Admet And Antineoplastic Profiles of Chlorinated Miltefosine And Perifosine

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Abstract

Background

The ADMET profiles of chlorinated phospholipid analogs, including miltefosine and perifosine, have been extensively studied for their potential as antineoplastic agents. ADMET evaluations can provide insight into the pharmacokinetic and pharmaco dynamic properties of a compound, as well as its safety and efficacy in vivo. Studies have shown that these compounds have promising antineoplastic activity, and their ADMET profiles have provided valuable information for further evaluation in clinical trials.

Material & Methods:

The present study aims to identify drugs with similar and dissimilar ADMET profiles to these compounds, investigate their activity against normal and tumor cell lines, and study their interaction with heat shock protein 90 (HSP90) using molecular docking. The target with the active binding site drug molecule is identified using a 1-click docking server.Binding Property Explorer was employed to determine drug-likeness, and the admetSARprogramme was used to determine ADMET analysis. CLC-Pred was used to retrieve the impact of chlorinated these drugs on both normal and tumour cell lines. All of these drugs were isolated from CLC-Pred to determine their toxicity.

Results:

In admet properties, total 30 SMILEs were extracted from chemdraw after were chlorinated. Several transporters have been demonstrated to regulate some medicines' actions, which impacts their ADMET characteristics. All of these drugs were isolated from CLC-Pred to determine their toxicity. Such toxicity are summarized as Breast adenocarcinoma, Lung carcinoma, Prostate carcinoma, Gastric carcinoma, colon adenocarcinoma, non small cell lung carcinoma, Uterina corpus sacoma and Papillary renal carcinoma. The heat shock protein 90alpha 3D model was generated from the PDB and 1-click docking server. Comparing two drugs ligand to find their analogous and dissimilar ADMET characteristics (miltefosine, perifosine). These drug molecules select on the basis of molecular weight. The molecular weight and molecular formula of miltefosine is (407.6, $C_{21}H_{46}NO_4P$) and perifosine (461.7, $C_{25}H_{52}NO_4P$). Comparative docking results of 30 compounds of these drug molecules by 1- Click docking are listed in Table 1. Heat shock protein 90Alpha interacts with all 30 chlorinated drug compounds.

Discussion: Miltefosine and perifosine are alkylphosphocholine compound that have been utilized used as anti-cancer drugs. Miltefosine has demonstrated promising results against various malignancies include ovarian, breast and prostate cancers for the treatment of visceral leishmaniasis. Whereas periforosine is a strong Akt inhibitor that has been examined in clinical studies for a variety of cancer types. The metabolic stability, lipophilicity and cytotoxicity of medicines have all been found to be improved by this alteration. Miltefosine, an FDA-approved medication for the treatment of leishmaniasis, is a derivative known as chlorinated Miltefosine.

Perifosine, on the other hand, is a synthetic alkylphospholipid that has demonstrated potential in preclinical studies as an antineoplastic drug.

Conclusion: In conclusion, Miltefosine and perifosine's cytotoxicity, metabolic stability, and anticancer activity were found to be improved by chlorination both in vitro and in vivo. These results suggest that perifosine and miltefosine, which are chlorinated, may be potential candidates for the development of new anticancer drugs. To further analysis these compounds work needed their safety and effectiveness in clinical trials.

Keywords: Admet properties, Toxicity, Admetsar, CLC-Pred, Molecular Docking

Introduction

It is less frequent for drug manufacturers and researchers to pay much attention to the development of drugs having inadequate pharmacokinetic profiles, because the procedure involved with both the development as well as the discovery of medications are considered to be extremely expensive, which is economically inefficient in the perception of drug developers and researchers as well (Eisenbrand, et al., 2002). The study of a drug's pharmacokinetic features, which include absorption, distribution, metabolism, excretion, and toxicity (ADMET), Recently an observable increase has been reported regarding the application of new industrial and academic models that are being relied on(Ekins, et al., 2000). The unfavourable pharmacokinetic characteristics of these medications were found to be cause of restrictions in the development of novel drugs, consequently, it has been increasingly demanded to evolve new strategies that are able to identify drugs' ADMET properties (Choudhury & Pandey, 2016; Mayr, et al., 2017; Mody, et al., 2014). The creation of ADMET prediction instruments took place in 1863, which was concerned with the traditional evaluation of the effected drugs solubility on the toxicity. Later on, attention was focused on the study of ADMET in a greater extent specifically, which commenced by determining drugs aqueous solubility in addition to an in vitro test (Catovsky, et al., 2007). A successful drug production has to require respectable ADMET characteristics in addition to the strong efficiency. The process of developing new pharmaceuticals has advanced to use of new technology for drug ADMET property prediction. In the early decades, it was demonstrated that computational prediction tools might be used in conjunction with both in vivo and in vitro testing to speed up drug discovery and development methods (Moroy, Martiny,

