Synthesis, Characterization, Antimicrobial and Antileishmanial Activities of Amide derivatives of *L*-tartaric acid

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Abstract: Sixteen (16) chiral, amides were synthesized from commercially available *L*-tartaric acid, having two asymmetric centers and C2 axis of symmetry. The diacid functionality of *L*-tartaric acid was protected as dimethyl ester and dihydroxy groups as acetonoid. The partial hydrolysis of acetonoid of dimethyl ester gave the corresponding monoester. Monoester upon treatment with different substituted aromatic amines gave desired amides (**1-8**). Amides (**1-8**) afforded deprotected compounds (**9-16**) after reacting with acetyl chloride and methanol. All the compounds were characterized by using spectroscopic techniques such as IR, ^{1}H-NMR, ^{13}C-NMR, and EIMS. The compounds gave reasonable elemental analyses. The structure of compound **6** was unambiguously obtained by X-ray crystallography. Protected (**1-8**) and deprotected amides (**9-16**) were tested for their antileishmanial (against *Leshmania tropica* KWH23 Promastigotes) and antimicrobial activities at different concentrations against different strains of bacteria and fungi.

Key Words: *L*-Tartaric acid, Protection and deprotection, Amides, Antileshmanial, Antimicrobial activity.

Introduction

Amide bonds are amongst the most stable attachments found in organic compounds and are the most common type of bonds occurring in living organisms in the form of proteins and peptides. The amide bond constitutes the key functional group in peptides, natural products, and pharmaceuticals [1]. Amides are usually prepared by coupling of carboxylic acids and amines in the presence of coupling reagent [2], or by prior conversion of the carboxylic acid into a reactive derivative [3]. Tartaric acid derivatives have been the subject of numerous studies including selective ion complexation or ion transport [4], asymmetric oxidation of prochiral sulfides [5a] and polyamide [5b] as bio-inspired antifreezing additives [6]. Synthetic development of new macrocyclic peptide antibiotics such as biphenomycin B [7] and vancomycine type glycopeptides antibiotics [8] has brought dramatic changes during the last few years. Synthesis of carbazolophane amides along with their antibacterial and antifungal activities has also been reported [9]. In the continuation of our research work on biologically active compounds [10-12] and owing to the importance of amides in organic synthesis, we aimed to synthesize some amides from *L*-tartaric acid and their biological screening. Thus, eight (8) protected amides (**1-8**) and eight (8) deprotected amide (**9-16**) were synthesized and tested for their antileshmanial activity using *Leishmania tropica* KWH23 promastigotes as parasites and antimicrobial activities at three different concentrations against different bacterial and fungal strains. All the protected and deprotected amides showed moderate to good activities against *Leishmania tropica* KWH23. In addition, protected and deprotected amides were active against all the three fungal as well as bacterial strains. The structures of synthetic compounds were identified by using spectroscopic techniques

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including IR, ^{1}H-NMR, ^{13}C-NMR, and EIMS. Elemental analyses of synthetic compounds were found to be satisfied. The structure of compound **6** was confirmed by X-ray crystallography.

Experimental

All reactions were carried out in anhydrous conditions and under static pressure of nitrogen gas using rubber septa and three way stopcock. Diethyl ether was dried and distilled over sodium and benzophenone. Chloroform was dried by refluxing with phosphorus pentoxide and methanol was dried over magnesium turnings and iodine crystals. Amines were dried by refluxing over potassium hydroxide. All the reactions were monitored through thin layer chromatography using pre-coated silica gel glass plates (layer thickness 0.25 mm, HF-254, E. Merck, Germany). Ethyl acetate: *n*-hexane and methanol: chloroform mixtures were used as eluent. Chromatograms were detected by using ultraviolet light (λ_{max} 254 and 365 nm). Column chromatography was performed on silica gel (0.063 - 0.200 mm) E. Merck, Germany. IR spectra were recorded on a Thermo scientific Nicolet Fourier Transform Infrared Spectrophotometer Model 6700. ^{1}H-NMR spectra were recorded on a NMR Bruker apparatus at 300 MHz in $CDCl_3$. ^{13}C-NMR spectra were recorded on a NMR Bruker apparatus at 75 MHz. Tetramethylsilane (TMS) was used as internal reference. Chemical shifts are given in δ (ppm). Abbreviations *s*, *d*, and *t* have been used for singlet, doublet, and triplet, respectively. Electron impact (EI) mass spectra were performed on a VG: 70 SE mass spectrometer JEOL MSRoute instrument with direct probe as inlet system. The optical rotations of the compounds were measured on a ATAGO, AP-100 Automatic polarimeter.

General Procedure for the Synthesis of Protected Amides **(1-8)**

In a 100 mL round-bottomed flask, 5-(methoxycarbonyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylic acid (1 equivalent, 5 mmol, 1.02 g) and *N,N*-dicyclohexylcarbodiimide (DCC) (1.2 equivalent, 06 mmol, 1.23 g) were placed under nitrogen and chloroform (40 mL) was added as a solvent. After half an hour substituted aniline (1 equivalent, 5 mmol) was added. The reaction mixture was stirred under nitrogen atmosphere for 8 hours. Dicyclohexyl urea was removed by multiple filtration and extracting the reaction mixture with ethyl acetate or chloroform and water. Crude was purified on a silica gel column.

(4R,5R)-Methyl-5-((2-fluorophenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate **(1).**

The compound (4*R*,5*R*)-methyl-5-((2-fluorophenyl) carbamoyl)-2, 2-dimethyl-1, 3-dioxolane-4-carboxylate, was synthesized by the general procedure as described earlier.

Yield: 72%. White crystalline solid. m.p = 85-86 °C. $[\alpha]_D^{25}$ = +44.79° (c = 24 mg / 2 mL CH_2Cl_2). IR (neat) cm^{-1}: 3399 (NH), 2967 (CH), 1739 ($COOCH_3$), 1700 (CONH), 1529 (Ar), 1112 (C-F). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.63 (bs, 1H, NH), 8.38-7.11 (m, 4H, Ar-H), 4.95 (d, J =5.5 Hz, 1H, CH), 4.89 (d, J = 5.5 Hz, 1H, CH), 3.88 (s, 3H, OCH_3), 1.55 (s, 3H, CH_3), 1.52 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.1 (CONH), 169.7 ($COOCH_3$), 148.6, 128.4, 125.7, 123.0, 122.1 (Ar-C), 143.4 (Ar-C-NH), 113.5 (qt C), 76.2 (CH), 75.6 (CH), 52.2 (OCH_3), 26.7 (CH_3), 25.9 (CH_3). Anal. Calc. For $C_{14}H_{16}FNO_5$ (297.1): C, 56.56; H, 5.42; F, 6.39; N, 4.71; O, 26.91 Found C, 56.12; H, 5.67; F, 6.70; N, 3.98; O, 26.45. EIMS *m/z* (%): 297.0 $(M)^+$ (85.5), 282.1 (72.4), 238.0 (29.6), 203 (100), 59.0 (30.7).

