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In Silico Studies of Aurantiamide Acetate: Conformational Characterization and Admet

Larisso Gustavo de Oliveira Lasaro[1], Francisco Nithael Melo Lucio[2], Emmanuel silva Marinho [3]

Department of Chemistry, University State of Ceará, Brazil
Department of Chemistry, University State of Ceará, Brazil
Department of Chemistry, University State of Ceará, Brazil
Email id - [3]emmanuel.marinho@uece.br

***Abstract*— The future of drug research involves the use of mechanisms for the development / modification of drugs that allow more specific therapies to treat diseases. One of the current focuses is natural products with therapeutic potential, which, combined with drug design techniques, are trends that aim to promote the development of new pharmacological tools. In this context, the present work aimed to use in silico molecular modeling techniques to perform initial studies of the Aurantiamide acetate molecule, a substance found in plants of the genus Zapotece, which has shown several biological activities (antiprotozoal, anti-inflammatory and trypanocidal activity. Using the MMFF94 algorithm, it was possible to characterize the connections, angles, dihedral angles, dipole moment and render the Van der Waals surface of the Aurantiamide acetate molecule.The virtual screening algorithm for target classes showed proteases and receptor coupled to the A G family protein as possible biological targets. With respect to pharmacokinetics, Aurantiamide acetate, showed a high gastrointestinal adsorption potential, which contributes to good oral bioavailability.The results presented in this study indicate acetate with the promising therapeutic tool, being indicated for future studies in vitro and in vivo.**

***Keywords*— ADMET. MMFF94. Theoretical Chemistry. virtual screening.**

I. INTRODUCTION

One of the trends in the global pharmaceutical market is the development of products with components of natural origin, or at least the incorporation of natural active ingredients in these products. This practice produced great interest both in the national and international market for substances extracted from plants, mainly with scientific study proving its effectiveness[1][2]. The worldwide interest, especially in developed countries, has been observed over the years, by natural products, such as phytochemicals, phytopharmaceuticals, cosmetics and food supplements, stimulating investments from industrialized countries in bioprospecting[3].

The future of drug research involves the use of mechanisms for the development / modification of drugs that allow more specific therapies to treat diseases, in addition to reducing side effects [4][5]. Thus, the study of natural products with therapeutic potential combined with drug design techniques are trends that aim to promote the development of new pharmacological tools.

Molecular modeling techniques can foster the development of new drugs, since using more efficient algorithms and computers with greater processing power[6][7][8][9], they can simulate the behavior of substances against therapeutic targets[10][11]. The first step for modeling studies, consists in the conformational characterization of the molecule of interest[12][13][14], as well as simulating its pharmacokinetic viability[15].

In this perspective, the present work aimed to use molecular modeling techniques in silico to carry out initial studies of the Aurantiamide acetate molecule, a substance found in plants of the genus Zapotece, which has shown several biological activities (antiprotozoal, anti-inflammatory and trypanocidal activity[16][17][18], as a fundamental

step for future drug design and molecular docking studies.

II. METHODOLOGY

Conformational analysis is performed by rotating bonds, with parallel changes in torsional and dihedral angles and by corresponding calculations of steric energy resulting from the spatial overlap of unbound atoms and torsional rotation barriers. Using the postulates derived from Newtonian Mechanics, Molecular Mechanics is used to describe molecular systems, representing chemical systems with bonds and atoms, and with the interactions between unbound atoms. In these systems, the potential energy is calculated by the sum of several energetic contributions, such as the bond length, the bond angle, proper twist of the angles, interactions of unbound atoms (Coulombian and van der Waals) Eq. (1)[19][20].

$$\Delta E = \sum El + \sum Ea + \sum Et + \sum Enl \quad (1)$$

where terms are defined as:

$\sum El$ Energy depending on connection length;

$\sum Ea$ Energy depending on the connection angle;

$\sum Et$ Energy as a function of the proper torsion of the angles;

$\sum Enl$ Energy as a function of the interactions of unbound atoms (Coulombian and van der Waals).

