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Research Article

Synthesis Characterization and Antimicrobial Activities Studies of N-{2-(4-Chlorophenyl) Acetyl} Amino Alcohols Derived From A-Amino Acids

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ABSTRACT

Amino acids play important roles in organisms to sustain in living state and perform as body constituents, enzymes, and antibodies. At insalubrious situations, the use of amino acid derivatives as drugs in the maintenance of normal health is a better choice than common unnatural synthetic drugs. This is due to the fact that the derivatives of the amino acid may be more biocompatible, biodegradable, and eliminate easily than others. In this sense we have made an effort and report herein the synthesis of N-{2-(4-chlorophenyl) acetyl} amino alcohols synthesized by reduction of N-{2-(4-chlorophenyl)acetyl} derivatives of (S)-amino acids such as (S)-phenylalanine, (S)-alanine, (S)-methionine, (S)-leucine, (S)-tryptophan and (S)-proline. These newly synthesized amino acid derivatives were analyzed by proton, carbon-13 NMR, and fourier-transform infrared spectroscopy (FTIR). The composition of solid derivatives was determined by elemental analysis. Further, antimicrobial activities of these derivatives were assessed on usual bacteria *K. aerogenes, E. coli, S. aureus* and *P. desmolyticum* and fungi *A. flavus* and *C. albicans*. The compounds were witnessed moderate activity than authorized antibacterial and fungal agents, Ciprofloxacin and Fluconazole, respectively. The antimicrobial studies also revealed that these derivatives could be better antifungal agents than antibacterial agents. Finally, we compared the experimental results of antimicrobial activities with docking studies.

Introduction

A wide range of proteinogenic and non-proteinogenic derivatives of amino acids and reduced amino acids (amino alcohols) have been synthesized and found applications in various fields. Peptides have been displayed properties that control the biological functions of other proteins and also antagonism towards pathogenic microorganisms; such peptides commonly have been used as therapeutic agents due to their behavior as peptidomimetics or enzyme inhibitors.[1-3] There are many simple amino alcohol derivatives exhibited various biological activities such as antitumor[4] and antibacterial.[5] Lipidic amino alcohol derivatives and their metal complexes showed good anti-carcinogenic, immune suppressor, anti-inflammatory, and analgesic[6] properties. Non-proteinogenic small and natural amino alcohol derivatives like Bestatin, Valinoctin-A are better in anticancer activities[7] and Microginin as ACE inhibitors.[8] Ethambutol is also an amino alcohol derivative that has been using for many decades to treat tuberculosis patients worldwide.[9] Nature always preferred to create microorganisms as an evolutionary adaptation, which will make upcoming microbial species has drug resistance[10] to overcome the adapted species. This process would be continuous and challenging in a contest of research and development that has been moved towards designing modern drugs. This made to explored or synthesize a large number of normal amino alcohol derivatives in the field of pharmaceutical chemistry to get control over multi-drug resistant species.

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However, there is limited research that has been taken on alpha-amino alcohol derivatives. In this context, herein, we have designed and synthesized the 4-chlorophenylacetyl derivatives of amino alcohols starting from natural proteinogenic α-L-amino acids by the well-known reported method[11] and investigated their antimicrobial activity and compared the experimental results with docking studies.

Materials and Methods

Reagents and various solvents procured from Spectrochem Ind. Pvt. Ltd., and SD Fine Chemicals Ind. Pvt. Ltd., and were used as received. Melting points were measured in an open capillary tube closed at one end and are reported uncorrected. FTIR spectra were recorded on the Perkin Elmer Frontier-I FTIR spectrophotometer using the ATR. Proton, carbon-13 NMR spectra were recorded on Agilent 400MR DD2 spectrometer and chemical shifts were measured with respect to TMS in δ ppm. TLC was carried on prefabricated silica gel plates (Merck, 60F254) and were developed using a suitable solvent system visualized under UV light, iodine vapor, and/or by KMnO4 spray. Bacterial strains *E. coli* [NCIM-5051], *K. aerogenes* [NCIM-2098], *P. desmolyticum* [NCIM-2028], *S. aureus* [NCIM-5022], and fungal strains *A. flavus* [NCIM-544] and *C. albicans* [NCIM-3100] were procured from National Chemical Laboratory, Pune, India. Standard antibiotics Ciprofloxacin and Fluconazole were obtained from Hi-Media, Mumbai, India.

