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Molecular docking studies and *in silico* pharmacokinetic property study of synthesized organotin complex of (1r, 2s, 5r)-2-isopropyl-5-methylcyclohexanol

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ABSTRACT

The main objective of our research was to synthesis organotin complex of (1R, 2S, 5R)-2-Isopropyl-5-Methylcyclohexanol having potential to work as antimicrobial agent. The synthesized complex was characterized by UV –Visible and ^{1}H NMR. Molecular docking was done using computational software iGEMDOCK (Graphical Drug Design system for Docking, Screening and Post-analysis). Docking was done using different Protein Data Bank files (3EOO, 3D2U, 2I42 and 3D2Y) to analyze the antibacterial study and the interaction of the potent complex against *Burkholderia pseudomallei, Human cytomegalovirus, Yersinia enterocolitica and Escherichia coli*. Organotin complex of (1R, 2S,5R)-2-isopropyl-5-methylcyclohexanol has shown good docking results on almost all the receptors, with interaction supporting the fitting of the drug to the target molecules. The complex was found to having potency to efficiently inhibit the microbes. Further pharmacokinetic study has shown that the complex has the potential to cross Blood Brain Barrier, pass human intestine, $CaCO_2$ permeable, it was found to be Non AMES toxic and non-carcinogenic.

KEY WORDS: Organotin complex, iGEMDOCK, computational studies, Protein Data Bank, admet SAR, Pharmacokinetic properties, Blood Brain Barrier.

1. INTRODUCTION

Organotin complex have many application in biological and potential activity such as antineoplastic and anti-tuberculosis (Rehman, 2006; 2009). It can likewise utilized as marine anti-biofouling, preservatives, fungicides, as bactericides, acaricides (killing ticks and mites), anticancer treatment, antifungal agents in paints and for the generation of tin dioxide on glass bottles (Warren, 1973).

For computer aided drug designing and structural molecular biology, molecular docking is exceptional tool. The general principal of ligand- protein dock that governs the uppermost binding of ligand with protein or nucleic acid target (3-dimensional structure). The interaction involves between ligand and proteins are vander waal, hydrogen and electrostatic. The principal provides the theoretical framework for designing the desired compound having potency and specificity of potential drugs lead for a given therapeutic target. Docking can execute the outcome and suggest structural hypotheses of how target is repressed by ligand that is vital in lead optimization.

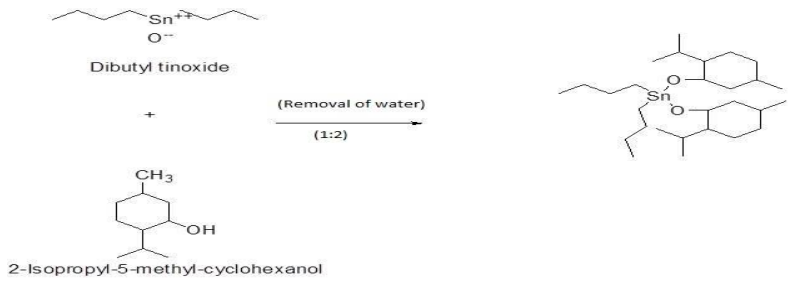
There are so many docking programs software programming accessible yet we have worked just on iGEMDOCK, a structure-based Virtual Screening system. An autogenous docking tool with offices from preparations to post-screening analysis. This is extremely useful software to provide associated interfaces to construct both the binding site of the target protein and the screening compound. The compounds is then docked with the binding sites and subsequently, iGemdock bring out protein interaction profiles of Vander Waal's (V) interactions, electrostatic (E) Hydrogen-bonding (H). Eventually, iGEMDOCK ranks and conceptualize the compound to be screened by combination of the energy-based scoring function and pharmacological interactions. (Balavignesh, 2013). This incorporates the virtual screening based on structure and post-screening analysis, thus it is a helpful framework for drug discovery. This is maintained by Drug Design and Systems Biology Laboratory of National Chiao Tung University, Taiwan. The precision of docking and the screening utility were superior to other docking methods. These results have been published (Yang and Chen, 2004).

2. MATERIALS AND METHODS

Material: Analytical Grade chemicals and solvents were used and all of them were obtained from commercial sources like, Spectrochem, Qualigen, Fischer scientific and Merck specialitics. Solvents were dried and purified by standard procedures (Armarego and Perrin, 1996). *In silico* study was carried out using software iGEMDOCK at ARSD College, University of Delhi.