Emphasizing that the energy of the covalent bonds as a function of the two connected particles is generally described by a simple harmonic term. Deviation from the reference length results in a potential energy Eq.(2)[19][20].

$$E_{bond} = \sum_{bond} k_l (l_l - l_l^{(0)})^2 \quad (2)$$

Where kl is defined as the bond constant and determines the bond strength, ll (0) is the reference length of the covalent bond.the Angular Energy, and calculated with a result of the deviation of a reference angle of the connections between three particles is described in a similar way to the energy of connection, using the same model eq.(3)[19][20].

$$E_{(langular)} = \sum_{angular} k_a (\theta_a - \theta_a^{(0)})^2 \quad (3)$$

where ka is called the angular constant and θa (0) is the reference angle.

The calculation of torsional energy has a great impact on the characterization of molecular conformation, being one of the main parameters that differentiate the force fields. These differences are evident mainly in the analysis of large molecules.Torsional energy is generally described using series of cosines eq.(4)[19][20].

$$E_{torsional} = \sum_{torsional} k_d [1 + cos(n\phi - d)] \quad (4)$$

Where kd is constant for each term and may be different or not for each, ϕ, ϕa (0) is the reference dihedral angle.

Van der Waals interactions are described using the Lennard-Jones function to describe in empirical terms the interactions that act on the pairs of particles.These interactions are the result of fluctuations in electronic density, present in all molecules,and dependent on polarizabilityeq.(5)[19][20].

$$E_{vdW}(R) = \sum_{I<J} 4\varepsilon_{IJ} \left[\left(\frac{\sigma_{IJ}}{R_{IJ}} \right)^{12} - \left(\frac{\sigma_{IJ}}{R_{IJ}} \right)^{6} \right] \quad (5)$$

Where the constant σIJ is the collision parameter and the constant ϵIJ odepth of interactions parameter.

The steepest descent algorithm consists of changing the coordinates of the particles in the negative gradient direction of the energy resulting from the interactions of the particles with the initial coordinates, it is the simplest gradient method to obtain a more stable conformation.Eq.(6) and Eq.(7)[19][20].

$$d_n = -\frac{\partial E(c_n)}{\partial c} \quad (6)$$

$$c_{n+1} = c_n + \Delta_n d_n \quad (7)$$

Where E (c) is the energy as a function of the coordinates c, cn are the coordinates in step n, Δn is always positive for the energy to always decrease.

As methodological steps, the PubChem® virtual online repository [https://pubchem.ncbi.nlm.nih.gov/][21] was first used to obtain the two-dimensional coordinates of the Aurantiamide acetate, IUPAC nomenclature and physicochemical properties. For the optimization process, the Avogadro®[22]package was used, configured to perform theoretical calculations of the classic Merck Molecular Force Field (MMFF94)[23] force level, performing cycles 500 interactions with speed descent algorithm and convergence parameter of the order of $10e^{-7}$. Noting that the MMF94 algorithm by Developed Merck Research Laboratories, was Initially parameterized with quantum calculations, having parameters for the Atoms of C, H, N, O, F, Si, P, S, Cl, Br, I and ions Fe +2, Fe + 3, F-, Cl-, Br-, Li +, Na +, K +, Zn + 2, Ca + 2, Cu + 1, Cu + 2 and Mg + 2, provides good precision for organic molecules[23], which fits the Aurantiamide acetate.Using the structural optimization output file, it was possible to characterize Aurantiamide acetate conformationally, as well as to identify the dipolar moment and to render the Van der Waals surface map.

The properties of Absorption, Distribution, Metabolization, Excretion and Toxicity (ADMET) including solubility, blood brain barrier (BBB) were predicted using the Swissadme code (http: // www. swissadme.ch/)[24], an online software written in JavaScript, HTML, and PHP5 with Python 2.7 encoded computing backend that allows you to accurately analyze 2D structures of drug candidates against ADMET descriptors [25][26][24]. lipophilicity was predicted according to Wildman et al [27],violations of oral bioavailability were assessed according to the Lipinski rule [28].At this stage we also examined the possible inhibitory character of Aurantiamide acetate Cytochrome Family (P450 CYP) isoforms such as CYP1A2 and CYP2D6, in addition to other pharmacokinetic predictions (gastrointestinal absorption, P-glycoprotein and blood brain barrier), as Ghose and Veber Rules and bioavailability [29][30].

