IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Synthesis, Characterization, Predicted ADME Value And Molecular Docking Of Vanadium Containing Metal Complexes As Potential Antimicrobial Activity

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Abstract

Sulfanilic acid (SNA) and trimethoprim (TMP) are two pharmacological compounds used to treat bacterial infections and urinary tract infections. Computational studies have been used to estimate molecular properties, including binding sites, electronic states, MEP, chemical reactivity, optical properties, and FTIR spectra. Schiff-bases and salen-type ligands are unusual classes of ligands with donor atoms and coordination modes towards transition metals The ChemOffice chemical software suite helps chemistry researchers and students create and use chemical papers and databases. It includes modules such as ChemDraw Ultra, Chem3D Ultra, E-Notebook Ultra, ChemFinder, CombiChem, Inventory, Bioassay. ChemDraw is a two-dimensional chemical editor. Molecular docking is used to predict the preferred binding orientation of molecules when they combine to form stable complexes, allowing for the structure-based drug development of new drugs. The interaction between pharmacokinetics, toxicity, and potency is crucial for effective drugs. The pharmacokinetic profile of a compound defines its absorption, distribution, metabolism, and excretion (ADME) properties. While optimal binding properties of a new drug to the therapeutic target are crucial, ensuring that it can reach the target site in sufficient concentrations to produce the physiological effect safely is essential for the introduction into the clinic.

Keywords: Transition metals, coordination modes, metallo-element, ADMET properties, toxicological ect.

1. Introduction

The computation time for quantum mechanical calculations increases with the quality of calculations and the size of the system. Such calculations are therefore quite successful in calculating gas phase reaction energies. Determining reaction energies in solution directly from quantum mechanical calculations is, however, a very challenging task. In a solution, there are very large numbers of molecules interacting and experimentally observed properties represent averages over large ensembles, accurate calculations on such large systems are extremely time-consuming. A widely used approach to calculate reaction energies in solution is to first calculate reaction energies in gas phase and then calculate the solvation energy with some form of solvation model. Solvation models are based on some simplified representation of the solvent, common forms are continuum models, where the solvent is represented as a dielectric continuum, and explicit models where solvent molecules are usually given a simplified molecular mechanics representation (some form of ball-and-stick model with fixed charges). In calculations, where quantum mechanical calculations and solvation models are combined, the solvation models are usually expected to be the main source of uncertainty. There is at present great interest both in finding optimal solvents for CO_2 absorption and in finding the optimal process conditions for a given solvent. Detailed understanding of the chemistry is of great value in accomplishing both of these tasks. For simple aliphatic amines, the species formed are known and the overall reactions are reasonably well understood. There is, however, uncertainties regarding some mechanisms that have not been resolved by experimental work. Molecular attributes such as binding sites, electronic states, MEP, optical characteristics, chemical reactivity, and FTIR spectra have all been estimated by computational research. Unusual kinds of ligands with donor atoms and coordination modes towards transition metals are Schiff - bases and salen-type ligands. Flexible ligands of the Salen type are used in coordination chemistry to enable metal ions to project various shapes in conjunction with other ligands. The search for more potent antibacterial chemicals is crucial since drug-resistant microbe strains are becoming more prevalent. Complexes created by synthesizing metals and sulphonamide's have a wide range of applications, and sulphonamides have a wide range of pharmacological actions. The chemical software suite known as Chem Office facilitates the creation and students use databases and produce chemical papers. Modules like Chem Finder, Combi Chem, E-Notebook Ultra, Chem Draw Ultra, Chem3D Ultra, Inventory, Bio Assay, and The Merck Index are among them. A two-dimensional chemical editor is called Chem Draw. Molecular docking facilitates structure-based medication discovery by predicting the preferred binding orientation of molecules when they come together to form stable complexes. In the process of developing new drugs, pharmacokinetics, efficacy, and safety must all be carefully balanced by maximizing drug-like properties. The interaction between pharmacokinetics, toxicity, and potency determines the effectiveness of drugs.

