BAOJ Microbiology

Shipra B, BAOJ Microbiology 2019, 5: 2
5: 045

Research

Synthesis, Characterization and Antimicrobial Activity of Some New Pyrimidine-5-Carboxylate Derivatives

Shipra Baluja[1*], Sumitra Chanda[2], Swati Oza[1] and Paras Ramavat[1]

[1]Department of Chemistry, Saurashtra University, Rajkot-360005 (Gujarat), India.

[2]Department of Biosciences Saurashtra University, Rajkot-360005 (Gujarat), India.

Abstract

Pyrimidine-5-carboxylate derivatives possess a broad spectrum of pharmacological action. A series of pyrimidine-5-carboxylate derivatives were synthesized and were characterized by IR, 1H NMR and mass spectroscopy. All these synthesized compounds were tested for in vitro antimicrobial against four Gram positive bacteria, four Gram negative bacteria and four fungal strains in DMF and DMSO. Further, some molecular lipophilicity and drug likeness score of synthesized compounds were also evaluated.

Keywords: Pyrimidine-5-carboxylate derivatives; Gram positive bacteria; Gram negative bacteria;

Introduction

The consequence of continued exposure to antibacterial environment is an enrichment of bacteria that are intrinsically resistant to antimicrobials or have acquired resistance mechanism to these substances [1]. In the family of heterocyclic compounds nitrogen containing heterocycles are an important class of compounds in the medicinal chemistry and also contributed to the society from biological and industrial point which helps to understand life processes [2] The pyrimidines represent one of the most active classes of compounds possessing wide spectrum of biological activities like significant in vitro activity against unrelated DNA and RNA, viruses including polioherpes viruses, diuretic, antitumour, anti-HIV, and cardiovascular [3]. Literature survey shows that large array of pyrimidine-5-carboxylate derivatives possess a variety of pharmacological properties, such anticancer [4], antifungal [5], analgesic [6], anti-tubercular [7], central nervous activities [8], antihypertensive [9], antimicrobial [10], antimalerial [11], anti HIV [12], etc. In the present work, some new pyrimidine-5-carboxylate derivatives were synthesized from aldehyde, urea and methyl isobutryl acetate. The characterization of synthesized compounds was done by IR, NMR and mass spectral analysis. The antimicrobial activity of the synthesized compounds was done against some pathogenic Gram positive and Gram negative bacteria and fungi in N, N-dimethyl formamide (DMF) and Dimethyl sulfoxide (DMSO). Molecular lipophilicity and drug likeness scores of synthesized compounds were also evaluated.

Material And Methods

Experimental

Material

Different substituted benzaldehydes, isobutyl propionate, urea and phenacyl bromide used for the synthesis, was supplied from Spectrochem Pvt. Ltd. (Mumbai, India) and was used without any treatment. The methanol and acetone used were of AR grade supplied by Spectrochem Pvt. Ltd. (Mumbai, India).

Synthesis

Synthesis of dihydropyrimidine-5-carboxylate derivatives

A methanolic solution of different substituted aldehyde (0.01mol),

***Corresponding Author:** Shipra Baluja, Department of Chemistry, Saurashtra University, Rajkot-360005 (Gujarat), India, Email: shipra_baluja@rediffmail.com

Sub Date: June 18th, 2019, **Acc Date:** June 19th, 2019, **Pub Date:** June 21st, 2019

Citation: Shipra B, Sumitra C, Swati O, Paras R (2019) Synthesis, Characterization and Antimicrobial Activity of Some New Pyrimidine-5-Carboxylate Derivatives. BAOJ Microbiology 5: 045.

isobutyl propionate (0.01mol) and urea (0.012mol) was refluxed for 16 hrs in presence of copper chloride and concentrated sulphuric acid. The completion of reaction was confirmed by analytical thin layer chromatography (TLC) (Performed on aluminum coated plates Gel 60F254 (E. Merck)) using (3:2-Hexane: Ethyl acetate) as mobile phase. After completion of reaction, the reaction mass was cooled and the resulting solid was filtered, washed with methanol to remove unreacted reagents and dried under vacuum to give crude product.

