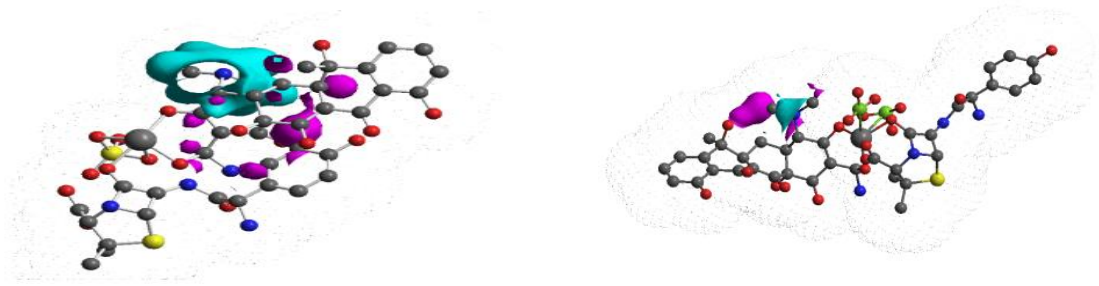
Biomolecular interaction simulation of supramolecular topologies of organometallic assemblies of Bi(V) with antibiotic Tetracycline Amoxicillin drugs and their experimental activities evaluation

Rajiv Kumar,[1,4,5,6,7] Kiran Gulia[2], Mina Chandra[3], Anil K Aggarwal[4], Anil Kumar[5], Sandeep Mittan[6] and Parashuram Mishra[7]

[1]University of Delhi. Delhi, India. [2]School of Engineering, Innovation Campus TELFORD Shropshire, Engineering, University of Wolverhampton, Birmingham, West Midlands, UK [3]Post Graduate Institute of Medical Education & Research (PGIMER) and Dr Ram Manohar Lohia Hospital (Formerly Willingdon Hospital), New Delhi-110001,India. [4]Shivaji College, University of Delhi, New Delhi 110027, India. [5]Gene Regulation Laboratory, National Institute of Immunology, Aruna Asaf Ali Marg, New Delhi, India. [6]Icahn School of Medicine at Mount Sinai, 1468 Madison Avenue, Annenberg Building 24th Floor, Suite 50 New York, NY 10029. [7]Bioinorganic and Materials Chemistry Research Laboratory, Tribhuvan University, M.M.A.M. Campus, Biratnagar, Nepal.

Corresponding Author: Dr. Rajiv Kumar, Email: chemistry_rajiv@hotmail.com

Abstract

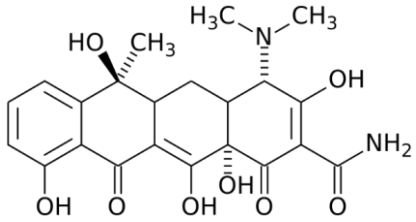


Antibiotic drugs i.e. tetracycline and amoxicillin, were used mixed ligands (ML), for designing, architecturing, tailoring and synthesis for synthesis of supramolecular topologies of organometallic assemblies of Bi(V), represented as OMCs-Bi(V), having O_5 set for bonding. Molecular models were proposed as a standard to judge specific interactions in topologies of molecules of ML and derived organometallic assemblies. In OMCs-Bi(V), on chelation, polarity of Bi(V) get reduced to great extent due to overlap of ML orbital. As a result, delocalization of π-electrons density clouds get spread over the surface of chelating ring and enhances penetration power of OMCs-Bi(V) into lipid membranes. This influenced binding with enzyme sites in microorganisms. Some electron set for bonding groups present in ligands moieties display extensive biological activity that may be responsible for increase in hydrophobic character and liposolubility of supramolecular topologies of organometallic of assemblies; ultimately enhanced biological activity of OMCs-Bi(V).

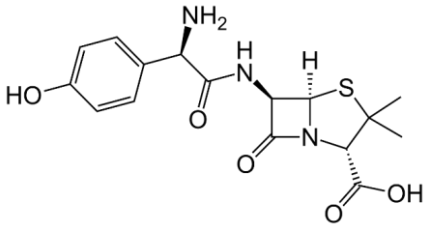
Keywords: *hydrophobic, liposolubility, supramolecular topologies, organometallic of assemblies and in topologies of molecules*

Introduction

Antibiotic drugs as ligands have been used in past decades to increase their efficacy and efficiency for the treatment of microbial infections.[1] The mechanism of action of such antibiotics through cellular uptake was a huge challenge in front of the scientific community.[2] Keeping such view, we were concentrating to understand inns and out of antibiotic drugs as mixed ligands to develop effective antimicrobial.[3] These drugs were used as mixed ligands with different metals or their ion(s), considering their medical and biological importance, for the synthesis of supramolecular topologies of organometallic assemblies of Bi(V).[4] These efforts concerning about mixed ligand constrain of antibiotic drugs were helped out to explore all possibilities within designed ligand for chelation with Bi(V) to produce perfect models of organometallic assemblies. Developed supramolecular topologies of OMCs-Bi(V) played a crucial role as a better option for treatment of microbial infections.[5]



(a) Tetracycline



(b) Amoxicillin

Figure 1 Molecular structure of antibiotic drugs used as mixed ligand, (ML).

Some metals, in biological systems, are involved in specific interactions with antibiotics, proteins, membrane components, nucleic acids, and other biomolecules in biochemical conversions.[6] Mixed antibiotics as ligands showed interesting coordinating behavior especially to over topology suitable for effective encapsulation of large metal ions and as a result formed effective supramolecular topologies of OMCs-Bi(V). Such transformations depend on binding abilities within organometallic assemblies. There was an enormous potential for numerous applications of OMCs-Bi(V) in medicine[7] and selection of the metal ions offered the possibility for discovery of metallodrugs with a novel mechanism of action.[8] Bismuth compounds were widely used for the treatment of peptic ulcers and Helicobacter pylori infections. It had been suggested that enzyme inhibition played an important role in antifungal activity of bismuth towards the microorganisms. OMCs-Bi(V) made off mixed antibiotic drugs showed characteristic features as a promising candidate in the area of medicinal chemistry. Some antibiotics drugs were the toxicological, and many of them had pharmacological properties.[9] In architecture and tailoring of such multidimensional networks of supramolecular topologies of organometallic

assemblies, tetracycline and amoxicillin were having O-set for bonding sites, due to deprotonation of the hydroxyl group in presence of Bi(V) and presence of anions. These coordination modes and intriguing architecture had possibilities of rational designing for synthesizing such supramolecular architectures based on bonding between oxygen atoms or supramolecular of OMCs-Bi(V).

To design tailoring methodologies for preparation of supramolecular topologies of organometallic assemblies of Bi(V), molecular modeling was employed to judge the coordinate performance of Bi(V) might be influenced by O_5 set. XRPD findings related to crystal lattice and crystal size were correlated with molecular modeling parameters. By converting antibiotics drugs into supramolecular topologies of organometallic assemblies change their physical, chemical and medicinal properties might be good as a medicine or might be good as antimicrobial agent.[10] In this communication, antibiotic drugs (tetracycline and amoxicillin), 2-(amino-hydroxy-methylidene)-4-dimethylamino-6,10,11,12a-tetrahydroxy-6-methyl-4,4a,5,5atetrahydro -tetracene-1,3,12-trione and 7-[2-amino-2-(4-hydroxyphenyl)-acetyl]amino-3,3-dimethyl-6-oxo-2-thia-5-azabicyclo [3.2.0]heptane4carboxylic acid, had been used as a mixed ligand and a novel class of OMCs-Bi(V) derived and synthesized. A complete set of spectral investigations, (IR, ^{1}H-NMR, ^{13}C-NMR, and MS), physiochemical investigations (elemental analyses), X-ray powder diffraction and molecular modeling on binding capabilities of antibiotic drugs with Bi(V), were displayed to investigate binding patterns with O_5, figure 01. The combined impact of these factors makes ML moiety competent as desired and having tailored architectures and antimicrobial effects are well known. Designed OMCs-Bi(V) is having appropriate metal/ligand stability within the system for bonding O_5 were discussed. Antifungal activity of supramolecular topologies of organometallic assemblies of Bi(V) was reported against these pathogens i.e. Candida glaberata, Candida albicans, and Aspergillus flavus by serial dilution method. MIC values and zone of inhibition (in mm) of OMCs-Bi(V) were performed against fungi using Ketoconazole as standard. It was found out that in most cases OMCs-Bi(V) was initiate to be more active than ML.

Table 1 Elemental analyses and % of analytical composition of OMCs-Bi(V)

OMCs-Bi(V)	Empirical Formula	Elemental analyses: Found/calculated (%)				
		C	H	N	S	Bi
$Bi(ML)SO_4$	$C_{38}H_{42}BiN_5O_{17}S_2$	40.01	3.78	6.00	5.70	18.70
		(40.97)	(3.80)	(6.29)	(5.76)	(18.76)
$Bi(ML)(OCLO_3)_3$	$C_{38}H_{42}BiCl_2N_5O_{21}S$	37.50	3.40	5.71	(2.58)	17.16
		(37.51)	(3.48)	(5.76)	(2.64)	(17.18)

The focus of this article was also on the synthesis, physical studies, the characterisation and metalloantibiotics effectiveness with concern their coordination and organometallic behavior. The compounds reported in this article constituted a new class of metal-based antimicrobial agents and thus their metalloantibiotics were investigated. OMCs-Bi(V) were screened against different plant pathogens i.e. Aspergillus flavus, Candida albicans, and Candida glaberata. On the basis of result and discussion, supramolecular architectures of organometallic assemblies, OMCs-Bi(V), showing very good antimicrobial activities as per their corresponding pharmacophore geometries specified by molecular modeling.