(4R,5R)-Methyl-2,2-dimethyl-5-((4-(trifluoromethoxy)phenyl)carbamoyl)-1,3-dioxolane-4-carboxylate **(2).**

Yield: 70%. White crystalline solid. m.p = 72-74 °C. $[\alpha]_D^{25}$ = +63.20° (c = 24 mg / 2 mL CH_2Cl_2). IR (neat) cm^{-1}: 3350 (NH), 2990 (CH), 1762 ($COOCH_3$), 1681 (CONH), 1605 (Ar), 1302 (C-F_3). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.34 (bs, 1H, NH), 7.64 (d, J= 8.5 Hz, 2H, Ar-H), 7.23 (d, J= 8.4 Hz, 2H, Ar-H), 4.92 (d, J = 5.4 Hz, 1H, CH), 4.88 (d, J = 5.4 Hz, 1H, CH), 3.87 (s, 3H, OCH_3), 1.57 (s, 3H, CH_3), 1.54 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.1 (CONH), 168.8 ($COOCH_3$), 142.1 (Ar-C-OCF_3), 137.3 (Ar-C-NH), 126.3 (OCF_3), 122.3 (2), 117.3 (2) (Ar-C) 113.6 (qt C), 76.3 (CH), 75.1 (CH), 53.5 (OCH_3), 26.8 (CH_3), 25.7 (CH_3). Anal. Calc. For $C_{15}H_{16}F_3NO_6$ (363.0): C, 49.59; H, 4.44; F, 15.69; N, 3.86; O, 26.42 Found C, 49.67; H, 3.97; F, 16.19; N, 3.38; O, 26.22. EIMS *m/z* (%): 363.1 $(M)^+$ (15.5), 348.1 (42.4), 161.0 (49.6), 159 (61.6), 59.0 (100).

(4R,5R)-Methyl-5-((2-bromophenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate **(3).**

Yield: 76%. White crystalline solid. m.p = 98-99 °C $[\alpha]_D^{25}$ = +61.41° (c = 24 mg / 2 mL CH_2Cl_2)

(IR υ cm^{-1}): 3277 (NH), 2927 (CH), 1737 ($COOCH_3$), 1680 (CONH), 1541 (Ar), 1050 (C-Br). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.28 (bs, 1H, NH), 7.34-7.32 (m, 4H, Ar-H), 4.90 (d, J = 5.3 Hz, 1H, CH), 4.80 (d, J = 5.3 Hz, 1H, CH), 3.78 (s, 3H, OCH_3), 1.55 (s, 3H, CH_3), 1.52 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.6 (CONH), 169.9 ($COOCH_3$), 137.4 (Ar-C-NH), 127.7, 126.0, 124.9, 122.1, 119.5 (Ar-C), 113.3 (qt C), 76.3 (CH), 75.6 (CH), 52.2 (OCH_3), 26.5 (CH_3), 25.8 (CH_3). Anal. Calc. For $C_{14}H_{16}BrNO_5$ (357.0) C, 46.95; H, 4.50; Br, 22.31; N, 3.91; O, 22.33 Found C, 46.90; H, 3.99; Br, 22.34; N, 4.14; O, 21.87. EIMS *m/z* (%): 357.1 $(M)^+$ (2.5), 342.1 (8.4), 298.0 (2.6), 59.0 (100).

(4R,5R)-Methyl-5-((4-bromophenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate **(4).**

Yield: 69%. White crystalline solid. m.p = 112-113 °C. $[\alpha]_D^{25}$ = +64.31° (c = 24 mg / 2 mL CH_2Cl_2) (IR υ cm^{-1}): 3345 (NH), 2983 (CH), 1755 ($COOCH_3$), 1681 (CONH), 1588 (Ar), 1020 (C-Br). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.30 (bs, 1H, NH), 7.51 (d, J = 8.6 Hz, 2H, Ar-H), 7.46 (d, J = 8.5 Hz, 2H, Ar-H), 4.90 (d, J = 5.6 Hz, 1H, CH), 4.86 (d, J = 5.5 Hz, 1H, CH), 3.86 (s, 3H, OCH_3), 1.56 (s, 3H, CH_3), 1.53 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.4 (CONH), 167.6 ($COOCH_3$), 135.7 (Ar-C-NH), 131.8 (2), 120.3 (2), 117.2 (Ar-C), 113.7 (qt C), 76.6 (CH), 75.2 (CH), 53.0 (OCH_3), 26.6 (CH_3), 26.1 (CH_3). Anal. Calc. For $C_{14}H_{16}BrNO_5$ (357.0) C, 46.95; H, 4.50; Br, 22.31; N, 3.91; O, 22.33 Found C, 46.90; H, 3.99; Br, 22.34; N, 4.14; O, 21.87. EIMS *m/z* (%): 357.1 $(M)^+$ (2.5), 342.1 (8.4), 298.0 (2.6), 59.0 (100).

(4R,5R)-Methyl-5-((2,4-dimethylphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4 carboxylate **(5).**

Yield: 79%. White crystalline solid. m.p = 150-151 °C. $[\alpha]_D^{25}$ = +45.91° (c =24 mg / 2 mL CH_2Cl_2). (IR υ cm^{-1}): 3392 (NH), 2928 (CH), 1750 ($COOCH_3$), 1675 (CONH), 1596 (Ar). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.21 (bs, 1H, NH), 7.88 (d, J = 8.7 Hz, 1H, Ar-H), 7.79 (d, J = 8.6 Hz, 1H, Ar-H), 7.05 (s, 1H, Ar-H), 4.95 (d, J = 5.4 Hz, 1H, CH), 4.88 (d, J = 5.4 Hz, 1H, CH), 3.87 (s, 3H, OCH_3), 1.60 (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 2.30 (s, 3H, Ar-CH_3), 2.25 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.5 (CONH), 167.4 ($COOCH_3$), 134.9 (Ar-C-NH), 132.1, 131.1, 128.2, 126.2 (Ar-C), 113.6 (qt C), 76.6 (CH), 75.7 (CH), 53.0 (OCH_3), 26.8 (CH_3), 26.2 (CH_3), 20.9 (Ar-CH_3), 17.5 (Ar-CH_3). Anal. Calc. For $C_{16}H_{21}NO_5$ (307.1) C, 62.53; H, 6.89; N, 4.56; O, 26.03 Found C, 61.90; H, 6.45; N, 4.45; O, 26.29. EIMS *m/z* (%): 307.1 $(M)^+$ (30.5), 248.1 (7.0), 121.0 (82.6), 59.0 (100).