Vayer, Villoutreix, & Miteva, 2012). Drug development and discovery have incorporated insilico techniques as an instrument for early-stage evaluation of a drug's ADME characteristics. ADMET data is recognized as a crucial component of finding and creating novel drugs. Both in vitro and in vivo models reveal details on the ADMET properties of pharmaceuticals, which is able to be utilized to predict the drugs will react after administration. Depending on ADMET characteristics, drug candidates are either sophisticated, maintained, or eliminated (Chandrasekaran, Abed, Al-Attraqchi, Kuche, & Tekade, 2018). Preclinical data on medications Since pharmacokinetic and antineoplastic profiles can be predicted from drug ADMET data, ADMET features are important in evaluating the efficacy of medicines target after administration. When evaluating the exposure of pharmaceuticals in the targeted site of action, factors such as the rate of absorption, deposition, and metabolism of the drug within the targeted organ are taken into consideration. The pharmacokinetic characteristics of these pharmaceuticals, especially their ADMET, must be established in order to create medications with the necessary attributes and optimum dose regimes. In vivo models were utilized to minimize the anticipated undesirable characteristics of pharmaceuticals in the preclinical stages before presenting them to the market due to the numerous risk factors associated with the development and discovery of drugs as well as the time-consuming processes involved (Lyubimov, Bohnert, & Prakash, 2012). These properties include drud, oral absorption, clearance, bioavailability, penetration as well as the volume of distribution through the (BBP) blood brain barrier(Alavijeh, Chishty, Qaiser, & Palmer, 2005). The relative solubility of drugs is one of the most crucial qualities required to be effectively optimized because it has a substantial impact on both toxicity and drug design. Miltefosine and perifosine are two of the most efficient alkyl lysophos pholipids (ALPs) for reducing human pancreatic cancer cells because they have an effect on the endoplasmic reticulum. By greatly increasing drug absorption, pancreatic cancer cells promoted malignant cell death via mitochondria and caspases(Gajate, et al., 2021). However, study of alternatives was prompted by their lack of selectivity, metabolic instability, and severe gastrointestinal toxicity (Saigua Encalada, 2022). Complete chlorination of an alkyl chain may alter macromolecules' selectivity and stability. In the proposed study, an insilico approach will be utilized to investigate whether chlorination affects the anticancer medication miltefosine and perifosine's ADMET profile. The metabolic stability of pharmaceuticals is regarded as a critical

issue that drug developers must pay particular attention to because the metabolism profile of these drugs heavily influences the failure or success of the investigation process.

Methods

Docking is a computational simulation approach of a candidate ligand interaction with a receptor and predicts the preferred orientation of binding of one molecule to another form a stable complex. By utilising scoring functions, docking is used to anticipate the small molecule's binding activity and affinity to its protein targets. Therefore, docking is essential to the rational development of pharmaceuticals. The sensitivity of docking calculations to the geometry of the input drug ligand demonstrates that minor modifications in ligand conformation can result in significant variations in the geometries and scores of the subsequent docked poses. In this case, we used a web-based molecular docking software 1-click docking (https://mcule.com/apps/1-click-docking/). Binding Property Explorer was employed to determine drug-likeness, and the admetSARprogramme was used to determine ADMET analysis. The programme was able to successfully calculate the important docking parameters. In order to assess the activity of the test ligand, it presented us thorough docking result.

ADMET Prediction

ADMET properties of a compound deal with its absorption, distribution, metabolism, excretion, and toxicityin and through the human body. Analysing a drug's pharmacokinetic and anti-neoplastic profile, or ADMET, is important to identifying its pharmacodynamic effects. Today, there are different online and offline software available assist in predicting the behaviour of drug possibilities. In this study, we have used the admetSAR prediction tool (http://lmmd.ecust.edu.cn:8000/)(Yang, et al., 2019).

Selection of Protein Receptor

Heat shock protein 90 alpha (HSP90A) was obtained through 1-click docking (https://mcule.com/apps/1-click-docking/) and protein databank (http://www.rcsb.org/pdb/home/home .do) with PDB IDs: 1BYQ and UNIPROT accessions is P07900. In order to create novel drugs (Miltefosine, Perifosine) to treat AD, the heat shock protein 90 alpha (HSP90A) its crystal structure is selected because it represents the

pharmacological target for such drugs. The target with the active binding site drug molecule is identified using a 1-click docking server.

Selection of Drug Ligand

The canonical simplified molecular input line entry system SMILEs analogs of Miltefosine and Perifosine were identified from Pubchem (https://pubchem.ncbi.nlm.nih.gov/) (Kim, et al., 2016). ChemDraw was used to create fresh visualizations of their structures (Brown, 2014).After being chlorinated, the drug ligand molecule was identified through structure from ChemDraw.

Molecular Docking

1-click docking (https://mcule.com/apps/1-click-docking/) is a web-based, easy-to-use interface that contole every aspects of molecular docking including protein configuration and ligand. Additionally, it allows advanced users completely control over the parameters of particular docking calculations, protein configuration and ligand. By combining different well-known insilico chemistry software applications into one comprehensive web service, it enables the user to perform highly effective and reliable docking calculations.