Docking studies of these compounds were carried by Discovery studio 3.5 work station equipped with Xeon processor E3e1225, 3.20 GHz, V2 quadcore personal computer with 8 GB total RAM.

Synthesis

N-(4-chlorophenyl acetyl) amino acid (1.574 mmol) and THF (100 mL) were placed into two-necked 100 mL round bottom flask. The main neck was closed by a balloon with an adopter. The reaction mixture was stirred on a magnetic stirrer at ice-cold temperature (0-4°C) for 10 minutes. Then, added the N-methyl morpholine (159.12 mg, 1.574 mmol) followed by ethyl chloroformate (170.75 mg, 1.574 mmol) and continued stirring for 10–15 minutes. Sodium borohydride (357.17 mg, 9.441 mmol) was put in a single portion into the above reaction mixture. Then, 25 mL of methanol was added slowly through the side neck of the round bottom flask using a pressure-equalizing funnel. The liberated hydrogen gas was collected in the balloon and continued the stirring under the same conditions for further 2–3 hours, then allowed the contents of the reaction mixture to attain the room temperature. After completion on total leucocyte count (TLC), the reaction system was treated with 1 N HCl; the product was extracted by using ethyl acetate (EtOAc, 100 mL). The EtOAc layer was washed with water (25 mLx3) followed by brine solution (25 mL × 3). The organic layer was dried with anhydrous sodium sulfate. The solvent was evaporated by rotary evaporator; white solid was persisted as a product. Except for methionine and proline, these derivatives are yellow liquids.

N-(4-Chlorophenyl acetyl) alaninol (4-CPA-OH)

^{1}H NMR (400 MHz, δ ppm): 1.079-1.096 (d, CH_3, *J*= 6.8 Hz, 3H), 3.427- 3.607 (d, CH_2O, 2H) 3.492 (s, Ar-CH_2, 2H), 3.527 (s, OH, 1H), 4.000-4.014 (m, CH_{Chiral}, 1H) 5.773 (s, NH_{Amide}, 1H), 7.169-7.303 (dd,ArCH);^{13}C NMR (100 MHz, δ ppm): 17.55 (CH_3), 41.98 (Ar-CH_2), 47.00 (CH_{Chiral}), 64.81 (OCH_2), 128.47-136.10 (ArC), 169.58 (CO_{Amide}). FT-IR ($\bar{\upsilon}$ cm^{-1}): 3348 (O-$H_{Stretching}$, N-$H_{Streching}$, ArC-$H_{Streching}$ and overtones of various out plane bending), 1695 (amide C=$O_{Streching}$), 1600 (ArC=$C_{Streching}$), 1554 (N-H Plane bending), 1492 (C-$H_{Bending}$), 1423 (C-$N_{Streching}$ and N-$H_{Bending}$), 1250 (C-$N_{Stretching}$), 1089 (C-$O_{Stretching}$), 735 (C-$H_{out\ of\ plane\ bending}$), 609 (N-$H_{outof\ plane\ bending}$); Colour: White; Elemental analysis Found (calcd.): C,58.10 (58.00); H,6.16 (6.14); N, 6.30 (6.14); Melting point: 119°C; Yield: 88%.

N-{2-(4-Chlorophenyl acetyl)} leucinol (4-CPL-OH)