Experimental Method: Synthesis of the organotin complex of (1R, 2S, 5R)-2-isopropyl-5-methylcyclohexanol was done by using conventional method that is aziotropic distillation method. Dry benzene (30 ml) along with absolute ethanol (10 ml) and 0.2489g dibutyltin (IV) oxide (1mmol) were added in round bottom flask. 0.31254g of ligand (1R, 2S, 5R)-2-isopropyl-5-methylcyclohexanol (2 mmol) was added maintaining the molar ratio of 1:2 (metal: ligand). The entire mixture was then refluxed azeotropically in a Dean Stark separator for 10-15 min. Refluxing was further proceeded for 6 hours till complete removal of water and excess solvent left was discarded using a rotator

evaporator (Aniyery Rohit Babu, 2015). After synthesis the complex was characterized by UV visible spectra studies and ^{1}H NMR spectral. The characteristic peaks observed confirmed the complex formation.



Scheme: Synthesis of organotin complex of (1R, 2S, 5R)-2-isopropyl-5-methylcyclohexanol

Preparation of Binding site: All the protein structure files were acquired from Protein Data Bank (http://www.rcsb.org/) (PDB ID: 2I42, 3EOO, 3D2U and 3D2Y). The best binding pocket was selected considering the site score and site's hydrophobic/hydrophilic areas, which bears better cavity.

Ligand Preparation: The ligand (organotin complex of (1R, 2S, 5R)-2-isopropyl-5-methylcyclohexanol) structure was drawn using chemdraw and chem. Draw 3D software. The structure was optimized prior docking using Gaussian software. iGEMDOCK software accepts MDL MOL, SYBYL MOL2 and PDB format for ligand files. Therefore the ligand file was converted into MOL 2 format by Open babel software (Noel, 2011). The ligand was docked with the binding site of each PDB files using accurate docking function (slow docking). Finally, the post analysis tool visualized and ranked the compound to be screened by merging the pharmacological interactions and energy-based scoring function

***In Silico* Pharmacokinetic Properties Study:** ADMET properties that is Absorption, Distribution, Metabolism and Toxicity were calculated using admetSAR database which provides latest and most inclusive manually created data for various chemicals with known ADMET properties (Feixiong Cheng, 2012).

3 RESULTS AND DISCUSSION

Physical study: Organotin complex of (1R, 2S, 5R)-2-isopropyl-5-methylcyclohexanol [$C_{28}H_{36}O_2Sn$] having molecular weight 455.18 g·mol^{-1}was obtained in good yield (0.4457 g), 82% and was white coloured viscous semisolid soluble in Dimethyl Sulphoxide (DMSO)and ethanol.

UV absorption spectra: The λ_{max} of ligand ((1R, 2S, 5R)-2-isopropyl-5-methylcyclohexanol) was found to be 220nm and absorbance 0.010000 which is generally assigned to π-π* transition. The λ_{max} of organotin complex was recorded at 249 nm and absorbance 1.150000; this was actually due to the coordination or attaching of ligand with the Dibutyl Tin Oxide. The shift in the peak from 220nm to 249nm (Redshift) is attributed to the n--$\boldsymbol{\pi}$* transition which indicates the ligand metal charge transfer (LCMT). Shifting of the UV peaks to higher wavelength shows 'Bathochromic shift or Red shift'. This gives an evidence of complex formation of ligand with dibutyl tin oxide (Leovacet, 2007; Norrihen San, 2012).

^{1}H NMR spectra: The Organotin complex showed resonance signals (ppm):3.16 (-CH, Cyclohexane), 1.50 (-CH cyclohexane), 1.61 (-CH, cyclohexane), 1.68, 1.42 (-CH_2, cyclohexane), 1.52, 1.27 (-CH_2, cyclohexane), 1.3 (-CH_2, methylene), 1.82 (-CH, methane), 0.96 (-CH_3, methyl), 1.26 (-CH_2, methyl), 1.31 (-CH_2, methyl), 0.91 (-CH_3, methyl). The absence of -OH proton signal in the ^{1}H NMR spectra of the organotin (IV) complexes (Jose and Casas, 2004) indicated that the phenolic oxygen is coordinated to the Sn (IV) atom after deprotonation.

***In Silico* Antimicrobial Studies Using Molecular Docking Software (iGEMDOCK):** iGEMDOCK is a tool which can allow a superior and starting point for reasoning pharmacological interaction which facilitate results in perceiving another novel and potentially active compounds for a specific protein, responsible for causing diseases. The highest binding energy of receptor - ligand interactions supports the fitting of the drug to the target molecules. The negative value of binding energy change (ΔG) reveals that the binding process is spontaneous. The binding energy with highest value supports the fitting of the drug to the target molecules. Larger the negative value of binding energy, greater the chemical be accepted as a drug (Balavignesh, 2013).