Swiss Target Prediction algorithm was used to screen possible targets for biological interactions. [31][32][33]. *Homo sap*iens receiver search identifier [34], the Aurantiamide acetate two-dimensional structure was used, which was converted to 3D format, using the Tanimoto coefficient as an adjustment factor and similarity, vectorized by the Manhattan distance, defined by by the equation using the vectors (X and Y) and equation 2 to calculate the final value 3D similarity between molecules of i and j, where d ij is the shortest Manhattan distance between the 20 × 20 calculated distances over all possible conformations of each molecule [31] Eq. (8) and Eq.(9).

$$d = \sum_{s=1}^{18} |x_n - x_s| \quad (8)$$

$$1/(1 + 1/18 d\ ij \quad (9)$$

III. RESULTS AND DISCUSSION

Technological developments have provided advances in the means of information, since the internet is a large database of diverse information. In this perspective, the online virtual repository PubChem®[21][35], [36][37][38] was used to obtain initial information on the Aurantiamide acetate (PubChem CID: 124319), as its official nomenclature by IUPAC ([(2S) -2 - [(2-benzamido-3-phenylpropanoyl) amino] -3-phenylpropyl] acetate), molecular formula (C27H28N2O4), Molecular Weight (444.5 g / mol), Exact Mass (444.204907 g / mol), XLogP3 -AA (4.4), Monoisotopic Mass (444.204907 g / mol), Topological Polar Surface Area (84.5 Å²)(Table I). Two-dimensional coordinates show in their structure 4 hydrogen bond acceptor atoms, 2 hydrogen bond donor atoms and it does not have stereocenter counters for both defined and undefined bonds (figure1).

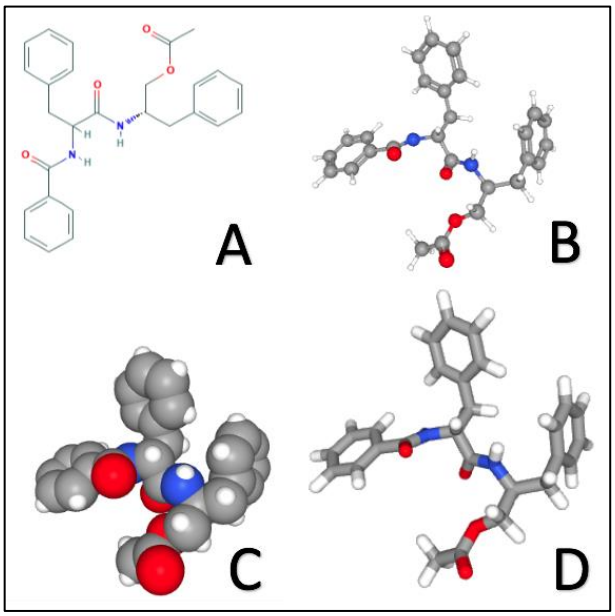

Fig. 1.Structural representations of the Aurantiamide acetate (A) two-dimensional (B) Ball and Stick (C) Space-Filling (D) Sticks

Table I
Physicochemical properties of Aurantiamide acetate

PropertyName	PropertyValue
Molecular Weight	444.5 g/mol
XLogP3-AA	4.4
Hydrogen Bond DonorCount	2
Hydrogen Bond AcceptorCount	4
Rotatable Bond Count	11
Exact Mass	444.204907 g/mol
Monoisotopic Mass	444.204907 g/mol
Topological Polar Surface Area	84.5 Å²
Heavy AtomCount	33
Formal Charge	0
Complexity	620
IsotopeAtomCount	0
DefinedAtomStereocenterCount	1
UndefinedAtomStereocenterCount	1
Defined Bond StereocenterCount	0
Undefined Bond StereocenterCount	0
Covalently-Bonded Unit Count	1
CompoundIsCanonicalized	Yes

Molecular modeling is an important tool for the study of molecules, since it consists of a set of computational techniques of visualizations and manipulations based on theoretical calculations that help in the study of complex molecular systems in order to obtain theoretical properties close to the real[39][40][41]. Structural and conformational analysis helps to understand the distribution of each atom of a molecule spatially, where it allowed us to investigate the molecular properties of a given compound[25]. When designing a molecule in software or removing it from online virtual repositories, it is not theoretically shaped in its native form [42]. Geometric optimization is one of the techniques used by molecular modeling with the intention of bringing complex molecular systems closer to their native forms[43][44]. This technique uses theoretical methods through the energy minimization process[45].

