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Bioactive 3-methyl-2,6-diarylpiperidin-4-one, oxime and its copper(II) complex

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ABSTRACT

A six membered nitrogenous heterocyclic ketone 3-methyl-2,6-diphenylpiperidin-4-one, its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime and copper(II) complex of this oxime was prepared by literature procedure. The purities of these ketone, oxime and copper complex was analyzed by physico-chemical and spectroscopic methods reported in the literature. The physicochemical analysis results confirmed that the structure of the complex was distorted octahedral. The antimicrobial activities of these substrates such as ketone, oxime and its copper complex were investigated using Bauer-Kirby disc diffusion technique against several antimicrobes by measuring the mm of zones of inhibitions. Further these activities were concluded using drug dilution method. From the analysis report, the copper (II) complex of the oxime shows significant antimicrobial activities against their antimicrobial stains. The oxime shows moderate antimicrobial activity. The ketone shows satisfactory antibacterial and antifungal activities against their stains in both disc diffusion and drug dilution methods.

Keywords: Piperidine-4-one, Piperidine-4-oneoxime, Copper(II) complex, Antimicrobial activities, Disc diffusion, Drug dilution

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1. INTRODUCTION

Alkyl, alicyclic, aromatic and heterocyclic ketones and its oximes are more important in organic chemistry, biochemistry, bio-technology and chemical biology. These have vital role for organic building blocks and many biological activities [1]. The Mannich base formation reaction is important for deriving piperidine-4-ones as a six membered nitrogenous heterocyclic ketone and its derivatives [2, 3]. The biological properties of the ketones were also determined by their stereochemistry. Many synthetic methods were reported in the literature for the syn thesis of piperidone and its derivatives. Petrenko-Kritschenko piperidone synthesis route is well known. In this method the chemists used alkyl-1,3-acetonedicarboxylate with benzaldehyde and an amine as reactants [4]. *L*-Proline-copper (I) complexes catalyzed Ullmann amination followed by hydrolysis of obtained ketals method used for synthesis of N-aryl substituted piperidin-4-ones [4].

A solid polymer-bound 4-benzylsulfonyl-l-triphenylphosphoranylidene-2-butanone supported hetero-cyclization process was useful for the synthesis 2-substitutedpiperidin-4-one derivatives from substituted divinyl ketones [5]. An acyclic α,γ-substituted β-keto esters and bis(aminol) ethers were converted into substituted 3,5-substituted- 4-piperidones high diastereoselectivity by double Mannich condensation [2]. A reaction of Chiral 2-amino-1,3-butadienes with aromatic *N*-trimethylsilyl aldimines and *N*-phenyl aldimines in the presence of $ZnCl_2$ to give high yields of 4-piperidones [6].

Various 2-aryl-4-piperidones, 3-piperidein-2-ones, 3-amino-2-arylpiperidin-4-ones, 3-aminopiperidin-2-ones, oxazolopiperidones, and hydroxy lactams were synthesized and visible in the literature by the reaction of aromatic aldehydes and active methylene compounds in ethanol in the presence of ammonium acetate [7]. In these reaction various catalysts were employed such as Ultrasound-Na_2CO_3 [8], DIBAL-H, DABCO [9], $NaHCO_3$ [10], I_2 [11], BPH [12], Na/EtOH [13], K_2CO_3 [14], TFA, TFSA [15], Et_3N [16], Zn-Hg/HCl [17], $Rh(acac)(C_2H_4)_2$ [18] and NaOEt [19]. These piperidones possess antimicrobial [13, 14, 16, 17], antitubercular [16], antioxidant [20], antitumor [20], cytotoxic [21], analgesic [3], anticancer [22], anti-HIV [3], antiviral [23] etc. The compounds bearing piperidone skeleton that mimic the naturally occurring alkaloids and steroids have been synthesized in order to study their biological activity.

The oximes have the general formula R–C=N–OH which are derived from carbonyl compounds condensed with hydroxylamine in the presence of base. The cyclic heterogeneous five and six membered ketones were condensed with hydrazine hydrochloride in presence of base gave their corresponding oximes. Some oximes were used as carbon building blocks. For example, benzanilide was prepared by the Beckmann rearrangement of benzophenone oxime by mineral acid or thionyl chloride catalyst. The piperidone oximes also prepared by the condensation of hydroxylamine hydrochloride and a corresponding piperidones. Various piperidones were prepared and the possess numerous biological activities [24].

Such compounds are 1-(propylsulfonyl)piperidin-4-one oxime, 1,3-dimethyl-2,6-diphenyl-piperidin-4-one oxime, 1-benzyl-4-piperidone oxime, 1-isopropylpiperidin-4-one oxime, oxiconazole, azolyl-2-methyl chromanone oxime ethers, piperidine-4-one oxime ethers [25], 3-methyl-2,6-diphenyl piperidine-4-one oxime, pyrazolo oximes, piperidine-4-one oxime esters, bicyclic oxime ethers, r-2, c-6-Bis(2-chlorophenyl)-t-3,t-5-dimethyl-1-nitrosopiperidin-4-one oxime, 2,6-bis(4-methoxyphenyl)-1-methylpiperidin-4-one oxime esters [26]. These oximes have many applications including industrial [27] and medicinal fields [28].