Table.1. Summary of Total energy, Vander-Waal interaction, Hydrogen bonding, and electrostatic energy of stannane of (1R, 2S, 5R)-2-isopropyl-5-methylcyclohexanol on interaction with PDB files

PDB File	Total Energy (kcal/mol)	VDW (kcal/mol)	Hydrogen Bond (kcal/mol)	Electrostatic (kcal/mol)	AverConPair (kcal/mol)
3D2U	-59.2155	-59.216	0	0	13.3548
3D2Y	-57.6844	-57.684	0	0	13.6129
3EOO	-62.3422	-59.877	-2.46509	0	27.129
2I42	-68.0088	-64.303	-3.70565	0	13.7742

PDB 3D2U is basically the Protein Data Bank file for Structure of UL18, a Peptide-Binding Viral MHC Mimic, Bound to a Host Inhibitory Receptor, Gene Names: H301, Glycoprotein UL18.

Human cytomegalovirus or herpes viruses expresses Glycoprotein UL18 which is essentially an intensely glycosylated transmembrane bestowing ≈25% sequence identity with class I MHC molecules and helps to prevent host lysis (Fahnestock, 1995). The role of UL18 has been accounted for to hinder the NK-cell-mediated lysis in some experimental conditions but not others (Wagner, 2008). Human cytomegalovirus infections are mainly associated with the salivary glands. Cytomegalovirus shed in the fluids discharged from the body of any infected person, and thus it can be found in urine, saliva, blood, tears, semen, and breast milk. Eventually, it may cause mucoepidermoid carcinoma and possibly other malignancies such as prostate cancer.

PDB 3D2U	
Amino acid residue	**Energy(kcal/mol)**
H-S-ASN-54	0
H-S-NAG-811	0
H-M-FUC-814	0
V-S-ASN-54	-7.38506
V-M-GLY-18	-4.79989
V-S-LYS-19	-6.41114
V-M-NAG-811	-4.33435
V-S-NAG-811	-8.52251
V-M-FUC-814	-5.37835

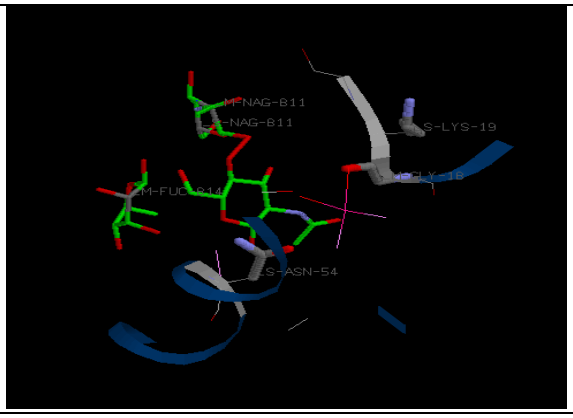


Figure.1. Docking pose of organotin complex of (1R,2S, 5R)-2-isopropyl-5-methylcyclohexanol with PDB 3D2U

Conclusion: From the results of docking, the synthesized organotin complex was found to fit well with the binding sites of the target protein. The complex interacted with the PDB file with total fitness value -59.2155 kcal/mol which comprises mainly of Van der waal interaction. The complex interacted with the residues V-S-ASN-54, V-M-GLY-18, V-S-LYS-19, V-M-NAG-811, V-S-NAG-811and V-M-FUC-814- of binding pocket (refer figure 1). The complex interacted with the residues of basic amino acid like N-Acetyl –Glucosamine at position 811 with binding energy value -8.52251 kcal/mol, Lysine at position 19 with binding energy value -6.41114 kcal/mol. Asparagine at position54 with binding energy value -7.38506kcal/mol and FUC at position 814 with binding energy value -5.37835 kcal/mol. The organotin complex has potency to effectively inhibit the Human cytomegalovirus' Glycoprotein UL18 Bound to a Host Inhibitory Receptor.

PDB 3D2Y is a Protein Data Bank file for Complex of the N-acetylmuramyl-L-alanine amidase AmiD from *E.coli* with the substrate anhydro-N-acetylmuramic acid-L-Ala-D-gamma-Glu-L-Lys.