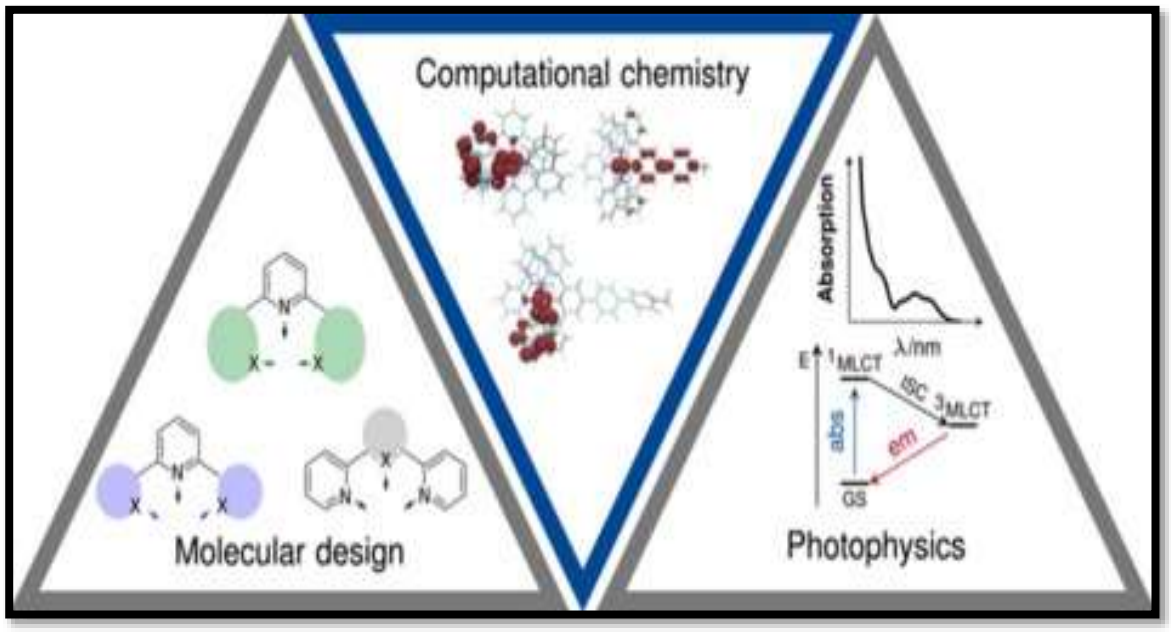


Fig No.1 Layout design of computational chemistry

This research paper provides a brief overview of V, its function, and the global progress made in V research to date in light of earlier findings, which could help interdisciplinary studies assess the ecological significance of V toxicity. Vanadium (Z = 23) is a strong, steel- gray metal that is a transitional element found in Group VB and the fourth row of the periodic table. There are two naturally occurring isotopes: stable 51V (99.75%) and long-lived (3.9 × 1017 years) 50V, which is broken down by electron capture and emission. Due to V's compound composition and oxidation state, its toxicity varies significantly; pentavalent vanadium is the most poisonous and mobile form. Approximately 80% of V generated worldwide is used as an addition in the steel industry. The antibacterial activity of these compounds is influenced by the various types of metal, ion, and ligand, as well as the surrounding complex, coordination sites, hydrophilicity, lipophilicity, and presence of co-ligands. Polar and lipophilic substitutes enhance the antibacterial effect. The best possibilities for bactericides are heterocyclic ligands with several functions that can interact with nucleotide bases or certain biological metal ions. To gain access to high coordination numbers, the heterocyclic ligands interfere with functional groups.

2. Overview of Coordination Chemistry

Schiff base complexes' easy synthesis, adaptability, and wide variety of uses have kept them a prominent and well-liked research topic. Due to their pharmacological characteristics.

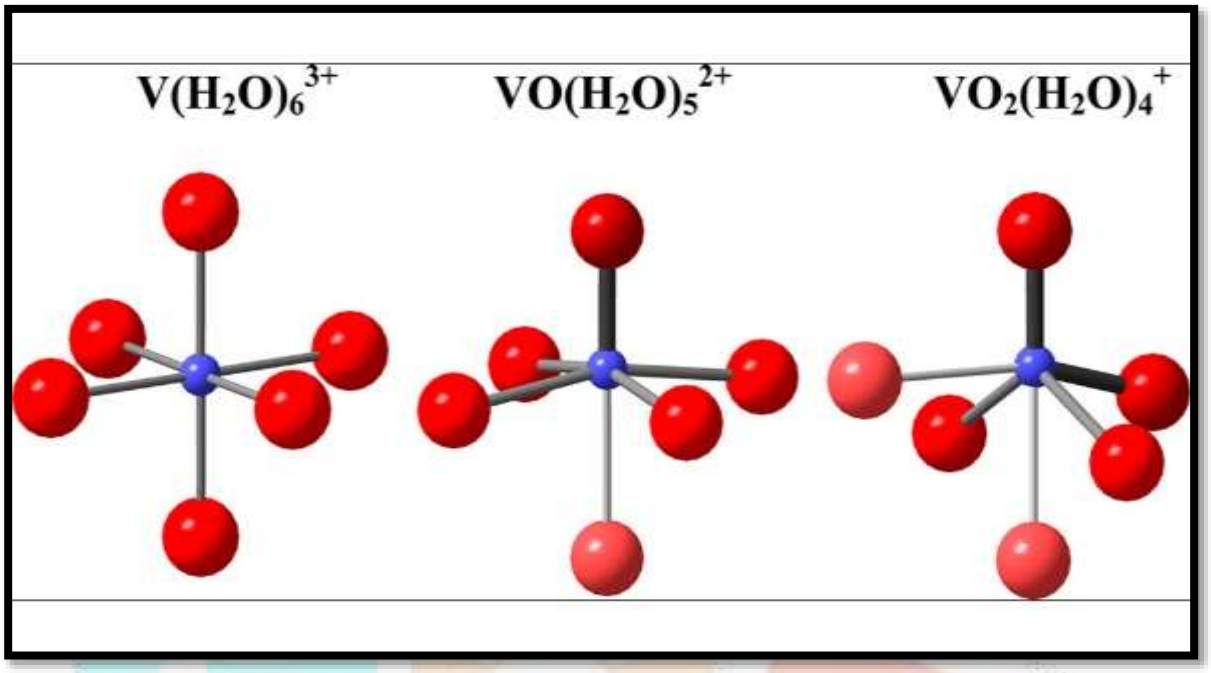


Fig.No.2 Coordination chemistry of vanadium metal complex structure

Many studies have demonstrated that when a medication binds to a metallo-element, it increases that element's activity and, in certain situations, the resulting complex has even more therapeutic potential than the original drug. Metal complexes provide a framework for creating novel medicinal substances. Large families of bidentate, tetradentate Schiff base ligated complexes, with broad applications as catalysts in various chemical processes, have been explored, taking into consideration the extremely desired properties of this kind of ligands.