Oxidation ofdihydropyrimidine-5-carboxylate derivatives

10 ml nitric acid (60%) was stirred at 00C for 10 min. and then above synthesized compound (0.01mol) was added fractionally to the chilled nitric acid. The mixture was then stirred at 00C temperature for 30 min. The progress of reaction was monitored by thin layer chromatography. The reaction mixture was then poured into cold water and was neutralized with saturated sodium bicarbonate solution. The solid was filtered, washed with water and dried. The crude product was directly used for the next step.

Synthesis of Methyl 4-Isopropyl-2-(2-Oxo-2-Phenylethoxy)-6-Phenylpyrimidine-5-Carboxylate-5-Carboxylate Derivatives

1Equimolar solution of above product and phenacyl bromide in dry acetone was refluxed in presence of dry K_2CO_3 for 1hr. The solvent from the reaction mixture was evaporated to get solid mass. This solid mass was poured into crushed ice to remove K_2CO_3. The solution was filtered. The resulting solid product was washed with cold water and dried under vacuum.The structure confirmation of these crystallized compounds was done by FTIR, ^{1}H NMR and mss spectral data. IR spectra were recorded on IR affinity 1S (furrier transport infra-red spectroscopy), ^{1}H NMR spectra were taken on a Bruker AVANCE II 400. In all the cases, ^{1}H NMR spectra were obtained in DMSO-d6 using TMS as an internal standard. The NMR signals are reported in δppm. Mass spectra were determined using direct inlet probe on a GCMS-QP-2010 mass spectrometer. The reaction scheme is given in Figure 1. Figures 2 to 4 show IR, ^{1}H NMR and mass spectra of RPD-1 compound respectively. The melting points of compounds were measured by Differential Scanning Calorimeter (DSC) (Model-Shimadzu-DSC-60).