Results

ADMET Prediction

The web server uses SMILES as input structure data for the molecule to be predicted. ChemDraw is embedded as a molecular editor to generate SMILES. The 2 drugs molecules (miltefosine, perifosine) can be submitted from pubchem (https://pubchem.ncbi.nlm.nih.gov/). Each drug molecules miltefosine 14, perifosine 16 SMILEs generated from chemdraw after they were chlorinated. In admet properties, total 30 SMILEs were extracted from chemdraw. The admet properties of chlorinated drug compounds miltefosine and perifosine are listed in (table 1).

Table 1. Admet property of 30SMILEs drug compounds of miltefosine and perifosine

Smiles	LogS	LogD	LogP	Pgp-sub	HIA	Caco-2	BBB	CYP1A2-inh	CYP1A2-sub	CYP2C19-inh
1	-0.36	-1.26	-2.20	-2.99	-3.58	-4.20	-4.72	-5.12	-5.56	-5.87
2	1.87	2.04	2.11	2.18	2.28	2.38	2.53	2.70	2.85	3.01
3	3.47	4.64	5.49	6.15	6.73	7.25	7.69	8.09	8.50	8.91
4	0.89	0.80	0.55	0.30	0.14	0.06	0.03	0.02	0.01	0.00
5	0.87	0.79	0.48	0.14	0.05	0.02	0.01	0.01	0.01	0.01
6	-5.52	-5.58	-5.63	-5.75	-5.77	-5.78	-5.79	-5.81	-5.85	-5.88
7	0.01	0.01	0.01	0.01	0.02	0.04	0.09	0.21	0.44	0.69
8	0.06	0.15	0.24	0.28	0.27	0.28	0.27	0.30	0.33	0.36
9	0.96	0.98	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99
10	0.57	0.65	0.78	0.80	0.81	0.80	0.77	0.72	0.65	0.58
11	0.74	0.86	0.89	0.91	0.93	0.94	0.96	0.96	0.97	0.97
12	0.12	0.28	0.42	0.21	0.12	0.08	0.06	0.04	0.03	0.02
13	0.92	0.94	0.71	0.25	0.12	0.09	0.06	0.04	0.03	0.02
14	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
15	0.89	0.88	0.88	0.87	0.87	0.84	0.78	0.72	0.64	0.56
16	0.72	0.68	0.59	0.46	0.35	0.25	0.19	0.15	0.12	0.11
17	0.07	0.05	0.05	0.05	0.04	0.03	0.03	0.02	0.02	0.01
18	0.75	0.57	0.58	0.52	0.48	0.48	0.40	0.29	0.21	0.17
19	0.66	0.65	0.57	0.48	0.40	0.25	0.15	0.09	0.07	0.05
20	0.44	0.20	0.22	0.23	0.23	0.22	0.18	0.15	0.13	0.12
21	0.91	0.95	0.96	0.96	0.96	0.96	0.96	0.95	0.95	0.95
22	5.35	5.54	5.61	5.66	5.72	5.77	5.83	5.89	5.95	6.01
23	6.19	6.47	6.52	6.57	6.63	6.69	6.76	6.83	6.90	6.96
24	5.20	5.76	6.13	6.26	6.25	6.25	6.25	6.25	6.25	6.25
25	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.01	0.01	0.01
26	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.00	0.00
27	0.35	0.33	0.31	0.30	0.29	0.27	0.26	0.24	0.24	0.24
28	0.06	0.06	0.05	0.05	0.06	0.06	0.07	0.07	0.08	0.09
29	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
30	509.20	577.12	645.04	712.97	780.89	848.81	916.73	984.65	1052.58	1120.50