They used as corrosion inhibitors. Many of the oximes possess biological activities such as antibacterial [29], antifungal [29], anticonvulsant [30], insecticidal [31], antioxidant [32], and cytotoxicity [28].

Copper complexes of oximes are interesting compounds and they have many chemical biological and industrial oriented properties of applications. The oximes namely, (2*E*,3*E*)-3-[(6-{[(1*E*,2*E*)-2-(hydroxyimino)-1-ethylpropylidene]amino}pyridin-2-yl)imino] butan-2-one oxime and 2-(hydroxyimino)-1-ethylpropylideneaminophenyliminobutan-2-one oximes were used for synthesizing some homodinuclear Cu(II) heterodinuclear Cu(II) and Ni(II) and mononuclear Cu(II) complexes [33]. These complexes have DNA binding, antioxidant and antimicrobial activities. Kunwar et al., reported the synthesis and antimicrobial activities of some copper complex of 2-formyl thymol oximes [34]. The structure and properties of complex of a tetradentate dioxime-diimine bridging oxime group with Cu(II) was studied by Bertrand et al., [35]. The copper (II) complexes with the ligand 4,4,9,9-tetramethyl-5,*s*-diazadodecane-2,l-dione dioxime, LH_2 was prepared and the spectroscopic properties of this complex was reported by Fraser et al., [36].

Wai [37] studied the Synthesis, structural characterization and biological activities such as anticancer, DNA binding, Nucleolytic study, Human Topoisomerase I inhibition assay, antibacterial and antifungal assays of copper(II) complexes of thiosemicarbazones and their N(4)-substituted derivatives derived from 2,4-dihydroxybenzaldehyde. Electrochemical and biological activities of dimethylglyoxime-amino acid mixed ligand copper complex was studied by Bougherra and his co-workers [38]. Tabl and his group of researchers [39] investigated the preparation, structure analysis and anti-cancer activities of some new copper complex's with 2-Hydroxy-3-(hydroxyimino)-4-oxopentan-2-ylidene)benzohydrazides.

Antimicrobial and antitubercular activities of some copper complexes of oxime was carried out and reported in literature by Donde et al., [40].

The copper(II) complex of Schiff base ligand 2-N-(1′,2′-diphenylethanone oxime) benzoic acid obtained and assessed the antimicrobial activities of the complex by Manikshete et al., [41]. Kurtoglu studied the antimicrobial activities of the copper complex of 2,4-dihydroxy-5-[(*E*)-phenyldiazenyl]benzaldehyde ligand [42]. Biological and entomological activities of some copper complex of oxime ligands was reported by Copper and his research group [43]. Singh et al., [44] have investigated the preparation, structure analysis and biological activity of complexes of 2-hydroxy-3,5-dimethylacetophenoneoxime (HDMAOX) with copper(II), cobalt(II), nickel(II) and palladium(II).

Some new copper complex of isonicotinoylhydrazide oxime wasz prepared and evaluated the antitumor activity- antiproliferative activity against the growth of human breast cancer tumor cell line MCF-7 by Tabl et al., [45].

The copper complex of the type $[Cu(penh)_2]$ with the ligand of (*E*)-N'-(1-(pyridin-2-yl)ethylidene) nicotinohydrazide possess anticancer activities [46]. Mangaiyarkkarasi and Arulantony [47] have investigated the DNA cleavage, cytotoxic activities, and antimicrobial activities of some novel Schiff's base transition metal complexes derived from 4-aminoantipyrine and dihydropyrimidone of vanillin ligand. Within the above there is no information reported regarding synthesis and evaluation of the antimicrobial activities of 3-methyl-2,6-diphenylpiperidin-4-one, its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime and copper (II) complex of this oxime. Hence the author has taken effort to investigates the antimicrobial activities of the compounds using Bauer-Kirby disc diffusion as well as drug dilution method.

2. EXPERIMENTAL

2. 1. Materials and methods

All chemicals used in this investigation were arranged from Sigma-Aldrich, E-Merck, CDH, BDH, SD-Fine and Qualigens chemical companies. Melting point of 3-methyl-2,6-diphenylpiperidin-4-one, its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime and copper (II) complex of this oxime were find from Guna make electrical melting point apparatus using capillary tubes and are un corrected [48, 49]. The micro analysis of the ketone, oxime and the complex were performed in Thermofennigan CHN analyzer. The chloride ion was estimated by Volhard's method. Cu ions was estimated by iodometry. The electrical conductance measurements are made in dimethylformamide solution at room temperature (35 ºC) using Elico conductivity bridge model CM 82T with dip type cell. The cell constant of the conductivity cell is used 1.009. The concentration of the solution used for the measurements were the order of 10^{-3}M. The magnetic susceptibility of the complex at room temperature was measured by Guoy method using $Hg[Co(SCN)_4]$ as the calibrant.