3. Antimicrobial Potency of vanadium complex

Vanadium's impact on the life sphere (geo-sphere, atmosphere, marine environments), as well as its potentiality in the treatment of diseases such as cancer, diabetes and bacterial infections. In particular, the following topics are addressed:

(1) vanadium in marine environments (halide oxidation by haloperoxidases in the seaweed *Ascophyllum nodosum* and by marine bacteria associated with macroalgae; accumulation and redox transformation of vanadium by ascidians and fan worms);

(2) the role of vanadium in nitrogen fixation by diazotrophs in the root nodules of legumes, and in liverworts and horn warts;

(3) amavadin in the fly agaric mushroom;

(4) vanadium speciation by unicellular organisms (bacteria, protozoa) and adjunctive medicinal applications;

(5) the potentiality of vanadium (coordination compounds) in the treatment of diseases such as cancer and diabetes, and bacterial infections.

4. Using Chemdraw Ultra 12.0 with Chem3D Software for Drug Design

Chemistry researchers and students can focus on and identify a number of daily tasks with the help of the ChemOffice chemical software suite. The computer is turned into a workstation for creating and using chemical papers and databases by the modules of the programme. The new ChemOffice Ultra includes the following applications: ChemDraw Ultra, Chem3D Ultra, E-Notebook Ultra, ChemFinder, CombiChem, Inventory, BioAssay, and The Merck Index. The ChemDraw/Excel and ChemFinder/Word modules are used for Microsoft Office integration. When conducting experiments, researchers can organize the storage of chemical data, documents, and information by using an electronic laboratory journal, or e-notebook. One of the components of the ChemOffice integrated software package is a program known as ChemDraw, which is a two-dimensional chemical editor. It is designed for molecular structure depiction in two dimensions.

5. Introduction of pkCSM profile for pharmacokinetics

Developing new drugs has become an increasingly challenging, costly, and risky endeavour with a low success rate. The vast majority of drugs evaluated in clinical trials do not reach the market due to either a lack of efficacy or unacceptable side effects. Drug development is a fine balance of optimizing drug like properties to maximize efficacy, safety, and pharmacokinetics. Many early stage drug discovery programs focus on identifying molecules that bind to a target of interest. While potency is a driving factor in these early stages, ultimately the pharmacokinetic and toxicity properties dictate whether it will ever advance its effectiveness and success therapeutically. The interaction between pharmacokinetics, toxicity, and potency is crucial for effective drugs. The pharmacokinetic profile of a compound defines its absorption, distribution, metabolism, and excretion (ADME) properties. While optimal binding properties of a new drug to the therapeutic target are crucial, ensuring that it can reach the target site in sufficient concentrations to produce the physiological effect safely is essential for the introduction into the clinic.

6. Molecular docking of vanadium complex

When two molecules, such ligands and receptors, join to form a stable complex, it can be easier to predict which way they will preferentially attach when using a computational modeling technique called molecular docking. Comprehending the preferred orientation of the bound molecules allows one to predict the strength and stability of complexes as well as their energy profile (including their binding free energy). To determine the preliminary binding characteristics of small molecules (possible medications) to biomolecular targets (proteins, polysaccharides, and nucleic acids), molecular docking is widely employed nowadays.

7. Synthesis of vanadium containing Metal Complexes

In order to create the metal complexes, a hot solution (60◦C) of the relevant metal (2 mmol) in an ethanol-water mixture (1:1, 25 mL) was added to a hot solution (60◦C) of complex formed (1.0 g, 2 mmol) in the same solvent (25 mL). After an hour of stirring the resultant mixture while it was under reflux, the complexes precipitated. After gathering them through filtration, they were cleaned multiple times using a petroleum ether and ethanol mixture of 1:1. We conducted the analysis of the data twice for C, H, N, and Cl. The resulting homogenous solution was then refluxed for 6 h, during which the product formed. This was filtered, washed

with ethanol and dried over sintered glass. The same procedure was used for the preparation of Vanadium metal. A hot solution (60◦C) of the relevant metal (2 mmol) in a methanol-water mixture (1:1, 25 mL) was added to a hot solution (60◦C) of complex formed (1.0 g, 2 mmol) in the same solvent (25 mL). After an hour of stirring the resultant mixture while it was under reflux, the complexes precipitated.

8. Metal complex surface chemistry

Assessing and comprehending surface behaviour necessitates first understanding the electrical structure and related chemical properties of surfaces, as well as the general and adsorbate structure on surfaces. approaches to surface structure determination. By modifying the structural model and atom locations to find the lowest energy configuration, abinitio methods are used to calculate the electrical and chemical properties. This article includes illustrations of the structural phenomena related to adsorbate bonding at surfaces as well as how surface structure characterization by experimental means can provide insight into the phenomenon. We start by providing a quick overview of the methods utilized to ascertain the structure of the adsorbate.