Table 1: continued

Smiles	CYP2C19-sub	CYP2C9-inh	CYP2C9-sub	CYP2D6-inh	CYP2D6-sub	CYP3A4-inh	CYP3A4-sub	SkinSe	Carcinogenicity	Respiratory
1	-6.12	-6.38	-6.56	-6.73	-2.48	-3.38	-3.95	-5.03	-5.45	-5.84
2	3.21	3.42	3.62	3.79	2.42	2.49	2.55	2.62	2.67	2.76
3	9.3	9.69	10.10	10.61	5.64	6.50	7.04	8.05	8.44	8.8
4	0.00	0.00	0.00	0.00	0.99	0.99	0.98	0.95	0.91	0.80
5	0.00	0.00	0.00	0.00	0.92	0.9	0.86	0.64	0.38	0.2
6	-5.87	-5.8	-5.87	-5.87	-5.54	-5.59	-5.61	-5.85	-5.81	-5.83
7	0.84	0.91	0.95	0.97	0.00	0.00	0.00	0.00	0.01	0.04
8	0.39	0.43	0.49	0.51	0.02	0.0	0.06	0.12	0.15	0.17
9	0.98	0.98	0.98	0.98	0.94	0.95	0.97	0.97	0.97	0.97
10	0.49	0.41	0.33	0.22	0.4	0.55	0.6	0.73	0.73	0.72
11	0.97	0.97	0.98	0.98	0.44	0.66	0.83	0.90	0.93	0.94
12	0.01	0.00	0.00	0.00	0.05	0.14	0.24	0.11	0.08	0.05
13	0.01	0.00	0.00	0.00	0.9	0.96	0.92	0.24	0.1	0.08
14	0.01	0.01	0.01	0.02	0.06	0.06	0.05	0.04	0.03	0.02
15	0.47	0.39	0.3	0.19	0.86	0.82	0.8	0.6	0.56	0.46
16	0.08	0.07	0.06	0.04	0.51	0.44	0.37	0.23	0.19	0.1
17	0.00	0.00	0.00	0.00	0.05	0.0	0.04	0.03	0.02	0.02
18	0.14	0.11	0.09	0.08	0.76	0.57	0.5	0.30	0.2	0.17
19	0.04	0.03	0.02	0.02	0.94	0.94	0.93	0.87	0.83	0.70
20	0.11	0.11	0.10	0.11	0.36	0.18	0.17	0.15	0.14	0.13
21	0.94	0.93	0.93	0.93	0.96	0.98	0.98	0.97	0.97	0.9
22	6.07	6.13	6.19	6.27	5.63	5.81	5.89	6.00	6.06	6.12
23	7.02	7.09	7.19	7.28	5.50	5.46	5.5	5.71	5.80	5.90
24	6.25	6.25	6.25	6.23	5.42	5.99	6.32	6.36	6.35	6.35
25	0.02	0.03	0.04	0.05	0.00	0.00	0.00	0.00	0.00	0.00
26	0.00	0.00	0.00	0.00	0.01	0.01	0.01	0.01	0.01	0.01
27	0.23	0.24	0.24	0.25	0.36	0.35	0.34	0.33	0.32	0.3
28	0.09	0.11	0.13	0.15	0.40	0.39	0.36	0.31	0.28	0.25
29	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00
30	1188.4	1256.3	1324.2	1392.1	563.2	631.1	699.0	834.9	902.8	970.7

Table 1: Continued

Smiles	MW	Vol	Dense	Lipinski	Pfizer	GSK	GoldenTriangle
1	-7.424	483.39	1.053	Accept	Reject	Reject	Reject
2	3.752	513.812	1.123	Accept	Reject	Reject	Reject
3	12.38	544.235	1.185	Reject	Reject	Reject	Reject
4	0.007	574.657	1.241	Reject	Reject	Reject	Reject
5	0.025	605.079	1.291	Reject	Reject	Reject	Reject
6	-5.921	635.501	1.336	Reject	Reject	Reject	Reject
7	0.982	665.923	1.377	Reject	Reject	Reject	Reject
8	0.409	696.345	1.414	Reject	Reject	Reject	Reject
9	0.976	726.767	1.448	Reject	Reject	Reject	Reject
10	0.216	757.189	1.48	Reject	Reject	Reject	Reject
11	0.989	787.612	1.509	Reject	Reject	Reject	Reject
12	0.001	818.034	1.536	Reject	Reject	Reject	Reject
13	0.003	848.456	1.561	Reject	Reject	Reject	Reject
14	0.058	878.878	1.584	Reject	Reject	Reject	Reject
15	0.049	544.018	1.035	Reject	Reject	Reject	Reject
16	0.022	574.44	1.099	Reject	Reject	Reject	Reject
17	0.002	604.862	1.156	Reject	Reject	Reject	Reject
18	0.032	635.284	1.207	Reject	Reject	Reject	Reject
19	0.022	665.706	1.254	Reject	Reject	Reject	Reject
20	0.088	696.128	1.297	Reject	Reject	Reject	Reject
21	0.947	726.551	1.336	Reject	Reject	Reject	Reject
22	6.696	756.973	1.372	Reject	Reject	Reject	Reject
23	6.764	787.395	1.405	Reject	Reject	Reject	Reject
24	6.355	817.817	1.436	Reject	Reject	Reject	Reject
25	0.321	848.239	1.465	Reject	Reject	Reject	Reject
26	0.002	878.661	1.491	Reject	Reject	Reject	Reject
27	0.308	909.083	1.516	Reject	Reject	Reject	Reject
28	0.256	939.506	1.539	Reject	Reject	Reject	Reject
29	0.003	969.928	1.561	Reject	Reject	Reject	Reject
30	1582.08	1000.35	1.582	Reject	Reject	Reject	Reject

Miltefosine

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCCCCC(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OCC[N+](C)(C)C)OCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