Peptidoglycan is an important segment of the cell wall that gives the shape to bacterial cells and guarantees them against high internal osmotic pressures. It is comprised of glycan chains with alternating units of *N*-acetylglucosamine (GlcNAc) and *N*-acetylmuramic acid (MurNAc) that are interconnected by covalent cross-links between short peptides. In *Escherichia coli*, four *N*-acetylmuramoyl-L-alanine amidases, AmiA, -B, -C, and -D, are found in the periplasm. AmiA, -B, and -C are soluble enzymes, whereas AmiD is a lipoprotein which anchored in the outer membrane. AmiD is the 5th recognized N-acetylmuramoyl-L-alanine zinc amidase of Escherichia coli. AmiD is efficient in cleaving the intact peptidoglycan (PG) also soluble fragments having N-acetylmuramic acid. Peptidoglycan fragments with at least three amino acids in their peptide chains is hydrolyzed by AmiD and the presence of an anhydro function on the *N*-acetylmuramic acid is not essential (Frederic Kerff, 2010).

PDB 3D2Y	
Amino acid residue	**Energy (kcal/mol)**
H-M-ALA-2	**0**
V-M-TRP-110	-4.24786
V-S-TRP-110	-16.1546
V-M-LYS-159	-1.47527
V-S-LYS-159	-6.31117
V-S-ASP-160	-1.98721

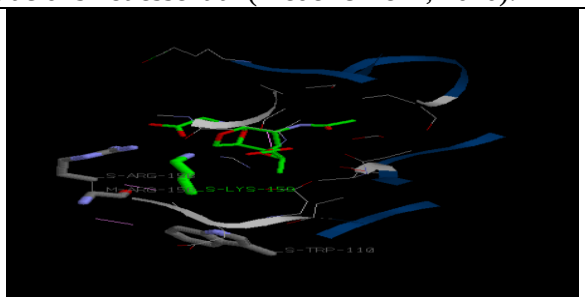


Figure.2. Docking pose of organotin complex of ` (1R,2S, 5R)-2-isopropyl-5-methylcyclohexanol with PDB 3D2Y

Conclusion: The complex interacted with the PDB file with total fitness Value -57.6844 kcal/mol which comprises mainly of Van der waal interaction. The complex also interacted with the residues of V-M-TRP-110, V-S-TRP-110, V-S-LYS-159 and V-S-ASP-160 of binding pocket (figure.2). The complex interacted with the residues of basic

amino acid like Trytophan at position 110 with binding energy value -16.1546 kcal/mol, Lysine at position 159 with binding energy value -6.31117kcal/mol and Aspartate at position 160 with binding energy value -1.98721kcal/mol. It easily binds to protein structure which plays an important role in hydrolyzing the link between N-acetylmuramoyl residues and L-amino acid residues in certain cell-wall glycopeptides. The function like bacterial cell wall organization, peptidoglycan turnover (continual breakdown and regeneration of peptidoglycan required to maintain the cell wall) and peptidoglycan catabolic process could be hindered if the complex interact with this protein. Thus it has the potency to hinder the growth of *Escherichia coli*.

PDB 3E00 is 2.9A crystal structure of methyl-isocitrate lyase from *Burkholderia pseudomallei*, the causative organism for disease called melioidosis. It symptoms include acute, chronic, and latent pulmonary infections. *B. pseudomallei* is an intracellular pathogen that causes lung pathology similar to that caused by tuberculosis

Catalytic activity/Lyase activity of the protein: Propionate is oxidized to yield pyruvate via the methylcitrate cycle in which 2-methylisocitrate lyase catalyzes the thermodynamically favoured C-C bond cleavage of (2R, 3S)-2-methylisocitrate to yield pyruvate and succinate.

(2S, 3R)-3-hydroxybutane-1, 2, 3-tricarboxylate ⇌ pyruvate + succinate

Propionate catabolic process: Methylcitrate cycle (Upton AM and McKinney JD (2007). a modified version of the Krebs cycle that metabolizes propionyl coenzyme A, instead of acetyl coenzyme A. The enzyme 2-methylcitrate synthase adds propionyl coenzyme A to oxaloacetate, which yields methylcitrate instead of citrate. Methylisocitrate lyase plays a supervisory function in this cycle; being activated by NAD but inhibited noncompetitively by NADH and NADPH.