The Infrared spectral measurement is obtained using Perkin Elmer 783 spectrophotometer. The measurements for ligand and the complex were recorded in KBr pellets in the region 4000-400 cm^{-1}. The electronic spectrum of the complex was measured in Ultraviolet – Visible region a HITACHI U – 3400 double beam UV-VIS-NIR spectrometer. The working range of the diffuse reflectance spectrophotometer is 200-900 nm. The UV range was not recorded dur to failure of the UV source lamp.

2. 2. Antimicrobial activity measurement

2. 2. 1. Materials and methods

The chemicals namely nutrient broth, Mueller-Hinton Agar, potato dextrose agar, tween-80 solution and other materials required have been procured from Himedia, Mumbai.

2. 2. 2. Collection of microorganisms

The bacterial stains such as *Bcillus subtilis, Micrococcus luteus, Streptococcus aureus, Escherichia coli, Klebsiella Pneumoniae Pseudomonas aeruginosa,* and the fungal stains such as *Aspergillus niger, Mucor species, Penicillium scup* and *Trichoderma viride* were procured from the Research department of Microbiology, Sengunthar Arts and Science College, Thiruchengode, Namakkal Dt., Tamil Nadu, Biochemical Laboratory PG and Research Department of Chemistry, Government Arts College, Chidambaram, Tamil Nadu and Pondicherry Centre for Biological Science, Boomiyanpet, Pondicherry. The stock cultures have been stored in the cooler machine for further studies.

2. 2. 3. Inoculum preparation

The liquid media for culturing microorganism was prepared by weighing 1.3 g of the broth and dissolved in 100 mL of disinfected distilled water. The bottle was swirled lightly while adding the nutrient broth and the pH of the medium was adjusted to 7.0. The Erlenmeyer flask was plugged with non-adsorbent cotton and pasteurized in an autoclave at 121 °C and 15 lbs/inc^2 pressure for 15 min. After chilling inside a Nonturbulent flow, a loopful of fresh bacterial sample was inoculated and incubated in an orbital shaker at 37 °C for 24 h. The cultures broth was diluted to 1:50 ratio with sterile functional saline and 0.5 mL of the inoculum

was used for the preparation of the spread plate. The similar process has been taken for all test bacterial samples.

2. 2. 4. Preparation of agar slants

Nutrients agar medium was prepared and sterilized in an autoclave at 121 °C and 15 lbs/inc^2 pressure for 15 min. After sterilization the medium was distributed into the test tubes. The test tubes were kept in the slanting position on a support. After whole solidification of the medium, streaking of the microorganism was done in the slant area using sterile inoculation loop. After the streaking the test tubes were incubated at 37 °C for 24 h. After good growth, the slants have been stored in a deep freezer (2 °C) for further studies.

2. 2. 5. Preparation of Mueller-Hinton agar slants

Exactly 38 g of the Mueller Hinton agar was dissolved in 1000 mL of sterile distilled water. The pH of the medium was adjusted to 7.0. The flask was plugged with non-adsorbent cotton and sterilized at 121 °C and 15 lbs/inc^2 pressure for 15 min. After sterilization, the medium was cooled to 45-47 °C, poured 15 mL of it in each sterile Petri-plate and allowed to solidify.

2. 2. 6. Preparation of test compounds

The synthesized sulfonamide compounds of weight 15 mg of each was dissolved in 1 mL of DMSO solvent. The discs were impregnated and placed on the Mueller Hinton solidified agar medium to find out the antimicrobial activity of the compounds on each organism. The antimicrobial activities of the five series of sulfonamide compounds have been studied by adopting the above procedure on ten microorganism and the results have been discussed with the available data and clustered column chart in each case.

2. 2. 7. Preparation of the potato dextrose agar medium

PDA agar medium was prepared in a conical flask by dissolving 3.9 g of the agar in 100 mL distilled water. It was sterilized in the autoclave for 15 min at 121 °C and 15 lbs/inch^2 pressure. Then the medium was allowed for solidification for an hour. After that the fungal species was inoculated in the medium and kept for 5 to 7 days at room temperature.

2. 2. 8. Preparation of the fungal inoculum

About 20 to 25 mL of sterile water (after cooling) is mixed with the medium. The water over the medium is swirled and decanted with the fungal species. Tween-80 (1 to 2 mL) may be added with this solution for uniform growth.