From the geometric optimization, Aurantiamide acetate (Figure 2) assuming its conformation thermodynamically closer to its native shape and potential energy 370,623 KJ / mol, it is possible to determine its structural properties. Table 2 shows the partial charges of each atom, where the presence of variations in charges of atoms of the same nature is noticed, since the carbons ranged from -0.062 to 0.304, those of oxygen from -0.463 to -0.251, the nitrogen -0.307 to -0.300 and hydrogens 0.033 to 0.150 (table II).

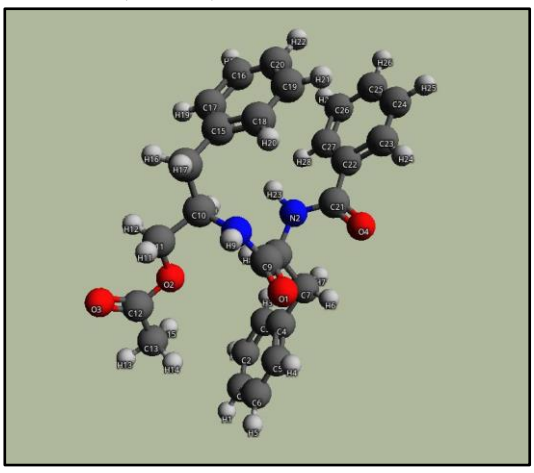

Fig. 2. Structural conformation of the Aurantiamide acetate.

Table II
Atomicproperties of Aurantiamideacetate

Atom	Type	Valence	Parcial Charge
1	03	2	-0.463
2	02	1	-0.274
3	02	1	-0.270
4	02	1	-0.251
5	Nam	3	-0.307
6	Nam	3	-0.300
7	C3	4	0.061
8	C3	4	0.104
9	C3	4	-0.006
10	C3	4	-0.001
11	C3	3	0.234
12	C3	4	0.111
13	Car	3	-0.046
14	Car	3	-0.045
15	Car	3	-0.059
16	Car	3	-0.059
17	C2	3	0.245
18	Car	3	-0.059
19	Car	3	-0.059
20	Car	3	-0.062
21	Car	3	-0.062
22	Car	3	0.037
23	Car	3	-0.062
24	Car	3	-0.062
25	Car	3	-0.062
26	Car	3	-0.062
27	C2	3	0.304
28	Car	3	-0.050
29	Car	3	-0.050
30	C3	4	0.033
31	Car	3	-0.061
32	Car	3	-0.061
33	Car	3	-0.062
34	H	1	0.149
35	H	1	0.150
36	H	1	0.053
37	H	1	0.060
38	H	1	0.033
39	H	1	0.033
40	H	1	0.034
41	H	1	0.034
42	H	1	0.072
43	H	1	0.072
44	H	1	0.062
45	H	1	0.062
46	H	1	0.062
47	H	1	0.062
48	H	1	0.062
49	H	1	0.062
50	H	1	0.062
51	H	1	0.062
52	H	1	0.062
53	H	1	0.062
54	H	1	0.063
55	H	1	0.063
56	H	1	0.034
57	H	1	0.034
58	H	1	0.034
59	H	1	0.062
60	H	1	0.062
61	H	1	0.062

Table III shows all identified connections, where we can highlight those that are of the second order of connection (O3 - C11), (O4 - C21), (O2 - C5), (C17 - C20), (C14 - C19), (C25 - C27), (C13 - C18), (C10 - C15), (C23 - C26), (C16 - C22), (C8 -C12), (C7 - C9). Regarding rotatable connections, the connections (C1 - C3), (C1 - C6), (C2 - C4), (C2 - C5), (C4 - C8), (C3 - C7), (C11 - C16) stand out), (C1 - N1), (C2 - N2), (O1 - C6), (N2 - C11), (N1 - C5), (O1 - C21).

Still on the connections, all connection angles were characterized (table 04) where the angles (C2 - N2 - H2) with an angle of 28.7482 ° and (C11 - N2 - H2) with an angle of 141.8608 ° stand out (Table IV).