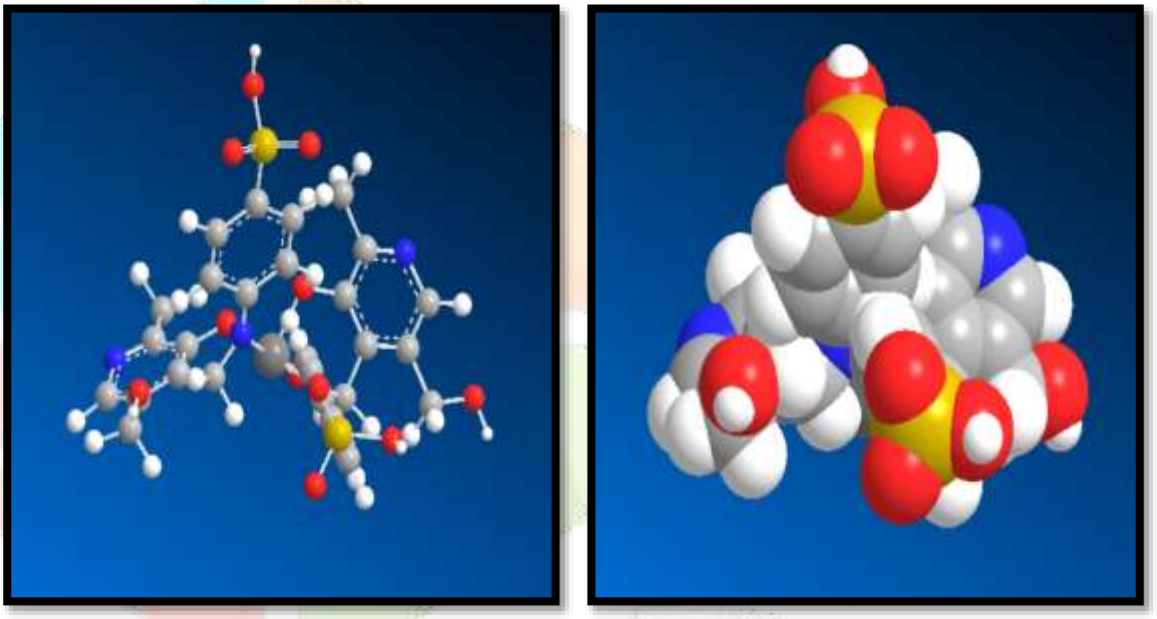
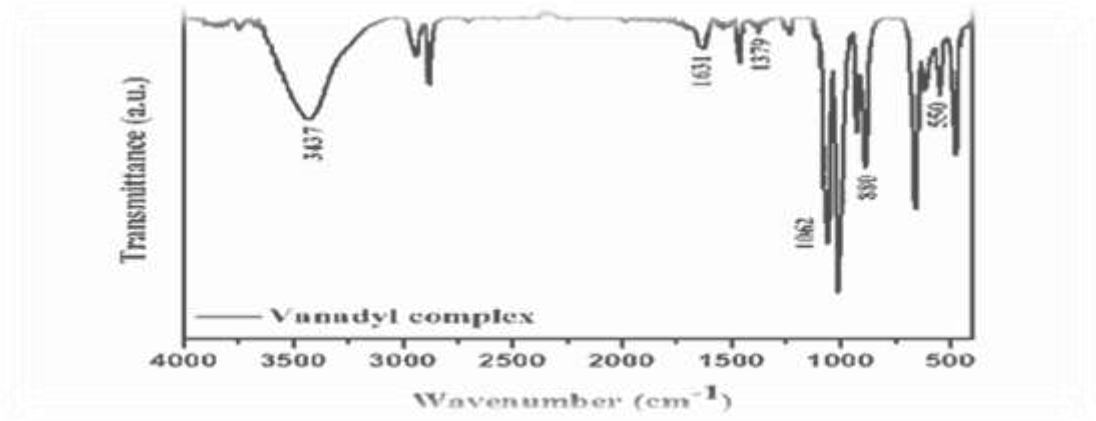


Fig.No.3 - Behaviour of surfaces including the electronic structure & their properties.

9. Charecterization of synthesize vanadium metal complexes

UV-Visible spectroscopy is an analytical technique that measures the amount of discrete wavelengths of UV or visible light that are absorbed by or transmitted through a sample in comparison to a reference or blank sample. This property is influenced by the sample composition, potentially providing information on what is in the sample and at what concentration. Humans are able to see a spectrum of visible light, from approximately 380 nm, which we see as violet, to 780 nm, which we see as red. UV light has wavelengths shorter than that of visible light to approximately 100 nm. Therefore, light can be described by its wavelength, which can be useful in UV-Visible spectroscopy to analyse or identify different substances by locating the specific wavelengths corresponding to maximum absorbance.