2. 3. Procedure for the synthesis of 3-methyl-2,6-diphenylpiperidin-4-one, its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime and copper (II) complex of oxime [48, 49]

2. 3. 1. Procedure for the synthesis of 3-methyl-2,6-diphenylpiperidin-4-one [48, 49]

The ketone, 3-methyl-2,6-diphenylpiperidin-4-one was prepared and their purities were examined by the data reported in literature. Based on the analysis report the structure of the ketone was illustrated in **Figure 1.**

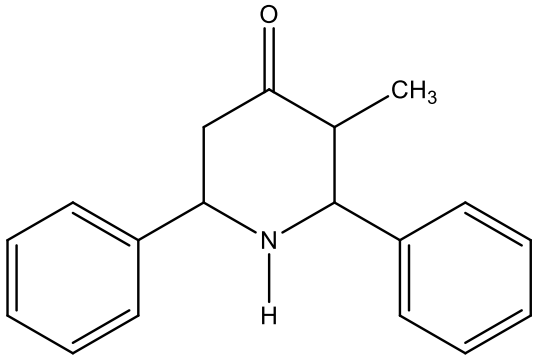

Figure 1. Structure of 3-methyl-2,6-diphenylpiperidin-4-one

2. 3. 2. Procedure for the synthesis of 3-methyl-2,6-diphenylpiperidin-4-one oxime [48, 49]

The oxime, 3-methyl-2,6-diphenylpiperidin-4-one oxime was prepared and their purities were examined by the data reported in literature. Based on the analysis report the structure of the ketone was illustrated in **Figure 2.**

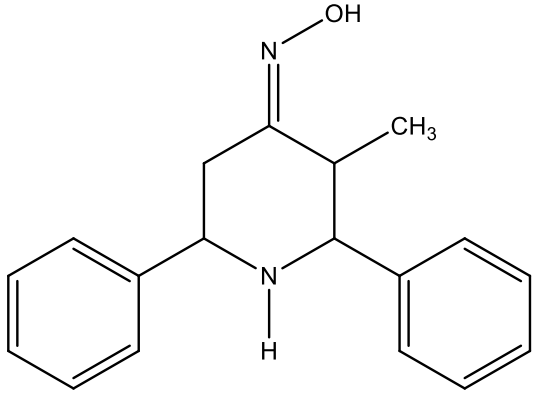

Figure 2. Structure of 3-methyl-2,6-diphenylpiperidin-4-one oxime [MDPO].

2. 3. 3. Procedure for the synthesis of copper (II) complex 3-methyl-2,6-diphenylpiperidin-4-one oxime

The copper complex of 3-methyl-2,6-diphenylpiperidin-4-one oxime **[$CuCl_2$·MDPO·$2H_2O$]** was prepared and their purities were examined by the data reported in literature. Based on the analysis report the structure of the ketone was illustrated in **Figure 3.**

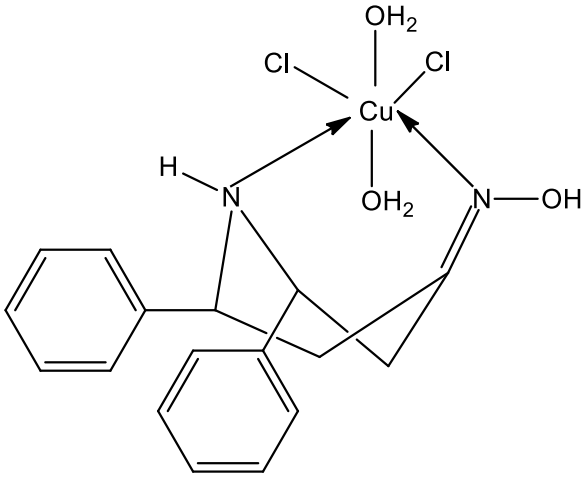

Figure 3. Structure of copper(II) complex of 3-methyl-2,6-diphenylpiperidin-4-one oxime **[$CuCl_2$·MDPO·2H_2O]**

3. RESULTS AND DISCUSSION

3. 1. Antibacterial sensitivity assay

3. 1. 1. Disc diffusion method

Table 1. Antibacterial activities of 3-methyl-2,6-diphenylpiperidin-4-one (**1**), its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime (**2**) and copper (II) complex of this oxime (**3**) by disc diffusion method.

Compound	Gram +ve bacteria			Gram -ve bacteria		
	Bcillus subtilis	***Micrococcus luteus***	***Streptococcus aureus***	***Escherichia coli***	***Klebsiella Pneumoniae***	***Pseudomonas aeruginosa***
1	4	5	4	4	4	4
2	6	7	5	4	3	6
3	9	10	8	10	11	9
Standard: Ciprofloxacin	12	14	13	13	12	13
Solvent: DMSO	---	---	---	---	---	---

Antibacterial sensitivity assay was performed using Kirby-Bauer [50] disc diffusion technique. In each Petri-plate about 0.5 mL of the test bacterial sample was spread uniformly over the solidified Mueller-Hinton agar using sterile glass spreader. Then the disc with 5 mm diameter made up of Whatman No. 1 filter paper, impregnated with the solution of the compound (ketone/oxime/complex) were placed on the medium using sterile forceps. The plates were incubated for 24 h at 37 °C by keeping the plates upside down to prevent the collection of water droplets over the medium. After 24 h the plates were visually examined and the diameter values of the zone of inhibition were measured. Triplicate results were recorded by repeating the same procedure. Ciprofloxacin and ketoconazole are used as standards for bacterial and fungal strains, respectively. The observed antibacterial activities of these compounds in terms mm of zone of inhibition was presented in **Table 1** and the clustered column chart was illustrated in **Figure 4.**