Results and Discussion

PHYSIOCHEMICAL INVESTIGATIONS

The reaction of mixed ligand (ML) with Bi(V) afforded light crystals of organometallic assemblies in good yields. The product shows partial solubility in acetone, methanol, ethanol, and acetonitrile, while considerably soluble in polar aprotic solvents like dimethylformamide (DMF), dimethylsulfoxide (DMSO), organic acids and pyridine. OMCs-Bi(V) having characteristic color were stable in air and practically insoluble in water, ethanol, methanol, chloroform and hexane. After elemental analysis, organometallic assemblies of antibiotic drugs i.e. tetracycline and amoxicillin under study were found to be monomeric in nature. Better insight of molecular structures achieved using topological analysis, i.e. using a multidimensional approach of spectral investigations. In results and discussion, there was a network of tactics of spectral observations at molecular level help to understand molecular arrangements of OMCs-Bi(V). The adjustability of concerned mixed ligand or connectivity or its selection abilities towards Bi(V) through specific coordination sites were explored. Elemental analyses (CHN) obtained was satisfactory and matched accurately with stereochemistry of corresponding organometallic assemblies. The empirical formula was derived and assigned to each OMCs-Bi(V) as per general composition. Elemental analyses were listed with the proposed empirical formula in table 1.

INFRARED SPECTRA OF OMCS-BI(V)

During infrared spectral investigations, especially binding abilities of ML towards Bi(V) ion(s) were demonstrated deeply within corresponding geometries of supramolecular topologies of organometallic assemblies. The infrared spectrum of ML showed strong bands and proves the presence of free hydroxyl (-OH) stretching located at ~3460-3445 cm^{-1} and 3380-3360 cm^{-1} whereas, very sharp bands at 1710-1715 and 1680-1685 cm^{-1}, assigned to carbonyl (>C=O) were presented, confirmed the presence of these groups A group of sharp and intense bands were observed at ~3346-3335 cm^{-1} corresponding to free primary amine ($-NH_2$) and broad medium bands at 3310, 3291 and 3260 cm^{-1} which were assigned to secondary amine (>NH) groups respectively, with absence of no change after complexation in infrared spectrum of ML and OMCs-Bi(V).[11] It clearly indicated that these groups had no role in coordination with metal ion and were free. The hetero-aromatic structure showed the presence of C-H stretching vibration in the region of 3100-3000 cm^{-1}, characteristic region for identification of C-H stretching vibration[12]. In this region, bands were not affected appreciably by the nature of substituents. Supramolecular topologies of organometallic assemblies of Bi(V) consisted with four adjacent C-H benzene ring systems, $>(CH_3)_2$, $-CH_2-$ and >CH-. The IR spectrum of ML has several prominent bands appearing at 3245, 1705 and 1635 cm^{-1} due to mN-H and C,O stretching modes, respectively. Comparison of IR spectra of ML and OMCs-Bi(V), indicated that -O- set for bonding were coordinated to Bi(V) by three sites, suggested that ML acts as a tridentate. This was also supported by the fact that bands for m(OH) in spectra of ML and OMCs-Bi(V) were observed. Instead, a band due to m(C-O) at

about 1245 cm^{-1} was observed for OMCs-Bi(V), supported the observation of their enolization during coordination.[13]

FTIR bands observed at 3062, 3019 and 2967 cm^{-1} were assigned to C-H stretching vibration. The in-plane aromatic C-H bending vibration occurs in the region of 1300-1000 cm^{-1}, bands were sharp but had weak-to-medium intensity. The C-H in-plane bending vibration computed at 1293-1146 and 1130 cm^{-1} showed excellent agreement with FTIR bands at 1317, 1259 and 1232 cm^{-1}. The bands observed at 1042-932, 862 and 790 cm^{-1} were assigned to C-H out-of-plane bending vibration for OMCs-Bi(V).[14] However, IR spectrum of OMCs-Bi(V), (M-S) bands did not observe because there is no such infrared spectra bands existed in OMCs-Bi(V), and not span M-S stretching mode.[15] The IR spectrum of ML exhibited a broad band centered at 1670 cm^{-1} due to asymmetric carboxyl mas (COO-)-stretching modes, which was probably broadened because of an overlap with aromatic ring carbon stretching and imidazole ring imido nitrogen-stretching frequency.[16] In addition, the band at 1410 cm^{-1} could be described to symmetric carboxyl ms (COO-) group. During the complexation they were not shifted to lower frequency indicating that there was no linkage between Bi(V) and carboxylato oxygen atom.[17] In addition, there were fascination bands near 1586-1575 cm^{-1} and 1413-1400 cm^{-1} due to the presence of five-membered heterocyclic ring in concerned mixed ligands and OMCs-Bi(V).

Deprotonation occurred from enol form on complexation. The amide-II band [m(NH+CO)] was split, displaced to higher frequency and reduced in intensity. The m(C-S-C) undergoes no negative shift in OMCs, indicating no coordination of ring sulfur to Bi(V). On the other hand, relatively strong bands at 1222-1220 and 1115-1112 cm^{-1} were assigned to ν(C-OH) and ν(>N-CH-) groups respectively. ML bonded to Bi(V) ion(s) through hydroxyl (O-H) and deprotonated phenolic groups, this confirmed origin of bonding patterns between metal ion(s)/ -O- atom and formation of supramolecular topologies of organometallic assemblies of Bi(V). This mode of bonding was suggested by following evidences: (i) there were so many phenolic groups available in organic moieties of ML and if some of them will show disappearance, then it would be very difficult to say which one was those phenolic groups (Ph-OH), (ii) those phenolic groups (Ph-OH) which supposed to interact with metal ion(s) indicating subsequent deprotonation of some phenolic proton prior to coordination. The new appearance of bands due to phenolic C-O- stretching vibrations were upward shifted due to Bi-O coordination (iii) Simultaneously appearance of new bands in the 531-516 cm^{-1} regions due to υ(Bi-O) vibrations. Bi(V) ion(s) also bonded through carbonyl (-NH-C=O), this mode of bonding was also suggested by formation of υ(Bi-O) vibrations as C-O-Bi stretching which were upward shifted and simultaneous appeared at 608-655 cm^{-1}. Formation of these bands was proved coordination to Bi(V) ions through ketonic carbonyl (>C=O) in OMCs-Bi(V). Because of this new bond formation, very strong bands of carbonyl groups were transformed into weak bands and these shifts were towards very lower region as mentioned in wavenumbers by 11-16 cm^{-1} from initial peaks. New stretching vibration bands assigned as υ(Bi-O), indicating coordination of carbonyl oxygen and phenolic groups with Bi(V) ion(s) (M-O). IR spectra of OMCs-Bi(V) showed characteristic change i.e. blue shift, confirmed bonding between Bi(V) and set for bonding atoms of ligand, especially observed bands for -O- from -OH. The Bi(V) bond between

metal/oxygen bond showed similar characteristics as reported earlier.[14] In lower frequency region weak bands were observed at 547-530 assigned to m(M-O) vibrations, respectively.[18] Thus, IR spectrum indicated that ligand acted as a pentadentate O_5 set for bonding set involving oxygen set for bonding atoms of -OH and (-NH-C=O).[13] By comparison of IR spectra of supramolecular topologies of organometallic assemblies of Bi(V) with that of free ligands, it was concluded, here ML behaves as triadentate ligand because ligand has different modes of coordination. Frequencies assigned to ML moieties associated with functional groups and corresponding peaks obtained in infrared spectra of OMCs-Bi(V) showed differences between the set for bonding atoms. This confirmed that binding sites of ML were played main role in the formation of OMCs-Bi(V). Data discussed and reported from IR spectra of components of ML and OMCs-Bi(V) correlated peak-by-peak in spectral characterization process. It was very difficult sometimes or may be very easy to find out difference between binding sites of ligand and metal ion(s) during the formation process of OMCs-Bi(V). During spectral analysis, shifting in frequencies of bands in the form of stretching vibrations were observed in the architecture of OMCs-Bi(V). Vibrational and stretching frequencies with their related assignments reported and discussed. In he infrared spectrum of $Bi(ML)SO_4$ shows absorption at 1108 and 937 cm^{-1} indicating bidentate coordinated sulphate group and because of this, symmetry is reduced to C_{2v}. The characterizing spectral appearances of sulphate groups influence its possible molecular configurations. The vibrational motions of participating atoms produce zero dipole moment in all vibrational positions, vibrational mode would be inactive in infrared. Perchlorate presence was observed in $Bi(ML)(OCLO_3)_3$ and confirmed by detection of vibrations of Bi-O-Cl=O transformation.