^{1}H NMR (400 MHz, δ ppm): 0.873-0.877 (d, $C(CH_3)_2$, *J*=1.6 Hz, 6H), 1.254-1.308 (t, CH_2, 2H), 1.437-1.537 (m, CH,1H), 2.159 (s, O-H_{weak}, 1H), 3.448-3.644 (d, OCH_2, 2H), 3.528 (s, Cl-Ar-CH_2, 2H), 3.962-4.022 (m, CH_{chiral},1H), 5.492-5.508 (d, NH_{Amide}, *J*= 6.4 Hz, 1H), 7.718-7.320 (dd, ArCH, 4H); ^{13}C{^{1}H} NMR (100 MHz, δ ppm): 22.27 (CH_3), 23.73 (CH), 24.70 (CH_2), 42.08 (Cl-Ar-CH_2), 49.23 (CH_{Chiral}), 64.25 (CH_2O), 128.44-136.21 (ArC), 169.73 (CO_{Amide}); FT-IR ($\bar{\upsilon}$ cm^{-1}): 3370 (O-$H_{Streching}$), 3257 (N-$H_{Streching}$), 2297 (ArC-$H_{Streching}$ and overtones of various out plane bending), 1644 (amide C=$O_{Streching}$), 1600 (ArC=$C_{Streching}$), 1571 (N-$H_{bending}$), 1490 (C-$H_{3Bending}$), 1436 (C-$N_{Streching}$ and N-$H_{Bending}$), 1267 (C-$N_{Stretching}$), 1091 (C-$O_{Stretching}$), 751 (C-$H_{Out\ plane\ bending}$), 658 (N-$H_{Out\ plane\ bending}$); Colour: White solid; Elemental analysis Found (calcd.): C, 62.20 (62.27); H, 7.35 (7.41); N, 5.19 (5.18); Melting Point: 137°C; Yield: 94%.

N-(4-Chlorophenyl acetyl)phenylalaninol (4-CPPA-OH)

^{1}H NMR (400 MHz, δ ppm): 2.550-2.841 (d, $PhCH_2$, 2H), 3.334 (Cl-Ar-CH_2), 3.262-3.388 (m, CH_2O, 2H), 3.830-3.885 (m, CH_{Chiral}, 1H), 4.858 (s, O-H, 1H), 7.041-7.259 (m, ArCH, 9H), 7.982- 8.002 (d, NH_{Amide}, *J* = 8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, δ ppm): 36.98 ($PhCH_2$), 42.051 (Cl-Ar-CH_2), 52.93 (CH_{Chiral}), 63.17 (CH_2O), 126.28-139.53 (ArC), 169.72 (CO_{Amide}); FT-IR ($\bar{\upsilon}$ cm^{-1}) 3470 (O-$H_{Streching}$), 3302 (N-$H_{Streching}$), 2654 (ArC-$H_{Streching}$ and overtones of various out plane bending), 1645 (amide C = $O_{Streching}$), 1600 (ArC = $C_{Streching}$), 1534 (N-$H_{Bending}$), 1491 (C-$H_{Bending}$), 1435 (C-$N_{Streching}$ and N-$H_{Bending}$), 1263 (C-$N_{Stretching}$), 1090 (C-$O_{Stretching}$), 748 (C-$H_{out\ plane\ bending}$), 671 (N-$H_{out\ plane}$

$_{bending}$); Colour: White solid; Elemental analysis Found (Calcd.): C, 67.07 (67.15); H, 6.01 (5.92); N 4.78 (4.6); Melting Point: 131°C; Yield: 95%.

N-(4-Chlorophenyl acetyl) Methioninol (4-CPM-OH)

^{1}H NMR (400 MHz, δ ppm): 1.675-1.787 (d, CH_2, 2H), 2.011 (s, SCH_3, 3H), 2.395-2.430 (t, SCH_2, 2H), 3.476 (s, Cl-Ar-CH_2, 2H), 3.500-3.600 (d, CH_2O, 2H), 3.699 (s, O-H, 1H), 3.979-3.991 (m, CH_{Chiral}, 1H), 6.196-6.217 (d, NH_{Amide}, *J*= 8.4 Hz, 1H), 7.155- 7.300 (d, ArCH, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, δ ppm): 15.11 (S-CH_3), 30.44 (S-CH_2), 31.11 (CH_2), 42.09 (Cl-PhCH_2), 50.50 (CH_{Chiral}), 63.42 (CH_2O), 128.47-136.12 (ArC), 170.04 (CO_{Amide}); FT-IR ($\bar{\upsilon}$ cm^{-1}): 3694 (O-$H_{Stretching}$ and N-$H_{Streching}$), 3137-2826 (ArC-$H_{Streching}$ and overtones of various out plane bending), 1655 (amide C=$O_{Streching}$), 1611 (ArC=$C_{Streching}$), 1554 (N-$H_{Bending}$), 1492 (C-$H_{Bending}$), 1445 (C-$N_{Streching}$ and N-$H_{Bending}$), 1245 (C-$N_{Stretching}$), 1093 (C-$O_{Stretching}$), 808 (S-$C_{Streching}$), 700 (C-$H_{out\ plane\ bending}$), 611 (N-$H_{Out\ plane\ Bending}$); Colour: Pale yellow viscous liquid; Yield: 78%.