PDB 3EOO	
Amino acid residue	**Energy (kcal/mol)**
H-M-ILE-428	**0**
H-M-GLY-429	**0**
V-S-GLU-307	**0**
V-S-LEU-353	**0**
V-M-GLY-429	-0.298167

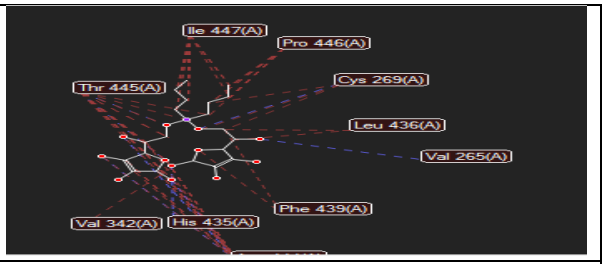


Figure.3. Docking pose of organotin complex of (1R,2S, 5R)-2-isopropyl-5-methylcyclohexanol with PDB 3EOO

Conclusion: The complex interacted with the PDB file with total fitness Value -62.3422 kcal/mol which comprises Van der waal interaction energy value of -59.877 kcal/mol and Hydrogen bonding with energy value -2.46509 kcal/mol. The complex interacted with the residue V-M-GLY-429 of binding pocket (refer figure 3). The complex interacted with residues of basic amino acid like Glycine at position 429 with binding energy value -0.298167 kcal/mol. This complex has the potency to use as antibiotic agent against *Burkholderia pseudomallei* .If proper antibiotics are not supplied in combination with isocitrate lyase inhibitors, the resulting *B. pseudomallei* infection overwhelms the host, resulting in death.

PDB 2I42 is Crystal structure of Yersinia protein tyrosine phosphate complexed with vanadate**.** *Yersinia enterocolitica* is a Gram-negative bacterium which causes the disease yersiniosis. Pathogenic species of *Yersinia* harbor an extra chromosomal that is crucial for *Yersinia* pathogenicity. This plasmid encodes the genes of a type III secrection system. On association with the host cell, the *Yersinia* type III secretion system transfers a set of effectors proteins termed Yops (*Yersinia* outer proteins) into the host cell. Six Yop effectors (YopH, YopE, YopJ/P, YpkA/YopO, YopT, and YopM) have been recoginized to date, and they function to constrict the host immune response during infection (Black, 1997). Five of the six Yops have catalytic activities that seem to be essential for their pathogenic functions (Wulff-Strobel, 2002). YopH, a protein tyrosine phosphatase (Cornelis, 1997), inhibits the tyrosine phosphorylation signaling that is essential for the assembly of focal adhesion complexes, resulting in the inhibition of macrophage phagocytosis.

PDB 2I42	
Amino Acid Residue	**Energy (kcal/mol)**
V-S-ARG-255	-6.61578

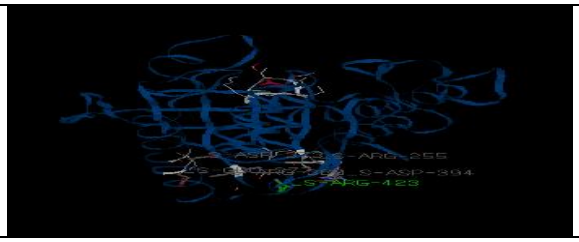


Figure.4. Docking pose of organotin complex of ` (1R,2S, 5R)-2-isopropyl-5-methylcyclohexanol with with PDB 2I42

Conclusion: The complex interacted with the PDB file with total fitness Value -68.0088 kcal/mol which comprises Van der waal interaction energy value of -64.303 kcal/mol and Hydrogen bonding with energy value -3.70565 kcal/mol. The complex interacted with the residue V-S-ARG-255 of binding pocket (refer figure 4). The complex

interacted with residues of basic amino acid like Arginine at position 225 with binding energy value -6.61578 kcal/mol. Protein tyrosine phosphatases (PTPs) are involved in the managing of various cell functions which includes growth, differentiation, motility, metabolism, gene transcription, and the immune response of *Yersinia enterocolitica*. Thus the complex has the potency to inhibit the growth of *Yersinia enterocolitica*.

***In Silico* Pharmacokinetic Properties Study:** The pharmacokinetic properties study was validated by comparative study of Organotin Complex of (1R, 2S, 5R)-2-Isopropyl-5-Methylcyclohexanol with standard reference drug Chloramphenicol (http://www.drugbank.ca/drugs/DB00446).