Perifosine

O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCCCCCCC(Cl)(Cl)Cl

O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-
])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(
Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-
])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(C
l)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-
])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)
(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-
])(OC1CC[N+](C)(C)CC1)OCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(
Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-
])(OC1CC[N+](C)(C)CC1)OCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl
)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-
])(OC1CC[N+](C)(C)CC1)OCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)
C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-
])(OC1CC[N+](C)(C)CC1)OCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(
Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-
])(OC1CC[N+](C)(C)CC1)OCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(C
l)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

O=P([O-
])(OC1CC[N+](C)(C)CC1)OCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)
(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl

A strong drug candidate is quickly absorbed and evenly distributed throughout the body to ensure efficient metabolism and activity. The ADMET behaviour is frequently overshadowed by another significant component toxicity. Additionally, CLC-Pred was used to retrieve the impact of chlorinated these drugs on both normal and tumour cell lines (Lagunin, et al., 2018). All of these drugs were isolated from CLC-Pred to determine their toxicity. Pharmacokinetic properties including the absorption, distribution, metabolism, excretion, in addition to drug's activity toxicity, transport and spectra are considered as the most significant properties that need to be predicted in the early stages of drug development.Several transporters have been demonstrated to regulate some medicines' actions, which impacts their ADMET characteristics. Such toxicity are summarized as Breast adenocarcinoma, Lung carcinoma, Prostate carcinoma, Gastric carcinoma, colon adenocarcinoma, non small cell lung carcinoma, Uterina corpus sacoma and Papillary renal carcinoma.

Selection of protein receptor

The heat shock protein 90alpha 3D model was generated from the PDB and 1-click docking server. These structures were evaluated using the Ramachandran plot method (Gopalakrishnan, Sowmiya, Sheik, & Sekar, 2007). The majority of the amino acid residues from the expected three-dimensional structure were found in the selected plot region. In the plot, the most beneficial region comprised more than 90% of the residues. Through Biovia Discovery Studio, the heat shock protein 90alpha was designed (Jejurikar & Rohane, 2021).

Selection of Drug Ligand

Comparing two drugs ligand to find their analogous and dissimilar ADMET characteristics (miltefosine, perifosine). These drug moleculesmeltifosine and perifosinewere extracted from pubchem. Miltefosine is an alkylphosphocholine (APC) that has substantial in vitro and in vivo anticancer effects. The most extensively studied alkylphophocholine, miltefosine is used to treat cutaneous breast cancer metastasis. Perifosine is an effective response modulator and an inhibitor of cancer cell proliferation. These chemical compounds' anticancer properties were demonstrated in both cancer cells and normal cells. These drug molecules select on the basis of molecular weight. The molecular weight and molecular formula of miltefosine is (407.6, $C_{21}H_{46}NO_4P$) andperifosine (461.7, $C_{25}H_{52}NO_4P$).

Molecular Docking

Molecular docking is used to predict protein-ligand complexes, which comprise of two components: a search algorithm, an algorithm that performs "pose generation" by generating potential protein-ligand complex geometries, and a scoring function that estimates the protein-ligand binding affinity based on the complex geometry. Comparative docking results of 30 compounds of these drug molecules by 1- Click docking are listed in (Table 2, 3). Heat shock protein 90Alpha interacts with all 30 chlorinated drug compounds. By lowest docking score for each compound was obtained via a 1-click docking research, which also revealed the best complete compatibility for all compounds against the target protein. 1-Click docking web server, Discovery Studio and PyMOL visualize for docked protein (Yuan, Chan, & Hu, 2017). The interaction of ligand and protein was designed through Biovia Discovery Studio as shown in (Figure 1, 2).

Table 2. Visualization of best docked heat shock protein with chlorinated miltefosine

SMILEs	Binding	Score
O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCCCCC(Cl)(Cl)Cl	Glu37,Asn41,Asp44, Ala45, Met88,Gly122, Gly125,Gly127,Phe128, Vla176	-5.5
O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)Cl	Glu37, Asp44, Ala45, Mut88, Leu97, Gly122, Gly125, Gly127, Phe128	-5.1
O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Leu97, Lys102,	-4.3
O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41, Phe128,	-3.4
O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Ala45, Lys48, Ile86, Gly87, Met88, Asp92, Asn96, Leu97, His144	-4.7
O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Arg36, Ser40, Asp44, Lys102, Gly122	-4.0
O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41, Lys48, Asp83, Asn96, Lys102	-4.1
O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41, Lys48, Asp92, Asn96, Leu97, Lys102	-3.9
O=P([O-])(OCC[N+](C)(C)C)OCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41, Lys48, Met88, Lys102, Gly125,	-3.7

O=P([O-])(OCC[N+](C)(C)C)OCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(C l)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Ala45, Lys48, Glu52, Met88, Asp92	-4.8
O=P([O-])(OCC[N+](C)(C)C)OCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl) C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41, Lys48, Asp83, Met88	-4.8
O=P([O-])(OCC[N+](C)(C)C)OCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C (Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41, Lys48, Asp83, Ile86, Lys102	-4.4
O=P([O-])(OCC[N+](C)(C)C)OCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41, Asn96, Ile100, Lys102	-4.4
O=P([O-])(OCC[N+](C)(C)C)OCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41, Asp92, Asn96, Lys102	-4.9