N-{2-(4-Chlorophenyl acetyl)}tryptophnnol (4-CPT-OH)

^{1}H NMR (400 MHz, δ ppm): 2.697-2.922 (d, Indo-CH_2, 2H), 3.316 (s, Cl-Ar-CH_2, 2H), 3.343-3.409 (m, CH_2O,2H), 3.918-3.952 (m, CH_{Chiral}, 1H), 4.724-4.750 (t, OH, 1H), 6.913-7.569 (m, ArCH, 9H), 7.911-7.932 (d, NH_{Amide}, *J*= 8.4 Hz, 1H), 10.750 (s, Indo-NH, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, δ ppm): 26.95 (Indo-CH_2), 42.04 (Cl-Ar-CH_2), 52.28 (CH_{Chiral}), 63.02 (CH_2O), 111.68-136.59 (ArC), 169.83 (CO_{Amide}); FT-IR ($\bar{\upsilon}$ cm^{-1}): 3480 (O-$H_{Streaching}$, Indole N-$H_{Streching}$, amide $NH_{Streching}$, ArC-$H_{Streching}$ and overtones of various out plane bending), 1655 (Amide C=$O_{Streching}$), 1599 (ArC=$C_{Streching}$), 1554 (N-$H_{Out\ of\ plane\ bending}$), 1494 (C-$H_{Bending}$), 1458 (Indole C-$N_{Streching}$ and N-$H_{Plane\ bending}$), 1457 (C-$N_{Streching}$ and N-$H_{In\ plane\ bending}$), 1259 (C-$N_{stretching}$), 1233 (Indole C-$N_{Stretch}$), 1090 (C-$O_{Stretching}$), 743 (C-$H_{Out\ plane\ bending}$), 677 (N-$H_{Out\ plane\ bending}$); Colour: White solid; Elemental analysis, Found (calcd.): C, 66.45 (66.50); H, 5.56 (5.54); N, 8.18 (8.16); Melting Point: 147°C; Yield: 98%.

N-(4-Chlorophenyl acetyl) prolinol(4-CPP-OH)

^{1}H NMR (400 MHz, δ ppm): 1.707-2.033 (m, $CH_{Pyrolidine}$ and OH, 5H), 3.400-3.755 (m, NCH_2, NCH_{chiral}, Cl-Ar-CH_2 and CH_2O, 7H), 7.160-7.505 (m, ArCH); $^{13}C\{^1H\}$ NMR (100 MHz, δ ppm): 23.89 ($C_{Pyrolidine}$), 27.15 ($C_{Pyrolidine}$), 37.54 (Cl-PhCH_2), 47.28 (NCH_2), 59.15 (CH_{Chiral}), 61.48 (CH_2O), 128.66-132.15 (ArCH), 167.32 (C=O_{Amide}); FT-IR ($\bar{\upsilon}$ cm^{-1}): 3626-3163 (O-$H_{stretching}$ and N-H $_{stretching}$), 3055-2797 (ArC-$H_{Streching}$ and overtones of various out plane bending), 1728 (AmideC=$O_{Streching}$), 1601 (ArC=$C_{Streching}$), 1492 (C-$H_{Bending}$), 1439 (C-$H_{Asymmetric}$), 1286 (C-$N_{Stretching}$), 1092 (C-$O_{Stretching}$), 746 (C-$H_{out\ plane\ bending}$); Colour: Pale yellow viscous liquid; Yield: 90%.