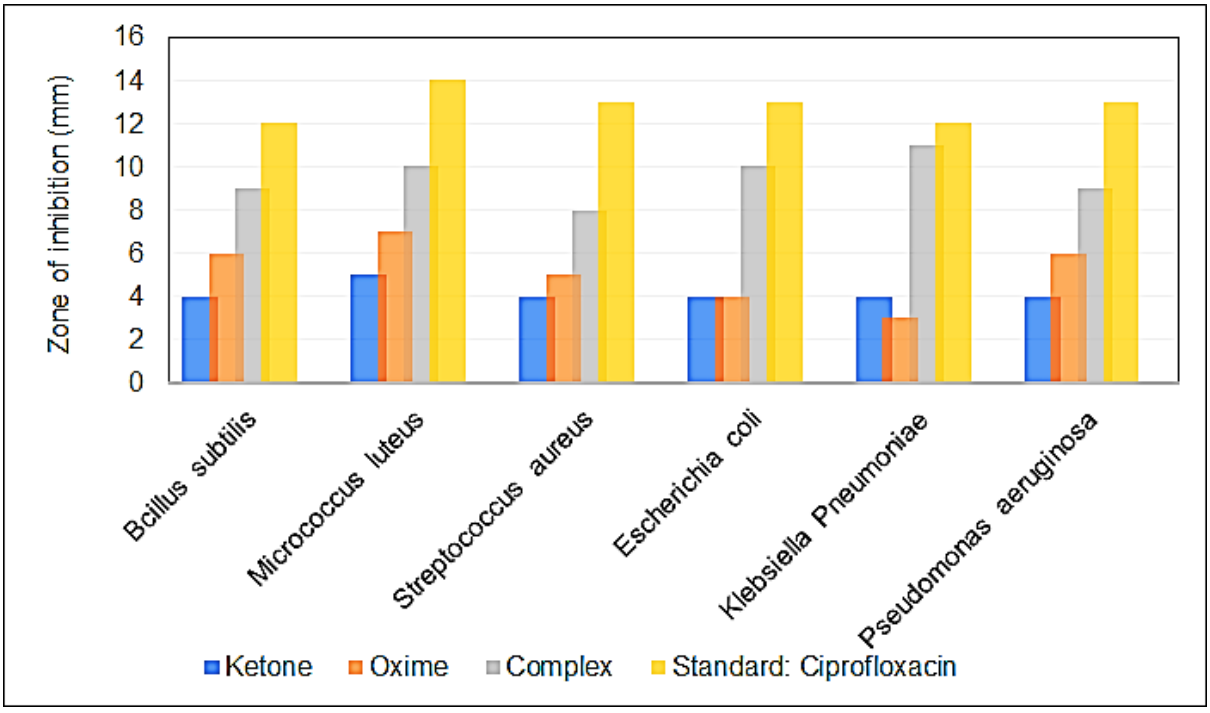

Figure 4. The clustered column chart of the antibacterial activities of 3-methyl-2,6-diphenylpiperidin-4-one (**1**), its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime (**2**) and copper (II) complex of this oxime (**3**).

3. 1. 2. Drug-dilution method

Further the author has investigated the anti-bacterial activity of these 3-methyl-2,6-diphenylpiperidin-4-one, its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime and copper (II) complex of this oxime. Determination of minimum inhibitory concentration of piperidine-4-one/oxime/copper complex using twofold serial dilution method Testing was done in the seeded broth (10^{-6} to 10^{-7} cfu/mL).

The test compounds were taken at different concentrations ranging from 200, 100, 50, 25, 12.5, 6.25, 3.13, 1.56, 0.78, and to 0.39 µg/mL for finding the minimum inhibitory

concentration (MIC) by using seeded broth as diluent. Similarly, the standard solution of ciprofloxacin drug prepared at the concentrations of 200, 100, 50, 25.5, 6.25, 3.13, 1.56, 0.78, and 0.39 μg/mL of sterile distilled water and DMSO were maintained throughout the experiment simultaneously as control.

The study involves a series of 11 assay tubes for the test compounds against each strain. In the first assay tube, 1.6 mL of seeded broth was transferred, and 0.4 mL of the test solution was added, followed by mixing it thoroughly to obtain a concentration of 200 μg/mL. To the remaining nine assay tubes, 1 mL of seeded broth was transferred, and then, from the first assay tube, per milliliter of the content was pipetted out and added into the second assay tube, followed by mixing thoroughly. This type of dilution was repeated up to the 11th assay tube serially. The same procedure was followed for standard drugs. Duplicates were also maintained; these were done under aseptic conditions.

