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Study of N-Arylanthranilic Acids Derivates as the Potential Anti-Inflammatory Agents

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ABSTRACT

Since about a decade, the modelling of the biological properties of molecules constitutes an important field of research, orienting not only the isolation of biologically active molecules from natural sources, but also the synthesis of active compounds as a potential drug. In this paper, an attempt was made to develop the docking studies of aspirin and a series of one hundred substituted N-arylanthranilic acids with cyclooxygenase protein (PDB-code 2AW1). Molecular docking analysis was carried out using arguslab 4.0.1. The results of the docking software suggested that 56 out 100 molecules have shown best ligand pose energy, the maximal energy is -8.40 kcal/mol and minimal is -11.18 kcal/mol, among these 56 molecules 20 show a good binding with cyclooxygenase protein, more than aspirin. A Lipinski rule was studied for the best five poses, four of these five molecules satisfy this rule. A computer system PASS (Prediction of Activity Spectra for Substances) was also used to predict the probability of this set of molecules to be anti-inflammatory active/inactive. PASS predict that 73 out of 100 molecules show a good probability of anti-inflammatory activity. All these results lead us to conclude that more than 50% anthranilic acids molecules are suitable for drug treatment of inflammation with less side effects.

Keywords: N-arylanthranilic, NSAIDS, Docking, Cyclooxygénase, Binding mode.

INTRODUCTION

In the field of molecular modeling, docking is a method which predicts the preferred orientation of one molecule to a second when bound to each other to form a stable complex [1]. Knowledge of the preferred orientation in turn may be used to predict the strength of association or binding affinity between two molecules. Docking is frequently used to predict the binding orientation of small molecule drug candidates to their protein targets in order to in turn predict the affinity and activity of the small molecule. Hence docking plays an important role in the rational design of drugs [2-8]. Given the biological and pharmaceutical significance of molecular docking, considerable efforts have been directed towards improving the methods used to predict docking. N-arylanthranilic acids belong to the category of NSAIDS. They are amino

isosteres of salicylates and are also known as fenemates [9,10]. Important molecules of this class include mefenamic acid, flufenamic acid and meclofenamic acid. Fenemates act by blocking the metabolism of arachidonic acid by the enzyme cyclooxygenase (COX), one of the key enzymes in the arachidonic acid cascade [11,12]. This enzyme bis-oxygenates arachidonic acid move to prostaglandine G2, wich is subsequently degraded to vasoactive and inflammatory mediators such as prostanglandins (PGS), prostacyclin (PGI2), and thromboxane-A2 [13]. Some fenemates also inhibit arachidonic acid lipoxygenase resulting in decreased synthesis of leukotrines, known mediators involved in inflammatory process [14]. Studies suggest that flufenamic and tolfenamic acids suppress proliferation of human peripheral blood lymphocytes by a mechanism; which involves inhibition of $Ca2^{+}$ influx and is not related to inhibition of prostanoid synthesis [15]. There are a good correlation between Minimum Effective Dose (MED), Structural Molecular Fragment (SMF) and N-anthranilic acids [16]. In this study, we are reporting probable binding mechanism of N-arylanthranilic acids analogs with COX by molecular docking. Some of these molecules show a good binding with COX, more than aspirin and has drug-like properties.

MATERIALS AND METHODS

Preparation of protein structure

The crystal structure of the protein (PDB: 2AW1) has been obtained from RCSB protein Data Bank [17]. All water molecules were removed and on the final stage hydrogen atoms were added to the target protein molecule.

Preparation of ligand structures

All the compounds used for docking study were selected from the literature see figure 1. Chemdraw, chemical intelligent drawing interface was used to construct the structure of the ligands. Using draw mode of chemdraw, the ligands were generated and three dimensional optimization were done and then save in mol file.

Protein ligand interaction using ArgusLab 4.0.1

Argus lab is the electronic structure program that is based on the quantum mechanics, it predicts the potential energies, molecular structures; geometry optimization of the structure, vibration frequencies of coordinates of atoms, bond length, bond angle and reactions pathway [18]. The protein was docked against the obtained one hundred ligand using Arguslab 4.0.1 [19]. Arguslab is used to find the reasonable binding geometries and explore the protein ligand interactions. Docking simulations were performed by selecting "ArgusDock" as the docking engine. The selected residues of the receptor were defined to be a part of the binding site.