Antimicrobial Activity

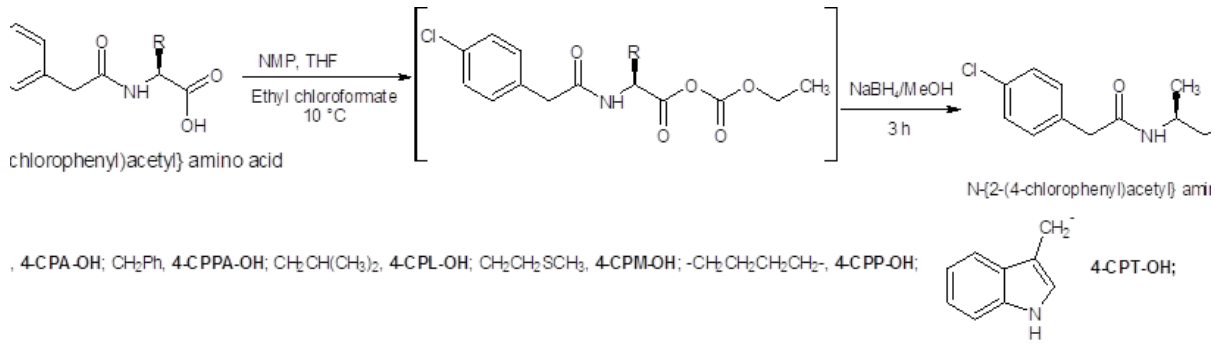
The new compounds 4-CPA-OH, 4-CPL-OH, 4-CPPA-OH, 4-CPM-OH, 4-CPT-OH, and 4-CPP-OH were screened for the antimicrobial activity using agar well diffusion method. [12] Matured broth cultures of selected bacteria and fungi strains were smeared on sterile nutrient agar and potato dextrose agar media containing plates respectively, with the help of steel cork-borer wells were made about 10 mm diameter on each inoculated plate. Synthesized samples solutions were prepared of concentrations 20 µg/µL and 10 µg/µL in DMSO. About 50 µL of differently concentrated solutions were put into the wells using a micropipette. Plates were incubated for 18–24 hours at 37°C. The activity indexes were calculated by measuring the inhibition zone.

Docking Studies

The C (30) carotenoid dehydrosqualene synthase (CDS) and N-myristoyl transferase with myristoyl-COA (NMT-CoA) are enzymes of *S. aureus* and *C. albicans*, respectively. The 3D crystallographic structures of the complexes of CDS – BPH-673[13] (PDB ID: 3ACX) and NMT-CoA-peptidic inhibitor[14] (PDB ID: 1IYK) were taken from protein data bank website. The synthesized compounds and enzymes complexes structures were optimized and minimized in protein preparation wizard[15] by using the CHARMn force field[16] to obtain the root mean square deviation (RMSD) value 0.3 Å. Synthesized 2D structures were minimized to possible conformation by using Ligprep[17] and placed into a grid of pre-processed protein for docking study by applying default parameters incorporated in maestro[18-19] applications. The extra precision (XP) mode was used to identify the binding modes of our samples with targets. The docking energy and hydrogen-bonded residues obtained from docking studies on bacteria and fungi were tabulated in Tables 1 and 2 with the binding receptor PDB ID: 3ACX and PDB ID: 1IYK, respectively.

Results and Discussion

The 4-chlorophenyl acetyl derivatives of six amino acids such as (*S*)-alanine (4-CPA), (*S*)-phenylalanine (4-CPPA), (*S*)-methionine (4-CPM), (*S*)-leucine (4-CPL), (*S*)-tryptophan (4-CPT) and (*S*)-proline (4-CPP) were synthesized and reduced using borohydride and methanol system via carbonate intermediate in the presence of ethyl chloroformate resulted corresponding six new alcohol derivatives 4-CPA-OH, 4-CPPA-OH, 4-CPM-OH, 4-CPL-OH, 4-CPT-OH and 4-CPP-OH. The synthesis reactions (Scheme 1) of these compounds were monitored by TLC using 70:30 n-hexane and ethyl acetate mixture as a solvent phase. The composition of solid compounds was confirmed by elemental analysis. The derivatives were characterized by ^{1}H, $^{13}C\{^1H\}$ NMR, and FTIR spectroscopy.



Scheme 1: Synthesis of N-{2-(4-chlorophenyl) acetyl} amino alcohols.