(4R,5R)-Methyl-5-((2,6-diethylphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate **(6).**

Yield: 74%. White crystalline solid. m.p = 160-161 °C $[\alpha]_D^{25}$ = +35.31° (c = 24 mg / 2 mL CH_2Cl_2).(IR υ cm^{-1}): 3244 (NH), 2929 (CH), 1731 ($COOCH_3$), 1681 (CONH), 1592 (Ar). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.86 (bs, 1H, NH), 7.28-7.15 (m, 3H, Ar-H), 5.01 (d, J = 5.5 Hz, 1H ,CH), 4.85 (d, J = 5.5 Hz, 1H ,CH), 3.86 (s, 3H , OCH_3), 2.63 (q, J = 7.6 Hz, 4H, 2×CH_2), 1.54 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.23 (t, J = 7.6 Hz, 6H, 2×CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.4 (CONH), 168.3 ($COOCH_3$), 141.2 (Ar-C-NH), 131.3 (2) (Ar-C-C_2H_5), 124.2, 123.5 (2) (Ar-C), 113.3 (qt C), 76.6 (CH), 75.9 (CH), 53.1 (OCH_3), 26.3 (CH_3), 25.6 (CH_3), 23.4 (CH_2), 15.6 (CH_3). Anal. Calc. For $C_{18}H_{25}NO_5$ (335.1) C, 64.46; H, 7.51; N, 4.18; O, 23.85 Found C, 64.65; H, 7.78; N, 4.12; O, 24.07. EIMS *m/z* (%): 335.1 $(M)^+$ (3.5), 276.1 (7.0), 218.0 (22.6), 59.0 (100).

(4R,5R)-Methyl-5-((4-bromo-2-methylphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4 carboxylate **(7).**

Yield: 81%. White crystalline solid. m.p = 141-143 °C. $[\alpha]_D^{25}$ = +37.21° (c = 24 mg / 2 mL CH_2Cl_2). (IR υ cm^{-1}): 3390, (NH), 2933, (CH), 1753 ($COOCH_3$), 1674 (CONH), 1602 (Ar), 1060 (C-Br). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.27 (bs, 1H, NH), 7.98 (s,1H, Ar-H), 7.35 (d, J = 8.4 Hz, 1H, Ar-H), 7.33 (d, J = 8.4 Hz, 1H, Ar-H), 4.93 (d, J = 5.4 Hz, 1H, CH), 4.85 (d, J = 5.4 Hz, 1H, CH), 3.86 (s, 3H, OCH_3), 2.26 (s, 3H, Ar-CH_3), 1.59 (s, 3H, CH_3), 1.53 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.4 (CONH), 167.5 ($COOCH_3$), 133.9 (Ar-C-NH), 130.6, 129.2, 122.7, 117.8 (Ar-C), 113.7 (qt C), 77.9 (CH), 76.6 (CH), 53.0 (OCH_3), 26.8 (CH_3), 26.1 (CH_3), 17.3 (Ar-CH_3). Anal. Calc. For $C_{15}H_{18}BrNO_5$ (371.0) C, 48.40; H, 4.87; Br, 21.47; N, 3.76; O, 21.49 Found C, 48.67; H, 5.03; Br, 21.78; N, 4.12; O, 21.42. EIMS *m/z* (%): 371.1 $(M)^+$ (9.5), 356.1 (7.0), 312.0 (22.6), 59.0 (100).

(4R,5R)-methyl-5-((2-chloro-4-methylphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate **(8).**

Yield: 79%. White crystalline solid. m.p = 113-115 °C. $[\alpha]_D^{25}$ = +59.49° (c = 24 mg / 2 mL

CH_2Cl_2). (IR υ cm^{-1}): 3373 (NH), 2994 (CH), 1749 ($COOCH_3$), 1695 (CONH), 1610 (Ar), 1090 (C-Cl). ^{1}H NMR (300MHz, $CDCl_3$): δ (ppm): 8.91 (bs, 1H, NH), 8.30 (s,1H, Ar-H), 7.19 (d, J = 8.4 Hz, 1H, Ar-H), 7.09 (d, J = 8.4 Hz, 1H, Ar-H), 4.92 (d, J = 5.4 Hz, 1H, CH), 4.86 (d, J = 5.4 Hz, 1H , CH), 3.85 (s, 3H, OCH_3), 2.29 (s, 3H, Ar-CH_3), 1.59 (s, 3H, CH_3), 1.52 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 170.4 (CONH), 167.9 ($COOCH_3$), 135.3 (Ar-C-NH), 131.0, 129, 127, 120 (Ar-C), 113.2 (qt C), 77.5 (CH), 76.6 (CH), 53.0 (OCH_3), 26.5 (CH_3), 25.2 (CH_3), 20.2 (Ar-CH_3). Anal. Calc. For $C_{15}H_{18}ClNO_5$ (327.0) C, 54.97; H, 5.54; Cl, 10.82; N, 4.27; O, 24.41 Found C, 55.12; H, 5.43; Cl, 10.17; N, 4.47; O, 24.30. EIMS *m/z* (%): 327.1 $(M)^+$ (12.5), 312.0 (22.6), 268.1 (7.0), 141.1 (94.8), 59.0 (100).

General Procedure for Deprotected Amides **(9-16).**

To a solution of the corresponding amide in MeOH (15 mL), acetyl chloride was added drop wise. After complete disappearance of the reactant the reaction mixture was concentrated on a rotary evaporator, the mixture was extracted with EtOAc (4 × 15 mL). The organic layer was collected and dried with appropriate drying agent and concentrated on a rotary evaporator. The crude was then purified by column chromatograpy using methanol and chloroform as eluent.