The racks of assay tubes were placed inside the incubator at 37 ± 1 °C for 24 h. After the incubation period, the assay tube concentrations were again streaked into the nutrient agar plate due to turbidity of the drug microorganism mixture. The lowest concentration of the test compounds, which caused apparently a complete inhibition of growth of organisms, was taken as the MIC. The solvent control tube was also observed to find whether there was any inhibitory action. The sterile distilled water and DMSO did not show any inhibition. The antimicrobial activity of all the synthesized piperidine-4-one/oxime/copper complex were examined by disc diffusion and two fold serial dilution methods. Bacterial strains, viz. *Bcillus subtilis, Micrococcus luteus, Streptococcus aureus, Escherichia coli, Klebsiella Pneumoniae Pseudomonas aeruginosa,* and fungal strains, viz. *Aspergillus niger, Mucor species, Penicillium scup* and *Trichoderma viride*. In the present study, DMSO is used as control, while ciprofloxacin and ketoconazole are used as standards for bacterial and fungal strains, respectively. The zone of inhibition and MIC values of compounds piperidine-4-one/oxime/copper complex against both the tested bacterial strains are given in **Table 2**.

Table 2. Antibacterial activities of 3-methyl-2,6-diphenylpiperidin-4-one (**1**), its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime (**2**) and copper (II) complex of this oxime (**3**) by serial dilution method.

Compound	**Gram +ve bacteria**			**Gram -ve bacteria**		
	Bcillus subtilis	***Micrococcus luteus***	***Streptococcus aureus***	***Escherichia coli***	***Klebsiella Pneumoniae***	***Pseudomonas aeruginosa***
1	15	15	20	15	25	50
2	35	15	15	30	20	45
3	30	25	30	40	35	40
Standard: Ciprofloxacin	7.35	7.85	5.25	8.35	4.75	5.65

The representative photographs of disc diffusion and serial dilution methods are depicted in **Figure 5**. The antibacterial activity of piperidine-4-one/oxime/copper complex produced a maximum zone of inhibition against all the bacterial strains. The copper complex shows significant antibacterial activity against all bacterial stains against standard (ciprofloxacin). This is due to the electron withdrawing group of chlorine and it have +I effect. This effect enhanced the antibacterial activity. The satisfactory antibacterial activity was observed for the oxime. This is due to the OH group in oxime moiety reduced the activity.

The Antibacterial activity of all synthesized piperidine-4-one/oxime/copper complex were measured by serial dilution method, and the MICs are presented in **Table 2**. From Table 5, compounds 1 to 3 showed the growth inhibitory concentration against the tested organism fall in the range of 1.5 to 200 µg/mL. However, compounds **3** showed the inhibition against all bacterial strains in the range from 25 to 100 µg/mL. The rest of the compounds are more effective against all bacterial strain MICs at 1.5 to 25 µg/mL. The copper complex (**3**) shows more significant antibacterial activity against all stains in dilution method than the oxime (**2**) and ketone (**1**).

