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Synthesis of 7-carbethoxyamino-4-arylaminomethyl coumarins and their biological studies

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ABSTRACT

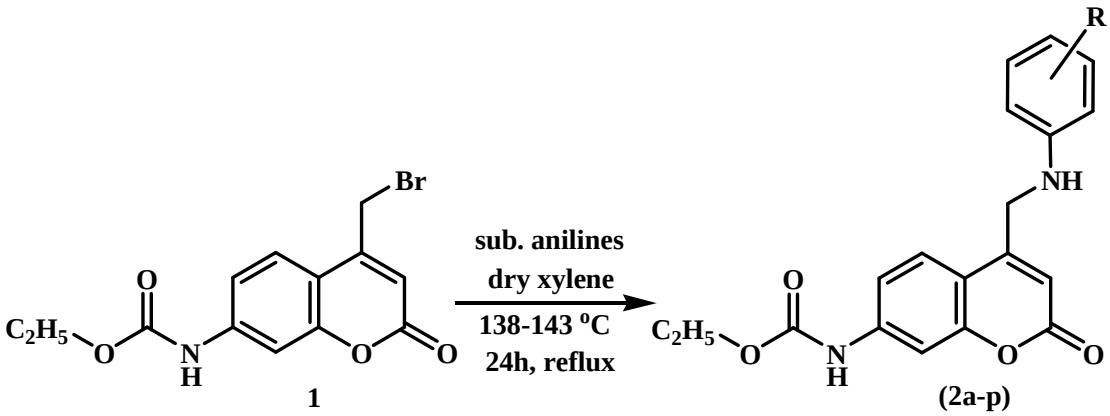
*As a part of our ongoing studies in developing new coumarin derivatives we describe the synthesis of novel 7-carbethoxyamino-4-(R) arylaminomethyl coumarins. The synthesized compounds were characterized by elemental, spectroscopic analysis (IR, Mass and NMR) and tested for their antibacterial and antifungal activity. The antimicrobial studies of the compounds (**2a-p**) showed significant activity against S. aureus and A. fumigatus. The compound (**2f**) was found to be more active against all the screened microbial.*

Keywords: coumarins, anti-microbial studies.

INTRODUCTION

The chemistry of heterocycles is known to overwhelm field of investigation in medicinal chemistry, since they have been found to reveal improved biological activity. Heterocyclic compounds display significant role in medicinal chemistry constituent to natural products as well as in materials chemistry. Among them, coumarin derivatives a class of oxygen heterocycles have received a solid attention in synthetic organic chemistry with countless significant and valuable applications in pharmaceutical industry. Coumarins are known as a large group of naturally occurring plant secondary metabolites mainly having a benzopyrene core emanated from the shikimic acid pathway. Their function in the plant tissues are far from clear, though suggestions include waste products, plant growth regulators, fungistats and bacteriostats[1].

Coumarins with a variety of pharmacophoric groups at C-3, C-4, and C-7 positions have been screened for various biological activities[2]. Among various coumarin derivatives, 7-substituted coumarins constitute an important group of compounds has resulted in their outstanding applications as fluorescent probes[3], in the study of biochemical mechanism (Cleo)and are widely used as emission layers in organic light-emitting diodes (OLED)[4], optical brighteners[5], and nonlinear optical chromophores[6]. 7-carbethoxyamino coumarin is also used as intermediate for the synthesis of bioactive compounds. Coumarins are known to possess many activities, such as, anti-microbial[7], anti-cancer[8], anti-inflammatory[9], anti-viral[10], anti-oxidant[11], anti-HIV[12], inhibitors[13], caged neurotransmitters[14], chemo sensors[15], biosensors[16], protein receptors[17]and Dye sensitized solar cell applications[18].