Table.2. ADMET Predicted Profile-Classification

Model	Result Chloramphenicol (reference)	Probability	Result Organotin Complex of (1R, 2S, 5R)-2-Isopropyl-5-Methylcyclohexanol	Probability
Absorption				
Blood-Brain Barrier	BBB+	0.9366	BBB+	0.6307
Human Intestinal Absorption	HIA+	0.9157	HIA+	0.7500
Caco-2 Permeability	Caco2+	0.7367	Caco2+	0.5971
P-glycoprotein Substrate	Non-substrate	0.7305	Substrate	0.7404
P-glycoprotein Inhibitor	Non-inhibitor	0.9216	Inhibitor	0.5076
	Non-inhibitor	0.8822	Non-inhibitor	0.9508
Renal Organic Cation Transporter	Non-inhibitor	0.9477	Non-inhibitor	0.8669
Distribution				
Metabolism				
CYP450 2C9 Substrate	Non-substrate	0.7775	Non-substrate	0.7689
CYP450 2D6 Substrate	Non-substrate	0.8934	Non-substrate	0.7908
CYP450 3A4 Substrate	Non-substrate	0.5936	Substrate	0.5000
CYP450 1A2 Inhibitor	Non-inhibitor	0.9046	Non-inhibitor	0.7530
CYP450 2C9 Inhibitor	Non-inhibitor	0.9071	Non-inhibitor	0.7921
CYP450 2D6 Inhibitor	Non-inhibitor	0.9231	Non-inhibitor	0.8712
CYP450 2C19 Inhibitor	Inhibitor	0.8994	Non-inhibitor	0.7538
CYP450 3A4 Inhibitor	Non-inhibitor	0.8309	Non-inhibitor	0.6270
CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	0.8682	Low CYP Inhibitory Promiscuity	0.8807
Excretion				
Toxicity				
Human Ether-a-go-go-Related Gene Inhibition	Weak inhibitor	0.9658	Weak inhibitor	0.6433
	Non-inhibitor	0.8764	Inhibitor	0.6671
AMES Toxicity	Non AMES toxic	0.9133	Non AMES toxic	0.6875
Carcinogens	Non-carcinogens	0.5483	Non-carcinogens	0.8676
Fish Toxicity	High FHM	0.7096	High FHMT	0.9884
Tetrahymena Pyriformis Toxicity	High TP	0.9917	High TPT	0.9937
Honey Bee Toxicity	Low HBT	0.8303	High HBT	0.5782
Biodegradation	Ready biodegradable	0.5053	Not ready biodegradable	0.9888
Acute Oral Toxicity	III	0.7521	III	0.5255
Carcinogenicity (Three-class)	Non-required	0.7280	Non-required	0.5759

Table.3. ADMET Predicted Profile --- Regression

Model	Value Chloramphenicol	Value Stannane of Pyridoxal phosphate	Unit
Absorption			
Aqueous solubility	-2.1726	-4.6528	LogS
$CaCO_2$ Permeability	0.9742	1.2426	LogPapp, cm/s
Rat Acute Toxicity	2.2247	2.0812	LD50, mol/kg

Fish Toxicity	1.2030	0.9598	pLC50, mg/L
Tetrahymena Pyriformis Toxicity	0.6795	0.9022	pIGC50, ug/L

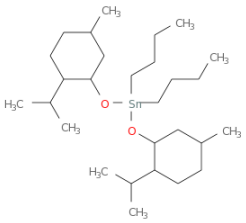
$CaCO_2$ permeability: The Complex has shown positive result in $CaCO_2$ permeability which shows that it is readily permeable**.** $CaCO_2$ cells are a human colon epithelial cancer cell line generally used as a model for human intestinal assimilation of drugs and other compounds.$CaCO_2$ cells specifies transporter proteins, efflux proteins, and Phase II conjugation enzymes which model a variety of transcellular pathways, also the metabolic transformation of test substances (Van Breemen, 2005).

Human Intestinal Absorption: Intestine is normally the primary site for absorption of drug from an orally administered solution. The complex has shown positive result, which shows that it, could be absorbed or assimilated through human intestine.

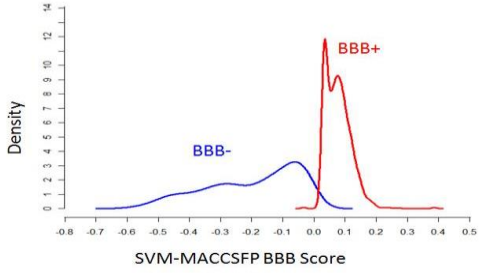
P-glycoprotein substrate: P-glycoprotein (P-gp) is one among the first members of the ATP-Binding Cassette (ABC) transporter which acts as a physiological barrier by ejecting toxins and xenobiotics out of cells it limits the bioavailability of orally administered drugs by pumping them back into the lumen .Drugs which induce or inhibit P-glycoprotein can interact with other drugs handled by the pump. P-gp is expressed primarily in certain cell types in the liver, pancreas, kidney, colon, and jejunum. (Konig, 2013; Igel, 2007; Ho RH, 2005). Substrates of P-glycoprotein can potentially act as inhibitors or inducers of its function. Inhibition of P-glycoprotein can result in increased bioavailability of the susceptible drug. Induction of P-glycoprotein reduces the bioavailability. The complex was found to be P- glycoprotein substrate and non-inhibitor.