A spacing of 0.4A between the grid points was used and an exhaustive search was performed by enabling '' High precision'' option in docking precision menu, ''Dock'' was chosen as the calculation type, ''flexible'' for ligand and the AScore was used as the scoring function.

At maximum 150 poses were allowed to be analyzed, binding site box size was set to 20 × 20 × 20 angstroms so as to encompass the entire active site.

The AScore function (1), with the parameters read from the AScore.prm file was used to calculate the binding energies of the resulting docked structures. A Score is based on terms taken from the HPScore piece of XScore [20].

All the compound in the dataset were docked into the active site of our protein, using the same protocol. After completion of docking, the docked protein (protein-ligand complex) was analyzed to investigate the type of interactions [21].

The docking poses saved for each compound were ranked according to their dock score function. The pose having the highest dock score

was selected for further analysis.

$$\Delta G_{bind} = \Delta G_{wdv} + \Delta G_{hydrophobic} + \Delta G_{H-bond} + \nabla G_{deformation} + \Delta G_0$$

$$With\ \Delta G_{wdv} = CD_{wdv} VDW \quad With\ CD = -0.00096$$

$$\Delta G_{hydrophobic} = C_{hydrophobic} HP \quad With\ C_{hydrophobic} = 0.037$$

$$\Delta G_{H-bond} = C_{H-bond} HB \quad With\ C_{H-bond} = 0.38$$

$$\Delta G_0 = C_{regression} \quad With\ C_{regression} = 2.783$$

$$And\ \ VDW = \sum_i^{ligand} \sum_j^{protein} \left[\left(\frac{d_{ij}}{r_{ij}} \right)^8 - 2 \left(\frac{d_{ij}}{r_{ij}} \right)^4 \right] + \sum_i^{ligand} \sum_{j>i}^{protein} \left[\left(\frac{d_{ij}}{r_{ij}} \right)^8 - 2 \left(\frac{d_{ij}}{r_{ij}} \right)^4 \right]$$

d_{ij} *is sum of vdw radii of atom i, j intra – ligand vdw excludes* $1-2,\ 1-3$ *bonded pairs.*

$$HB = \sum_i^{ligand} \sum_j^{protein} f(\ \ With\ \ )$$

sum of over hydrophobic ligand – protein atom pairs

$$\begin{cases} f(d_{ij}) = 1 \quad With\ \ \mathrm{d} < d_{ij} + 0.5A^{\circ} \\ f(d_{ij}) = \frac{2}{3}(d_0 + 2 - d) \quad With\ d_{ij} + 0.5A^{\circ} < \mathrm{d} \le d_{ij} + 2.0A^{\circ}, \\ f(d_{ij}) = 0 \quad With\ \ \mathrm{d} > d_{ij} + 2.0A^{\circ} \end{cases}$$

$$\begin{cases} HB = \sum_i^{ligand} \sum_j^{protein} HB_{ij} \\ HB_{ij} = f(r_{ij}) f(\theta_{1,ij}) f(\theta_{2,ij}) \end{cases}$$

r_{ij} *distance between donor / acceptor atoms*

$\theta_{1,ij}$ *angle between donor root – donor – acceptor*

$\theta_{2,ij}$ *angle between donor – acceptor – acceptor root*

$$RT = \sum_i^{ligand} RT_i$$

$$RT_i = \begin{cases} 0\ atom\ i\ not\ involved\ in\ any\ torsion \\ 0.5\ atom\ i\ involved\ in\ 1\ torsion \\ 1\ atom\ i\ involved\ in\ 2\ torsion \\ 1.5\ atom\ i\ involved\ in\ >2\ torsion \end{cases}$$

Prediction activity spectra for substances (pass)