(2R,3R)-Methyl-4-(2-fluorophenylamino)-2,3-dihydroxy-4-oxobutanoate **(9).**

Yield: 79%. White crystalline solid. m.p = 110-111 °C. $[\alpha]_D^{25}$ = +48.91°(c = 24 mg / 2 mL CH_2Cl_2). (IR υ cm^{-1}): 3450 (OH), 3309 (NH), 2977 (CH), 1749 ($COOCH_3$), 1678 (CONH), 1527 (Ar), 1118 (C-F). ^{1}H NMR (300MHz, DMSO-d_6): δ (ppm): 8.93 (bs, 1H, NH), 7.88-7.57 (m, 4H, Ar-H), 4.86 (d, J = 5.6 Hz, 1H, CH), 4.66 (d, J = 5.6 Hz, 1H, CH), 3.78 (s, 3H, OCH_3), 2.98 (bs, 2H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 170.9 (CONH), 169.7 ($COOCH_3$), 152.6, 128.4, 125.7, 123.0, 122.1 (Ar-C), 146.4 (Ar-C-NH), 74.2 (CH), 73.3 (CH), 51.2 (OCH_3). Anal. Calc. For $C_{11}H_{12}FNO_5$ (257.0) C, 51.36; H, 4.70; F, 7.39; N, 5.45; O, 31.10 Found C, 51.12; H, 4.90; F, 7.67; N, 5.18; O, 31.33. EIMS *m/z* (%): 257.1 $(M)^+$ (9.0), 198.0 (5.7), 111.0 (100), 59.0 (18.9).

(2R,3R)-Methyl-2,3-dihydroxy-4-oxo-4-(4-(trifluoromethoxy)Phenylamino)butanoate **(10).**

Yield: 72%. White crystalline solid. m.p = 87-88 °C. $[\alpha]_D^{25}$ = +60.29° (c = 24 mg / 2 mL CH_2Cl_2). (IR υ cm^{-1}): 3509 (OH), 3358 (NH), 2996 (CH), 1752 ($COOCH_3$), 1671 (CONH), 1615 (Ar), 1312 (C-F_3). ^{1}H NMR (300MHz, DMSO-d_6): δ (ppm): 9.89 (bs, 1H, NH), 7.86 (d, J= 8.4 Hz, 2H, Ar-H), 7.33 (d, J= 8.4 Hz, 2H, Ar-H), 4.51 (d, J = 5.3 Hz, 1H, CH), 4.40 (d, J = 5.3 Hz, 1H, CH), 3.68 (s, 3H, OCH_3), 3.12 (bs, 2H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 172.8 (CONH), 170.8 ($COOCH_3$), 144.2 (Ar-C-OCF_3), 138.1 (Ar-C-NH), 127.3 (OCF_3), 125.3 (2), 119.3 (2), (Ar-C), 74.0 (CH), 72.5 (CH), 52.2 (OCH_3). Anal. Calc. For $C_{12}H_{12}F_3NO_6$ (323.0)C, 44.59; H, 3.74; F, 17.63; N, 4.33; O, 29.70 Found C, 44.23; H, 3.45; F, 17.79; N, 4.88; O, 29.35. EIMS *m/z* (%): 323.1 $(M)^+$ (13.7), 264.1 (6.7), 177.0 (100), 59.0 (38.0).

(2R,3R)-Methyl-4-(2-bromophenylamino)-2,3-dihydroxy-4-oxobutanoate **(11).**

Yield: 80%. White crystalline solid. m.p = 145-146 °C. $[\alpha]_D^{25}$ = +62.41°(c = 24 mg / 2 mL CH_2Cl_2). (IR υ cm^{-1}): 3500 (OH), 3272 (NH), 2937 (CH), 1747 ($COOCH_3$), 1670 (CONH), 1521 (Ar), 1030 (C-Br). ^{1}H NMR (300MHz, DMSO-d_6): δ (ppm): 9.28 (bs, 1H, NH), 7.84-7.72 (m, 4H, Ar-H), 4.80 (d, J = 5.4 Hz, 1H, CH), 4.70 (d, J = 5.4 Hz, 1H, CH), 3.77 (s, 3H, OCH_3), 3.21 (bs, 2H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.6 (CONH), 170.9 ($COOCH_3$), 138.4 (Ar-C-NH), 128.7, 127.0, 125.9, 123.1, 121.5 (Ar-C), 74.3 (CH), 72.8 (CH), 51.2 (OCH_3). Anal. Calc. For $C_{11}H_{12}BrNO_5$ (316.9) C, 41.53; H, 3.80; Br, 25.12; N, 4.40; O, 25.15 Found C, 41.67; H, 4.30; Br, 25.06; N, 4.75; O, 25.45. EIMS *m/z* (%): 317.1 $(M)^+$ (2.9), 197.1 (5.9), 119.0 (11.2), 60.1 (100).

(2R,3R)-Methyl-4-(4-bromophenylamino)-2,3-dihydroxy-4-oxobutanoate **(12).**

Yield: 84%. White crystalline solid. m.p = 115-116 °C. $[\alpha]_D^{25}$ = +68.39° (c = 24 mg / 2 mL CH_2Cl_2). (IR υ cm^{-1}): 3499 (OH), 3301 (NH), 2947 (CH), 1735 ($COOCH_3$), 1661 (CONH), 1591 (Ar), 1025 (C-Br). ^{1}H NMR (300MHz, DMSO-d_6): δ (ppm): 9.90 (bs, 1H, NH), 7.51 (d, J = 8.4 Hz, 2H, Ar-H), 7.46 (d, J = 8.4 Hz, 2H, Ar-H), 4.50 (d, J = 5.4 Hz, 1H, CH), 4.38 (d, J = 5.4 Hz, 1H, CH), 3.67 (s, 3H, OCH_3), 3.02 (bs, 2H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 170.9 (CONH), 167.4 ($COOCH_3$), 138.3 (Ar-C-NH), 132.3 (2), 120.9 (2), 118.6 (Ar-C), 74.1 (CH), 72.6 (CH), 52.2 (OCH_3). Anal. Calc. For $C_{11}H_{12}BrNO_5$ (316.9) C, 41.53; H, 3.80; Br, 25.12; N, 4.40; O, 25.15 Found C, 41.67; H, 4.30; Br, 25.06; N, 4.75; O, 25.45. EIMS *m/z* (%): 317.1 $(M)^+$ (2.9), 197.1 (5.9), 119.0 (11.2), 60.1 (100).