R = H, 4-F, 4-Cl, 4-CH_3, 4-OH, 4-OCH_3, 4-Br, 4-NO_2, 3-F, 3-Cl, 3-CH_3, 3-OH, 3-OCH_3, 3-NO_2, 2,4-CH_3, 2,5-Cl

SCHEME 1: Synthesis of compounds (2a-p)

MATERIALS AND METHODS

Melting points were determined in open capillaries and are uncorrected. The FT-IR spectra were recorded on Nicolet Impact 5200 USA FT-IR using KBr pellets. ^{1}H NMR spectra in DMSO-$d_6$solution were recorded on Bruker 300-MHz NMR spectrometer. The mass spectra were recorded on Shimadzu Japan QP2010 S model spectrometer and elemental analyses were carried out using Heraus CHN rapid analyzer. All the compounds gave satisfactory elemental analysis. 7-carbethoxyamino-4-bromomethyl coumarin was prepared by Pechman condensation using 3-carbethoxyamino phenol. The purity of the compounds was checked by thin layer chromatography (TLC) on silica gel plate.

General procedure for the preparation of 7-carbethoxyamino-4-[(R) arylaminomethyl] coumarins (2a-2p):
A mixture of substituted 7-carbethoxyamino-4-bromomethyl coumarin (**1**) (0.004 mol) and substituted anilines (0.004 mol) in super dry xylene (20 mL) was refluxed on an oil bath for 24 hr at 135-148 ^{o}C. After the completion of the reaction, the separated solid was filtered, washed with excess of cold ethanol, dried and crystallized from suitable solvent.

ethyl 4-((phenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2a**):colorless solid, Recrystallized from Ethanol, Yield (81 %), MP. 240-242^{o}C; IR (KBr, cm^{-1}): 1714 (lactom C=O), 1678 (amide C=O), 3422 (NH), 3281 (carbonyl NH); MS (m/z, 70 eV): 338;^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.26 (t, 3H, CH_3), 4.08 (s, 1H, NH), 4.28 (q, 2H, CH_2), 5.76 (s, 2H, CH_2), 6.32 (s, 1H, Ar-H), 6.77 (d, 2H, Ar-H), 7.23 (s, 1H, Ar-H), 7.36 (d, 2H, Ar-H), 7.54 (d, 1H, Ar-H), 7.65 (s, 1H, Ar-H), 7.97 (d, 1H, Ar-H), 10.28 (s, 1H, NH); Anal. Calcd $C_{19}H_{18}N_2O_4C$, 67.44; H, 5.36; N, 8.28 found C, 67.38; H, 5.31; N, 8.22.

ethyl 4-((4-fluorophenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2b**): colorless solid, Recrystallized from Ethanol+1,4-Dioxane, Yield (77%), MP. 256-258 ^{o}C; IR (KBr, cm^{-1}): 1702 (lactom C=O), 1671 (amide C=O), 3369 (NH), 3278 (carbonyl NH); MS (m/z, 70 eV): 356; ^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.29 (t, 3H, CH_3), 3.92 (s, 1H, NH), 4.68 (m, 2H, CH_2), 5.88 (s, 2H, CH_2), 6.42 (s, 1H, Ar-H), 6.73 (d, 2H, Ar-H), 7.31 (d, 2H, Ar-H), 7.59 (d, 1H, Ar-H), 7.70 (s, 1H, Ar-H), 7.95 (d, 1H, Ar-H), 10.32 (s, 1H, NH); Anal. Calcd $C_{19}H_{17}FN_2O_4C$, 64.04; H, 4.81; N, 7.86 found C, 63.94; H, 4.75; N, 7.81.

ethyl 4-((4-chlorophenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2c**): colorless solid, Recrystallized from Ethanol+1,4-Dioxane, Yield (88%), MP. 260-262 ^{o}C; IR (KBr, cm^{-1}): 1739 (lactom C=O), 1697 (amide C=O), 3438 (NH), 3280 (carbonyl NH); MS (m/z, 70 eV): 374 (m+1), 372; ^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.26 (t, 3H, CH_3), 4.10 (s, 1H, NH), 4.59 (q, 2H, CH_2), 5.79 (s, 2H, CH_2), 6.38 (s, 1H, Ar-H), 6.82 (d, 2H, Ar-H) ,7.28 (d, 2H, Ar-H), 7.47 (d, 1H, Ar-H), 7.67 (s, 1H, Ar-H), 7.89 (d, 1H, Ar-H), 10.27 (s, 1H, NH); Anal. Calcd $C_{19}H_{17}ClN_2O_4C$, 61.21; H, 4.60; N, 7.51 found C, 61.14; H, 4.54; N, 7.45.