This computer system can predict biological activity based on structural formula of a chemical compound. The PASS approach is based on the suggestion, Activity=Function (Structure).Thus, “comparing” structure of a new substance with that of the standard biologically active substances, it is possible to find out whether a new substance has a particular effect or not. PASS estimates the probabilities of a particular substances belonging to the active and inactive sub-sets from the SAR Base (Structure-Activity Relationships Base) [22]. The result of prediction is returned in the form of a table containing the list of biological activity with the appropriate probability values (i.e) the values defining the likelihood for a given activity type to be either revealed PASS Activity (Pa probability of presence of anti-inflammatory activity) or not revealed PASS Inactivity (Pi probability of absence of anti-inflammatory activity) for each activity type from the predicted biological activity spectrum. Their values vary from 0.000 to 1.000. Only those activity types for which Pa>Pi are considered possible. Usual interpretation of prediction results is based on the Pa values. If Pa>0.7 the chance to find the activity in experiment is high, but in many cases the compound may occur to be the close analogue of known pharmaceutical agents. If 0.5<Pa<0.7 the chance to find the activity in experiment is less, but the compound is not so similar to known pharmaceutical agents. If Pa<0.5 the chance to find the activity in experiment is even more less, but if it will be confirmed the compound might occur to be a New Chemical Entity.

ADME/Toxicity testing

ADME (absorption, distribution, metabolism, and excretion) determines drug like activity of the ligand molecules based on Lipinski Rule of 5 [23,24]. Lipinski'rule states that, in general, an orally active drug has no more than one violation of the following criteria:

No more than 6 hydrogen bond donors (the total number of nitrogen or oxygen-hydrogen bonds)

No more than 12 hydrogen bond acceptors (all nitrogen or oxygen atoms)

A molecular mass less than 600 Daltons

An octanol-water partition coefficient that does not exceed 6

The polar surface area less than 150.

A dataset

Our dataset possesses of 100 molecules of N-arylanthranilic acids, one molecule of aspirin and target protein 2AW1 (Figures 1-3).

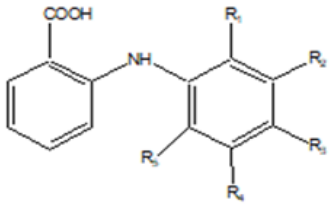

Figure 1: Chemical structure of anthranilic acids.

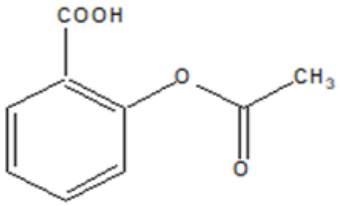

Figure 2: Chemical structure of aspirin.

Figure 3: The target 2AW1.

$$A = \log(\frac{4000}{MED}). \quad (2)$$

The experimental activity A was calculated from the Minimal Effective Dose (MED mg/kg body) by formula (2). In the literature, the molecules with a value of biological activity less than 3.20 are considered to be inactive molecules and the compounds with a value of biological activity greater than or equal to 3.20 are considered as active molecules [25,26] (Table 1).