(2R,3R)-Methyl-4-(2,4-dimethylphenylamino)-2,3-dihydroxy-4-oxobutanoate **(13).**

Yield: 78%. White crystalline solid. m.p = 160-161 °C. $[\alpha]_D^{25}$ = +47.99° (c = 24 mg / 2 mL CH_2Cl_2). (IR υ cm^{-1}): 3456 (OH), 3376 (NH), 2954 (CH), 1749 ($COOCH_3$), 1662 (CONH), 1506 (Ar). ^{1}H NMR (300MHz, DMSO-d_6): δ (ppm): 8.81 (bs, 1H, NH), 7.89 (d, J = 8.4 Hz, 1H, Ar-H) , 7.69 (d, J = 8.4 Hz, 1H, Ar-H) , 7.60 (s, 1H, Ar-H) , 4.58 (d, J = 5.5 Hz, 1H, CH), 4.56 (d, J = 5.5 Hz, 1H, CH), 3.76 (s, 3H, OCH_3), 3.11 (bs, 2H, OH), 2.31 (s, 3H, Ar-CH_3), 2.28 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 170.9 (CONH), 168.2 ($COOCH_3$), 135.9 (Ar-C-NH), 132.8, 131.8, 128.5, 126.8 (Ar-C), 74.9 (CH), 72.5 (CH), 52.2 (OCH_3), 20.5 (Ar-CH_3), 17.8 (Ar-CH_3). Anal. Calc. For $C_{13}H_{17}NO_5$ (267.1) C, 58.42; H, 6.41; N, 5.24; O, 29.93 Found C, 58.66; H, 6.12; N, 5.68; O, 30.05. EIMS *m/z* (%): 267.2 $(M)^+$ (8.1), 208.1 (2.7), 147.2 (30.8), 121.2 (100), 59.0 (20.5).

(2R,3R)-Methyl-4-(2,6-diethylphenylamino)-2,3-dihydroxy-4-oxobutanoate **(14).**

Yield: 79%. White crystalline solid. m.p = 123-124 °C. $[\alpha]_D^{25}$ = +42.91° (c = 24 mg / 2 mL CH_2Cl_2). (IR υ cm^{-1}): 3422 (OH), 3269 (NH), 2965 (CH), 1735 ($COOCH_3$), 1665 (CONH), 1525 (Ar). ^{1}H NMR (300MHz, DMSO-d_6): δ (ppm): 8.73 (bs, 1H, NH), 7.37-7.35 (m, 3H, Ar-H), 5.34 (bs, 2H, OH), 4.70 (d, J = 5.4 Hz, 1H ,CH), 4.40 (d, J = 5.4 Hz, 1H ,CH), 3.81 (s, 3H , OCH_3), 2.67 (q, J = 7.6 Hz, 4H, 2×CH_2), 1.16 (t, J = 7.6 Hz, 6H, 2×CH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 172.6 (CONH), 169.9 ($COOCH_3$), 141.2 (Ar-C-NH), 133.3 (2) (Ar-C-C_2H_5), 124.4 123.3 (2) (Ar-C), 73.3 (CH), 72.5 (CH), 51.5 (OCH_3), 24.5 (CH_2), 14.1 (CH_3). Anal. Calc. For $C_{15}H_{21}NO_5$ (295.1) C, 61.00; H, 7.17; N, 4.74; O, 27.09 Found C, 60.78; H, 7.46; N, 4.34; O, 27.29. EIMS *m/z* (%): 295.2 $(M)^+$ (3.9), 236.2 (2.7), 176.1 (100), 119.1 (19.1), 59.1 (20.3).

(2R,3R)-Methyl-4-(4-bromo-2-methylphenylamino)-2,3-dihydroxy-4-oxobutanoate **(15).**

Yield: 85%. White crystalline solid. m.p = 155-157 °C. $[\alpha]_D^{25}$ = +43.99° (c = 24 mg / 2 mL CH_2Cl_2). (IR υ cm^{-1}): 3411 (OH), 3387 (NH), 2949 (CH), 1732 ($COOCH_3$), 1673 (CONH), 1579 (Ar), 1084 (C-Br). ^{1}H NMR (300MHz, DMSO-d_6): δ (ppm): 8.73 (bs, 1H, NH), 7.42 (s,1H, Ar-H), 7.35 (d, J = 8.4 Hz, 1H, Ar-H), 7.05 (d, J = 8.4 Hz, 1H, Ar-H), 4.67 (d, J = 5.4 Hz, 1H, CH), 4.60 (d, J = 5.4 Hz, 1H, CH), 3.82 (s, 3H, OCH_3), 3.24 (bs, 2H, OH), 2.28 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 172.6 (CONH), 171.0 ($COOCH_3$), 134.4 (Ar-C-NH), 133.6, 129.4, 124.7, 117.8 (Ar-C), 73.4 (CH), 72.2 (CH), 51.4 (OCH_3), 16.2 (Ar-CH_3). Anal. Calc. For $C_{12}H_{14}BrNO_5$ (331.0) C, 43.39; H, 4.25; Br, 24.06; N, 4.22; O, 24.08 Found C, 43.69; H, 4.65; Br, 24.16; N, 3.90; O, 24.50. EIMS *m/z* (%): 331.1 $(M)^+$ (34.0), 271.1 (8.4), 185.1 (100), 59.1 (29.5).

(2R,3R)-Methyl-4-(2-chloro-4-methylphenylamino)-2,3-dihydroxy-4-oxobutanoate **(16).**

Yield: 81%. White crystalline solid. m.p = 89-90 °C. $[\alpha]_D^{25}$ = +62.99°(c = 24 mg / 2 mL CH_2Cl_2). (IR υ cm^{-1}): 3489 (OH), 3345 (NH), 2958 (CH), 1724 (CO OCH_3), 1670 (CONH), 1610 (Ar), 1092 (C-Cl). ^{1}H NMR (300MHz, DMSO-d_6): δ (ppm): 8.30 (bs, 1H, NH), 7.79 (s,1H, Ar-H), 7.59 (d, J = 8.4 Hz, 1H, Ar-H), 6.99 (d, J = 8.4 Hz, 1H, Ar-H), 5.91 (bs, 2H, OH), 4.74 (d, J = 5.3 Hz, 1H, CH), 4.64 (d, J = 5.3 Hz, 1H , CH), 3.76 (s, 3H, OCH_3), 2.22 (s, 3H, Ar-CH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 171.1 (CONH), 168.8 ($COOCH_3$), 136.9 (Ar-C-NH), 131.9 (Ar-C-CH_3), 129.6, 127.3, 120.6 (Ar-C), 74.3 (CH), 73.5 (CH), 53.9 (OCH_3), 21.2 (Ar-CH_3). Anal. Calc. For $C_{12}H_{14}ClNO_5$ (287.0) C, 50.10; H, 4.90; Cl, 12.32; N, 4.87; O, 27.81 Found C, 50.43; H, 5.13; Cl, 12.63; N, 4.33; O, 28.20. EIMS *m/z* (%): 287.1 $(M)^+$ (13.1), 228.0 (5.6), 141.2 (100), 59.0 (24.5).