^{1}H-NMR SPECTRA OF OMCS-BI(V)

^{1}H NMR spectra of ML and organometallic assemblies in $CDCl_3$ were compared to authenticate chelation, the main difference observed in peaks of -OH groups and compared to authenticate metalation and this confirmed deprotonation followed by complexation to form OMCs-Bi(V). The ML showed a complex pattern in the region of δ 8.15-6.90 ppm for aromatic protons, and the same were observed in spectra of OMCs-Bi(V). A very strong singlet was observed at δ 4.1-4.25 ppm due to (-NH-C=O) proton. The magnetic characteristic of (-OH) protons was not equivalent for ML, and this behavior showed a different complex formation after chelation of free metal ion(s) with ML. During mononuclear OMCs-Bi(V) formation, the signals which were observed earlier at 14.12 and 13.05 ppm in free ML disappeared completely, confirmed deprotonation of this one -OH group during chelation occur. This confirmed involvement of hydroxyl group information of a new bond between Bi(V) and -O- for OMCs-Bi(V). In addition, amide chains acted as a bridge between -O- and Bi(V) atom s at 3.322-3.13 ppm. Other multiplets were observed at 8.82-7.32 ppm due to the presence of main group substituent of i.e. $-C_6H_3-$. ^{1}H NMR spectra show multiplets observed at 6.75- 6.81 ppm for phenyl protons in ML and OMCs-Bi(V). ^{1}H NMR spectra of ML showed singlet at δ11.31-12.60 ppm, and same presented in spectra of OMCs-Bi(V), confirmed the presence of carboxylic protons within Bi(V) architecture and there was no its role in chelation. Signals appearance due to secondary (-NH-) or primary ($-NH_2$) protons

at same positions in ligand and OMCs-Bi(V) show non-involvement of these groups in coordination. Methyl protons on carbon linked to –N< moieties recognize at δ 2.20-2.10 ppm. This signal was a singlet arise from nonequivalent methylene protons in OMCs-Bi(V). In general, OMCs-Bi(V) obtained were found to exhibit no additional resonances to confirm neat and pure encapsulation of OMCs-Bi(V).

^{13}CNMR SPECTRA OF OMCS-BI(V)

^{13}C NMR spectral peaks of ML and organometallic assemblies along with possible assignments were presented. Experimental values of all carbons within ML and OMCs-Bi(V) were reported which found as per architectural features of OMCs-Bi(V). ^{13}C NMR spectra of >C=O of ML appeared at 192.7 ppm. Peaks belong to those carbons attached with hydroxyl groups of ML appeared at 157.1 ppm. The ^{13}C spectra of hydroxyl phenyl moiety attached to Bi(V) appeared at 133.5-115.1 ppm while some carbons appeared at 150.5 ppm due to electron-withdrawing effect metal towards hydroxyl groups at this position. ^{13}C NMR spectra of all carbons of amino, phenyl and thio moieties of ML appeared at 114.9-152.8 ppm. In case of one part of ML, the spectra of different carbons appeared in an up-field direction as compared with other carbon atoms in phenolic moieties of OMCs-Bi(V) due to new bond formation of oxygen with a metal ion(s).[19]

ELECTRONIC SPECTRA OF OMCS-BI(V)

The coordination behavior of Bi(V) with ML investigated using electronic spectroscopy in solution and electronic absorption spectra were recorded in methanolic solution in 15 cm^3 cuvette with concentration. Electronic spectra of Bi(V)-OMCs showed two peaks at 331-317 and 460-431 nm which were assigned as ($\pi\rightarrow\pi^*$) and ($n\rightarrow\pi^*$) transition respectively. The transition of $ArCOCH_3$ and the existence of C,O and C,S bands can be observed. The absorption bands for C,O and C,S chromophores can be indicated at ƛmax in range of 281-295 nm. Therefore, it can be assigned as $\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$ overshadowed transitions. For $\pi\rightarrow\pi^*$ transition around 217 nm, the band might be due to ArCOMe and also ArCOAR group that affected the hypsochromic shift of phenyl ring. The presence of 'shoulder peak' explained the effect of an extended conjugation from aromatic rings of OMCs-Bi(V).[20] OMCs-Bi(V) displayed a broad emission spectral transition indicating charge-transfer. The emission spectral features of OMCs-Bi(V) was because of their ability of intramolecular energy transfer between triplet levels of ML and emitting energy levels of Bi(V), which depended on energy differentiation. In organic solvents, the energy gap between ML triplet level and emitting level of Bi(V) may be in favor of the energy transfer process.[21] Because of this, Bi(V)-OMCs displayed blue emission wavelength, and maximum emission peaks shifted towards the longer wavelength. It can be also seen that emission intensities of $Bi(ML)SO_4$ and $BI(ML)(OCLO_3)_3$ were stronger than ML.[22]

TIME-OF-FLIGHT (TOF) MASS SPECTRA OF OMCS-BI(V)

Time-of-flight mass spectral displayed molecular ion species [M]+ and other peaks corresponding to fragmentation patterns of supramolecular topologies of organometallic assemblies of Bi(V). The patterns of peaks in mass spectra reflected a clear indication of successive degradation with a series of

peaks corresponding to different fragments of studied OMCs-Bi(V). The intensities of peaks were directly related to the stability of concerned fragments patterns evidenced in mass spectra with a clear impression of successive degradation of OMCs-Bi(V). All fragments (ligand or fragments of ligand with metal or metal + ligand) discussed to confirm their molecular formula (Zeng, et. al., 2012).[23] In the mass spectra of $Bi(ML)SO_4$ and $Bi(ML)(OCLO_3)_3$ molecular ion peaks (ligand + metal) were observed at 730 and 824 (m/z) respectively which represented final molecular ion peak (m/z) for OMCs-Bi(V). Complete set of mass spectra of OMCs-Bi(V), molecular ion peaks of all fragments (ligand or fragments of ligand with metal or metal + ligand) observed as MS (EI, m/z (%): 1113 (M+) and MS (EI, m/z (%): 1214 (M+) as per molecular formula of OMCs.[6] Mass degradation patterns proved the presence of the isotropic ratio corresponding to metal ion(s) i.e. sulphate and chlorate of Bi(V) with ML fragments. The results obtained were discussed to show breaking and chelation patterns of OMCs-Bi(V). Mononuclear nature of OMCs-Bi(V) was assigned as [M (fragments of the ligand)]+.

In TOF-mass spectra of $Bi(ML)SO_4$ and $Bi(ML)(OCLO_3)_3$, initial fragmentation patterns were found similar to the ligand and also showed an additional peak indicating the mass loss of substitutes and

Table 2 Crystallographic data of OMCs-Bi(V)

Compound	$Bi(ML)SO_4$	$Bi(ML)(OClO_3)_2$
Empirical formula	$C_{38}H_{42}BiN_5O_{17}S_2$	$C_{38}H_{42}BiC_{l2}N_5O_{21}S$
Formula weight	1113.87	1215.13
Temp °K	302	298 °C
Wave length (λ)	1.02356 Å	1.54056 Å
2θ range	12-20	12-80
Unit	a = 15.25631 (A); b = 15.12548 (A); c = 16.25631 (A); α = 90.00°	a = 15.95464 (A); b = 15.95464 (A); c = 16.47710 (A); α = 90.00°
Cell dimension	β = 90.00°; γ = 120.00°	β = 90.00°; γ = 120.00°
Volume (A3)	3345.256	3632.32
Crystal system	Hexagonal	Hexagonal
Space group	P63/mmc	P63/mmc
Density (g/cc)	1.56	1.08
Z	2	2
Index ranges	$1\leq h\leq 8; 0\leq k\leq 5; 0\leq l\leq 10$	$1\leq h\leq 8; 0\leq k\leq 5; 0\leq l\leq 10$
Avs. Eps	M(9) = 5; F(9) = 1; 0.00002320	M(9) = 6; F(9) = 2; 0.0000650
Particle Size (nm)	12.03	11.66

degradation of double bond bonded oxygen fragments -O- from parent molecule of tetracycline observed at 690 and 687 (ligand fragments + metal)for these complexes respectively. Mass degradations patterns provide the most important information about the fragmentations of a particular compound in the studied spectra and proved the presence of isotopic ratio corresponding to the metals i.e. Bi(V) with the ligand fragments. On the basis of the above discussion, a mononuclear nature of the studied OMCs has been proved and may be assigned as [M+(fragments of the ligand)].