mol	R_1	R_2	R_3	R_4	R_5	A		mol	R_1	R_2	R_3	R_4	R_5	A
1	H	H	H	H	H	1,3		51	Cl	Cl	H	Cl	H	3,1
2	H	CF_3	H	H	H	3,0		52	H	Cl	Cl	Cl	H	1,3
3	H	CH_3	H	H	H	1,6		53	CH_3	CH_3	H	CH_3	H	2,2
4	H	Cl	H	H	H	2,2		54	CH_3	H	CH_3	CH_3	H	1,6
5	H	NH_2	H	H	H	1		55	H	Cl	CH_3	Cl	H	1,6
6	H	OCH_3	H	H	H	1,9		56	CH_3	H	CH_3	H	CH_3	1
7	H	$SO_2N(CH_3)_2$	H	H	H	1,9		57	Cl	$SO_2N(CH_3)_2$	H	H	Cl	3,4
8	H	$COCH_3$	H	H	H	1,3		58	Cl	OCH_3	H	H	Cl	4,1
9	H	$N(CH_3)_2$	H	H	H	1,6		59	CH_3	Br	H	H	CH_3	3,4
10	H	H	Cl	H	H	1,3		60	Cl	CN	H	H	Cl	3,4
11	H	C_4H_9	H	H	H	1,3		61	CH_3	Cl	H	H	Cl	3,1
12	H	CN	H	H	H	2,2		62	CH_3	Cl	H	H	CH_3	4
13	H	C_3H_7	H	H	H	1,9		63	Cl	OC_2H_5	H	H	Cl	3,7
14	H	SCH_3	H	H	H	1,6		64	CH_3	$COCH_3$	H	H	CH_3	3,6
15	H	NO_2	H	H	H	1,6		65	CH3	$N(CH_3)_2$	H	H	CH_3	3,4
16	H	OC_2H_5	H	H	H	1,6		66	C_2H_5	NO_2	H	H	C_2H_5	2,5
17	H	Br	H	H	H	1,9		67	NH_2	Cl	H	H	CH_3	2,2
18	H	C_2H_5	H	H	H	2,2		68	CH_3	CH_3	H	Cl	H	2,2
19	Cl	H	H	H	H	1,9		69	CH_3	CN	H	H	CH_3	4
20	CH_3	H	H	H	H	1,3		70	CH_3	SCH_3	H	H	CH_3	4
21	H	H	CH_3	H	H	1		71	CH_3	NO_2	H	H	Cl	3,4
22	Cl	H	Cl	H	H	1,6		72	CH_3	C_3H_7	H	H	CH_3	2,8
23	H	Cl	Cl	H	H	1,6		73	C_2H_5	$SO_2N(CH_3)_2$	H	H	C_2H_5	2,5
24	CH_3	CH_3	H	H	H	2,5		74	C_2H_5	$COCH_3$	H	H	C_2H_5	2,2
25	CH_3	CF_3	H	H	H	3,6		75	Cl	H	CF_3	H	Cl	3,7
26	CH_3	$SO_2N(CH_3)_2$	H	H	H	2,8		76	CH_3	$SO_2N(CH_3)_2$	H	H	CH_3	3,9
27	CH_3	NH2	H	H	H	1,9		77	CH_3	NH_2	H	H	Cl	2,8
28	CH_3	$N(CH_3)_2$	H	H	H	2,8		78	CH_3	CH_3	H	H	Cl	2,5
29	CH_3	Cl	H	H	H	2,8		79	Cl	Cl	H	H	CH_3	3,7
30	CH_3	OCH_3	H	H	H	2,8		80	Cl	H	C_2H_5	H	Cl	3,7
31	H	CF_3	H	CF_3	H	1,6		81	Cl	H	Cl	Cl	H	1

32	Br	CF_3	H	H	H	3,4	82	Cl	Cl	Cl	H	H	1,3
33	Br	Br	H	H	H	3,1	83	Cl	H	Cl	H	Cl	1,6
34	H	CH_3	H	CH_3	H	1,6	84	NH_2	CH_3	H	H	CH_3	2,2
35	Cl	H	H	H	CH_3	2,5	85	CH_3	CH_3	H	H	CH_3	2,8
36	Br	CN	H	H	H	3,4	86	Cl	CH_3	H	H	CH_3	3,1
37	F	Cl	H	H	H	3,1	87	CH_3	Cl	H	CH_3	H	3,4
38	H	Cl	H	Cl	H	1,9	88	CH_3	C_2H_5	H	H	CH_3	3,4
39	Cl	Cl	H	H	H	3,2	89	CH_3	NH_2	H	H	Cl	3,4
40	CH_3	NO_2	H	H	H	3,1	90	CH_3	SO_2CH_3	H	H	CH_3	3,8
41	CH_3	CN	H	H	H	3,1	91	Cl	$N(CH_3)_2$	H	H	Cl	3,8
42	CH_3	C_2H_5	H	H	H	3,1	92	CH_3	$SOCH_3$	H	H	CH_3	3,9
43	Cl	H	H	H	Cl	3,1	93	Cl	Cl	Cl	H	CH_3	2,5
44	Cl	CH_3	H	H	H	2,8	94	CH_3	CH_3	H	CH_3	CH_3	1,6
45	Cl	H	H	Cl	H	2,5	95	Cl	Cl	Cl	H	Cl	2,5
46	CH_3	H	H	H	CH_3	1,9	96	Cl	CH_3	Cl	H	Cl	2,5
47	CH_3	H	H	CH_3	H	1,3	97	Cl	Cl	Cl	Cl	H	1,6
48	H	CH_3	CH_3	H	H	1,3	98	Cl	Cl	H	Cl	Cl	3,3
49	CH_3	H	CH_3	H	H	1	99	Cl	Cl	Cl	Cl	Cl	2,2
50	CH_3	$SO_2N(CH_3)_2$	H	H	Cl	3,7	100	CH_3	CH_3	Cl	CH_3	Cl	1,6