Material and Methods

Assay for Antifungal Activity

In the present experiment three concentrations (100%, 80%, and 60%) of synthetic compounds were used to study the inhibition potential against three fungal and three bacterial strains.

The agar tube dilution method is used for determination of antifungal activity of the compounds [13]. DMSO was used as a control solvent, terbinafine was used as standard. The fungal strains were used in this study include *Fusarium solani, Helminthosporium sativum and Aspergillus niger*. Each fungal strain was maintained on Sabouraud dextrose agar (SDA) medium at 4 °C.

Assay for Antibacterial Bioassay

Three strains of bacteria were used in the study i.e *Enterobacter sp*, *Vibrio cholerae* and

Klebsiella sp. Nutrient broth medium was prepared by dissolving 0.4 g of nutrient broth per 50 mL of distilled water for the growth of bacterial inoculate, pH was adjusted at 7.0 and was autoclaved. Nutrient agar medium was prepared by dissolving 2.3 g agar in 100 mL of distilled water; pH was adjusted at 7.0 and was autoclaved at 121 °C. The standard was prepared by adding 0.5 mL (0.048 M) barium chlorides to 99.5 ml (0.36 N) sulfuric acid. Barium sulfate turbidity standard (4-6 mL) and was taken in screw capped test tube and poured to inoculums till the inoculums give the same color as that of turbidity standard [14].

Antileishmanial Assay

Antileishmanial activity of the synthesized protected (**1a-1h**) and deprotected amides (**2a-2h**) was assayed by modified Zhai's method [15] using a pre established culture of *L. tropica* KWH23. Parasites were cultured in medium M199 with 10% fetal bovine serum; 30 mM of HEPES, and 100 units/ml of penicillin and 100ug/ml of streptomycin at 24 °C in a shaking incubator for four hours and later in general incubator at 24 °C for five days.

Results and Discussion

Chemistry

For the synthesis of biologically important amides, we started our research work with selection of an inexpensive and commercially available starting material *L*-(+)-tartaric acid which has two chiral centers (Fig. 1).

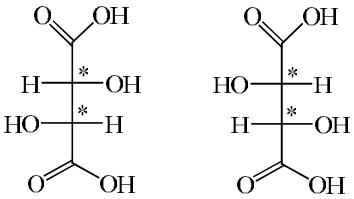
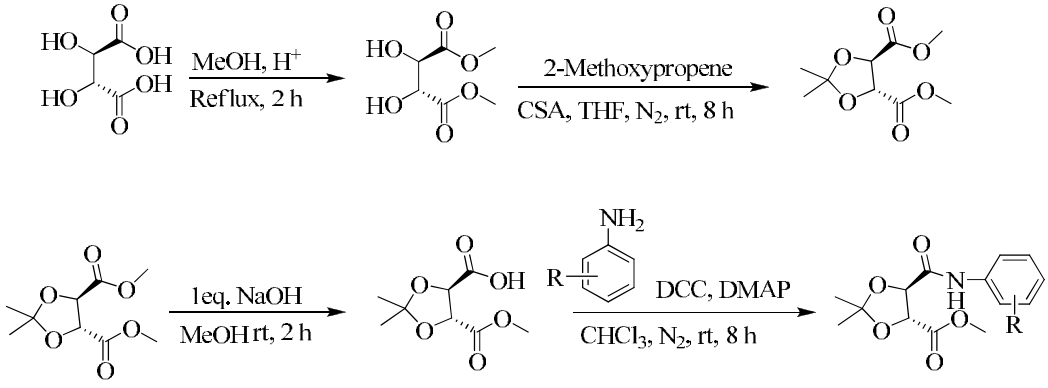


Fig. 1: L-(+)-tartaric acid which shows the Chiral centers.

Bifunctional *L*-tartaric acid was protected and partially hydrolyzed to get monoester as shown in Scheme-1. The basic hydrolysis of dimethyl 2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate by using 1N NaOH, afford 5-(methoxycarbonyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylic acid (monoester) which was treated with different substituted aromatic amines in dry chloroform as solvent and 1.2 equivalent *N,N*-dicyclohexylcarbodiimide (DCC) as dehydrating agent, the reaction mixture was stirred at room temperature for 8 h so that amides were synthesized. After the completion, reaction mixture was filtered to get rid of the byproduct *N,N*-dicyclohexyl urea. The crude was then purified by column chromatography using *n*-hexane/ethyl acetate as eluent. All the synthetic compounds were characterized by using spectroscopic techniques such as IR, ^{1}H-NMR, ^{13}C-NMR, and EIMS.



(1- 8)

S. No.	compounds	R	R_f values*	Yield (%)
1	1	2-Fluoroaniline	0.52	72
2	2	4-Trifluoromethoxylaniline	0.71	70
3	3	2-Bromoaniline	0.69	76
4	4	4-Bromoaniline	0.72	69
5	5	2,4-Dimethylaniline	0.47	79
6	6	2,6-Diethylaniline	0.66	74
7	7	4-Bromo-2-methylaniline	0.85	81
8	8	2-Chloro-4-methylaniline	0.68	79

*Solvent System: Ethyl acetate: Hexane (2:8)

Scheme-1: Synthesis of protected amides (**1-8**).

