiotics on human health. With the help of network pharmacology, we can now gain a deeper understanding of how xenobiotics interact with various biological pathways and networks within the body. This knowledge has the ability to transform the way we approach drug development and toxicity testing, ultimately leading to safer and more effective treatments for a wide range of diseases. As we continue to push the boundaries of possibilities with network pharmacology, we can look forward to a brighter future where the adverse effects of xenobiotics are minimized and human health is protected.

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