X-RAY POWER DIFFRACTION ANALYSIS OF OMCS-BI(V)

XRPD spectra were obtained from good quality of powder of organometallic assemblies. The density was resolute by the Archimedes method. Crystal methodologies (direct methods and Patterson synthesis) were utilized from XRPD data, all the diffraction peaks were pointed out which lead to extract

intensities of particular reflections. Indexing methodologies were performed using (CCP_4, UK) the Crysfire program with different crystal systems with varying space group.[24] The merit of fitness and particle size of supramolecular topologies of organometallic assemblies of Bi(V) were derived from

Table 2 Crystallographic data of OMCs-Bi(V)

Compound	$Bi(ML)SO_4$	$Bi(ML)(OClO_3)_2$
Empirical formula	$C_{38}H_{42}BiN_5O_{17}S_2$	$C_{38}H_{42}BiC_{l2}N_5O_{21}S$
Formula weight	1113.87	1215.13
Temp °K	302	298 °C
Wave length (λ)	1.02356 Å	1.54056 Å
2θ range	12-20	12-80
Unit	a = 15.25631 (A); b = 15.12548 (A); c = 16.25631 (A); α = 90.00°	a = 15.95464 (A); b = 15.95464 (A); c = 16.47710 (A); α = 90.00°
Cell dimension	β = 90.00°; γ = 120.00°	β = 90.00°; γ = 120.00°
Volume (A3)	3345.256	3632.32
Crystal system	Hexagonal	Hexagonal
Space group	P63/mmc	P63/mmc
Density (g/cc)	1.56	1.08
Z	2	2
Index ranges	$1\leq h\leq 8; 0\leq k\leq 5; 0\leq l\leq 10$	$1\leq h\leq 8; 0\leq k\leq 5; 0\leq l\leq 10$
Avs. Eps	M(9) = 5; F(9) = 1; 0.00002320	M(9) = 6; F(9) = 2; 0.0000650
Particle Size (nm)	12.03	11.66

Table 4 Bond angles of OMCs-Bi(V)

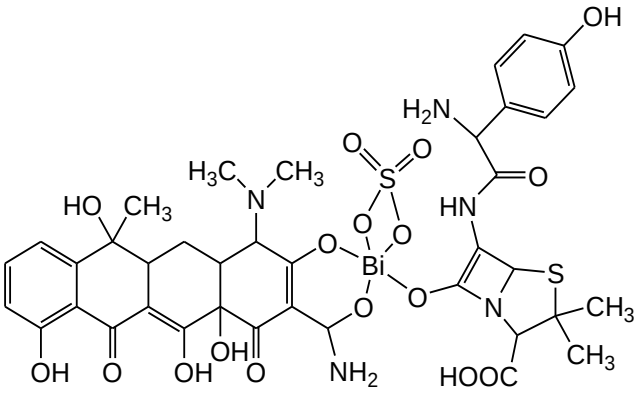
Bond length of $Bi(ML)ClO_4$			Bond length of $Bi(ML)SO_4$	
S. No.	Atoms numbering and their location	Bond Angle [º]	Atoms numbering and their location	Bond Angle [º]
1.	O(58)-Bi(57)-O(56)	145.8	O(58)-Bi(57)-O(56)	145.8
2.	O(58)-Bi(57)-O(31)	164.0	O(58)-Bi(57)-O(31)	160.0
3.	(58)-Bi(57)-O(29)	124.1	(58)-Bi(57)-O(29)	124.1
04.	Bi(57)-O(56)-C(43)	120.0	Bi(57)-O(56)-C(43)	120.0
05.	Bi(57)-O(31)-C(28)	99.84	Bi(57)-O(31)-C(28)	97.84
06.	Bi(57)-O(29)-C(17)	109.5	Bi(57)-O(29)-C(17)	107.0

Table 3 Bond length of OMCs-Bi(V)

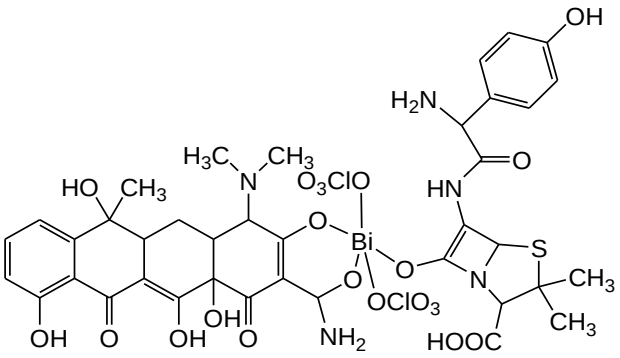
Bond length of $Bi(ML)ClO_4$			Bond length of $Bi(ML)SO_4$	
S. No.	Atoms numbering and their location	Bond Distance [Å]	Atoms numbering and their location	Bond Distance [Å]
1.	Bi(57)-O(63)	2.1	Bi(57)-O(63)	2.1
2.	Bi(57)-O(58)	2.1	Bi(57)-O(58)	2.1
3.	O(56)-Bi(57)	2.1	O(56)-Bi(57)	2.1
4.	O(31)-Bi(57)	2.0	O(31)-Bi(57)	2.0
5.	O(29)-Bi(57)	2.1	O(29)-Bi(57)	2.1

XRPD. The cell dimensions and other related parameters of OMCs-Bi(V) discussed to reveal crystalline nature. GSAS program for space group and density were performed by the Archimedes method. XRPD data was a very good source to deduce accurate cell parameters of OMCs-Bi(V) and particle sizes of OMCs-Bi(V) were calculated using Debye-Scherer equation. Crystalline nature of OMCs-Bi(V) was confirmed from reflectance patterns. Efforts to prepare single crystals of these complexes were unsuccessful due to the high molecular mass of metal ions. Hence, powder X-ray diffraction pattern of ML and OMCs-Bi(V) were recorded. The diffraction pattern revealed the crystalline nature of

complexes for crystal system and observed to know straightforwardly substantiate alignments in sequence about the stereochemistry of ML and OMCs-Bi(V), specified in table 2.



(a) $Bi(ML)SO_4$



(b) $Bi(ML)(OClO_3)_3$

Figure 2 Molecular structure of supramolecular topologies of organometallic assemblies of Bi(V)
The indexing procedures a pentagonal crystal system for OMCs-Bi(V), figure 02.

Molecular modeling of OMCs-Bi(V)

Molecular modeling was a mathematical concept to impersonate correlated significant features (bond angles, bond energies, torsion angles, and Cartesian coordinates demonstrates) in three-dimensional arrangements within certain topological assemblies to demonstrate molecular models for organometallic assemblies. Coordination abilities of ML with Bi(V) were performed through molecular mechanics calculations to get refined models of OMCs-Bi(V) to display sequence of new bonds formation between ML and Bi(V). Finally, a large number of deviations were noticed in distances, angles, or torsion because of specific electronic interactions to ascertain architectural features energy-minimized models of OMCs-Bi(V). Molecular coordinates depended on the hybridization of an atom and mode of bonding as a standard to judge specific interactions in topologies of molecules.[6] If deviations in distances, angles or torsion were evidenced, specific electronic interactions should perhaps be pursued to ascertain structural and geometrical features of OMCs-Bi(V) further confirmed spectral pieces of evidence and coordination capabilities of Bi(V).[25] In order to ascertain structural features and related coordination capabilities of supramolecular topologies of organometallic assemblies of Bi(V) towards metal ion(s) along with its impact on bond lengths and bond angles, thereby, were presented through molecular models of ML and OMCs-Bi(V).

Physical dimensions of molecules helped out to demonstrate changes occurred during their topological assemblies. The process of determining energy minimization was repeated several times to find global minimum energy. Data analysis of bond lengths and angles were presented in table 3 to 5. On the basis reported data, following remarks were concluded as follows: Bond angles between metal and set for bonding atoms in the moiety were altered somewhat upon coordination; bonds angles among O(58)-Bi(57)-O(31) was 164.0, a consequence of bonding was quite near to distorted trigonal-bipyramidal geometry. It was clear that all active groups taking part in coordination and had wider bonds than already existing in -O- linkages of ligand moiety. Coordination significantly shortens as for 2.0 [Å] as compared to 2.1 [Å] for Bi(57)- O(63). Conclusions might be drawn for the ligating properties of ML which could help in elucidating molecular modes of OMCs-Bi(V). One part of ML showed chelation occurring via -O- of -OH, through deprotonated phenolic oxygen. The second part of ML shows bidentate nature of anions and coordination occurred via -O- of –OH, and –NH-C=O.

Table 5 Atomic coordinates of $Bi(L)ClO_4$

Atom	X	Y	Z	Atom	X	Y	Z
C	-1.1217	5.8791	6.4057	C	7.5678	0.8417	4.4367
C	-2.0751	4.3323	7.4140	C	8.6414	0.8100	5.2329
C	-1.3425	3.3562	6.8681	C	6.5011	1.1909	2.2526
C	-1.1186	3.3457	5.5500	N	5.5647	2.1623	2.7501
C	-1.6272	4.3115	4.7779	C	5.8510	-0.1707	2.2316
C	-1.6287	5.5782	5.2057	C	4.1083	-1.4489	2.6021
C	-0.3957	2.3772	4.9462	C	2.7482	-2.0529	2.5705
C	-0.7970	2.0609	3.6956	C	4.4957	-2.8949	2.6021
C	-2.1431	2.4986	3.2083	N	3.0758	-3.2754	2.6021
C	-2.2481	4.0151	3.3008	S	5.0634	-3.3172	0.9307
C	0.0257	1.3464	2.9209	C	3.4187	-3.3495	0.1639
C	-0.3553	0.9611	1.5254	C	2.6928	-3.8815	1.3188
C	-1.8436	0.6416	1.4754	C	3.3566	-4.2790	1.0409
C	-2.6417	1.9387	1.4792	C	2.9104	-2.0352	0.4138
C	0.3975	-0.2835	1.1239	C	1.2189	-3.6403	1.1031
C	0.2259	-0.6652	0.1606	O	0.4591	-4.5759	1.0231
C	-1.0143	-0.6245	0.6585	O	0.7537	-2.3900	1.0004
C	-2.1742	-0.1730	0.1733	O	6.4731	-1.1311	1.8443
O	-0.8271	2.3774	7.6506	N	4.6537	-0.3065	2.6197
O	0.5397	1.8345	5.4844	O	1.5262	-1.4694	2.5225
O	1.2300	0.9627	3.4094	Bi	-0.2045	-2.6583	2.4897
O	1.1011	-0.8931	1.8937	O	-0.9987	-4.5804	2.7809
C	-3.6972	4.4748	3.2087	Cl	-0.1375	-5.8931	2.3425
O	-1.5868	4.6904	2.2652	O	-0.8704	-7.0521	2.6335
N	-2.9057	-1.3459	0.5698	O	1.0718	-5.9157	3.0510
C	-4.0767	-0.9534	1.3064	O	0.1264	-5.8404	0.9668
C	-3.2994	-2.0829	0.6005	O	-0.5518	-2.2085	4.5113
C	1.3837	-1.1291	0.9884	Cl	-1.7937	-1.2388	4.9288
O	-1.3420	-0.9867	1.9224	O	-1.8213	-1.0875	6.3222
O	-0.0499	2.0220	0.6611	O	-2.9983	-1.8117	4.4978
O	1.0482	-1.0518	2.3474	O	-1.6296	0.0160	4.3259
N	2.5237	-0.2920	0.7285	O	10.9384	1.0599	5.5434
C	7.7032	1.1554	3.1441				