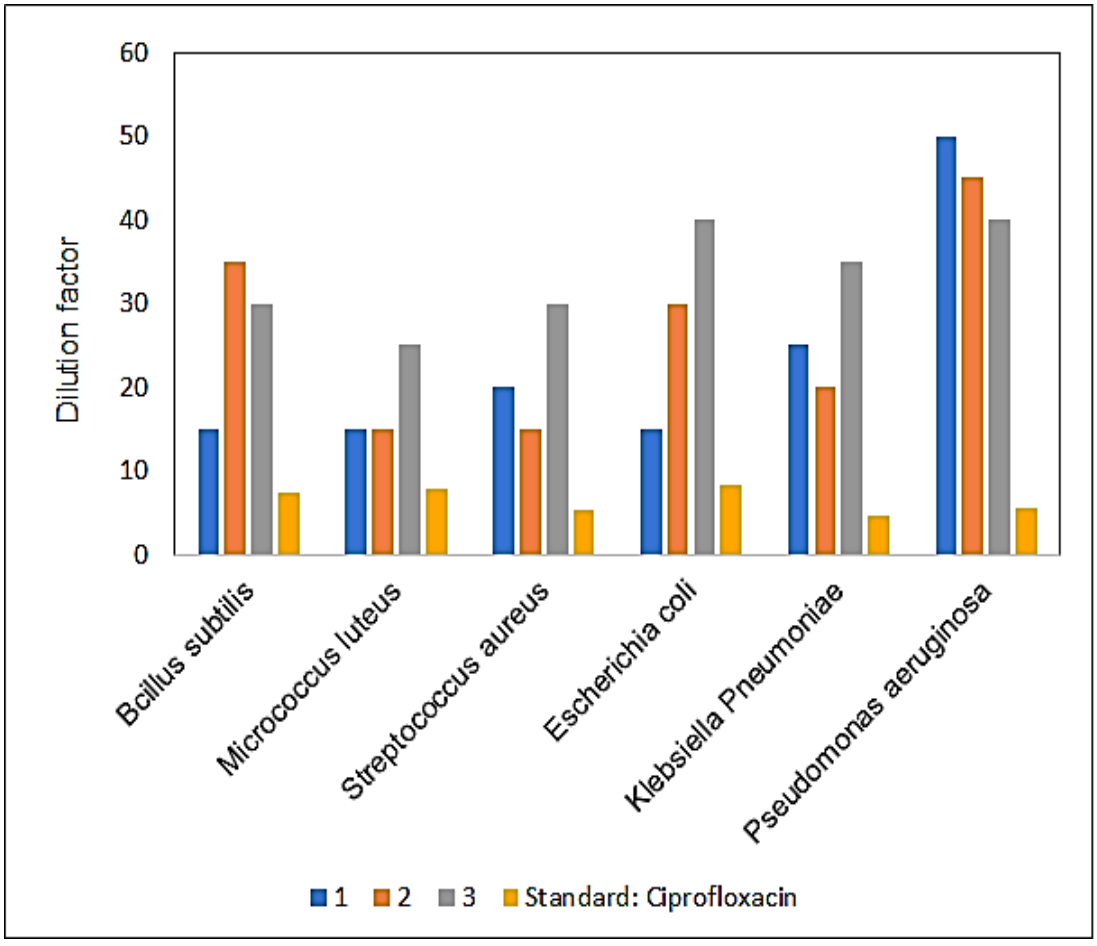

Figure 5. The clustered column char of the antibacterial activities of 3-methyl-2,6-diphenylpiperidin-4-one (**1**), its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime (**2**) and copper (II) complex of this oxime (**3**). by serial dilution method.

3. 2. Antifungal sensitivity assay

3. 2. 1. Disc diffusion method

Table 3. Antifungal activities of 3-methyl-2,6-diphenylpiperidin-4-one (**1**), its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime (**2**) and copper (II) complex of this oxime (**3**) by disc diffusion method.

Compound	*Aspergillus niger*	*Mucor species*	*Penicillium scup*	*Trichoderma viride*
1	6	7	8	6
2	7	7	6	7
3	9	10	8	7
Standard: Ketoconazole	15	13	11	12
Solvent: DMSO	---	---	---	---

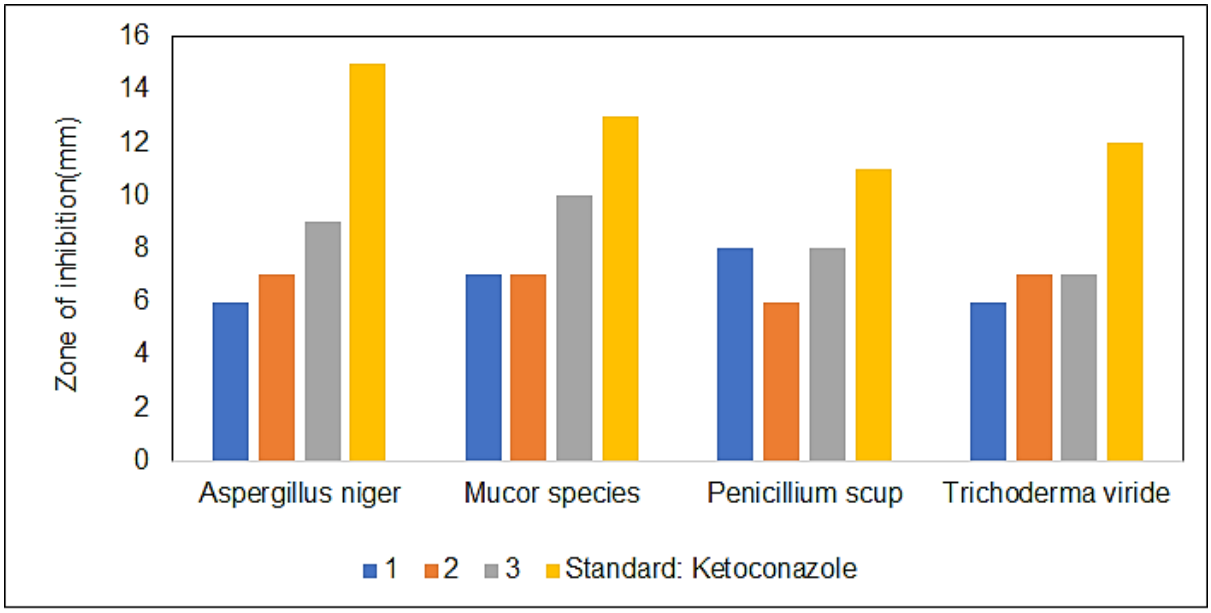

Figure 6. The clustered column chart of the antifungal activities of 3-methyl-2,6-diphenylpiperidin-4-one (**1**), its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime (**2**) and copper (II) complex of this oxime (**3**) by disc diffusion method.

Antifungal sensitivity assay was performed using Kirby-Bauer [50] disc diffusion technique. PDA medium was prepared and sterilized as above. It was poured (ear bearing heating condition) in the Petri-plate, which was already filled with 1 mL of the fungal species. The plate was rotated clockwise and counter clockwise for uniform spreading of the species. The discs were impregnated with the test solution. The test solution was prepared by dissolving 15 mg of the compounds (ketone/oxime/complex) in 1 mL of DMSO solvent. The medium could solidify and kept for 24 h. Ketoconazole are used as standard for evaluation of anti-fungal activity against their strains. Then the plates were visually examined and the diameter values of zone of inhibition were measured. Triplicate results were recorded by repeating the same procedure. The measured antifungal activities of the compounds **1-3**(ketone/oxime/complex) were presented in Table 3 and the correlated cluster column chart was illustrated in **Figure 6**. From the Table 3, the copper (II) complex 3-methyl-2,6-diphenylpiperidin-4-oneoxime (**3**) shows significant antifungal activities against their standard. The oxime (**2**) shows satisfactory antifungal activity. The ketone, 3-methyl-2,6-diphenylpiperidin-4-one (**1**), has least antifungal activity.