The infrared absorption spectra of the synthetic amides (**1-8**) showed characteristic stretching bands at 1762 and 1700 cm^{-1} for CO (ester) and CO (amide), respectively. The NH stretching frequencies for all the amides appeared in the range of 3399-3244 cm^{-1}. The structures were further supported by ^{1}H and ^{13}C-NMR data. Broad singlets appeared in 8.63-8.32 ppms which were attributed to NH protons. Singlets in 3.88-3.78 ppm were appearing due to 3 protons of the methoxy group, two singlets at 1.55 and 1.52 ppm were attributed to methyl protons of the isopropylidene moiety. The aromatic protons showed doublet in *para* substituted anilines while *ortho* and *meta* substituted anilines showed multiplet and a singlet, respectively. In ^{13}C-NMR the carbonyl carbon of carboxamide appeared at 170.6-170.1 ppm, while quaternary carbon appeared at 113.7-113.1 ppm, respectively. EIMS and elemental analysis of the synthetic compounds, described in the experimental protocol further supported the structures of all the compounds. Finally the assigned structure were supported by single crystal X-ray diffraction study of amide 4*R*,5*R*-methyl-5-((2,6-diethylphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (**6**) (Fig. 2).

Crystal system, space group: Monoclinic, C2. Selected bond lengths (Å) and angles (deg): N(1)-C(11) = 1.336(4), N(1)-C(1) = 1.435(4), O(3)-C(14) = 1.451(5), O(1)-C(11) = 1.215(4), N(2)-C(29) = 1.334(4), N(2)-C(24) = 1.428(4), C(11)-N(1)-C(1) = 121.9(3), C(2)-C(1)-C(6) = 121.9(4), C(29)-N(2)-C(24) = 123.4(3), C(13)-O(2)-C(14) = 106.7(2), C(12)-O(3)-C(14) = 110.4(2), C(30)-O(8)-C(33) = 110.5(2).

Deprotected Amides

All the protected amides were deprotected by using methanol and freshly distilled acetyl chloride. Acetyl chloride was added dropwise. The *in situ* generation of anhydrous HCl is enough to deprotect the acid labile acetonide. The progress of the reaction was monitored through thin layer chromatography to give compounds (**9-16**) Scheme-2.

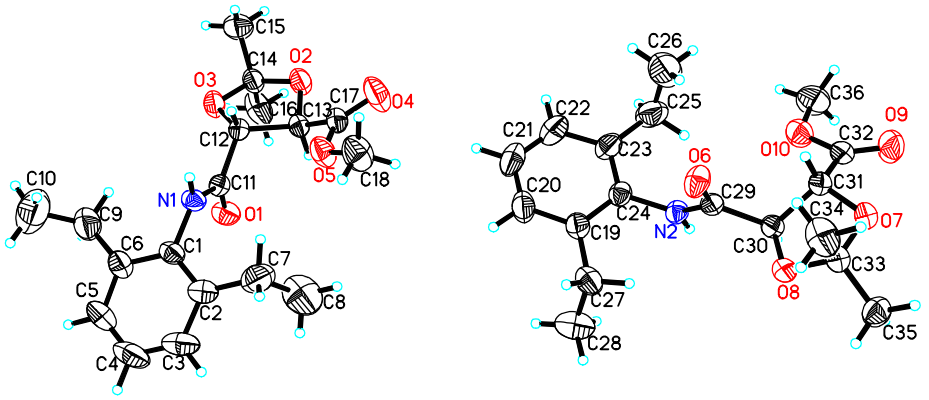
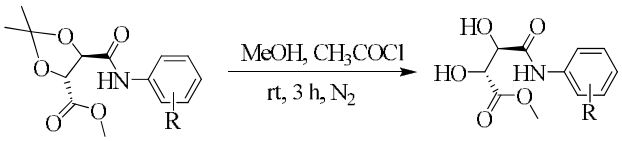


Fig. 2: X-ray crystal structure of 4*R*,5R-methyl-5-((2,6-diethylphenyl)carbamoyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (**6**).



(1-8) **(9-16)**

S. No.	Compounds	R	R_f values*	Yield (%)
1	9	2-Fluoroaniline	0.67	79
2	10	4-Trifluoromethoxylaniline	0.59	72
3	11	2-Bromoaniline	0.64	80
4	12	4-Bromoaniline	0.70	84
5	13	2,4-Dimethylaniline	0.65	78
6	14	2,6-Diethylaniline	0.69	79
7	15	4-Bromo-2-methylaniline	0.78	85
8	16	2-Chloro-4-methylaniline	0.72	81

* Solvent system: MeOH: Chloroform (2:8).

Scheme-2: Synthesis of deprotected amides (**9-16**).

The deprotection of the diol group was confirmed by ^{1}H-NMR and IR spectra which showed the disappearance of the ketal, resonance at 1.55 ppm and the presence of broad OH stretching bands in 3509 and 3411 cm^{-1} (**9-16**). In ^{13}C-NMR the disappearance of the quaternary carbon further supported the deprotection. EIMS and elemental analysis of these compounds, described in the experimental protocol further supported the structures of all the synthesized compounds.

Bioassay

All synthetic protected and deprotected amides (**1-16**) were screened for their *in vitro* antibacterial and antifungal potential against different strains of bacteria (*Enterobacter sp*, *Vibrio cholera* and *Klebsiella sp*) and fungi (*Fausarium solani*, *Helminthosporium sativum*, and *Aspergillus niger*). The results are listed in Table-1 and 2.

Antifungal Activity

All the compounds showed good activity against *Fusarium solani, Helminthosporium sativum* and *Aspergillus niger* at 100% concentration. Compounds **1**, (55%, 67%, 66%), **2** (71%, 77%, 77%), **3** (79%, 88%, 88%), **4** (79%, 56%, 75%), **5** (56%, 66%, 90%) and **8** (76%, 68%, 78%) displayed good zones of inhibition, respectively. However, as the concentration decrease to 80% and 60% these compounds showed a decline in activity. Compound **6** with diethyl substitution showed (71%, 79%, and 78%) inhibition at 100% concentration in all the three strains of fungi, respectively. When the concentration was decreased to 80% and 60%, a decrease in activity in all the compounds was also observed. The results reveal that the same type of inhibition is observed in the activity of compounds of **9-16**. Compound **11** with *ortho* bromo substitution was found to be the most active compound and showed inhibition 88%, 91%, 91%, at 100% concentration against all three strains. Compound **12** with *para* bromo substitution showed 83%, 64%, 89% activity at 100% concentration. Compounds **15** and **16** with *para* and *ortho* halogens showed inhibitions at 100% concentration (77%, 83%, 83%), (81%, 79%, 83%), respectively.