Table III
Bonding property of the Aurantiamide acetate molecule

Typer	Start Atom	EndAtom	Bond Order	Length(Å)
O-C	O1	C6	1	1.44015
O-C	O1	C21	1	1.35573
O-C	O2	C5	2	1.2371
O-C	O3	C11	2	1.22617
O-C	O4	C21	2	1.22704
N-C	N1	C5	1	1.3614

N-H	N1	H1	1	1.01506
N-C	N2	C11	1	1.37705
N-H	N2	H2	1	1.01298
C-N	C1	N1	1	1.47517
C-C	C1	C3	1	1.5438
C-C	C1	C6	1	1.54125
C-H	C1	H3	1	1.09891
C-N	C2	N2	1	1.46503
C-C	C2	C4	1	1.53871
C-C	C2	C5	1	1.53391
C-H	C2	H4	1	1.08875
C-C	C3	C7	1	1.51128
C-H	C3	H5	1	1.09808
C-H	C3	H6	1	1.09546
C-C	C4	C8	1	1.51578
C-H	C4	H7	1	1.09784
C-H	C4	H8	1	1.09828
C-H	C6	H9	1	1.09605
C-H	C6	H10	1	1.09076
C-C	C7	C9	2	1.40143
C-C	C7	C10	1	1.40177
C-C	C8	C12	2	1.40083
C-C	C8	C13	1	1.40512
C-C	C9	C14	1	1.39522
C-H	C9	H11	1	1.08841
C-C	C10	C15	2	1.39591
C-H	C10	H12	1	1.08731
C-C	C11	C16	1	1.48548
C-C	C12	C17	1	1.39738
C-H	C12	H13	1	1.08777
C-C	C13	C18	2	1.39586
C-H	C13	H14	1	1.08983
C-C	C14	C19	2	1.39317
C-H	C14	H15	1	1.08697
C-C	C15	C19	1	1.39355
C-H	C15	H16	1	1.08689
C-C	C16	C22	2	1.39984
C-C	C16	C23	1	1.40088
C-C	C17	C20	2	1.39268
C-H	C17	H17	1	1.08727
C-C	C18	C20	1	1.39163
C-H	C18	H18	1	1.0871
C-H	C19	H19	1	1.08672
C-H	C20	H20	1	1.08667
C-C	C21	C24	1	1.50126
C-C	C22	C25	1	1.39564
C-H	C22	H21	1	1.08797
C-C	C3	C26	2	1.39665
C-H	C23	H22	1	1.08717
C-H	C24	H23	1	1.0914
C-H	C24	H24	1	1.09242
C-H	C24	H25	2	1.09486
C-C	C25	C27	1	1.3948
C-H	C25	H26	1	1.08716
C-C	C26	C27	1	1.39522
C-H	C26	H27	1	1.08751
C-H	C27	H28	1	1.08747

Table IV
Aurantiamideacetateangleproperties

Typer	**Start Atom**	**Vertex**	**EndAtom**	**Angle(Å)**
COC	C6	O1	C21	121.4578
CNH	C5	N1	H1	109.9579
CNC	C1	N1	C5	131.9632
CNH	C1	N1	H1	114.3981
CNH	C11	N2	H2	118.6663
CNC	C2	N2	C11	120.7315
CNH	C2	N2	H2	115.2193
NCC	N1	C1	C3	112.9469
NCC	N1	C1	C6	115.6505
NCH	N1	C1	H3	102.7517
CCC	C3	C1	C6	110.6515
CCH	C3	C1	H3	108.3183
CCH	C6	C1	H3	105.7024
NCC	N2	C2	C4	111.8663
NCC	N2	C2	C5	105.8408
NCH	N2	C2	H4	108.7656
CCC	C4	C2	C5	108.4408
CCH	C4	C2	H4	112.1582
CCH	C5	C2	H4	109.5601
CCC	C1	C3	C7	113.3836
CCH	C1	C3	H5	109.7300
CCH	C1	C3	H6	110.4209
CCH	C7	C3	H5	107.8889
CCH	C7	C3	H6	109.5421
HCH	H5	C3	H6	105.5490
CCC	C2	C4	C8	116.3905
CCH	C2	C4	H7	108.7139
CCH	C2	C4	H8	110.0948
CCH	C8	C4	H7	107.2767
CCH	C8	C4	H8	107.6668
HCH	H7	C4	H8	106.2034
OCN	O2	C5	N1	117.9813