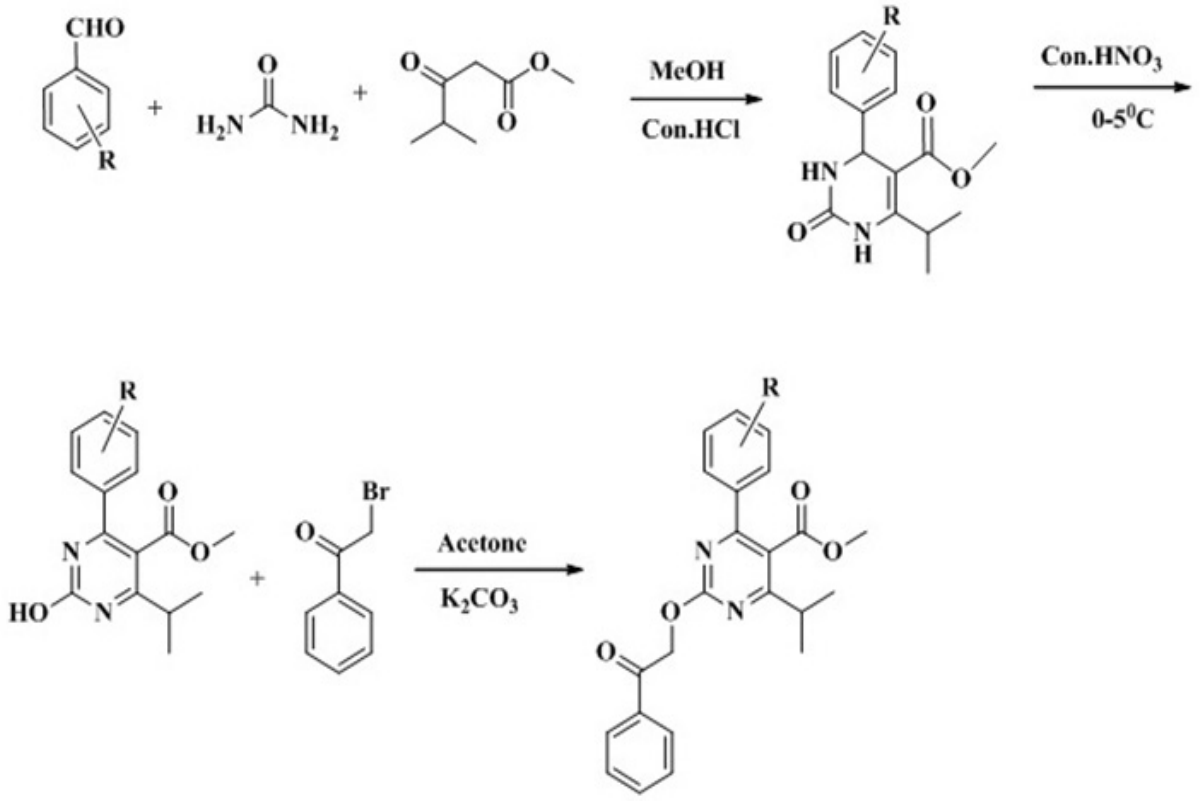

Figure 1: Reaction Scheme

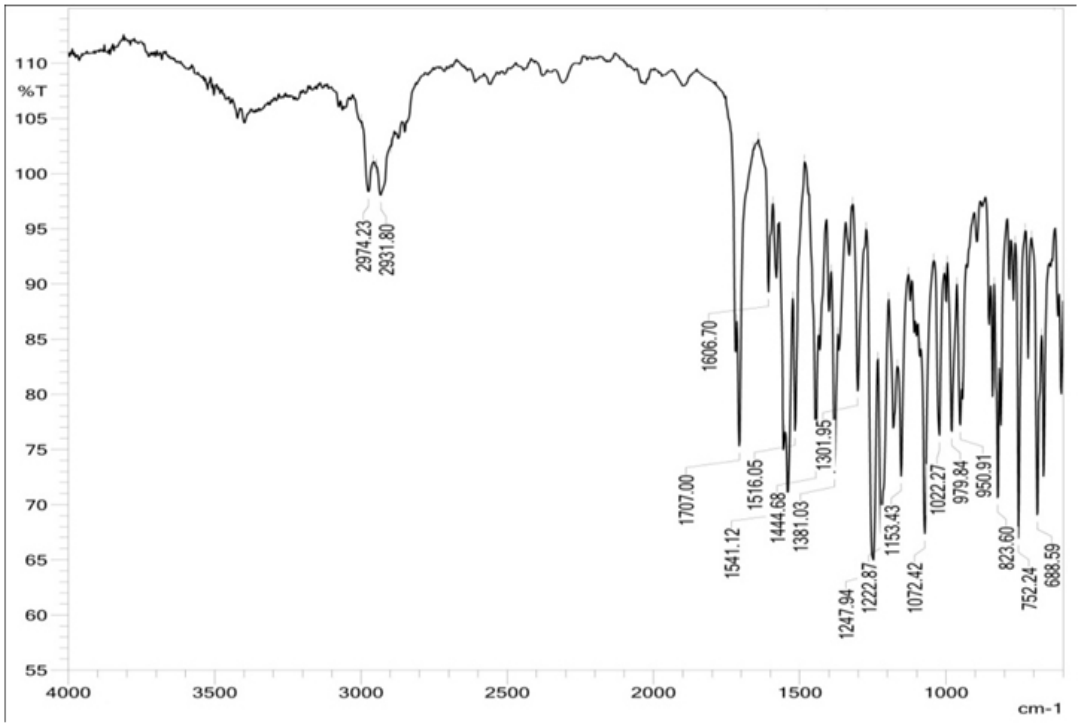

Figure 2: IR spectrum of compound RPD-1

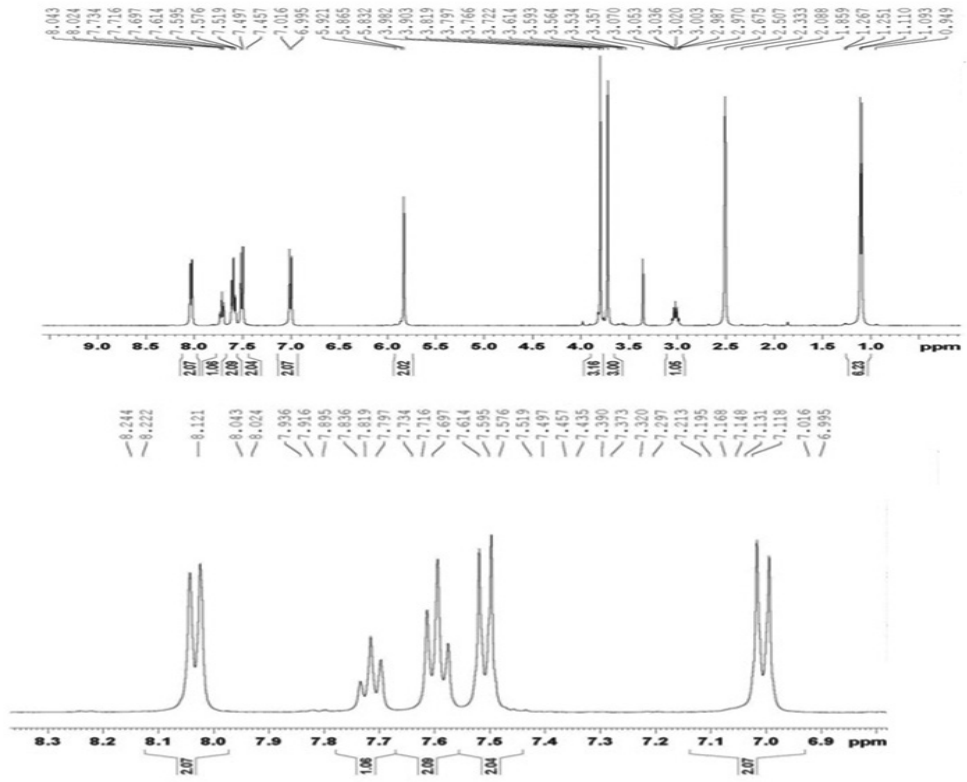

Figure 3: ^{1}H NMR spectrum of compound RPD-1

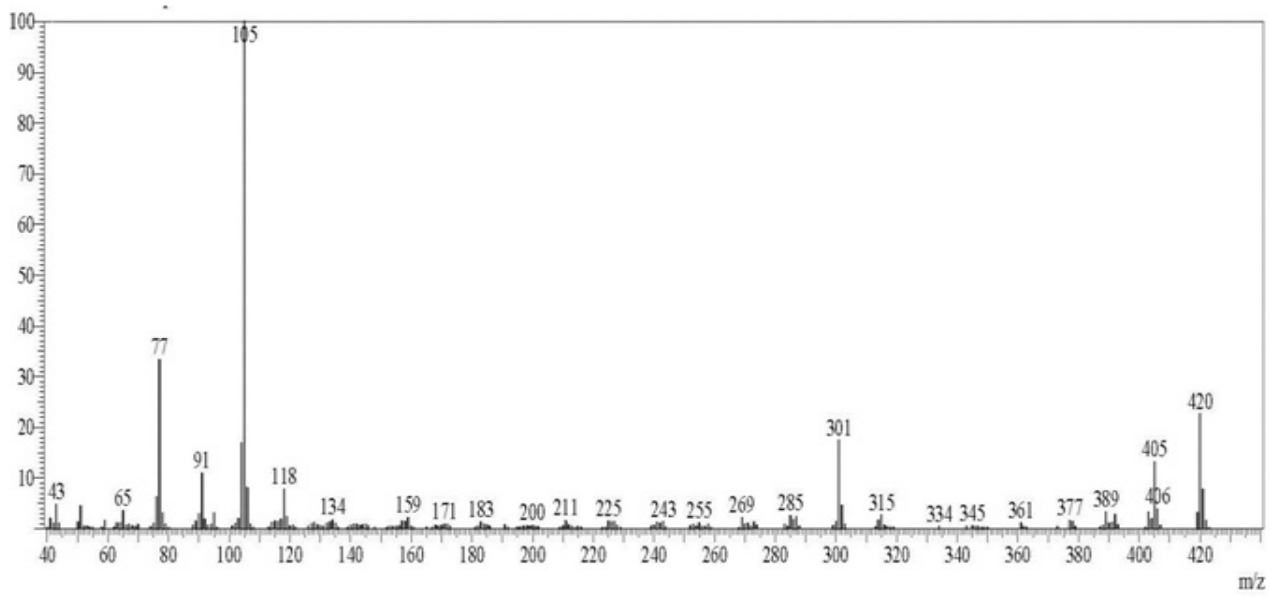

Figure 4: Mass spectrum of compound RPD-1

Microorganisms Tested

The studied microorganisms were obtained from National Chemical Laboratory (NCL), Pune, India. The microorganisms were maintained at 4°C. The Gram positive bacteria studied were *Staphylococcus aureus* ATCC29737 (SA), *Corynebacteriumrubrum* ATCC14898 (CR), *Listeria monocytogenes* ATCC19112 (LM), *Bacilluscereus* ATCC11778 (BC); Gram