Renal Organic Cation Transporter (OCT): The complex was found to be non-inhibitor of Renal Organic Cation Transporter. The significance of the organic cation transporter OCT2 in the renal excretion of cationic drugs shows the possibility of drug-drug interactions (DDIs) in which an inhibitor (perpetrator) drug decreases OCT2-dependent renal clearance of a victim (substrate) drug (Kristina Hacker, 2015).

BBB permeability: The brain is safeguarded from exogenous compounds by the blood brain barrier (BBB). The potential of a drug to cross into brain is an essential parameter to consider which help to reduce the side effects and toxicities or to improve the efficacy of drugs whose pharmacological activity is within the brain. The complex has shown positive result hence it can easily cross the blood –brain barrier. The result generated by admet SAR database was further validated by using BBB predictor (http://www.cbligand.org/BBB/predictor.php).



Query Structure
SVM_MACCSFP BBB Score: 0.092



Threshold of BBB-/BBB+ Score is 0.02

This compound is predicted as BBB+

Figure 5: BBB permeability of organotin complex of ` (1R, 2S, 5R)-2-isopropyl-5-methylcyclohexanol

Cytochrome P450 inhibitors: Cytochrome P450 proteins are monooxygenases that catalyze various reactions involved in drug metabolism and synthesis of cholesterol, steroids, and other lipids components. Cytochrome P450 inhibitors is an substantial detoxification enzyme in the body, generally found in the liver .It oxidizes xenobiotics to assist its excretion from the body .Numerous drugs are deactivated by the Cytochrome P450 inhibitors and some can be activated by it. Inhibitors could affect drug metabolism and are contraindicated. Hence it is important to access a compound's ability to inhibit the Cytochrome P450. Cytochrome P450 enzymes are subdivided into classes based on their structure. The complex were predicted to be CYP450 2C9 and CYP450 2D6 Non substrate, forms substrate with CYP450 3A4 .the complex was predicted to be Non inhibitor for CYP450 1A2, CYP450 2C9, CYP450 2D6, CYP450 2C19and CYP450 3A4. It is important to identify whether a new drug is a substrate, inducer or inhibitor in drug development (Wang, 2009). Drugs that inhibit will predictably increase the plasma concentrations of the medication and in some cases adverse outcomes will occur.

AMES toxicity: AMES test is a broadly used method to assess a compound's mutagenic potential using bacteria .A positive test shows that the compound is mutagenic and might be carcinogenic. Organotin complex of (1R, 2S, 5R)-2-isopropyl-5-methylcyclohexanol gave negative result in AMES toxicity test and also found to be a non-carcinogenic agent in Carcinogenicity test .In some toxicity models, some negative results were recorded (regression profiles) indicates that they have very low probability values, Fish Toxicity, Tetrahymena Pyriformis Toxicity and Honey Bee Toxicity were reported since complex contains central metal atom which is Tin.

Human ether-a-go-go related gene (hERG): Potassium (K^+) channels play a vital role in cardiac action potential repolarization. Mutations could reduce hERG conductance or surface expression and it results in congenital fatal long QT syndrome (LQTS), this may cause loss of hERG function (Ping-zheng Zhou, 2011). The complex was found to be non-inhibitor for Human Ether-a-go-go-Related Gene.

4. CONCLUSION

From the *In silco* studies carried out, the organotin complex of (1R, 2S, 5R)-2-isopropyl-5-methyl cyclohexanol has the potency to be used as a drug.

5. ACKNOWLEDGMENT

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REFERENCES

Aniyery Rohit Babu, Organotin Bis-Complexes: Synthesis, Characterization, antimicrobial activity and Anticancer (computational) studies, Int. J. of Adv. Res., 3 (7), 2015, 262-273.

Armarego W.L.F, and Perrin D.D, Purification of Laboratory Chemicals, Butterworth Heinemann, Oxford, UK, 4th edition, 1996.

Balavignesh V, Srinivasan E, Molecular docking study on NS5B polymerase of hepatitis c virus by screening of volatile compounds from Acacia concinna and ADMET prediction, International Journal of Pharmaceutical Life sciences, 4, 2013, 2548-2558.

Black D.S, and Bliska J.B, Identification of p130Cas as a substrate of *Yersinia* YopH (Yop51), a bacterial protein tyrosine phosphatase that trans locates into mammalian cells and targets focal adhesions, The EMBO Journal, 16, 1997, 2730-2744.