Table 1: A dataset of 100 N-arylanthranilic acids with their experimental activities.

RESULTS AND DISCUSSION

Molecular docking of ligands with the target proteins are routinely and extensively used to reduced cost and time of drug discovery. The target 2AW1 is docked with the geometrically optimized ligands: Aspirin and one hundred analogues N-anthranilic acids. Among the compounds, 56 out of 100 showed interaction energies. In Table 2, we can see the best poses ligands of our docking study. In Figures 4-8, we show the binding mode of the five best ligands: molecules N°11, 42, 53, 55, 97 (Table 2).

mol	**Docking method**	**PASS prediction**		**mol**	**Docking method**	**PASS prediction**	
N°	**Energy: (Kcal/mol)**	**Pa**	**Pi**	**N°**	**Energy: (Kcal/mol)**	**Pa**	**Pi**
1	-9,3	0,66	0,021	53	-10,31	0,638	0,025
2	-9,04	0,584	0,035	54	-10,19	0,604	0,031
3	-9,3	0,626	0,027	55	-10,51	0,677	0,019
4	-9,09	0,595	0,033	56	-	0,617	0,028
5	-8,46	0,533	0,043	57	-	0,54	0,046
6	-8,79	0,584	0,035	58	-	0,641	0,024
7	-8,73	0,499	0,057	59	-	0,374	0,109
8	-9,12	0,636	0,025	60	-	0,667	0,02
9	-8,53	0,499	0,057	61	-	0,67	0,02
10	-9,16	0,611	0,029	62	-	0,725	0,013
11	-10,4	0,543	0,045	63	-	0,615	0,028

12	-9,29	0,544	0,045		64	-	0,641	0,024
13	-9,88	0,542	0,045		65	-	0,475	0,065
14	-9,43	0,633	0,21		66	-	0,453	0,072
15	-8,77	0,479	0,063		67	-	0,461	0,069
16	-9,01	0,559	0,041		68	-9,82	0,592	0,034
17	-9,3	0,461	0,069		69	-	0,541	0,045
18	-9,63	0,556	0,042		70	-	0,562	0,04
19	-9,3	0,61	0,029		71	-	0,315	0,147
20	-9,42	0,631	0,026		72	-	0,577	0,037
21	-9,65	0,636	0,025		73	-	0,577	0,037
22	-10,1	0,589	0,034		74	-	0,585	0,035
23	-10,02	0,57	0,038		75	-	0,284	0,177
24	-9,53	0,061	0,021		76	-	0,45	0,073
25	-9,58	0,605	0,03		77	-	0,368	0,112
26	-8,6	0,456	0,071		78	-	0,537	0,046
27	-8,7	0,465	0,068		79	-	0,468	0,067
28	-8,4	0,484	0,062		80	-	0,634	0,025
29	-9,81	0,744	0,011		81	-10,21	0,55	0,043
30	-9,09	0,526	0,049		82	-10,16	0,482	0,063
31	-9,08	0,581	0,036		83	-	0,712	0,014
32	-9,26	0,0	0,0		84	-	0,483	0,062
33	-9,78	0,0	0,0		85	-	0,642	0,024
34	-9,86	0,621	0,028		86	-	0,635	0,025
35	-	0,505	0,055		87	-9,76	0,717	0,014
36	-8,77	0,0	0,0		88	-	0,591	0,034
37	-9,6	0,539	0,046		89	-	0,39	0,101
38	-9,29	0,582	0,036		90	-	0,723	0,013
39	-9,53	0,573	0,038		91	-	0,171	0,014
40	-8,69	0,404	0,094		92	-	0,596	0,033
41	-9,53	0,533	0,042		93	-	0,37	0,112
42	-10,3	0,602	0,031		94	-	0,653	0,022
43	-	0,729	0,012		95	-	0,595	0,033
44	-9,54	0,718	0,014		96	-	0,795	0,007
45	-9,62	0,59	0,034		97	-11,18	0,466	0,067
46	-	0,63	0,026		98	-	0,686	0,018
47	-9,53	0,621	0,029		99	-	0,653	0,022
48	-9,98	0,62	0,028		100	-	0,772	0,009
49	-8,25	0,618	0,028		101	-9,24	0,770	0,018
50	-	0,38	0,106					
51	-10,01	0,538	0,046					
52	-10,27	0,48	0,063					