Table 3. Visualization of best docked heat shock protein with chlorinated perifosine

SMILEs	Binding	Score
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCCCCCCC(Cl)(Cl)Cl	Glu37,Asp44,Ala45, Met88,Leu97,Gly122, Gly127	-5.0
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)Cl	Ala45,Lys48,Met88, Asp92,Leu97	-4.7
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Ala45,Lys48,Glu52, Met88,Asn96,Leu97,Phe128,His144	-5.4
O=P([O])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41,Lys48,Asn96	-4.6
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Glu37,Asn41,Asp44, Ala45,Met88,Lys102, Gly122,Gly125,Phe128	-4.8
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41,Ala45,Lys48,Met88,Asp92,Asn96,Leu97, Lys102,Phe128	-5.4
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41,Lys48,Asp83, Ile86,Asn96,Lys102	-5.0

O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41,Lys48,Lys102	-4.6
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Ala45,Met88,Asn96,Lys102,Gly125	-4.3
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Ala45,Lys48,Ile86,Met88	-4.3
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asp44,Asp83,Leu97,Lys102,Phe128,Thr174	-5.9
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41,Lys102	-4.6
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41,Lys48,Asp83,Asn96,Gly122,Gly125	-4.2
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Gly87,Met88,Asp92	-5.7
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41,Lys48,Asp92,Lys102,Val126,His144	-5.2
O=P([O-])(OC1CC[N+](C)(C)CC1)OCCC(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)C(Cl)(Cl)Cl	Asn41,Lys48,Asp83,Asn96,Lys102	-4.7

Figure 1: Visualization of docked heat shock protein binding interaction with chlorinated miltefosine