3. 2. 2. Serial dilution method

Further the author has investigated the antifungal activities of these 3-methyl-2,6-diphenylpiperidin-4-one (**1**), its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime (**2**) and copper (II) complex of this oxime (**3**) by serial dilution method. For this study the author applied the same procedure for evaluating the antimicrobial activity. The Antibacterial activity of all synthesized piperidine-4-one/oxime/copper complex were measured by serial dilution method, and the MICs are presented in Table 4. From Table 4, compounds 1 to 3 showed the growth inhibitory concentration against the tested organism fall in the range of 1.5 to 200 µg/mL. However, compounds (3) showed the inhibition against all bacterial strains in the range from 25 to 100 µg/mL. The rest of the compounds are more effective against all bacterial strain MICs at 1.5 to 45 µg/mL. The copper complex (3) shows more significant antibacterial activity against all stains in dilution method than the oxime (2) and ketone (1).

Table 4. Antifungal activities of 3-methyl-2,6-diphenylpiperidin-4-one (1), its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime (**2**) and copper (II) complex of this oxime (**3**)by serial dilution method.

Compound	***Aspergillus niger***	***Mucor species***	***Penicillium scup***	***Trichoderma viride***
1	75	55	45	90
2	45	35	70	30
3	25	30	25	45
Standard: Ketoconazole	7.5	4.5	6.25	8.15

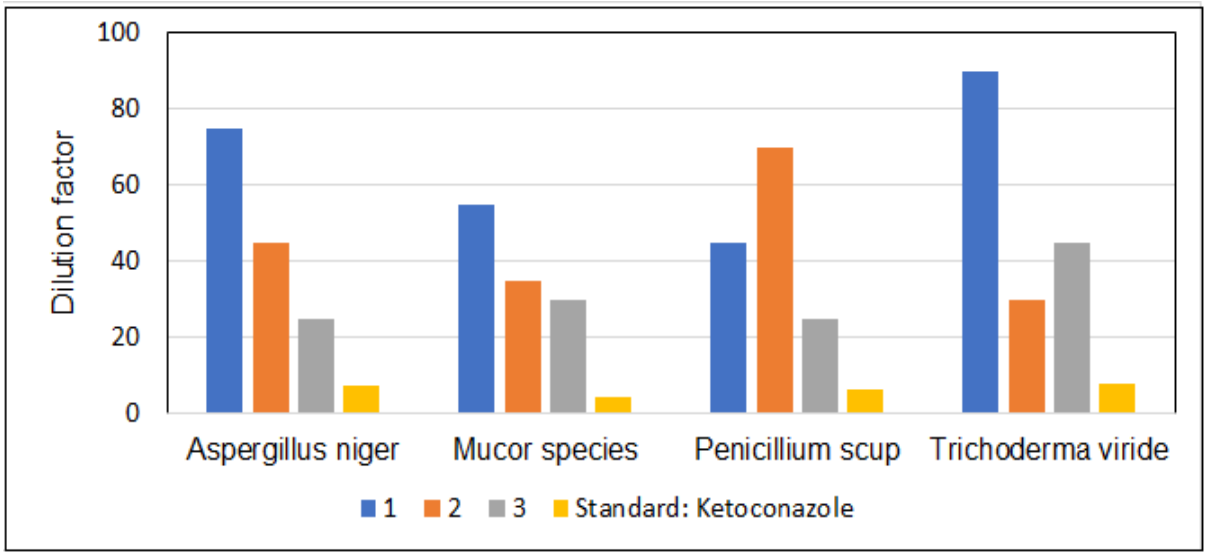

Figure 7. The clustered column chart of the antifungal activities of 3-methyl-2,6-diphenylpiperidin-4-one (1), its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime (2) and copper (II) complex of this oxime (3) by serial dilution method.

4. CONCLUSION

Six membered nitrogenous alicyclic ketone, 3-methyl-2,6-diphenylpiperidin-4-one (1), its oxime namely 3-methyl-2,6-diphenylpiperidin-4-oneoxime (2) and copper (II) complex of this oxime (3) were prepared and their purities were analyzed by literature method. The antibacterial and antifungal activities of these compounds were assessed by Bauer-Kirby disc diffusion as well as serial dilution method. All compounds show antimicrobial activities against their stains. The complex (3) shows significant antibacterial as well as antifungal activities by both disc diffusion and serial dilution method. This is due to the electron with-drawing +I effect nature as well as the distorted octahedral geometry of the complex. The oxime shows satisfactory antibacterial and antifungal activity. The ketone showed least antimicrobial activity against their microbes in both the methods.

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