negative bacteria were *Pseudomonasaeruginosa* ATCC27853(PA), Escherichia coli NCIM2931 (EC), *KlebsiellapneumoniaeNCIM2719* (KP), *Salmonella typhimurium* ATCC23564 (ST) and fungal strains were Candida albicans ATCC2091 (CA), *Cryptococcusneo formans* NCIM3542 (CN), *Candida glabrata*NCIM3448 (CG) and *Candida epicola* NCIM3367 (CE).The microorganisms studied are clinically important ones causing several infections and food spoilage. In vitro antimicrobial activity of the pyrimidine-5-carboxylate derivatives were studied against these pathogenic microbial strains by the agar well diffusion method [13].

Results and Discussion

Table 1 shows the physical constant of synthesized compounds. The spectral data of all the compounds are given below

Table 1: The physical constants of all the synthesized compounds

Compound Code	*Substitution R*	*Molecular Formula.*	*Molecular weight (g)*	*Yield (%)*	*M.P. ^0C*
RPD-1	4-OCH_3	$C_{24}H_{24}N_2O_5$	420	85	102
RPD-2	-4-CH_3	$C_{24}H_{24}N_2O_4$	404	83	103
RPD-3	-H	$C_{23}H_{22}N_2O_4$	390	80	109
RPD-4	3-Cl	$C_{23}H_{21}ClN_2O_4$	424	86	109
RPD-5	-2,5-di-OCH_3	$C_{25}H_{26}N_2O_6$	450	84	163
RPD-6	-4-F	$C_{23}H_{21}FN_2O_4$	408	86	118
RPD-7	-4-Br	$C_{23}H_{21}BrN_2O_4$	469	85	112
RPD-8	-3,4-di-OCH_3	$C_{25}H_{26}N_2O_6$	450	87	115
RPD-9	-3-OCH_3	$C_{24}H_{24}N_2O_5$	420	82	97
RPD-10	-4-Cl	$C_{23}H_{21}ClN_2O_4$	424	84	101