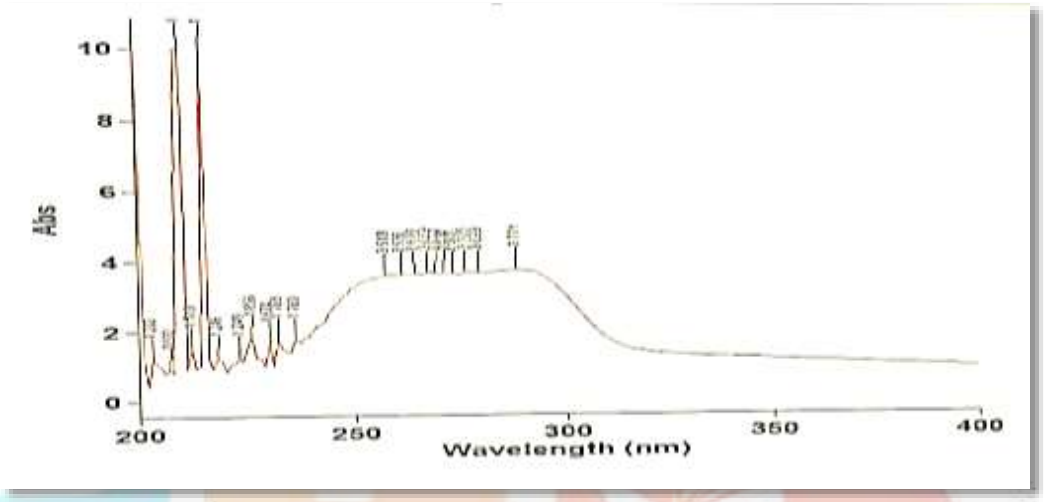


Fig.No.4 UV-Visible graph of vanadium metal complexes

IR spectral data of vanadium(III) complexes

Infrared spectroscopy is based on molecular vibrations caused by the oscillation of molecular dipoles. Bonds have characteristic vibrations depending on the atoms in the bond, the number of bonds and the orientation of those bonds with respect to the rest of the molecule. Thus, different molecules have specific spectra that can be collected for use in distinguishing products or identifying an unknown substance (to an extent.) Collecting spectra through this method goes about one of three general ways. Nujol mulls and pressed pellets are typically used for collecting spectra of solids, while thin-film cells are used for solution-phase IR spectroscopy.

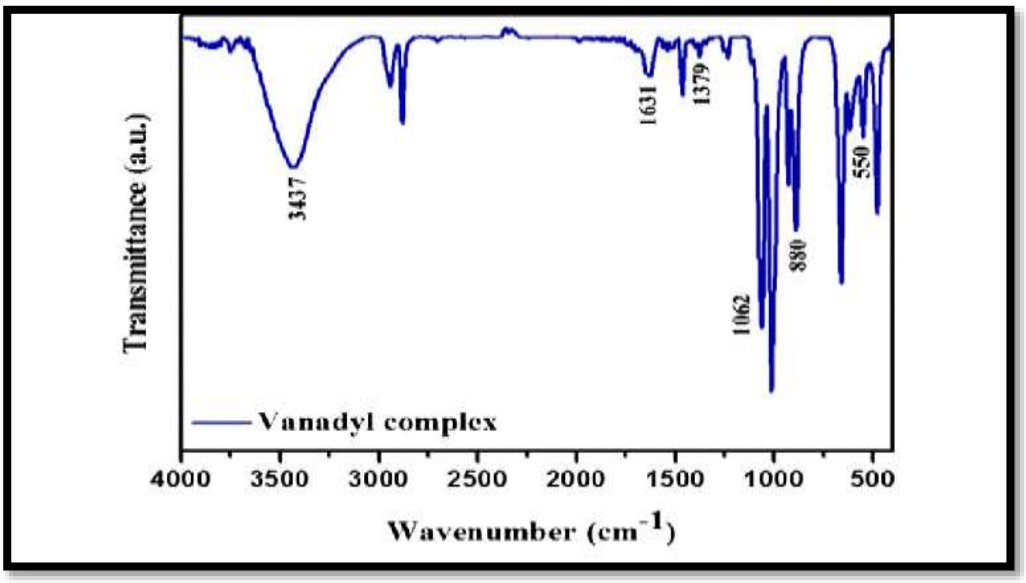


Fig.No.5 IR spectroscopy of vanadium metal complexes

10.Forecasting Pharmacokinetic and Toxicity Characteristics of Small-Molecules via Graph-Based Signatures.

The characteristics for absorption, distribution, metabolism, and excretion (ADME) of a substance are determined by its pharmacokinetic profile. While the optimal therapeutic target binding properties of a new drug are vital, the drug's ability to safely reach the target site at adequate concentrations to generate the physiological impact is just as important for its safe introduction into the clinic. Because early-stage pharmaceutical research takes ADMET properties into account, the number of drugs that failed in clinical trials due to inadequate ADMET attributes has considerably decreased. In addition to providing a platform for the study and optimization of pharmacokinetic and toxicological aspects combined in an approachable, publicly available web interface, the pkCSM technique is a helpful tool to help medicinal chemists achieve the best results. There is balance in pharmacokinetics, safety, and potency. According to the findings of several comparative tests we conducted, pkCSM performs as well as or better than several other popular methods.

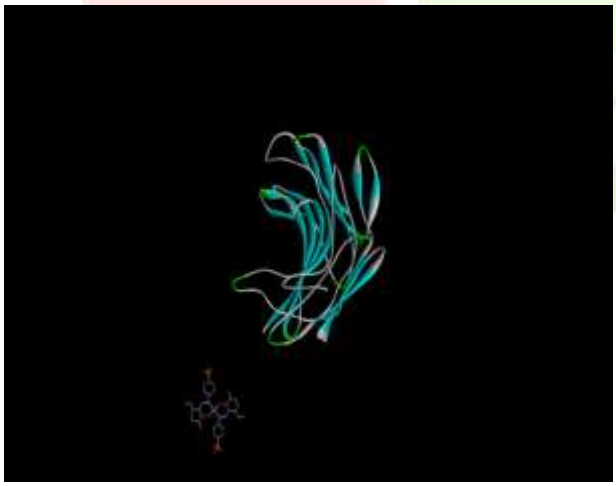
Table No.1 Predicted ADME properties of synthesize vanadium metal complexes