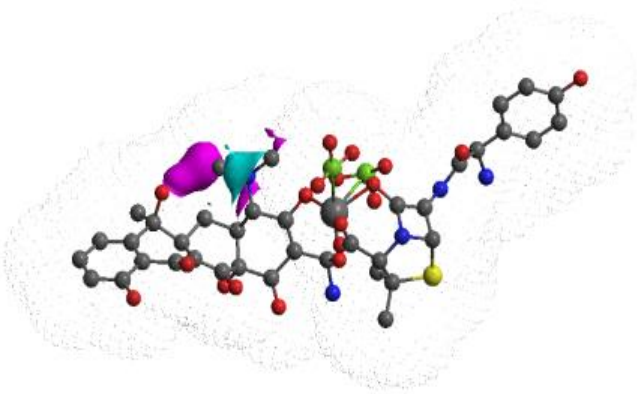


Figure 3 Optimized structure showing HOMO of Bi(ML)SO_4; Color Code: C, Blackish Grey; N, Blue; O, Red; Bi , Dark Grey, and S, Yellow

The coordination geometry was best described as distorted trigonal-bipyramidal geometry. Another important distortion was caused by asymmetric Bi-O bond lengths. Therefore, O-Bi-O angle of 145.8º was not consistent with true distorted trigonal-bipyramidal geometry in which basal plane was defined by five -O- backbone for Bi(ML)$(OCLO_3)_3$.[26] Bond angles between metal and set for bonding atoms in ML moiety were altered somewhat upon coordination; bonds angles O(58)-Bi(57)-O(31) and O(58)-Bi(57)-O(31) were 164.0° and 160.0° respectively as a consequence of bonding. Bond angles in OMCs-Bi(V) were quite near to distorted trigonal-bipyramidal geometry. It was clear that three active groups taking part in coordination and had longer bonds than already existing in ligand in -O-Bi-O- linkages. Coordination significantly shortened as 2.0 [Å] to 2.1 [Å] for O(31)-Bi(57). This was because of bond lengths in ML between set for bonding atoms probably gets affected due to the presence of hydrogen in -OH. There was a large variation in O(63)-Bi(57) bond lengths on complexation and becomes slightly longer as coordination took place via O atom of O_5.

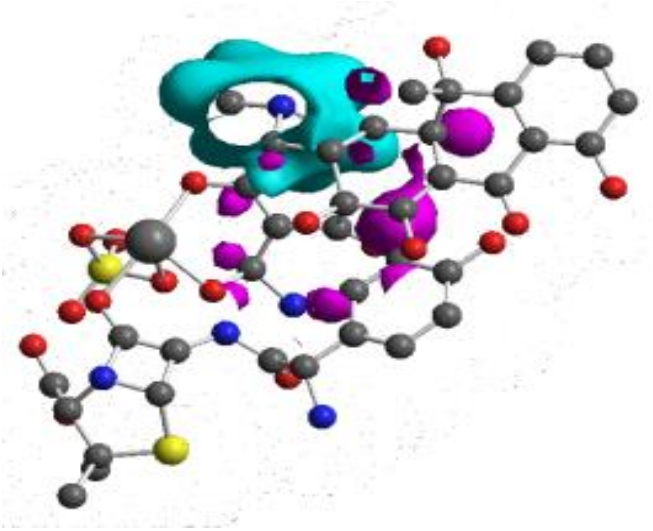


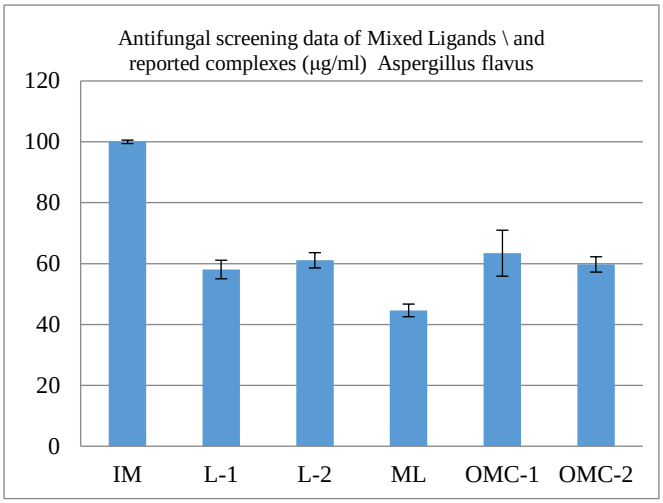
Figure 4 Optimized structure with HOMO of Bi(ML)ClO_4; Color Code: C, Blackish Grey; N, Blue; O, Red; Bi , Dark Grey, Cl, Green and S, Yellow

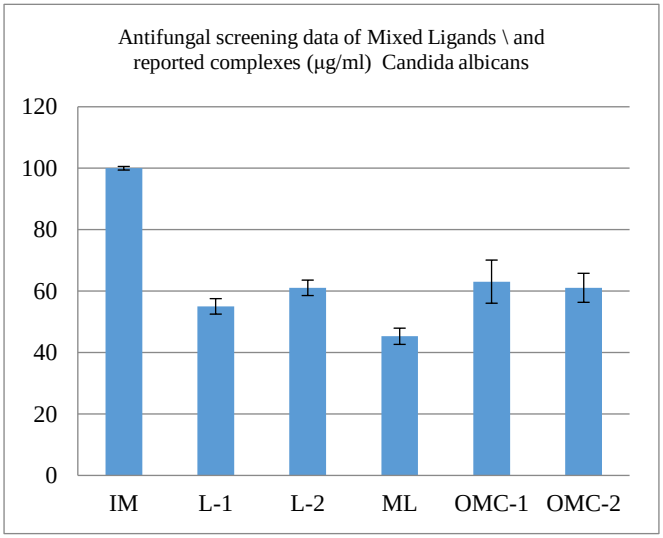
The overall geometry of Bi(V) was a trigonal-bipyramidal in which equatorial plane was formed from O_5 set for bonding set, while carboxyl oxygen and oxygen occupy axial positions for Bi(ML)SO_4 and

$Bi(ML)(OCLO_3)_3$. These were a first structure where coordination of a -O- atom from hydroxyl moiety in OMCs-Bi(V), the particular characteristics of these systems facilitated by coordination of -O-atom to Bi(V), which showed that coordination to -O-, favored rather than other atoms. Statistical findings of spectral and physiochemical analytical analysis (IR, ^{1}H NMR, ^{13}C NMR, and MS) analysis and molecular modeling, molecular structure of supramolecular topologies of organometallic assemblies of Bi(V) derived from ML matched with results of XRPD data, molecular models of supramolecular topologies of organometallic assemblies of Bi(V) with HOMO, and showed that essentially Bi(V) metal center, having five-coordinated geometry. Molecular and solvent accessible surface model of ML and OMCs-Bi(V) of Bi(V) were designed and presented as figure 3 and 4.[27]

ANTIFUNGAL ACTIVITY OF OMCS-BI(V)

Designing and tailoring of new biologically active of supramolecular topologies of organometallic assemblies were crucial and depended on the utilization of new methodologies and implemented techniques significantly. Antimicrobial effects of OMCs-Bi(V) depended upon several factors i.e. metal ion(s), chromophore set of ML moiety and other geometrical features. The combined impact of these factors makes ML moiety competent as desired and having tailored architectures and antimicrobial effectiveness are well known. Designed OMCs-Bi(V) having appropriate metal/ligand stability within a system for bonding O_5 were discussed.[28] Moreover, coordination reduced polarity of metal ion(s) because of the partial sharing of its positive charge with a set for bonding atoms within set for bonding set of ML.[29] During this process, the lipophilic nature of the central metal atom increased as a result favored permeation more efficiently through the lipid layer of a microorganism to destroy them more aggressively. Besides this, probably there might be other factors such as solubility (as shown in figure 3 and 4), dipole moment and conductivity which may be influenced by metal ions.[30] These could be major reasons behind higher antimicrobial effectiveness of OMCs-Bi(V) than ML.[1] Antifungal activity of supramolecular topologies of organometallic assemblies of Bi(V) was reported against these pathogens i.e. Candida glaberata, Candida albicans, and Aspergillus flavus by serial dilution method. MIC values and zone of inhibition (in mm) of OMCs-Bi(V) were performed against fungi using Ketoconazole as standard. It was found out that in most cases OMCs-Bi(V) was set up to be more active than ML. On the basis of reported results, a new methodology can be developed for designing of high standard antifungal agents. Organometallic assemblies were directly mixed in a medium of different concentrations. The fungus was positioned in the medium with the help of an inoculum's needle. Petri dishes wrapped in polythene sheets containing some drops of C_2H_5OH were put in an incubator at 30±3 °C for 70-90 hrs. The enlargement of the fungal colony was measured in diameter. Antifungal activity of ML and OMCs-Bi(V) were performed by agar plate technique and screened values were arranged graphically in figure 5.