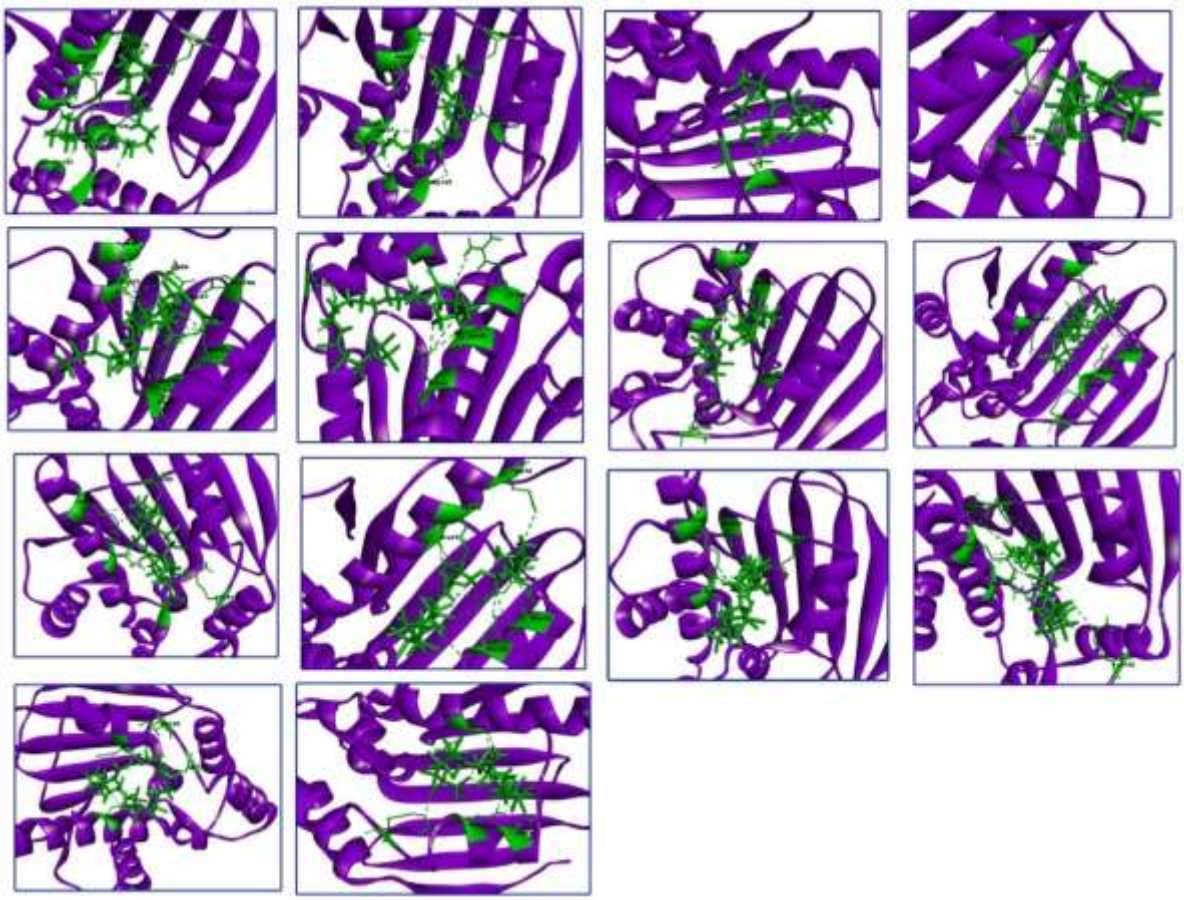
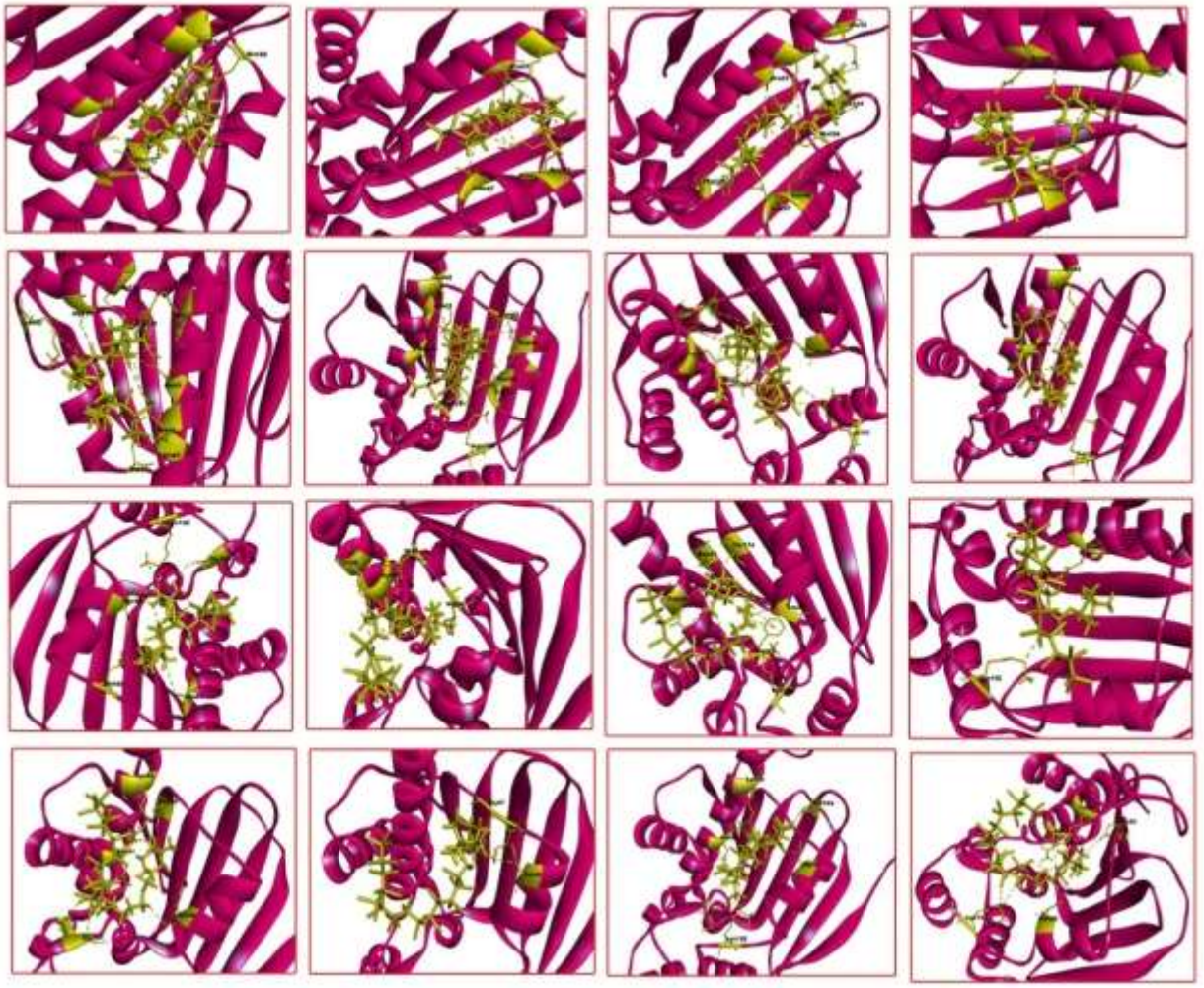


Figure 2: Visualization of docked heat shock protein binding interaction with chlorinated perifosine