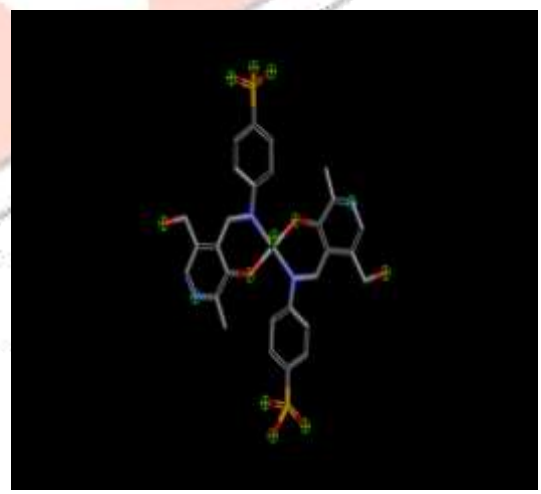
Property	Model Name	Predicted Value
Absorption	Water solubility	-2.892
Absorption	Caco2 permeability	-0.91
Absorption	Intestinal absorption (human)	22.449
Absorption	Skin Permeability	-2.735
Absorption	P-glycoprotein substrate	No
Absorption	P-glycoprotein I inhibitor	No
Absorption	P-glycoprotein II inhibitor	No
Distribution	VDss (human)	-0.651
Distribution	Fraction unbound (human)	0.398
Distribution	BBB permeability	-2.584
Distribution	CNS permeability	-4.758
Metabolism	CYP2D6 substrate	No
Metabolism	CYP3A4 substrate	No

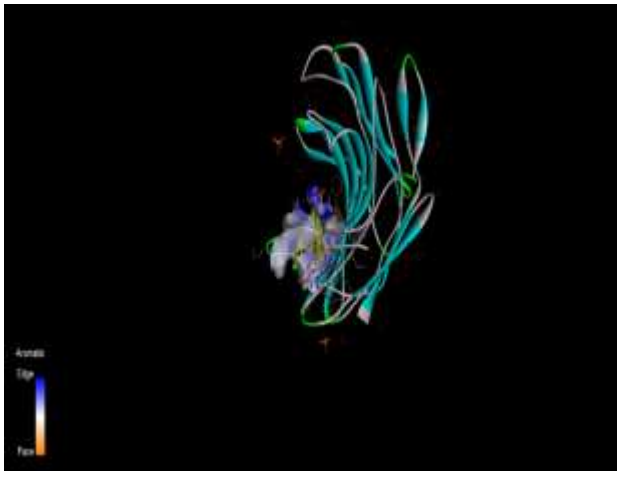
Metabolism	CYP1A2 inhibitior	No
Metabolism	CYP2C19 inhibitior	No
Metabolism	CYP2C9 inhibitior	No
Metabolism	CYP2D6 inhibitior	No
Metabolism	CYP3A4 inhibitior	No
Excretion	Total Clearance	-1.105
Excretion	Renal OCT2 substrate	No
Toxicity	AMES toxicity	No
Toxicity	Max. tolerated dose (human)	0.438
Toxicity	hERG I inhibitor	No
Toxicity	hERG II inhibitor	No
Toxicity	Oral Rat Acute Toxicity (LD50)	2.481
Toxicity	Oral Rat Chronic Toxicity (LOAEL)	2.415
Toxicity	Hepatotoxicity	No
Toxicity	Skin Sensitisation	No
Toxicity	*T.Pyriformis* toxicity	0.285
Toxicity	Minnow toxicity	3.366

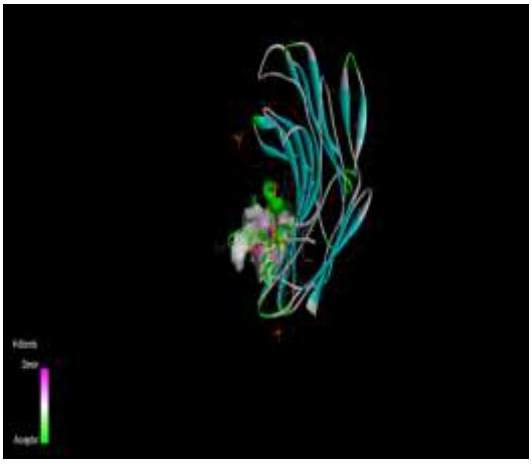
11.Molecular docking of Vanadium containing metal complexes

The molecular docking approach can be used to model the interaction between a small molecule and a protein at the atomic level, which allow us to characterize the behavior of small molecules in the binding site of target proteins as well as to elucidate fundamental biochemical processes.









Most scoring functions are physics based molecular mechanics force fields that estimate the energy of the pose; a low (-ve) energy indicates stable system and thus a likely binding interaction. Drug complex dock with receptor pd file "1y43" having certain types of results showing various graphical representation. In docking results showing maximum binding affinity of drug complex.

12. Antimicrobial studies of vanadium metal complexes

Antibacterial screening of the free ligands and the synthesized complexes were tested in vitro using Agar diffusion method. Prepared culture plates were inoculated with different environmental strains of gram-positive, gram-negative bacteria and fungi: Bacillus subtilis, Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Aspergillus niger and Candida albicans. The bacteria were cultured using the pour-plate method. From the diluted organisms (10^{-2}) 0-2ml was injected into the prepared sterile nutrient agar which was at 45ºC, then aseptically poured into sterile petri dishes, which were allowed to solidify for about 45-60 minutes. Wells were made on the agar surface (Nutrient agar) with 6mm sterile cork borer. The prepared different graded (50µg/ml and 10µg/ml) concentrations of the complexes and ligands were poured into the well using sterile syringes. The plates were incubated at 37 ºC ± 2 ºC for 24 hours. The plates were observed for the zone clearance around the wells. The zone of inhibition was calculated by measuring the diameter of the inhibition zone around the well (in mm) including the well diameter.