ethyl 4-((p-toluidino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2d**): colorless solid, Yield (78%), MP. 224-226 ^{o}C; IR (KBr, cm^{-1}): 1735 (lactom C=O), 1694 (amide C=O), 3435 (NH), 3284 (carbonyl NH); MS (m/z, 70 eV): 352;^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.30 (t, 3H, CH_3), 2.21 (s, 3H, Ar-CH_3), 4.20 (q, 2H, CH_2), 5.14 (s, 1H, NH), 5.34 (s, 2H, CH_2), 6.41 (s, 1H, Ar-H), 6.67 (s, 1H, Ar-H), 6.79 (s, 1H, Ar-H), 7.45 (m, 2H, Ar-H), 7.62 (s, 1H, Ar-H), 7.79 (d, 2H, Ar-H), 10.21 (s, 1H, NH); Anal. Calcd $C_{20}H_{20}N_2O_4C$, 68.17; H, 5.72; N, 7.95 found C, 68.11; H, 5.65; N, 7.90.

ethyl 4-((4-hydroxyphenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2e**): colorless solid, Recrystallized from Ethanol, Yield (90 %), MP. 230-232 ^{o}C; IR (KBr, cm^{-1}): 1700 (lactom C=O), 1668 (amide C=O), 3394 (OH), 3363 (NH), 3265 (carbonyl NH); MS (m/z, 70 eV): 354;^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.25 (t, 3H, CH_3), 4.02 (s, 1H, NH), 4.57 (m, 2H, CH_2), 5.32 (s, 1H, O-H), 5.88 (s, 2H, CH_2), 6.39 (s, 1H, Ar-H), 6.76 (d, 2H, Ar-H) ,7.32 (d, 2H, Ar-H), 7.58 (d, 1H, Ar-H), 7.72 (s, 1H, Ar-H), 7.95 (d, 1H, Ar-H), 10.23 (s, 1H, NH); Anal. Calcd $C_{19}H_{18}N_2O_5$C, 64.40; H, 5.12; N, 7.91 found C, 64.33; H, 5.08; N, 7.85.

ethyl 4-((4-methoxyphenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2f**): pale yellow solid, Recrystallized from Ethanol+1,4-Dioxane, Yield (90 %), MP. 212-214 ^{o}C; IR (KBr, cm^{-1}): 1720 (lactom C=O), 1686 (amide C=O), 3338 (NH), 3283 (carbonyl NH); MS (m/z, 70 eV): 368;^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.31 (t, 3H, CH_3), 2.82 (s, 3H, Ar-OCH_3), 3.93 (s, 1H, NH), 4.60 (m, 2H, CH_2), 5.88 (s, 2H, CH_2), 6.41 (s, 1H, Ar-H), 6.78 (d, 2H, Ar-H), 7.33 (d, 2H, Ar-H), 7.59 (d, 1H, Ar-H), 7.71 (s, 1H, Ar-H), 7.78 (d, 1H, Ar-H), 10.72 (s, 1H, NH); Anal. Calcd $C_{20}H_{20}N_2O_5$C, 65.21; H, 5.47; N, 7.60 found C, 65.15; H, 5.41; N, 7.54.

ethyl 4-((4-bromophenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2g**): colorless solid, Recrystallized from Ethanol+1,4-Dioxane, Yield (84 %), MP. 220-222 ^{o}C; IR (KBr, cm^{-1}): 1702 (lactom C=O), 1676 (amide C=O), 3387 (NH), 3269 (carbonyl NH); MS (m/z, 70 eV): 418 (m+2), 416;^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.28 (t, 3H, CH_3), 4.08 (s, 1H, NH), 4.57 (q, 2H, CH_2-H), 5.86 (s, 2H, CH_2), 6.40 (s, 1H, Ar-H), 6.77 (d, 2H, Ar-H), 7.28 (d, 2H, Ar-H), 7.57 (d, 1H, Ar-H), 7.73 (s, 1H, Ar-H), 7.93 (d, 1H, Ar-H), 10.52 (s, 1H, NH); Anal. Calcd $C_{19}H_{17}BrN_2O_4$C, 54.69; H, 4.11; N, 6.71 found C, 54.62; H, 4.06; N, 6.66.