Table 1: Antibacterial activity of 4-CPA-OH, 4-CPL-OH, 4-CPPA-OH, 4-CPM-OH, 4-CPT-OH, and 4-CPP-OH.

Sample	*Treatment (....µg/ 50 µL)*	*K. aerogenes (mean ± SE)*	*E. coli (mean ± SE)*	*S. aureus (mean ± SE)*	*P. desmolyticum (mean ± SE)*	*A. flavus (mean ± SE)*	*C. albicans (mean ± SE)*
Ciprofloxacin	5	12.33 ± 0.03	13.67 ± 0.03	14.00 ± 0.00	15.60 ± 0.03	-	-
Fluconazole	200	-	-	-	-	10.27 ± 0.03	11.50 ± 0.06
4-CPA-OH	500	0.50 ± 0.00	1.30 ± 0.06	1.10 ± 0.06	2.00 ± 0.00	3.12 ± 0.00	3.50 ± 0.06
	1000	1.17 ± 0.17	2.53 ± 0.03	3.43 ± 0.12	4.00 ± 0.00	4.87 ± 0.03	5.74 ± 0.00
4-CPP-OH	500	1.00 ± 0.00	1.10 ± 0.06	2.07 ± 0.07	1.00 ± 0.00	1.55 ± 0.00	1.60 ± 0.03
	1000	2.50 ± 0.07	2.00 ± 0.00	3.23 ± 0.07	2.53 ± 0.03	2.57 ± 0.03	2.63 ± 0.00
4-CPM-OH	500	2.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	4.67 ± 0.17	2.80 ± 0.00	2.57 ± 0.00
	1000	3.43 ± 0.23	1.67 ± 0.17	2.50 ± 0.07	6.67 ± 0.17	4.50 ± 0.06	4.27 ± 0.00
4-CPT-OH	500	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.50 ± 0.03	1.00 ± 0.00
	1000	2.37 ± 0.09	2.60 ± 0.06	3.00 ± 0.00	3.67 ± 0.17	2.47 ± 0.03	1.68 ± 0.00
4-CPL-OH	500	1.00 ± 0.00	0.50 ± 0.00	1.00 ± 0.00	2.00 ± 0.00	2.50 ± 0.06	2.00 ± 0.00
	1000	2.00 ± 0.00	1.67 ± 0.17	2.67 ± 0.17	3.23 ± 0.07	4.07 ± 0.00	3.33 ± 0.33
4-CPR-OH	500	1.80 ± 0.10	3.30 ± 0.42	1.40 ± 0.00	1.50 ± 0.00	2.85± 0.06	2.60 ± 0.00
	1000	2.10. ± 0.21	3.80 ± 0.32	2.43 ± 0.26	2.42 ± 0.00	4.62 ± 0.00	4.50 ± 0.07

In ^{1}H spectra of these compounds, the peak for CH_2O protons observed at δ, 3.262 to 3.755 ppm based on the number and nature of neighboring protons and the absence of signal for the carboxylic group confirmed the reduction of the amino acid derivative into amino alcohol. A broad singlet or a multiplet observed at δ, 3.9 to 4.2ppm, attributed to the chiral CH proton.[20] A broad singlet for alcoholic OH proton was appeared the spectra of all the compounds. All other signals are self-explanatory.

In $^{13}C\{^{1}H\}$ spectra, the signal for CH_2O carbon observed in the range of δ, 47–52 ppm. The signal for CONH carbon observed in the range δ, 169.58 to 170.04 ppm in all the compounds. The peak for chiral CH carbon appeared between δ, 62-64 ppm.

In the FTIR spectra, a band observed in the range 1644 to 1728 cm^{-1} attributed to the stretching of C = O group of amide. The band for O-H and N-H stretching observed in the range of 3694- 3163 cm^{-1}.[21] The band for acid C=O stretching was found vanished, and the bands at 1331 and 1627 cm^{-1} for COO due to symmetric and asymmetric stretching also found vanished in the products. These observations from the ^{1}H and $^{13}C\{^{1}H\}$ NMR, FTIR spectra confirmed the formation of desired products.