Cornelis G.R, and Wolf-Watz H, The *Yersinia* Yop virulon: a bacterial system for subverting eukaryotic cells, Molecular Microbiology, 23, 1997, 861-867.

Fahnestock ML, The MHC class I homolog encoded by human cytomegalovirus binds endogenous peptides, Immunity, 3, 1995, 583–590.

Feixiong Cheng, Weihua Li, admetSAR: A Comprehensive Source and Free Tool for Assessment of Chemical ADMET Properties, J.Chem.Inf.Model., American Chemical Society, 2012, 52 (11), 2012, 3099–3105.

Frederic Kerff, Raphael Herman, Specific Structural Features of the N-Acetylmuramoyl-L-Alanine Amidase AmiD from *Escherichia coli* and Mechanistic Implications for Enzymes of This Family, J. Mol. Biol., 397, 2010, 249–259.

Ho RH, Kim RB, Transporter and drug therapy: implications for drug disposition and disease, Clin Pharmacol Ther., 78, 2005, 260-77.

Igel S, Drescher S, Murdter T, Hofmann U, Heinkele G, Tegude H, Increased absorption of digoxin from the human jejunum due to inhibition of intestinal transporter- mediated efflux, Clin Pharmacokinet., 46, 2007, 777-85.

Jose S, Diorganotin (IV) complexes of diprotonated pyridoxine (PN, Vitamin B6), The crystal structure of [SnEt2 (PN-2H).CH_3OH, [SnEt2 (PN-2H) (DMSO)] and [SnBu2 (PN-2H)], Elsevier, Journal of Organometallic Chemistry, 2004, 620-626.

Konig J, Muller F, Fromm MF, Transporters and drug-drug interactions: Important determinants of drug disposition and effects, Pharmacol. Rev, 65, 2013, 944-66.

Kristina Hacker, and Renke Maas, Substrate-Dependent Inhibition of the Human Organic Cation Transporter OCT2: A Comparison of Metformin with Experimental Substrates, 2015.

Leovac, Synthesis and Charecterization of salicylaldehyde Girad-T hydrazine complexes, Structural Chemistry, 18, 2007, 113-119.

Noel M O' Boyle, Michael Banck and Geoffrey R Hutchison, Open Babel: an open chemical Tool box, Journal of chemo informormatics, 3, 2011, 33.

Ping-zheng Zhou, Joseph Babcock, Lian-qing Liu, Min Liand Zhao-bing Gao, Activation of human ether-a-go-go related gene (hERG) potassium channels by small molecules, Acta Pharmacologica Sinica, 32, 2011, 781–788.

Rehman W, Badshah A, Khan S, L. Tuyet L, Synthesis, Characterization, antimicrobial and antitumor screening of some diorganotin (IV) complexes of 2-[(9H-purin-6-ylimino)]-phenol, Eur. J. Med. Chem., 44, 2009, 3981–3985.

Rehman W, Baloch M, Badshah A, Ali S, Synthesis, Characterization and biological study of diorganotin (IV) complexes of monomethyl phthalate, Spectrochim. Acta A, 65, 2006, 689–694.

Upton AM, and McKinney JD, Role of the methylcitrate cycle in propionate metabolism and detoxification in *Mycobacterium smegmatis*, Microbiology, 153 (Pt 12), 2007, 3973–3982.

Van Breemen RB, Li Y, Caco-2 cell permeability assays to measure drug absorption, Expert Opin Drug Metab Toxicol., 1 (2), 2005, 175-85.

Wagner CS, Ljunggren HG, Achour A, Immune modulation by the human cytomegalovirus-encoded molecule UL18, a mystery yet to be solved, J Immunol., 180, 2008, 19–24.

Wang B, Zhou SF, Synthetic and natural compounds that interact with human cytochrome P450 1A2 and implications in drug development, Curr Med Chem., 16 (31), 2009, 4066-218.

Warren T. Piver, Organotin Compounds: Industrial Application and Biological Investigation, Environmental Health perspective, 1973, 61-77.

Wulff-Strobel C.R, Williams A.W, Straley S.C, LcrQ and SycH function together at the Ysc type III secretion system in *Yersinia pestis* to impose a hierarchy of secretion, Molecular Microbiology, 43, 2002, 411-423.

Yang J.M, and Chen C.C, GEMDOCK: A generic evolutionary method for molecular docking, Proteins: Structure, Function and Bioinformatics, 55, 2004, 288-304.