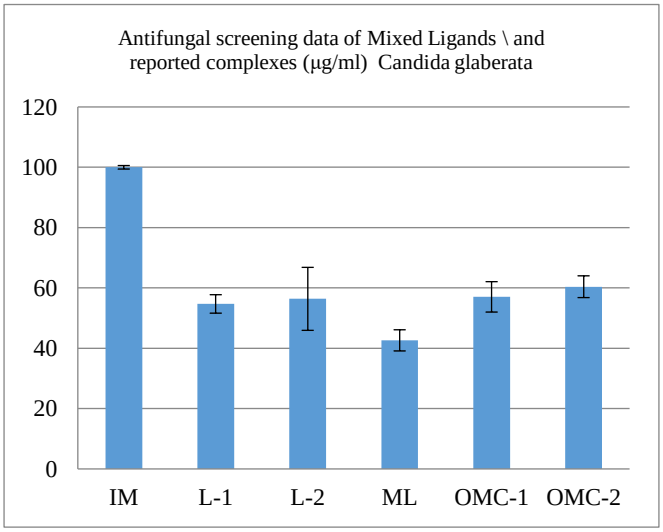


Figure 5 Graphical representation of antifungal activity of OMCs-Bi(V)

Results indicated that OMCs-Bi(V) had the potential to generate novel antimicrobial agent by displaying moderate to high affinities for most of receptors particularly in case of OMCs. Cell

permeability was due to its surrounding by the lipid membrane and acts as a special passage for the lipid soluble materials. So, it showed liposolubility and increased antimicrobial resistance in a cell.[31] This was known as the most important biological phenomenon in regard to antifungal aspects. Keeping in view, the problem of antimicrobial resistance, OMCs-Bi(V) showed good antimicrobial character. Polarity was directly influenced by the coordination abilities of metal because of partial sharing of its positive charge within ML system having π-electron delocalization.[32] OMCs-Bi(V) had higher activity than free ligand because of increased activity of metal chelates according to Overtone's concept. The inhibition activity of compounds seemed to govern with the certain degree as per availability percentile of sulphur, nitrogen and oxygen atoms in ML and OMCs-Bi(V). This was because O_5 set for bonding set with the presence of sulphur shows more activity against Aspergillus-flavas compared to those having a lesser number of sulphur atoms within the system. In this present study, concerned spectral results proved metal to be bonded through oxygen atom of hydroxyl group of substituents ring and another the hydroxyl group of the neighbouring ring and O=C-NH- group as O_5 set organometallic assemblies.[33] In the construction of novel OMCs-Bi(V), tetracycline and amoxicillin have been used to synthesize well computed designed organometallic assemblies through molecular modeling to have refined models in three dimensions of OMCs-Bi(V) specified as figures 6-7.

Reported organometallic assemblies showed good biological activity. By making a comparison between biological activities of ML and organometallic assemblies, it was pointed out that OMCs-Bi(V) have moderate activity as compared ML.[34] The higher inhibition zone of OMCs-Bi(V) comparatively ML could be explained on basis of Overtone's concept and Chelation theory. On chelation, the polarity of Bi(V) would be reduced to a greater extent due to overlap of ML orbital. Because of this, partial sharing of the positive charge of Bi(V) and partial negative charge of the set for bonding atoms exchanged with each other. As a result, delocalization of π-electrons density clouds spread over the surface of the chelating ring. This enhanced penetration power of organometallic assemblies into lipid membranes and influenced binding sites of enzymes within microorganisms.[35]

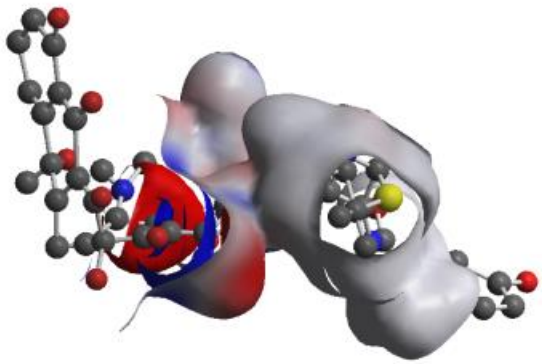


Figure 6 Achieve pharmacophore geometries of $Bi(ML)(OClO_3)_2$

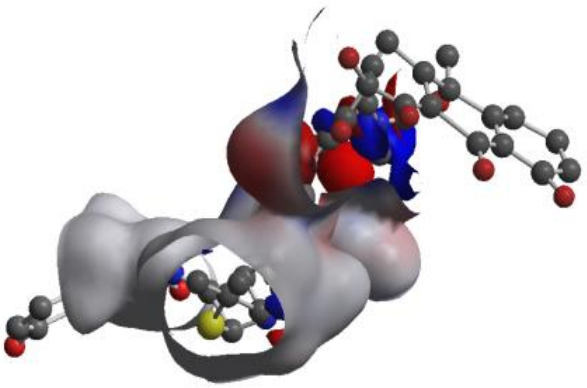


Figure 7 Achieve pharmacophore geometries of $Bi(ML)SO_4$

Due to interaction between aqueous Bi(V) (cations) and anionic constituents of the fungal cell wall, metal uptake decreased and hence toxicity decreased. But in case of OMCs-Bi(V), since metal cation was already coordinated to a ligand, it easily entre into fungal cells and hence exerts higher metal toxicity. The toxicity of metal ions on metabolic activity of fungal cells was resulting from organometallic assemblies and inactivation of cellular functional macromolecules.[36] It has also been suggested that some electron set for bonding groups present in ligands displayed extensive the biological activity that may be responsible for increase in hydrophobic character and liposolubility of organometallic assemblies that ultimately enhances the biological activity of compounds. There was so many other aspects such as solubility, conductivity, dipole movement and bond length between Bi(V) and ML which may influence the biological effectiveness of these organometallic assemblies. Spectral findings was compared peak by peak shifting to find out the molecular provision of considered metal ion(s) in OMCs-Bi(V).[37] A comparative analysis showed higher antifungal activity of organometallic assemblies than free ligands, mixed ligands and the metal salt. Some of the organometallic assemblies exhibited moderate activities as compared with standard drug ciprofloxacin. It was also observed that one of organometallic assemblies were more potent fungicides than mixed ligands. This enhancement in antifungal activity was rationalized on the basis of Overtone's concept[38] and Tweedy's chelation theory and partial sharing of the positive charge of metal ions with setting for bonding groups. This may support this argument that some type of bimolecular binding to metal ions or intercalation or electrostatic interaction caused inhibition of biological synthesis and prevented organisms from reproducing.[39]

Microorganisms were increasingly becoming resistant to make sure their existence contrary to the resource of antimicrobial agents to which they were being bombarded. They attained this over and done with dissimilar resources but mainly centered on the chemical assembly of antimicrobial agent and machineries through which such mediators act on behalf of. The resistance mechanisms, therefore depended on which specific pathways were inhibited by drugs and alternative ways available for those pathways that organisms can modify to get a way around in order to survive. Resistance could be described in two ways: a) intrinsic or natural whereby microorganisms naturally did not possess target sites for drugs and therefore drug did not affect them or they naturally had low permeability to those

agents because of differences in chemical nature of drug and microbial membrane structures especially for those that required entry into microbial cell in order to affect their action or b) acquired resistance whereby a naturally susceptible microorganism acquired ways of not being affected by drug. The results of our studies indicated that organometallic assemblies have good activity against ligand and all fungal strains. The strong antimicrobial activities of organometallic assemblies against tested organisms suggested further investigation on these supramolecular topologies of organometallic assemblies of Bi(V).[40-41]

MATERIALS AND METHODS

All the chemicals and solvent used in this study were of analytical grade and used as procured from Aldrich and dried over 4 Å molecular sieves. Solvents were purified by standard procedures (Riddick and Bunger, 1970).[42]

MATERIALS AND INSTRUMENTS

The stoichiometric analysis (C, H and N) of organometallic assemblies were performed using a Carlo-Ebra 1106 elemental analyzer. Metal content was estimated on AA-640-13 Shimadzu flame atomic absorption spectrometer in solution arranged by decaying the particular complex in hot concentrated HNO_3. IR spectra were recorded on a Perkin-Elmer FTIR spectrometer in KBr. The electronic spectra were recorded in water on a Beckman DU-64 spectrometer with quartz cells. ^{1}H and ^{13}C NMR spectra were recorded at ambient temperatures on Bruker AMX400 and DRX500 spectrometers with TMS as internal reference and D_2O as solvent. Chemical shifts (δ) were expressed in parts per million (ppm) relative to (TMS) tetramethylsilane. The crystals needed for X-ray diffraction analysis were tried to produce three dimensional crystalline models as follows: one gm of OMCs-Bi(V) was dissolved at 40 °C in minimum amount of methanol. A clear solution was obtained and heated for 4 to 5 minutes under reflux and was then filtered off at a high temperature. The solution was cooled down to room temperature and closed with a semipermeable membrane so that methanol cannot evaporate but still a very slow evaporation was there. The mixtures were stored at room temperature for a period of three to five weeks. Very small crystals were filtered off and dried.