OCC	O2	C5	C2	120.6357
NCC	N1	C5	C2	121.2484
OCC	O1	C6	C1	109.4297
OCH	O1	C6	H9	108.7866
OCH	O1	C6	H10	109.4639
CCH	C1	C6	H9	108.6850
CCH	C1	C6	H10	111.8437
HCH	H9	C6	H10	108.5753
CCC	C3	C7	C9	120.2364
CCC	C3	C7	C10	120.7742
CCC	C9	C7	C10	118.9876
CCC	C4	C8	C12	123.9876
CCC	C4	C8	C13	118.4622
CCC	C12	C8	C13	118.3541
CCC	C7	C9	C14	120.4950
CCH	C7	C9	H11	120.5042
CCH	C14	C9	H11	119.0008
CCC	C7	C10	C15	120.4135
CCH	C7	C10	H12	120.6036
CCH	C15	C10	H12	118.9828
OCN	O3	C11	N2	123.2061
OCC	O3	C11	C16	120.2900
NCC	N2	C11	C16	116.5029
CCC	C8	C12	C17	120.6462
CCH	C8	C12	H13	121.2904
CCH	C17	C12	H13	118.0627
CCC	C8	C3	C18	120.9371
CCH	C8	C13	H14	120.3331
CCH	C18	C13	H14	118.7292
CCC	C9	C14	C19	120.0648
CCH	C9	C14	H15	119.8269
CCH	C19	C14	H15	120.1082
CCC	C10	C15	C19	120.0964
CCH	C10	C15	H16	120.0241
CCH	C19	C15	H16	119.8794
CCC	C11	C16	C22	118.3715
CCC	C11	C16	C23	121.7514
CCC	C22	C16	C23	119.8383
CCC	C12	C17	C20	120.2763
CCH	C12	C17	H17	119.7494
CCH	C20	C17	H17	119.9745
CCC	C13	C18	C20	119.9757
CCH	C13	C18	H18	119.8701
CCG	C20	C18	H18	120.1531
CCC	C14	C19	C15	119.9414
CCH	C14	C19	H19	119.9691
CCH	C15	C19	H19	120.0894
CCC	C17	C20	C18	119.7873
CCH	C17	C20	H20	120.0954
CCH	C18	C20	H20	120.1126
OCO	O1	C21	O4	120.8366
OCC	O1	C21	C24	117.2940
OCC	O4	C21	C24	121.8539
CCC	C16	C22	C25	120.0701
CCH	C16	C22	H21	120.1464
CCH	C25	C22	H21	119.7834
CCC	C16	C23	C26	119.8440
CCH	C16	C23	H22	121.2983
CCH	C26	C23	H22	118.8249
CCH	C21	C24	H23	111.0781
CCH	C21	C24	H24	110.2315
CCH	C21	C24	H25	108.8556
HCH	H23	C24	H24	111.2657
HCH	H23	C24	H25	107.5467
HCH	H24	C24	H25	107.7368
CCC	C22	C25	C27	119.9721
CCH	C22	C25	H26	120.0697
CCH	C27	C25	H26	120.1170
CCC	C23	C26	C27	120.1170
CCH	C23	C26	H27	119.9443
CCH	C27	C26	H27	119.9349
CCC	C25	C27	C26	120.1392
CCH	C25	C27	H28	119.9218
CCH	C26	C27	H28	119.9355

Using the Van de Waals radius to represent the atoms of a molecule as a sphere, it is possible to plot a three-dimensional rendering of the molecule, which we define as the van der Waals surface map[46]. the sum of the individual van der Waals surfaces due to the overlap of intersecting spheres. From the conformational calculations[14], it is possible to verify the dipole moment and the Van Der Waals surface of the Aurantiamide acetate molecule(figure 3).

The polarity of the molecules is a very important aspect, as the characteristics of the substances are determined, among other factors, by the fact that their molecules are polar or nonpolar, which is preponderant to predict their solubility and adhesion to biological systems. a molecule expresses the measurement of molecular polarity[47][48]. Aurantiamideacetateobtainedthe dipolar moment 6,241 D, indicating high polarity and preferentialsolubility in polar solvents.