The new derivatives containing 4-chlorophenyl, amide, and alcoholic groups were screened for antimicrobial and antifungal activity studies against selected bacteria and fungi. The results of antimicrobial activities are presented in Table 3 and are also depicted as bar diagrams Fig. 1. Ciprofloxacin and Fluconazole were used as standard antibacterial and antifungal agents for these studies.

The antibacterial activity results demonstrated that all the compounds showed activity against all the bacterial strains. Further, the compound 4-CPM-OH showed the highest activity against two bacteria *K. aerogenes* and *P. desmolyticum*, whereas the compounds 4-CPA-OH and 4-CPP-OH showed the highest activity against *S. aureus* and *E. coli* respectively. All the compounds exhibited moderate activity against both the fungal strains *A. flavus* and *C. albicans*. In addition, the compound 4-CPA-OH showed the highest activity against both of these fungal strains.

The docking studies on the refined structure of C(30) carotenoid dehydrosqualene synthase complexed with BPH-673 had been found that most of the compounds depicted specific van der Waals interactions with the surrounding hydrophobic residues and form hydrogen bonds through hydroxyl group and amide linkage with residues (Ser19, Tyr41, Asn168, Arg171, Tyr248, Asp48, Val133) in the cavity of target protein and the docking score found in the least range -0.157 to -1.385 kcal/mol. Antifungal molecular docking studies were carried out to investigate the binding affinities of newly synthesized

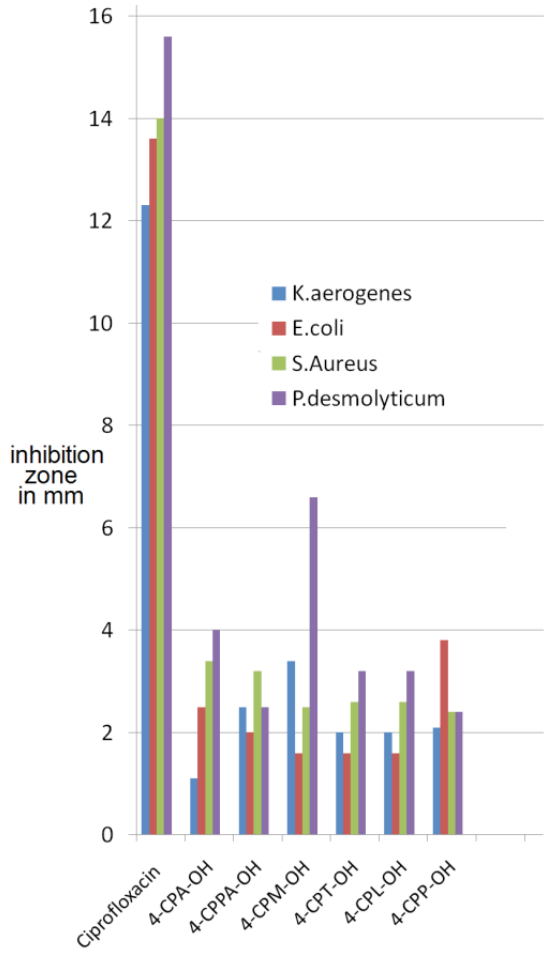


Fig. 1: Antibacterial activities of new compounds 4-CPA-OH, 4-CPL-OH, 4-CPPA-OH, 4-CPM-OH, 4-CPT-OH and 4-CPP-OH and standard Ciprofloxacin.

Table 2: Lowest binding energy for the compounds in the binding receptor PDB ID: 3ACX.

Compound	*Docking score (Kcal/mol)*	*Amino alcohols residue bonded via hydrogen bond*
4CPA-OH	-1.15	SER19, TYR41, ASN168
4CPL-OH	2.814	ARG171, TYR248
4CPM-OH	3.385	ARG171, TYR248
4CPP-OH	-0.157	ARG171, TYR248
4CPPA-OH	1.947	ASP48, VAL133
4CPT-OH	-1.385	ASP48, ASP48, ASN1608
Ciprofloxacin	-9.185	

Table 3: Lowest binding energy for the compounds in the binding receptor PDB ID: 1IYK.