BIO ASSAY

The free ligands, mixed ligands and supramolecular topologies of organometallic assemblies were tested against various fungal strains with the agar well diffusion method. The antifungal activity against various fungi was also tested and the results are presented as comparative manor graphically.

HANGING DROP METHOD-ANTIFUNGAL ACTIVITY

The concentration of test compounds was 500 ppm used to revision the antimicrobial doings on propagation of fungal spores by the hanging drop method. The germination of the spores was observed under microscope after 8 hours of incubation at 30°C for incubation period 6-9 days. The percentage inhibition of spore germination was calculated as follows, % Inhibition of spore germination = Total number of germinated spore/ Total number of spore.[37]

XRD MEASUREMENTS

XRD powder patterns were recorded on a vertical-type Philips 1130/00 X-ray diffractometer, operated at 40 kV and 50 mA generator using Cu-Kα line at 1.54056 A° as the radiation sources. Sample was scanned between 5° to 70° (2θ) at 25 °C. Crystallographic data was analyzed using CRYSFIRE-2000 powder indexing software package and the space group was found by CHECK CELL programme. Debye-Scherer relation was derived with the help of 100% peak width to determine the particle size. Experimental density was observed through Archimedes method.

3D MOLECULAR MODELING

The correct sequence of atoms in three dimensions was obtained to get reasonable low energy molecular geometries. The molecular modeling described application of classical mechanics to determine molecular equilibrium in proposed molecules Emphasize were taken on molecular structures of ML and organometallic assemblies help us to understand mechanism of biochemical transformations and in designing new methodologies to get perfect molecules for such purpose. 3D molecular models of organometallic assemblies were created using CS Chemdraw 3D program package. The correct stereochemistry was confident through operation and alteration of molecular coordinates to acquire sensible low energy molecular geometries. The optimized structures of OMCs were performed by MM2. The potential energy of molecule was sum of following terms: E = Estr + Eang + Etor + Evdw + Eoop + Eele. where all E's represent energy values and found corresponds to given types of interaction. The subscripts str, ang, tor, vdw, oop and ele denote bond stretching, angular bonding, torsion deformation, vander waals interactions, out of plain bending and electronic interaction respectively.

GENERAL PROCEDURE FOR SYNTHESIS OF OMCS-BI(V)

PREPARATION OF SOLUTIONS (MIXED LIGAND-ML-SOLUTION) AND OMCS-BI(V)

A required amount of corresponding antibiotic drugs were mixed in 1:1 ratio, equimolar amount of the drugs, and dissolved in CH_3OH.

PREPARATION OF BI(V) SOLUTION

Sodium bismathate was dissolved in 1:1 $HCLO_4$ or 0.1 M H_2SO_4 respectively as source of Bi(V). The transparent filtrate was obtained as metal salt, further used for complexation. Bi(V) solution was prepared by drop-wise addition of metal salts solution to 100 ml of 0.01 M Bi(V) solution in methanol with continuous stirring at room temperature. The pH of the solution was adjusted by drop-wise addition of NaOH in the range of 2-3 using a pH-meter separately.

GENERAL METHOD FOR SYNTHESIS OF OMCS-BI(V)

Organometallic assemblies i.e. OMCs-$Bi(OClO_3)_5$ or $Bi_2(SO_4)_5$ was prepared by dissolving equimolar amounts of mixed ligand (ML, gm, 0.5 mmol) and solution of $Bi(OClO_3)_5$ (gm, 0.5 mmol) or $Bi_2(SO_4)_5$ (gm, 0.5 mmol) respectively in minimum quantity of CH_3OH (20 cm^3, absolute) in 100 ml round bottom flask. The mixture was heated for 6 h, until volume was reduced to half original at

~82-85 °C on a water bath. A solid mass separated out on cooling at ~5 °C was refrigerated for better crystallization. It was then filtered, washed with CH_3OH and dried over P_2O_5 in vacuum. The formed crystals were re-dissolved for re-crystallization in excess amount of warm methanol. The clear solution obtained was left undisturbed for weeks to get very small fine crystals.

CONCLUSION

Supramolecular topologies of organometallic assemblies, OMCs-Bi(V) of Bi(V), having O_5 set for bonding, coordinate performance of Bi(V) ion(s) might be influenced by the number of a set for bonding atoms and their pharmacophore geometries. Bi-bound with different groups come into existence because of bonding between O-Bi and it further affected by the presence of -O- atoms of anions. These bonding between O-Bi were at origin of moderate fungal efficiency detected for OMCs-Bi(V). Tuning spacer toward higher polarities by incorporation of electronegative atoms such as oxygen was not offer a new track toward improved antifungal performances of grafted OMCs-Bi(V). To avoid any additional source of coordination expansion of Bi(V) atom, except for one caused by ML reaction components themselves.[43]

Moreover, coordination reduced the polarity of metal ion(s) because of partial sharing of its positive charge with set for bonding atoms within a set for bonding set of ML. During this process, the lipophilic nature of the central metal atom increased as a result favored permeation more efficiently through the lipid layer of the microorganism to destroy them more aggressively. Antifungal activity of supramolecular topologies of organometallic assemblies of Bi(V) was reported against these pathogens i.e. Candida glaberata, Candida albicans, and Aspergillus flavus by serial dilution method. It was found out that in most cases OMCs-Bi(V) was found to be more active than ML. On the basis of reported results, a new methodology can be developed for designing of high standard antifungal agents. Organometallic assemblies were directly mixed in a medium of different concentrations.[44]

ACKNOWLEDGMENTS

One of the authors (Rajiv Kumar) gratefully acknowledges his younger brother Bitto for motivation. Authors acknowledge IIT Delhi for recording ^1H NMR spectra respectively.

REFERENCES AND NOTES

1. R. Johar, R. Kumar. Computational approach on architecture and tailoring of organicmetal complexes derived from streptomycin and Zn, Cd and Pb: antimicrobial effectiveness. *Appl. Organometal. Chem.* **2011,** 25, 791-798.
2. R. Johar, R. Kumar, P. Mishra. Molecular modeling of Bi(V)-MCs derived from streptomycin derivatives: synthesis and spectroscopic studies. *J Integr Sci Technol,* **2015,** 3(1), 18-21
3. O.R. Sipahi. Effects of Antibiotic Resistance on Industrial Antibiotic R&D. *Expert Rev Anti Infect Ther*. **2008**, 6(4), 523–39.
4. R. Kumar, P. Mishra. Bi(V) organic framework in an asymmetric system: Synthesis, spectroscopic, XRPD and molecular Modeling, *Main Group Chemistry,* **2007**, 6, 85-95.

5. B. Spellberg, R. Guidos, D. Gilbert, et al. The Epidemic of Antibiotic-resistant Infections: A Call to Action for the Medical Community from the Infectious Diseases Society of America. *Clin Infect Dis*. **2008**, 46(2), 155–64.
6. R. Kumar, B.S. Chhikara. Organometallic assemblies: p-electron delocalization, m-bridging spacers, flexibility, lipophilic nature, bio-accessibility, bioavailability, intracellular trafficking pathways and antimicrobial assimilation. *J. Organometallic Chem.,* **2015,** 776, 64-76.
7. R. Kumar, Parashuram, M. Main group metal-organic frameworks of Bi(V) and Pb(II) derived from 2-[4,6-diamino-3-[3-amino-6-(1-methyamino-ethyl)tetrahydropyran-2-yl]oxy-2-hydroxy-cyclohexoxy]-5-methyl-4-methylaminotetrahydropyran-3,5-diol and their molecular modeling. *Main Group Chemistry* **2007,** 1-14.
8. R. Kumar, P. Mishra. Spectroscopic, thermal and X-ray powder diffraction patterns of Bi(V) complexes with [2S-[2a, 5a, 6b(S*)]-6-[amino(4-hydroxyphenyl) acetylamino]-3, 3-dimethyl-7-oxo-4-thia-1-azabicyclo[3,2,0] hepatane- 2-carboxylic acid and (6R)-6-(a-phenyl-D-glycyamino) penicillinic acids, *Main Group Chemistry*, **2008,** 7, 1, 1-14
9. R. Johar, R. Kumar, A.K. Aggarwal. Tailoring methodologies for the architecture of organometallic frameworks of Bi(V) derived from antibiotics: Spectral, MS, XRPD and molecular modeling with antifungal effectiveness. J Integr Sci Technol, 2013, 1(1), 54-64.
10. M. M. Cowan. Plant products as antimicrobial agents, *Clinical Microbiology Reviews*, **1999**, 12, 564-582.
11. J. Backmann, C. Schultz, H. Fabian, U. Hahn, W. Saenger, D. Naumann. Thermally induced hydrogen exchange processes in small proteins as seen by FTIR spectroscopy. *Proteins: Structure, Function and Genetics.* **1996**, 24, 379-87.
12. J.P. Coates. Once more into the unknown, *Spectroscopy*, **1996**, 11, 14-23.
13. B.J.M. Rajkumar, V. Ramakrishnan, *Journal of Raman Spectroscopy*. **2000**, 31, 1107.
14. S. Ramaswamy, R.K. Rajaram, V. Ramakrishnan, *Journal of Raman Spectroscopy*. **2002**, 33, 689.
15. E. Scrocco, J. Tomasi. Electronic Molecular Structure, Reactivity and Intermolecular Forces: An Euristic Interpretation by Means of Electrostatic Molecular Potentials. *Adv Quant Chem* **1978**, 11, 115-121.
16. M. Gussoni, C. Castiglioni, M.N. Ramos, M.C. Rui, G. Zerbi. Infrared intensities: from intensity parameters to an overall understanding of the spectrum. *J. Mol. Struct.* **1990,** 224, 445-449.
17. A.E.L. Ouf, M.S. Ali, E.M. Saad, S.I. Mostafa. pH-metric and spectroscopic properties of new 4-hydroxysalicylidene-2-aminopyrimidine Schiff-base transition metal complexes. *J. Mol. Struct.* **2010**, 973, 69.
18. I. F. Leshcheva, N. M. Sergeev, G. V. Grishina, V. M. Potapov. The ^{13}C NMR spectra, isomerism, and conformational analysis of substituted piperidin-4-ones, *Chemistry of Heterocyclic Compounds*, **1986**, 22, 1214-1225.
19. S.A. Khan, N. Singh, K. Saleem. Synthesis, characterization and *in vitro* antibacterial activity of thiourea and urea derivatives of steroids. *Eur. J. Med. Chem.* **2008**, *43*, 2272-2277.