ethyl 4-((4-nitrophenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2h**): yellow color solid, Recrystallized from Ethanol+1,4-Dioxane, Yield (68 %), MP. 226-228 ^{o}C; IR (KBr, cm^{-1}): 1719 (lactom C=O), 1689 (amide C=O), 3392 (NH), 3288 (carbonyl NH); MS (m/z, 70 eV): 383;^{1}H NMR (DMSO-d_6 300MHz, δ ppm): 1.25 (t, 3H, CH_3), 3.98 (s, 1H, NH), 4.21 (q, 2H, CH_2), 5.66 (s, 2H, CH_2), 6.55 (s, 1H, Ar-H), 7.23-7.56 (m, 5H, Ar-H), 7.68 (s, 1H, Ar-H), 7.88 (d, 1H, Ar-H), 10.18 (s, 1H, NH); Anal. Calcd $C_{19}H_{17}N_3O_6$C, 59.53; H, 4.47; N, 10.96 found C, 59.45; H, 4.41; N, 10.92.

ethyl 4-((3-fluorophenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2i**): colorless solid, Recrystallized from Ethanol+1,4-Dioxane, Yield (77 %), MP. 238-240 ^{o}C; IR (KBr, cm^{-1}): 1716 (lactom C=O), 1691 (amide C=O), 3369 (NH), 3282 (carbonyl NH); MS (m/z, 70 eV): 356;^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.29 (t, 3H, CH_3), 3.86 (s, 1H, NH), 4.28 (q, 2H, CH_2), 5.83 (s, 2H, CH_2), 6.28 (s, 1H, Ar-H), 6.51-7.67 (m, 5H, Ar-H), 7.77 (s, 1H, Ar-H), 7.98 (d, 1H, Ar-H), 10.25 (s, 1H, NH); Anal. Calcd $C_{19}H_{17}FN_2O_4$C, 64.04; H, 4.81; N, 7.86 found C, 63.96; H, 4.77; N, 7.80.

ethyl 4-((3-chlorophenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2j**): colorless solid, Recrystallized from Ethanol+1,4-Dioxane, Yield (72 %), MP. 246-248 ^{o}C; IR (KBr, cm^{-1}): 1723 (lactom C=O), 1698 (amide C=O), 3381 (NH), 3271 (carbonyl NH); MS (m/z, 70 eV): 374 (m+1), 372;^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.27 (t, 3H, CH_3), 3.90 (s, 1H, NH), 4.22 (q, 2H, CH_2), 5.62 (s, 2H, CH_2), 6.25 (s, 1H, Ar-H), 6.62-7.56 (m, 5H, Ar-H), 7.72 (s, 1H, Ar-H), 8.02 (d, 1H, Ar-H), 10.19 (s, 1H, NH); Anal. Calcd $C_{19}H_{17}ClN_2O_4$C, 61.21; H, 4.60; N, 7.51 found C, 61.15; H, 4.53; N, 7.45.

ethyl 4-((m-toluidino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2k**): colorless solid, Recrystallized from Ethanol+1,4-Dioxane, Yield (66 %), MP. 204-206 ^{o}C; IR (KBr, cm^{-1}): 1718 (lactom C=O), 1691 (amide C=O), 3380 (NH), 3288 (carbonyl NH); MS (m/z, 70 eV): 352;^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.33 (t, 3H, CH_3), 2.21 (s, 3H, Ar-CH_3), 3.77 (s, 1H, NH), 4.32 (q, 2H, CH_2), 4.42 (s, 2H, CH_2), 6.28 (s, 1H, Ar-H), 6.56-7.41 (m, 5H, Ar-H), 7.75 (s, 1H, Ar-H), 7.88 (d, 1H, Ar-H), 10.13 (s, 1H, NH); Anal. Calcd $C_{20}H_{20}N_2O_4$C, 68.17; H, 5.72; N, 7.95 found C, 68.11; H, 5.65; N, 7.88.