Table 2: Arguslab docking scores for aspirin and N-arylanthranilic acids, Probability of anti-inflammatory.

For the ligand 11, there is one hydrogen bond: atom of oxygen in the water residue h bonds with atom of oxygen in the molecule 11. The interatomic distance of hydrogen bonding between OH and water is 2.974 Å shown in Figure 4.

For the ligand 42, there are two hydrogen bonds: —atom of azote N in the residue His-94 h bonds with atom of oxygen in the molecule. The interatomic distance of hydrogen bonding is 2.873 Å.—atom N in the residue His-119 h bonds atom of oxygen O of the molecule. The interatomic distance of hydrogen bonding is 2.899 Å shown in Figure 5.

For the ligand 53, there is one hydrogen bond: atom of oxygen in the residue His-94 h bonds with atom of oxygen in the molecule 53. The interatomic distance of hydrogen bonding is 2.909 Å shown in Figure 6.

For the ligand 55, there are three hydrogen bonds: —atom of oxygen in the residue Thr-199 h bonds with atom of oxygen in the molecule. The interatomic distance of hydrogen bonding is 2.9 Å.—atom of oxygen in the residue Thr-199 h bonds with atom of oxygen of the molecule. The interatomic distance of hydrogen bonding is 2.841 Å. —atom of N in the residue Thr-199 h bonds with atom oxygen of the molecule. The interatomic distance of hydrogen bonding is 2.462 Å shown in Figure 7.

For the ligand 97, there are four hydrogen bonds: —atom of N in the residue Thr-199 bonds with atom of oxygen in the molecule. The interatomic distance of hydrogen bonding is 2.796 Å.—atom of N in the residue Thr-199 h bonds with atom of oxygen of the molecule. The interatomic distance of hydrogen bonding is 2.221 Å. —atom of oxygen in the residue Thr-199 h bonds with atom oxygen of the molecule. The interatomic distance of hydrogen bonding is 2.692 Å. —atom of N in the residue Thr-200 h bonds with atom oxygen of the molecule. The interatomic distance of hydrogen bonding is 2.997 Å shown in Figure 8.

In this graph we show the binding mode of the five-best ligand with their energies and the graph of binding mode of aspirin shown in Figure 9 (Figures 4-9).

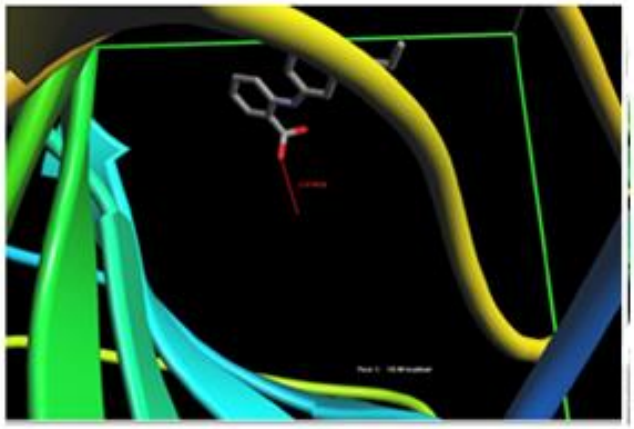

Figure 4: Binding mode of ligand 11 with 2AW1.