Table.No.4 Antifungal activity of vanadium metal complexes

S.No	Metallic extract	Aspergillus niger	Candida albanicans
01	Vanadium contain complexes	37mm	15mm

Aspergillus niger **Candida albicans**

13. Results and Discussion

White complexes with varying shades of hue were produced in low to moderate yields (17-60%) by combining sulfanilic acid with N-donor heterocycles; 1,10 phenanthroline with metal (II) salts of vanadium. When melted at temperatures exceeding 300°C, the metal complexes of the ligands sulfanilic acid and 1,10 phenanthroline completely broke down, although the ligands themselves melted at 168°C. Except for water, ethanol, and dimethyl sulfoxide (DMSO), they were insoluble in the vast majority of solvents. The data for analysis has been prepared. We reran the calculations for C, H, N, and Cl two times. A homogeneous solution was produced; the product was made by refluxing the mixture for 6 hours. Next, it was ethanol washed, filtered, and finally dried on sintered glass. Vanadium metal was also prepared using this method. It is essential to be familiar with the pros and cons of the facts derived from the various methodologies in order to analyse the following information. The wavelengths of ultraviolet light are around 100 nm, which is much shorter than the wavelengths of visible light. Thus, the wavelength is a valuable metric for describing light, which may be applied in UV-Visible spectroscopy to investigate or identify various compounds by determining the wavelengths at which they absorb the most. It is becoming more difficult, expensive, risky, and less productive to produce new pharmaceuticals. Due to insufficient efficacy or very negative side effects, many medications that undergo clinical testing never make it to market. During medication development, it is crucial to strike a compromise between optimising pharmacokinetics, efficacy, and safety while preserving drug-like characteristics. When there are a lot of chemical structures to explore but not many compounds available, computer models have been promoted as a viable alternative to experimental approaches for ADME prediction, particularly at the beginning stages. Predicting ADME parameters from molecular structure is the goal of many different in silico approaches. The majority of scoring functions are molecular mechanics force fields grounded in physics that attempt to estimate the pose's energy; a stable system, as indicated by a low (-ve) energy, is likely to have a binding contact. There are a number of visual representations in the drug complex dock with receptor pd file "1y43" that correspond to specific kinds of results. As shown by the docking studies, the drug compound had the highest binding affinity.

Acknowledgements

The author Dr. Reetesh Yadav is thankful to Chairman R.V. Karsoliya , Shri Ram Institute of Pharmacy, Jabalpur, Madhya Pradesh, India for for providing Central library and laboratory facilities.

Conflict of Interests

The authors have no conflict of interests.

References

1. Annoji Reddy R, Vibha, Pracha Lith N.C., Ravikanth M.N., Shilpa K.G., Thipperudrappa J ; Mapana–Journal of Sciences 2023, Vol. 22, No. 1, 205-243.
2. 2.Nahoko Kuroki, Yuji Mochizuki, and Hirotoshi Mori; s: J. Chem. Educ. 2023, 100, 647−654;
3. Mert Metin, Tomonori Kawano, Tadashi Okobira; Journal of the Indian Chemical Society
4. Volume 100, Issue 2, February 2023, 100895.
5. William F. Polik, J. R. Schmidt; Volume12, Issue1; January/February 2022; e1554; First published: 02 June 2021.
6. Dr. Markus Bursch, Dr. Jan-Michael Mewes, Dr. Andreas Hansen, Prof. Dr. Stefan Grimme
7. First published: 14 September 2022
8. Herry Saputra, Chepi Nur Albar, Dedi Sulistiyo Soegoto; Moroccan Journal of Chemistry ISSN: 2351-812X http://revues.imist.ma/?journal=morjchem&page=login Saputra & al. / Mor. J. Chem. 10 N°1 (2022) 037-049.
9. Xiaoyue M; Journal of Physics: Conference Series, Volume 2386, The International Conference on Computing Innovation and Applied Physics (CONF-CIAP 2022), 20 August 2022, online.
10. Melek Hajji a, Nadeem Abad b c, Mohamed A. Habib d, Salima Moftah H. Elmiric d, Taha Guerfel rhi;
11. Wenjie Fu, Guang-Jie Xia, Yixiang Zhang, Jiahui Hu, Yang-Gang Wang, Jun Li, Xiaoyan Li, Bing Li https://doi.org/10.1016/j.watres.2021.117391.
12. G. Wilkinson, R. D. Gillard and J. A. McCleery (Ed.) “Comprehensive Coordination Chemistry”, Pergamon, Oxford, 1987.
13. J. A. McCleery and T. J. Meyer, “Comprehensive Coordination Chemistry II, From Biology to Nanotechnology” Elsevier, Amsterdam, 2003.
14. F. A. Cotton, G. Wilkinson, C. A. Murillo and M. Bochmann, “Advanced Inorganic Chemistry” 6th Edn., John Wiley and Sons, Inc., 1999.
15. C. R. Samy and S. Radhey, Indian J. Chem., 35 A, 1, 1996.
16. X. Shen, Q. L. C. Yang and Xie, Synth. React. Inorg. Met. Org. Chem., 26, 1135, 1996.
17. Guojie Li; Dan Li, Mutasem Alshalalfeh, Joseph Cheramy, Hui Zhang and
18. Yunjie Xu Molecules 2023, 28(6), 2571; https://doi.org/10.3390/molecules28062571
19. Taghreed. H. Al-Noor1† --- Amer. J. Jarad2 ---Abaas Obaid Hussein; Article · August 2014.
20. Jiayue Chen1, Keita Fukuzumi2, Benny Ip2, Florence1, Abigail P. Cid3; METAL coordination chemistry in the study of biological pathway and processes: a review; July 2014.
21. 19.R. Jayachitra, M. Padmavathy, A. Kanagavalli, G. Thilagavathi, N. Elangovan, S. Sowrirajan, Renjith Thomas; Journal of the Indian Chemical Society Volume 100, Issue 1, January 2023, 100824
22. 20. Mohamed H. Abdel-Rhman, Ahmed A. El-Asmy, Reyad Ibrahim, Nasser M. Hosny; Journal of Molecular Structure; Volume 1279, 5 May 2023, 135023;
23. 21.Manoj Kumar, Atres Kumar Singh, Alok Kumar Singh, RajeshK. Yadav, Satyam Singh, Atul P. Singh, Amit Chauhan; Coordination Chemistry Reviews Volume 488, 1 August 2023.
24. 22. Filiz Öztürk; Journal of Molecular Structure Volume 1271, 5 January 2023, 133945.
25. 23. Rita Vaickelionienė, Vilma Petrikaitė, Irena Vaškevičienė, Alvydas Pavilonis,2023; 18(3): e0283289. Published online 2023 Mar 23.
26. 24. Morgan Vanderwall and Madison S. Strine; Yale J Biol Med. 2022 Dec; 95(4): 405–406.
27. 25. Olagboye S.A. And Ige S.E; International Journal of Innovative Science and Research Technology ISSN No: -2456-2165; Volume 7, Issue 2, February – 2022; www.ijisrt.com; 716-721.
28. 26. Tulqin Abduvalievich Julboev; Marat Mrazovich Sultonov & Komila Khudoyberdievna Abduvalieva; European Journal of Research and Reflection in Educational Sciences Vol. 9 No. 3, 2021 ISSN 2056-5852.