ethyl 4-((3-hydroxyphenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2l**): colorless solid, Recrystallized from Ethanol, Yield (81 %), MP. 194-196 ^{o}C; IR (KBr, cm^{-1}): 1720 (lactom C=O), 1688 (amide C=O), 3416 (OH), 3375 (NH), 3258 (carbonyl NH); MS (m/z, 70 eV): 354;^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.29 (t, 3H, CH_3), 3.71 (s, 1H, NH), 4.27 (q, 2H, CH_2), 5.42 (s, 2H, CH_2), 5.76 (s, 1H, OH), 6.44 (s, 1H, Ar-H), 6.52-7.44 (m, 6H, Ar-H), 7.96 (d, 1H, Ar-H), 10.12 (s, 1H, NH); Anal. Calcd $C_{19}H_{18}N_2O_5$C, 64.40; H, 5.12; N, 7.91 found C, 64.33; H, 5.08; N, 7.85.

ethyl 4-((3-methoxyphenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2m**): colorless solid, Recrystallized from Ethanol+1,4-Dioxane, Yield (84 %), MP. 186-188 ^{o}C; IR (KBr, cm^{-1}): 1709 (lactom C=O), 1686 (amide C=O), 3356 (NH), 3262 (carbonyl NH); MS (m/z, 70 eV): 368;^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.33 (s, 3H, CH_3), 2.81 (s, 3H, OCH_3), 3.93 (s, 1H, NH), 4.33 (q, 2H, CH_2), 4.68 (s, 2H, CH_2), 6.45 (s, 1H, Ar-H),

6.68-7.62 (m, 5H, Ar-H), 7.65 (s, 1H, Ar-H), 7.96 (d, 1H, Ar-H), 10.13 (s, 1H, NH); Anal. Calcd $C_{20}H_{20}N_2O_5C$, 65.21; H, 5.47; N, 7.60 found C, 65.16; H, 5.40; N, 7.53.

ethyl 4-((3-nitrophenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2n**): yellow color solid, Recrystallized from Ethanol+1,4-Dioxane, Yield (58 %), MP. 214-216 ^oC; IR (KBr, cm^{-1}): 1719 (lactom C=O), 1694 (amide C=O), 3368 (NH), 3274 (carbonyl NH); MS (m/z, 70 eV): 383;^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.20 (t, 3H, CH_3), 3.89 (s, 1H, NH), 4.27 (m, 2H, CH_2), 5.82 (s, 2H, CH_2), 6.51 (s, 1H, Ar-H), 7.86-7.48 (m, 6H, Ar-H), 7.82 (d, 1H, Ar-H), 10.18 (s, 1H, NH); Anal. Calcd $C_{19}H_{17}N_3O_6C$, 59.53; H, 4.47; N, 10.96 found C, 59.45; H, 4.41; N, 10.92.

ethyl 4-((2,4-dimethylphenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2o**): colorless solid, Recrystallized from Ethanol+1,4-Dioxane, Yield (74 %), MP. 226-228 ^oC; IR (KBr, cm^{-1}): 1712 (lactom C=O), 1683 (amide C=O), 3350 (NH), 3276 (carbonyl NH); MS (m/z, 70 eV): 366;^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.30 (t, 3H, CH_3), 2.28 (t, 3H, CH_3), 2.53 (s, 3H, CH_3), 4.21 (q, 2H, CH_2), 4.94 (s, 1H, NH), 5.48 (s, 2H, CH_2), 6.50 (s, 1H, Ar-H), 7.47-7.55 (m, 3H, Ar-H),7.63-7.69 (m, 2H, Ar-H), 7.83 (d, 1H, Ar-H), 10.22 (s, 1H, NH); Anal. Calcd $C_{21}H_{22}N_2O_4C$, 68.84; H, 6.05; N, 7.65 found C, 68.77; H, 5.97; N, 7.58.