20. A.M. Cotero-Villegas, R.-A. Toscano, M. Muoz-Hernández, M. López-Cardoso, P. García Y García, and R. Cea-Olivares. Synthesis, spectroscopic characterization of O,O′-alkylene dithiophosphates of tellurolane and 1-oxa-4-tellurane. Single crystal structures of $C_4H_8Te[S_2P(OCH_2)_2CMe\text{-}nPr]_2$ and $C_4H_8OTe[S_2P(OCH_2)_2CEt_2]_2$, *Journal of Organometallic Chemistry*, **2005**, 12, 2872-2879.
21. P. U. Jain, P. Munshi, M. G. Walawalkar, S. P. Rath, K. K. Rajak, G. K. Lahiri,Ruthenium dithiophosphates: synthesis, X-ray crystal structure, spectroscopic and electrochemical properties, *Polyhedron*, **2000**, 19, 801-808.
22. J. Roithová, J. Jašík, J.J. D. P. Mellado and D. Gerlich. Electronic spectra of ions of astrochemical interest: from fast overview spectra to high resolution, *Faraday Discussions*, **2019,** 217, 98-113.
23. A. Le Bail, H. Duroy, J.L. Fourquet. Ab-initio structure determination of LiSbWO6 by X-ray powder diffraction. *Mat. Res. Bull.* **1998**, 23, 447-452
24. R.B. Streit, D.K. Geiger. Structure and Bonding in Group 14 Congeners of Ethene: DFT Calculations in the Inorganic Chemistry Laboratory. *Journal of Chemical Education* **2005,** *82*, 111.
25. B. Ren. Application of novel atom-type AI topological indices in the structure-property correlations. *Theochem*, **2002c**, 586, 137-148.
26. A. K. Patra, M. Ray, R. Mukherjee. Synthesis, crystal structure and properties of trigonal bipyramidal $[M(L^5)_2(H_2O)].H_2O$ complexes [M cobalt(II) (S 3/2) or copper(II) (S 1/2); HL^5 N-(2-chloro-6-methylphenyl)pyridine-2- carboxamide]. *J. Chem. Soc., Dalton Trans.*, **1999**, 2461-2466
27. H. Gonzalez-Diaz, F. J. Prado-Prado. Unified QSAR and network-based computational chemistry approach to antimicrobials, part 1: Multispecies activity models for antifungals. *J. Comput. Chem.* **2008**, 4, 656-667.
28. G. Merino, A. Vela, T. Heine. Description of electron delocalization via the analysis of molecular fields, *Chem. Rev.* **2005**, 105, 3812-3841.
29. A. Ahmedova. Biomedical Applications of Metallosupramolecular Assemblies-Structural Aspects of the Anticancer Activity, *Front Chem.* **2018**, 6, 1-20.
30. A. Dehsorkhi, V. Castelletto, I.W. Hamley, J. Seitsonen, J. Ruokolainen, Interaction between a Cationic Surfactant-like Peptide and Lipid Vesicles and Its Relationship to Antimicrobial Activity. *Langmuir* **2013**, 29, 14246-14253.
31. V. Castelletto, R.H. Barnes, K.A. Karatzas, C.J.C. Edwards-Gayle, F. Greco, I.W. Hamley, R. Rambo, J. Seitsonen, J. Ruokolainen,. Arginine-Containing Surfactant-Like Peptides: Interaction with Lipid Membranes and Antimicrobial Activity. *Biomacromolecules* **2018**, 19, 2782-2794.
32. R.K. Naviaux, Metabolic features of the cell danger response. *Mitochondrion*, **2014**, 16, 7-17
33. M.A. Malik, O.A. Dar, P. Gull, M.Y. Wani and A.A. Hashmi, Heterocyclic Schiff base transition metal complexes in antimicrobial and anticancer chemotherapy, *Med. Chem. Commun.*, **2018**, 9, 409-436.

34. Y. Jadegoud, O. B. Ijare, B. S. Somashekar, G. A. N. Gowda, and B. H. M. Mruthyunjayaswamy, "Synthesis, characterization and antimicrobial activity of homodinuclear complexes derived from 2,6-bis[3′-methyl-2′-carboxamidyliminomethyl(6′,7′)benzindole]-4-methylphenol, an end-off compartmental ligand," *Journal of Coordination Chemistry*, **2008,** 61, 508-527.
35. Y. Jadegoud, O.B. Ijare, B.S. Somashekar, G.A.N Gowda, B.H.M. Mruthyunjayaswamy. Synthesis, characterization and antimicrobial activity of homodinuclear complexes derived from 2,6-bis[3′-methyl-2′-carboxamidyliminomethyl(6′,7′)benzindole]-4-methylphenol, an end-off compartmental ligand. *Journal of Coordination Chemistry*. **2008**, 61, 508-527
36. K. Singha, R. Thakura V. Kumar. Co(II), Ni(II), Cu(II), and Zn(II) complexes derived from 4-[{3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-ylmethylene}-amino]-3-mercapto-6-methyl-5-oxo-1,2,4-triazine. *Beni-Suef University Journal of Basic and Applied Sciences.* **2016,** 1, 21-30
37. Z.H.A. El-Wahab, M.M. Mashaly, A.A. Salman, B.A. El-Shetary, A.A. Faheim. Co(II), Ce(III) and UO2(VI) bissalicylatothiosemicarbazide complexes: binary and ternary complexes, thermal studies and antimicrobial activity. *Spectrochimica Acta A.* **2004**, 60, 2861-73.
38. N. Raman, R. kumar, M.M. Packiaraj Synthesis and characterization of efficient chemical nucleases: A joint refinement from XRD, antimicrobial screening, DNA binding and cleavage investigations. *Inorganic Chemistry Communications*, **2014**, 47, 20-26.
39. R.M. Epand, C.W. Raquel. F.E. Nathan, A.Magarvey, Molecular mechanisms of membrane targeting antibiotics. *Biochimica et Biophysica Acta (BBA) – Biomembranes*, **2016,** 1858, 980-987.
40. V. Selvarani, B. Annaraj, M.A. Neelakantan, S. Sundaramoorthy,S, Velmurugan. Synthesis, characterization and crystal structures of copper(II) and nickel(II) complexes of propargyl arm containing N2O2 ligands: antimicrobial activity and DNA binding. *Polyhedron*, **2013**, 54 74.
41. K. Lewis. Multidrug resistance: Versatile drug sensors of bacterial cells. *Current Biology*, **1999**, 9, R403-R407.
42. J.A. Riddick, W.B. Bunger. Organic Solvents: Physical Properties and Methods of Purification (3rd edn), Wiley: New York, 1970.; The crystals needed for X-ray crystal structure analysis were tried to produce but not succeed as follows: one gm of the bismuth OMC was dissolved at 40 °C in a very small amount of methanol as small as possible. A clear solution was obtained and heated for 4 to 5 minutes under reflux and was then filtered off at a high temperature. The solution was cooled down to room temperature and closed with a semipermeable membrane so the methanol cannot evaporate but a very slow evaporation was there. The mixtures were stored at room temperature for a period of three to five weeks. Very small crystals were filtered off and dried.
43. Z. Yue, H. Wang, D.J. Bowers, M. Gao, M. Stilgenbauer, F. Nielsen, et al. Nanoparticles of metal-organic cages designed to encapsulate platinum-based anticancer agents. *Dalton Trans.* **2018**, 47, 670-674.

44. Y.-Y. Zhang, W.-X. Gao, L. Lin, G.-X. Jin. Recent advances in the construction and applications of heterometallic macrocycles and cages. *Coord. Chem. Rev.* **2017**, 344, 323-344.