Compound	*Docking score (Kcal/ mol)*	*Amino alcohols residue bonded via hydrogen bond*
4CPA-OH	-5.263	ASP412, GLY409
4CPL-OH	-3.13	ILE111, ASP110
4CPM-OH	-2.624	TYR119, TYR119
4CPP-OH	-0.127	ASP412
4CPPA-OH	0.554	ASP412
4CPT-OH	2.204	-
Flucanozole	-7.3	

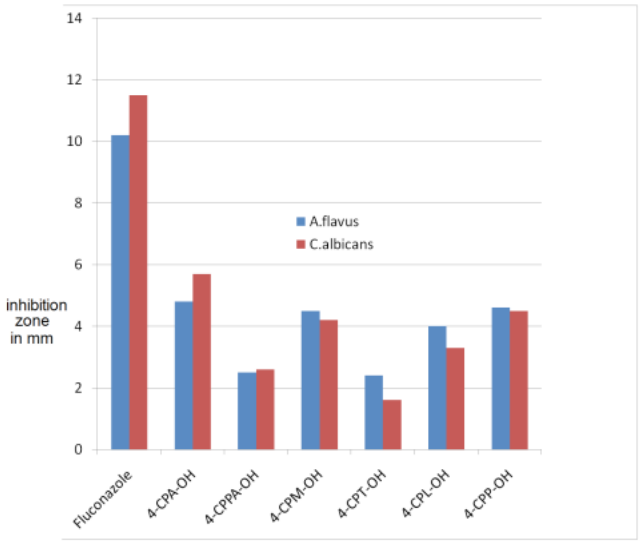


Fig. 2: Antifungal activities of new compounds 4-CPA-OH, 4-CPL-OH, 4-CPPA-OH, 4-CPM-OH, 4-CPT-OH and 4-CPP-OH and standard fluconazole.

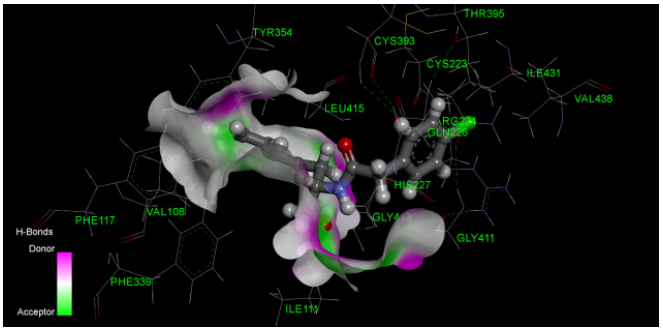


Fig. 3: 4-CPT–OH in of 1IYK protein pocket.

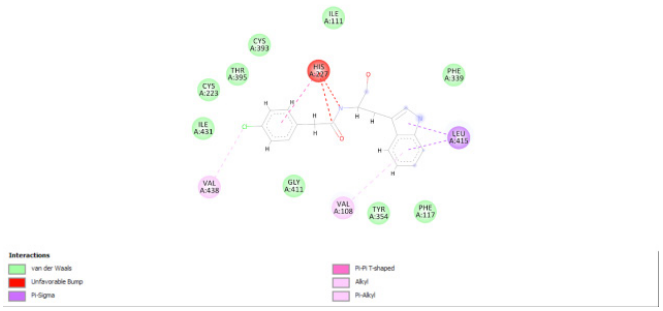


Fig. 4: Types of interaction of 4-CPT-OH with different amino acids of 1IYK protein.

compounds and target protein 1IYK. The docking results revealed that all the compounds except 4-CPT-OH showed hydrogen bonding interactions in the binding pocket of 1IYK (Figs. 3 and 4) with docking score in the range –0.127 to –5263 kcal/mol.

Conclusions

The N-{2-(4-chlorophenyl)acetyl} derivatives of amino alcohols were synthesized and characterized by FTIR, ^{1}H, and ^{13}C-NMR spectroscopic techniques. The compounds found moderate antimicrobial activity when compared

with standard drugs. Activity had been increased with an increased dosage of the respective compounds. The results also revealed that synthesized compounds could be better antifungal agents than antibacterial. Some of the compounds showed antimicrobial activity with positive docking score; hence, the compounds reduced the activities of the strains by noncompetitive inhibition manner.

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