ethyl 4-((2,5-dichlorophenylamino)methyl)-2-oxo-2*H*-chromen-7-ylcarbamate (**2p**): colorless solid, Recrystallized from Ethanol+1,4-Dioxane, Yield (68 %), MP. 234-236^oC; IR (KBr, cm^{-1}): 1725 (lactom C=O), 1691 (amide C=O), 3342 (NH), 3293 (carbonyl NH); MS (m/z, 70 eV): 408 (m+1), 406;^{1}H NMR (DMSO-d_6 300MHz, δppm): 1.23 (t, 3H, CH_3), 3.88 (s, 1H, NH), 4.59 (q, 2H, CH_2), 5.79 (s, 2H, CH_2), 6.36 (s, 1H, Ar-H), 6.73 (d, 1H, Ar-H), 7.24 (d, 2H, Ar-H), 7.56 (d, 1H, Ar-H), 7.69 (s, 1H, Ar-H), 8.37 (d, 1H, Ar-H), 10.45 (s, 1H, NH); Anal. Calcd$C_{19}H_{16}Cl_2N_2O_4C$, 56.04; H, 3.96; N, 6.88 found C, 55.96; H, 3.91; N, 6.82.

RESULTS AND DISCUSSION

Synthesis of7-carbethoxyamino-4-bromomethyl coumarin was brought about by the Pechman cyclization[19]of 3-carbethoxyamino phenol with 4-bromoethylacetoacetate[20]. The substituted 7-carbethoxyamino-4-(*R*) arylaminomethylcoumarins (**2a-p**) were synthesized (**Scheme 1**) by refluxing the reaction mixture of substituted anilines and 7-carbethoxyamino-4-bromomethyl coumarin(1) in dry xylene at 135-148ºC.

The title compounds further confirmed by IR, ^{1}H NMR, Mass spectral and elemental analyses. The FT-IR spectrum of compound(**2c**)in KBr showed theamide absorption bands at 3438 cm^{-1}, 3280 cm^{-1} and the carbonyl stretching frequencies at 1739 cm^{-1}, 1697 cm^{-1} respectively.

The ^{1}H NMR spectra analysis of compound (**2o**) a triplet was observed at 1.30 ppm due to methyl protons of carbethoxy group. Two singlets were observed at 2.28 ppm, 2.63 ppm due to methylprotons of aniline ring. The methylene protons were observed at 4.20 ppm, 5.48 ppm as a quartet & singlet, respectively. A singlet at 4.94 ppm was observed due to NH proton. The C3-H of coumarin observed as singlet at 6.50 ppm. Two multiplets at 7.47-7.55ppm for three protons, 7.63-7.69ppm for two protons were observed for aromatic protons of aniline and coumarin rings. A doublet at 7.83 ppm observed due to C8 proton of coumarin.

All this evidence plus molecular ion peaks at their respective molecular masses and micro-analytical data strongly support the structure of compounds (**2a-p**).

1. Antimicrobial activity

The newly synthesized compounds (**2a-p**) were screened via broth microdilution methodfor their antibacterial and antifungal activity at different concentrations of 100, 50, 25, 12.5, 6.25, 3.125, 1.6, 0.8, 0.4 and 0.2 µg/mL. The MIC values for the *in vitro* antibacterial studies of the compounds (**2a-p**) and the standard are represented in **Table 1**by serial dilution method [21].

3.1 Antibacterial activity

Antibacterial activity was carried out against three Gram positive bacteria, namely, *Staphylococcus aureus*, *Enterococcus faecalis*, and *Streptococcus mutans*, and three Gram-negative bacteria, namely, *Escherichia coli*, *Klebsiella pneumonia*, and *Pseudomonas aeruginosa*. Ciprofloxacin was used as a standard.

The antibacterial screening data showed that most of the compounds exhibited good bacterial inhibition. The compound (**2f**) (4-OCH_3) was very high active at MIC of 0.2 µg/mL& the compounds (**2d**) (4-CH_3), (**2e**) (4OH), (**2h**) (4-NO_2), (**2k**) (3-CH_3), (**2l**) (3-OH), (**2o**) (2,4-CH_3)were active at MIC of 0.4 µg/mL against *S. aureus* bacteria. The compound (**2f**) (4-OCH_3)was very high active at MIC of 0.2 µg/mL & the compound (**2m**) (3-OCH_3) active at