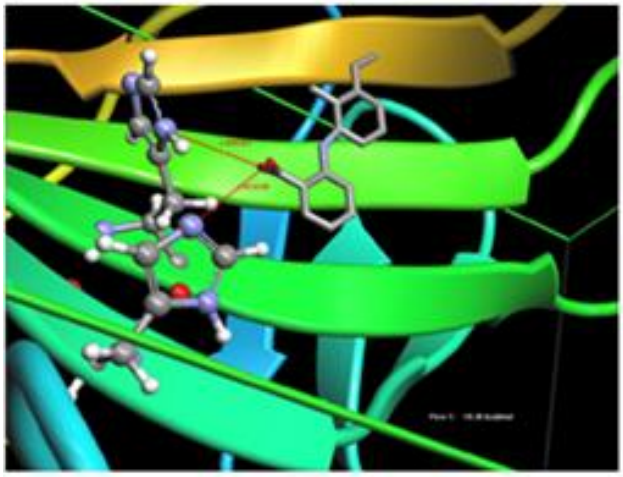

Figure 5: Binding mode of ligand 42 with 2AW1.

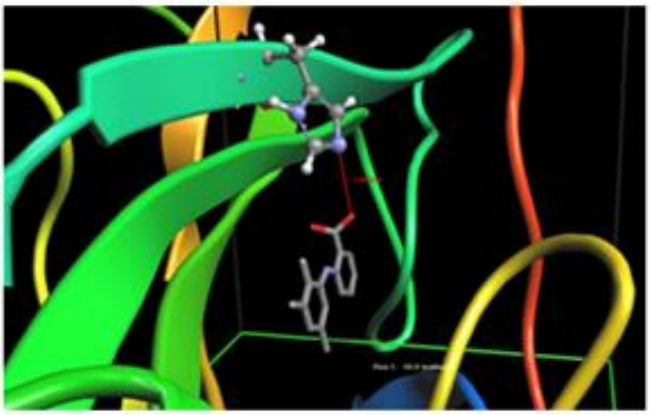

Figure 6: Binding mode of ligand 53 with 2AW1.

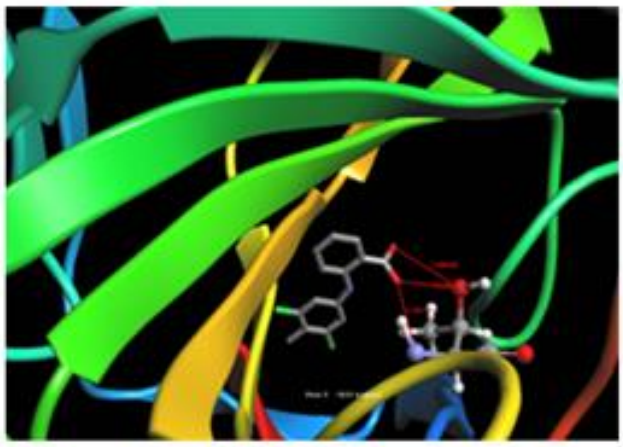

Figure 7: Binding mode of ligand 55 with 2AW1.

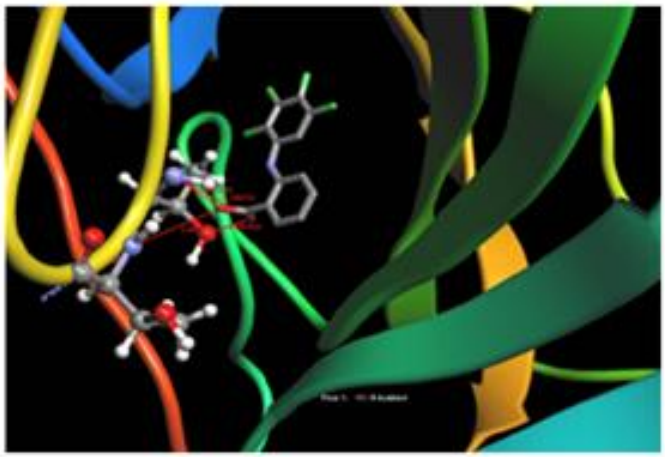

Figure 8: Binding mode of ligand 97 with 2AW1.