Antibacterial Activity

In addition, all the synthetic (**1-16**) were tested for their antibacterial activity and the results are collected in Table-2. All the compounds demonstrated good activity against all the three bacterial strains *i.e. Enterobacter sp, Vibrio cholera* and *Klebsiella sp.* at 100% concentration. The antibacterial activity of the compounds also decreases at 80% and 60% concentration, respectively. Compounds **3**, **4**, **7**, and **8** with halogen substituents at *ortho* and *para* position show significant activity (21, 17, 25, 21, for *Enterobacter sp*, 18, 25, 21, 21 for *Vibrio cholerae,* and 20, 19, 18, 20 mm zone of inhibition, for *Klebsiella sp,* respectively) against three bacterial strains at 100% concentration. However, the deprotected compounds **11**, **12**, **15**, **16**, (29, 19, 30, 29, for *Enterobacter sp*, 26, 29, 24, 29 for *Vibrio cholerae,* and 18, 31, 26, 22 mm zone of inhibition for *Klebsiella sp,* respectively) were found to be more active as compared to the protected amides.

Table-1: Antifungal activity of the protected **(1-8)** and deprotected amides (9-16) at three different concentrations against three fungal strains.

Compounds	*Fausarium solani*			*Helminthosporium sativum*			*Aspergillus niger*		
	100%	80%	60%	100%	80%	60%	100%	80%	60%
1, 9	**55, 68**	**22,58**	**23,33**	**67,80**	**44,33**	**22,45**	**66,79**	**33,67**	**23,60**
2, 10	**71, 79**	**66,49**	**23,46**	**77,81**	**44,42**	**11,33**	**77,80**	**33,42**	**23,34**
3, 11	**79, 88**	**69,78**	**22,43**	**88,91**	**26,44**	**22,33**	**88,91**	**33,32**	**33,44**
4, 12	**79, 83**	**44,54**	**43,50**	**56,64**	**22,20**	**44,36**	**75,89**	**37,43**	**31,42**
5, 13	**56, 69**	**28,56**	**35,34**	**66,77**	**42,54**	**27,32**	**90,93**	**63,75**	**33,55**
6, 14	**71, 82**	**33,30**	**19,31**	**79,88**	**18,42**	**26,55**	**78,81**	**40,56**	**32,44**
7, 15	**67, 77**	**55,51**	**33,42**	**66,83**	**51,57**	**30,25**	**77,83**	**25,50**	**43,65**
8, 16	**76, 81**	**32, 46**	**20,24**	**68,79**	**37,57**	**15,43**	**78,83**	**64,50**	**15,40**
Terbinafine	**94**	**94**	**94**	**98**	**98**	**98**	**98**	**98**	**98**

Table-2: Antibacterial activity of the protected (**1-8**) and deprotected amides (**9-16**) at three different concentrations against three bacterial strains.

Compound No.	*Enterobacter sp.*			*Vibrio cholerae*			*Klebsiella sp.*		
	100%	80%	60%	100%	80%	60%	100%	80%	60%
1, 9	**11,21**	**12,12**	**08,11**	**17,10**	**18,20**	**25,29**	**11,20**	**03,11**	**11,13**
2, 10	**17,19**	**15,18**	**13,19**	**18,29**	**12,15**	**11,12**	**18,20**	**13,16**	**11,12**
3, 11	**21,29**	**12,13**	**11,13**	**18,26**	**19,21**	**09,12**	**20,18**	**18,17**	**12,15**
4, 12	**17,19**	**14,17**	**14,13**	**25,29**	**11,13**	**08,11**	**19,31**	**14,17**	**11,16**
5, 13	**21,26**	**13,14**	**12,15**	**20,22**	**11,10**	**12,11**	**17,19**	**13,11**	**11,12**
6, 14	**21,24**	**12,19**	**13,15**	**28,30**	**12,15**	**11,12**	**23,27**	**19,22**	**14,16**
7, 15	**25,30**	**13,11**	**12,12**	**21,24**	**14,10**	**12,11**	**18,26**	**10,20**	**12,11**
8, 16	**21,29**	**17,19**	**16,19**	**21,29**	**11,16**	**10,13**	**20,22**	**15,19**	**06,11**
Chloramphenicol	**32**	**25**	**34**	**32**	**25**	**34**	**32**	**25**	**34**

[a]Zone diameter (Activity): Below 9 mm (no activity), 9-12 mm (non significant), 13-15 mm (low activity), 16-18 mm (good activity), above 18 mm (significant activity).

Antileshmanial Activity

Moreover, all the synthetic compounds (**1-16**) were tested for their anti-leishmanial activity using *Leishmania tropica* KHW23 promastigotes for *in vitro* screening. The results are shown in Table-3. Compounds **1**, **9**, **2**, **10**, **4**, **12**, **5**, and **13** showed good activity, however, the compounds **3**, **6**, and **8** exhibited moderate activity. The deprotected amides **11**, **14** and **16** showed good activity as compared to their protected analogs.

Table-3: % Inhibition of protected (**1-8**) and deprotected amides (**9-16**) against *L. tropica* KWH23.

Compound	*L. tropica* KWH23[a] (μg/mL± S.D.)
1, 9	**0.63 ± 0.01, 0.60 ± 0.02**
2, 10	**0.67 ± 0.09, 0.62 ± 0.09**
3, 11	**0.81 ± 0.16, 0.62 ± 0.16**
4, 12	**0.69 ± 0.27, 0.65 ± 0.27**
5, 13	**0.61 ± 0.09, 0.60 ± 0.09**
6, 14	**0.71 ± 0.15, 0.69 ± 0.16**
7, 15	**0.91 ± 0.26, 0.78 ± 0.27**
8, 16	**0.77 ± 0.13, 0.68 ± 0.11**
Amphotericin B	**0.59 ± 0.20**

[a]percentage inhibition activity: 100 = (non-significant; 0.95-0.80 = low; 0.79−0.70 = Moderate;
0.69−0.60 = Good; below 0.59-0.56 = Significant activity).

Conclusion

The deprotected amides were found more active against fungal and bacterial strains as compared to protected amides. The emerging resistance in bacteria, to currently available antibiotics is a serious threat to patients suffering from various bacterial diseases. There is need for new therapeutics to be evaluated as antibacterial agents. The protected and deprotected amides may serve as lead compounds for further research. In addition, all the protected and deprotected amides showed moderate to good activities against *Leishmania tropica* KWH23 promastigotes. The deprotected amides were found more active as compared to the protected amides. Drug resistance has been reported in various species of *Leishmania* against various antileishmanial drugs like antimonials, amphotericin B, pentamidine and miltifosine etc. In the current scenario these synthetic compounds may be further explored may prove to be good candidates against leshmaniasis.

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