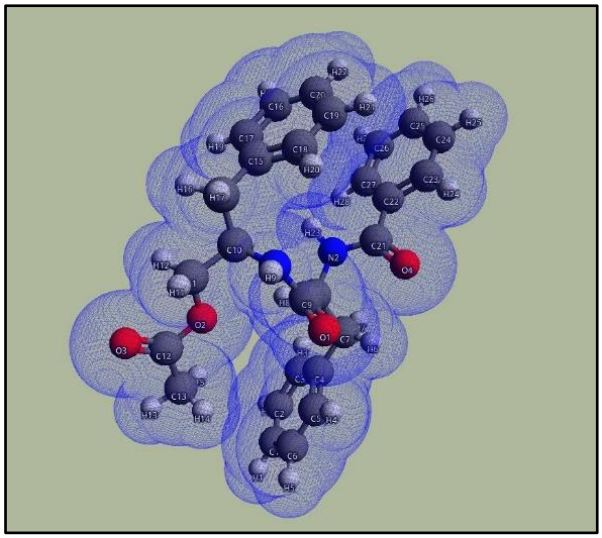

Fig.3. Van der Waals surface from Aurantiamide acetate

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The search for more effective pharmacological tools has fostered the development of computational algorithms, which allow to simulate the interaction of receptor drugs (molecular coupling) with greater precision [[11][49][50][6][51], as well as predicting the pharmacokinetics, being able to identify within a set of molecules those that can become an efficient drug with fewer side effects, thus promoting the development of drugs. The algorithms use mechanisms, based on molecular descriptors, that adjusted within facets (models) and rules allow structures to be quickly related to pharmacokinetic properties [[31][52][53][53].

The chemical structure of Aurantiamide acetate was subjected to ADMET in silico screening using SwissADME online software to predict overall absorption, distribution, metabolism, excretion and toxicity hazards. In the silico evaluation, we analyzed different descriptors that were calculated, partition coefficient (octanol / water), , number of H^+ donor groups and acceptor groups that compounded moderate solubility in waterand Consensus lipophilicity in the order of 3.89. Absorption or permeation of a molecule is more likely when the molecular weight is below the log P value is less than 5 and the value. Aurantiamide acetate has a maximum of $2H^+$ donors and 4 H^+ acceptor atoms as shown in Table V.

Table V

Aurantiamide acetate physicochemical and solubility descriptors generated by the ADMET algorithm

PhysicochemicalProperties	
Molecular weight	444.52 g/mol
Num. heavy atoms	33
Num. arom. heavy atoms	18
Fraction Csp3	0.22
Num. rotatablebonds	13
Num. H-bondacceptors	4
Num. H-bonddonors	2
Molar Refractivity	126.35
TPSA	84.50 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	3.57
Log $P_{o/w}$ (XLOGP3)	4.45
Log $P_{o/w}$ (WLOGP)	3.32
Log $P_{o/w}$ (MLOGP)	3.41
Log $P_{o/w}$ (SILICOS-IT)	4.73
Consensus Log $P_{o/w}$	3.89
WaterSolubility	
Log *S* (ESOL)	-4.95
Solubility	5.04e-03 mg/ml ; 1.13e-05 mol/l
Class	Moderatelysoluble
Log *S* (Ali)	-5.94
Solubility	5.06e-04 mg/ml ; 1.14e-06 mol/l
Class	Moderatelysoluble
Log *S* (SILICOS-IT)	-8.70
Solubility	8.87e-07 mg/ml ; 2.00e-09 mol/l
Class	Poorlysoluble

According to its pharmacokinetic properties, Aurantiamide acetate showed a high level of gastrointestinal adsorption which contributes to good oral bioavailability. Aurantiamide acetate showed inhibitory potential on P-gp substrate, CYP2C19

inhibitor CYP2C9 inhibitor CYP2D6 inhibitor CYP3A4 inhibitor, with p skin permeation Log Kp in the order of -5.85 cm / s.

The prediction of similarity with other drugs was also carried out according to the rules of Ghose and Veber and the molecule has characteristics of bioavailability [29]. Aurantiamide acetate did not violate the rules of Lipinski, Ghose, Egan, Muegge, showing only one violation of the Veber rule (Rotors> 10).