MIC of 0.4 µg/mL against *E. faecalis* bacteria. The compounds(**2b**) (4-F), (**2f**) (4-OCH_3)were very high active at MIC of 0.2 µg/mL & the compounds (**2e**) (4OH), (**2m**) (3-OCH_3) active at MIC of 0.4 µg/mL against *E. coli* bacteria. The compounds (**2b**) (4-F), (**2e**) (4OH), (**2f**) (4-OCH_3)were very high active at MIC of 0.2 µg/mL & the compounds (**2c**) (4-Cl), (**2g**) (4-Br), (**2m**) (3-OCH_3) active at MIC of 0.4 µg/mL against *S. mutans* bacteria. The compounds (**2b**) (4-F), (**2f**) (4-OCH_3) were very highly active at MIC of 0.2 µg/mL against *P. aeruginia* bacteria. It is to be noted that most of these compounds inactive against *K. pneumonia*.

3.2 Antifungal activity results

Antifungal activity of compounds was carried out against two fungi, namely, *Candida albicans* and *Aspergillus fumigatus*. Fluconazole was used as a standard. The compound (**2b**) (4-F), (**2c**) (4-Cl), (**2f**) (4-OCH_3), (**2g**) (4-Br) were very high active at MIC of 0.2 µg/mL & the compounds (**2d**) (4-CH_3), (**2e**) (4OH), (**2m**) (3-OCH_3) were active at MIC of 0.4 µg/mL against *C. albicans* fungi. The compounds (**2f**) (4-OCH_3), (**2h**) (4-NO_2) were very high active at MIC of 0.2 µg/mL & the compounds (**2b**) (4-F), (**2c**) (4-Cl), (**2d**) (4-CH_3), (**2e**) (4OH), (**2g**) (4-Br) were active at MIC of 0.4 µg/mL against *A. fumigatus* fungi.

TABLE 1: Results of antimicrobial activities of the synthesized compounds (2a-p)

Compounds		Gram-positive			Gram-negative			Fungi	
No	***R***	***S. aureus***	***E. faecalis***	***S. mutans***	***E. coli***	***K. pneumonia***	***P.aeruginia***	***C. albicans***	***A. fumigatus***
2a	H	0.8	1.6	3.12	6.25	100	6.25	12.5	0.8
2b	4-F	0.6	0.8	0.2	0.2	50	1.6	0.2	0.4
2c	4-Cl	0.6	0.8	0.4	0.8	50	3.12	0.2	0.4
2d	4-CH_3	0.4	3.12	1.6	0.8	100	6.25	0.4	0.4
2e	4-OH	0.4	0.8	0.2	0.4	100	6.25	0.4	0.4
2f	4-OCH_3	0.2	0.2	0.2	0.2	25	1.6	0.2	0.2
2g	4-Br	0.6	3.12	0.4	0.2	50	6.25	0.2	0.4
2h	4-NO_2	0.4	6.25	6.25	3.12	100	50	1.6	0.2
2i	3-F	0.6	3.12	3.12	3.12	100	100	0.8	0.8
2j	3-Cl	0.8	3.12	50	50	100	100	0.8	0.8
2k	3-CH_3	0.4	50	100	100	100	>100	1.6	0.8
2l	3-OH	0.4	0.8	50	100	100	50	3.12	0.8
2m	3-OCH_3	0.6	0.4	0.4	100	50	25	0.4	0.8
2n	3-NO_2	0.6	1.6	3.12	-	-	100	6.25	0.8
2o	2,4-CH_3	0.4	50	>100	100	-	100	50	3.12
2p	2,5-Cl	0.6	50	50	-	100	100	>100	6.25
Ciprofloxacin		2	2	2	1	1	4	-	-
Fluconazole		-	-	-	-	-	-	16	8

CONCLUSION

In conclusion, the tested 7-carbethoxyamino coumarin derivatives (**2a-p**) were exhibited better bacterial activity against *Staphylococcus aureus* than standard *Ciprofloxacin* and better fungal activity *A. Fumigatus* than the standard *Fluconazole*. Amongst, all the compounds (**2f**) showed better activity against all bacterial & fungal strains.

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