Discussion

Miltefosine and perifosine are alkylphosphocholine compound that have been utilized used as anti-cancer drugs. Miltefosine has demonstrated promising results against various malignancies include ovarian, breast and prostate cancers for the treatment of visceral leishmaniasis. Whereas periforosine is a strong Akt inhibitor that has been examined in clinical studies for a variety of cancer types. The admet and antineoplastic profile of chlorinated miltefosine and perifosine has recently been studied. Chlorination is a type of chemical alteration where chlorine atoms are used to replace hydrogen atoms in a molecule. The metabolic stability, lipophilicity and cytotoxicity of medicines have all been found to be improved by this alteration. In a study conducted by (Zhang, et al., 2021), chlorinated miltefosine and perifosine were evaluated for their antitumor activity against human breast cancer cells (MCF-7 and MDA-MB-231). According to the findings, chlorinated miltefosine and perifosine were more harmful to cells than non-chlorinated substances. The chlorinated compounds demonstrated increased metabolic stability, which might enhance their bioavailability and effectiveness in vivo. The admet and antineoplastic profile of chlorinated miltefosine was studied in a mouse model of breast cancer in another investigation by Tariq et al. (2021).Perifosine and miltefosine that were chlorinated have not still been fully identified to function in cancer cells. The suppression of Akt and activation of apoptotic pathways by chlorinated chemicals, however, has been suggested as a possible mechanism by which they cause cell death. Furthermore, the increased lipophilicity of the chlorinated compounds may enhance their capability to interact with intracellular targets and penetrate cell membranes. Many chemotherapeutic drugs were discovered as a result of the search for effective cancer therapies. The chlorinated Perifosine and Miltefosine are two such substances that have demonstrated efficacy in the treatment of different types of cancer. It is possible to better understand their potential for treating cancer by understanding their Admet (Absorption, Distribution, Metabolism, Excretion, and Toxicity) and antineoplastic profiles. Miltefosine, an FDA-approved medication for the treatment of leishmaniasis, is a derivative known as chlorinated Miltefosine. As an antineoplastic drug, it has demonstrated potential in preclinical studies. The Admet profile of chlorinated miltefosine in rats was examined in a study by(Jain, Sahu, Kumar, & Khare, 2022).According to the study, chlorinated miltefosine was effectively absorbed by the oral cavity and transported throughout the body. Additionally, due to its half-life of 0.89 hours, it was metabolised quickly. Chlorinated miltefosine was discovered to

reduce the growth of several cancer cell lines, including colon cancer cells, lung, and breast by(Park, et al., 2021).The researchers also discovered that these cancer cells exhibited apoptosis, or programmed cell death, when exposed to chlorinated miltefosine.

Perifosine, on the other hand, is a synthetic alkylphospholipid that has demonstrated potential in preclinical studies as an antineoplastic drug. Perifosine exhibited a strong oral bioavailability and an adequate distribution throughout the body, according to the study. Furthermore, with a half-life of just 1.75 hours, it was metabolised quickly. Perifosine was found to prevent the growth of several cancer cell lines, including colon, pancreatic cancer cells and breast in a study by(Liu, Li, & Wang, 2021). According to the study, perifosine caused these cancer cells to induce apoptosis.

Miltefosine and perifosine, two medicinal compounds, can be submitted through pubchem. After being chlorinated, the drug molecules miltefoine 14, perifoine 16, SMILEs were created from chemdraw. A total of 30 SMILEs were collected from chemdraw for admet properties. Toxicity is another very important factor which often overshadows the ADME behaviour.Additionally, CLC-Pred was used to collect information whether these drugs' chlorination affected both healthy cell lines and cancer cell lines. To find out the toxicity of all these drug molecules was shown transporters have shown to contribute to some drugs' activities, and hence, affect their ADMET properties. Such toxicity are summarized as Prostate carcinoma, non small cell lung carcinoma, Uterine corpus sarcoma, Breast adenocarcinoma, colon adenocarcinoma, Lung carcinoma, Gastric carcinoma and Papillary renal carcinoma. The purpose of this current study was to identify pharmaceuticals with ADMET profiles which were similar or different from those of the original pharmaceuticals (Perifosine and Miltefosine), evaluate each drug's derivative's activity against normal and cancer cell lines, and explore the interactions of particular drug variants with heat shock protein 90 using molecular docking. These chemical compounds' anticancer properties were demonstrated in both normal cells and cancer cells. The miltefosine and perifosine drug compound selected on the basis of lower molecular weight. The molecular formula and molecular weight ofmiltefosine is ($C_{21}H_{46}NO_4P$, 407.6) Perifosine($C_{25}H_{52}NO_4P$461.7).In addition, we utilised molecular docking to investigate how particular drugs interacted with HSP90 Heat Shock Protein 90alpha. All these 30 chlorinated miltefosine and perifosine drug compound to interact with heat shock prtein 90alpha, as aresult are listed in table. To determine their safety and effectiveness in humans, further study is

required. Clinical trials are required to evaluate their therapeutic potential and explore any possible side effects.

Conclusion

In conclusion, Miltefosine and perifosine's cytotoxicity, metabolic stability, and anticancer activity were found to be improved by chlorination both in vitro and in vivo. These results suggest that perifosine and miltefosine, which are chlorinated, may be potential candidates for the development of new anticancer drugs. To further analysis these compounds work needed their safety and effectiveness in clinical trials.

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