Thus, the screening process with the Lipinski rule showed that there were no compound violations, as the screening process with the Ghose rules shows that the substance Aurantiamide acetate can be accepted for not showing violations of the drug similarity rules (figure 10).

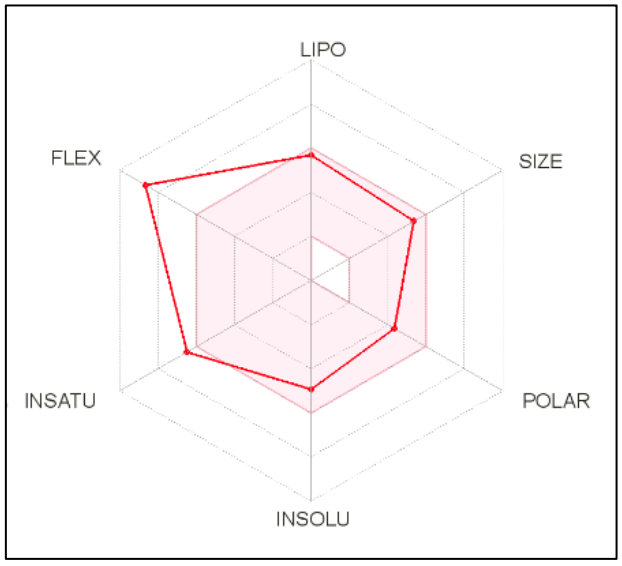

Fig. 4. Biovailability and pharmacokinetic parameters Aurantiamide acetate using Swiss ADME

The Virtual screening for target classes algorithm, presented the targets of possible interactions with possible biological targets, and can be a descriptor for therapeutic improvement [72]. As for possible classes of biological targets, Aurantiamide acetate had a higher probability of interactions with proteases (66.7%), and Family A G protein-coupled receptor (33.3%) (Figure 5).

Regarding specific goals, it was more likely to interact with the 11-beta-hydroxysteroid dehydrogenase 1, 3-phosphoinositide dependent protein kinase-1, 5-lipoxygenase activating protein, Acyl coenzyme A:cholesterol acyltransferase 1, Angiotensin-converting enzyme, Beta-secretase 1, Bile acid receptor FXR, Bromodomain-containing protein 2 and 4,C-C chemokine receptor type 3, c-Jun N-terminal kinase 1, Calpain 1,Carbonic anhydrase II,Caspase-1

Cathepsin (B and K)which was classified as the best binging probability in the SwissTarget Prediction report .

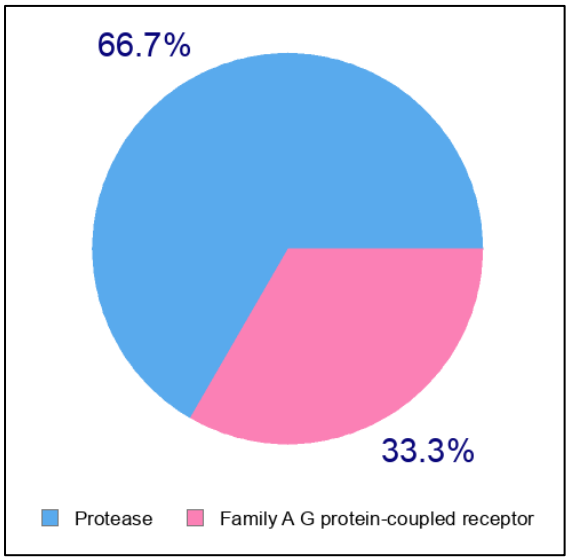

Fig. 5. Virtual Screening for Target Classes for Aurantiamide acetate.

IV. CONCLUSIONS

The future of drug research involves the use of mechanisms for the development / modification of drugs that allow more specific therapies to treat diseases.. Aurantiamide acetate molecule was characterized (connections, angles, dihedral angles, dipolar moment and rendering the surface of Van der Waals). The virtual screening algorithm for target classes showed proteases and receptor coupled to the A G family protein as possible biological targets. With respect to pharmacokinetics, Aurantiamide acetate, showed a high gastrointestinal adsorption potential, which contributes to good oral bioavailability. The results presented in this study

indicate acetate with the promising therapeutic tool, being indicated for future studies in vitro and in vivo.

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