29. 27. Dr. Monika Gupta; International Research Journal of Modernization in Engineering Technology and Science (Peer-Reviewed, Open Access, Fully Refereed International Journal) Volume:05/Issue:01/January-2023 Impact Factor- 6.752
30. 29. https://guides.libraries.uc.edu/chembio-software/chemdraw
31. 30. https://library.bath.ac.uk/chemistry-software/chem3d
32. 31. Aysha Fatima, Ghazala Khanum, Arun Sharma, Km Garima, Sandhya Savita, Indresh Verma, Nazia Siddiqui, Saleem Javed; 23 September 2021
33. 32. Douglas E. V. Pires, Tom L. Blundelland David B. Ascher ;2015 American Chemical Society; . Med. Chem. 2015, 58, 9, 4066–4072.
34. 33. Geary WJ. The use of conductivity measurements in organic solvents for the characterisation of coordination compounds. Coord Chem Rev., 1971; 7: 81-
35. 34. Kriza A, Pirnau C, Popa N. Complex combinations with 1-H-indole-2,3-dione. 1. Sn(IV) and Zr(IV) complex combinations with 1-H-indole-2,3 dione. Revista de Chim, 2001; 52(6): 346-48.
36. 35. Michael F. Primik, Simone Göschl, Samuel M. Meier, Nadine Eberherr, Michael A. Jakupe, Éva A. Enyedy, Ghenadie Novitchi, Vladimir B. Arion. Dicopper (II) and Dizinc (II) Complexes with Nonsymmetric Dinucleating Ligands Based on Indolo[3,2-c] quinolines: Synthesis, Structure, Cytotoxicity and Intracellular Distribution. Inorg Chim Acta, 2008; 10: 137-46.
37. 36. Crouch RK, Kensler TW, Oberley LW, Sorenson JRJ, Karlin KD, Zubieta J. Advanced Inorganic Chemistry, 3rd ed. New York: Adenine Press; 1986.
38. 37. Gerber TIA. J Coord Chem, 2003; 56: 1397-407.
39. 38. Bomigboye M O, Obaleye J A and Aluko O M. Synthesis, characterization and Antimicrobial Study of Mixed Isoniazid-Trimethoprim Metal Drug Complexes. Chemistry and Materials Research, 2012; 2: 1-8.
40. 39. Lever ABP. Inorganic Electronic Spectroscopy. 4 ed. New York: Elsevier; 1984.128 Kola, I.; Landis, J. Can the pharmaceutical industry reduce attrition rates? Nature Rev. Drug Discovery 2004, 3, 711– 715
41. 40.https://www.researchgate.net/publication/371376478_Vanadium_A_US_Perspective_on_an_Understudied_Metal.
42. 41.https://www.researchgate.net/publication/275277741_Vanadium_recent_advancements_and_research_prospects_A_review.
43. 42.https://www.elsevier.es/en-revista-boletin-sociedad-espanola-ceramica-vidrio-26-articulo-contribution-vanadium-particles-thermal-movement-S0366317522000140.
44. 43.https://asu.elsevierpure.com/en/publications/spectrally-selective-vanadium-dioxide-based-tunable-metafilm-emit.
45. 44. Merlot, C. Computational toxicology—a tool for early safety evaluation Drug Discovery Today 2010, 15, 16– 22