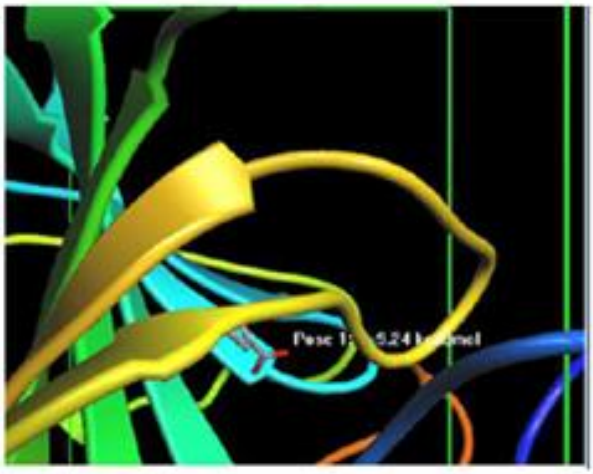

Figure 9: Binding mode of ligand aspirn with 2AW1.

Molecular modeling (docking) study was carried out for series of 100 N-anthranilic acids and aspirin, 56 out of 100 molecules show a good binding interaction. Among the 56 ligands, 41 molecules of N-anthranilic acids showed best binding energies than aspirin. The best five ligands of N-anthranilic acids and aspirin poses were shown in Figures 4 to 9. These best five compounds are the molecules N° 11, 42, 53, 55, 97, they possess respectively: -10.40 Kcal/mol, -10.30 Kcal/mol, -10.31 Kcal/mol, -10.51 Kcal/mol, -11.18 Kcal/mol. Binding interaction energy of aspirin is -9.24 Kcal/mol [27].

For a molecule to be considered as a potential drug, even if the latter has an acceptable anti-inflammatory activity, must obey Lipinski's rule. The drug likeness activity of the best five ligands molecules and aspirin are characterized using ADMET properties. They satisfy Lipinski's rule and ADMET properties results are shown in Table 3.

ligands	**M.W**	**Logp**	**PSA**	**DRS**	**ARS**
	Min : 200	Min : 2	Min : 0	Min : 0	Min : 0

	Max : 600	Max : 6	Max : 150	Max : 6	Max : 12
Molecule 11	255.31	5.37	49.33	2	3
Molecule 42	255.31	5.84	49.33	0	3
Molecule 53	255.31	5.52	49.33	2	3
Molecule 55	296.15	5.62	49.33	2	3
Molecule 97	351	6.19	49.33	2	2
aspirin	180.16	1.2	63.6	1	3

Table 3: Shows ADMET properties of five best ligands.

In Table 3, these five best ligands satisfy the "rule of five" except the compound 97. This compound possesses the partition coefficient (LogP) greater than 6, because of the present of four atoms of chloral (Cl) in the molecule.

The results of PASS prediction are also listed in the Table 3. For Pa>Pi, 73 out of 100 molecules possess a probability to be anti-inflammatory. For Pa>0.7, one has 9 molecules, the chance to find the activity in experiment is high. For 0.5<Pa<0.7, one have 64 molecules, the chance to find the activity in experiment is less. For Pa<0.5, one have 27 molecules.

CONCLUSION

We have reviewed the scoring functions currently used for protein–ligand interactions in molecular docking with arguslab. We have also described the computer system PASS (Prediction of Activity Spectra for Substances).The results and discussions made above lead to the conclusion that a serie of the 100 molecules of anthranilic acids have an anti-inflammatory properties. This has proven in a study using molecular docking and Prediction Activity Spectra for Substances (PASS). For the study using molecular docking, 100 N-anthranilic acids and aspirin were used, 56 out of 100 molecules show a good binding interaction with the target protein (2AW1). For Computer system PASS (Prediction of Activity Spectra for Substances), the same 100 N-anthranilic acids and aspirin were used, for Pa>Pi, 73 out of 100 molecules possess a probability to be anti-inflammatory. The results of our present study can be useful for the design and development of novel compounds having better inhibitory activity against several type of inflammation.

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