*2:3 - Hexane:Ethyl acetate

RPD-1

IR (cm^{-1}): 1708.00 (carbonyl str. in -$COOCH_3$), 1606.76 (Acyclic carbonyl str.), 1550.82 (Ar-C=C str.), 1384.94 (alkane C-H bending), 1300 (C-O str. of ester), 1026.16 (C-O str. of ether), 840.99 (p-di substituted aromatic ring), ***^{1}H NMR (DMSO-d_6)*** δ(***ppm***) :1.251 (6H, doublet, -CH_3 of isopropyl), 3.020 (1H, multiplet, C-H of isopropyl), 3.534 (3H, singlet, -$COOCH_3$), 3.819 (1H, singlet, -OCH_3), 5.865 (2H, singlet, -OCH_2), 7.016 (2H, doublet, Ar-CH), 7.519 (2H, doublet, Ar-CH),7.595 (2H, triplet, Ar-CH),7.734 (1H, triplet, Ar-CH) and 8.043 (2H, doublet, Ar-CH), **MS**: (***m/z***) = 420.

RPD-2

*IR (**cm^{-1}**):* 1726.35 (carbonyl str. in -$COOCH_3$), 1695.49 (Acyclic carbonyl str.), 1531.53 (Ar-C=C str.), 1369.50 (alkane C-H bending), 1327.07 (C-O str. of ester), 1082.10 (C-O str. of ether), 821.70 (p-di substituted aromatic ring), ***^{1}H NMR (DMSO-d_6) δ(ppm)*** : 1.214 (6H, doublet, -CH_3 of isopropyl), 2.333 (3H,singlet,-CH3), 3.054 (1H, multiplet, C-H of isopropyl), 3.547 (3H, singlet, -$COOCH_3$), 5.852 (2H, singlet, -OCH_2), 7.268 (3H, singlet, Ar-CH), 7.520 (2H, doublet of doublet, Ar-CH), 7.698 (2H, doublet of doublet, Ar-CH), 8.055 (2H, singlet, Ar-CH), ***MS: (m/z)*** = 404.

RPD-3

IR (cm-1): 1725.30 (carbonyl str. in -$COOCH_3$), 1680.84 (Acyclic carbonyl str.), 1549.86 (Ar-C=C str.), 1380.25 (alkane C-H bending), 1330.38 (C-O str. of ester), 1025.88 (C-O str. of ether), ***^{1}H NMR (DMSO-d_6) δ(ppm)*** : 1.234 (6H, doublet, -CH_3 of isopropyl), 3.023 (1H, multiplet, C-H of isopropyl), 3.530 (3H, singlet, -$COOCH_3$), 5.852 (2H, singlet, -OCH2), 7.481 (1H, multiplet, Ar-CH), 7.585 (5H, multiplet, Ar-CH), 7.803 (2H, doublet, Ar-CH), 7.946 (2H, doublet, ***MS: (m/z)*** = 390.

RPD-4

IR (cm^{-1}): 1730.21 (carbonyl str. in COOCH3), 1670.00 (Acyclic carbonyl str.), 1554.68 (Ar-C=C str.), 1383.01 (alkane C-H bending), 1334.78 (C-O str. of ester), 1082.10 (C-O str. of ether), 721.40 and 792.77 (m-di-substituted aromatic ring), ***^{1}H NMR (DMSO-d_6) δ(ppm) :*** 1.144 (6H, doublet, -CH_3 of isopropyl), 3.108 (1H, multiplet, C-H of isopropyl), 3.713 (3H, singlet, -COOCH3), 5.981 (2H, singlet, -OCH_2), 7.560 (7H, multiplet, Ar-CH), 8.071 (2H, singlet, Ar-CH), ***MS: (m/z)*** = 424.

RPD-5

IR (cm^{-1}): 1728.28(carbonyl str. in COOCH3), 1703.20(Acyclic carbonyl str.), 1554.68 (Ar-C=C str.), 1390.72 (alkane C-H bending), 1307.78 (C-O str. of ester), 1031.95 (C-O str. of ether), ***^{1}H NMR (DMSO-d_6) δ(ppm)*** : 1.260 (6H, doublet, -CH_3 of isopropyl), 3.025 (1H, multiplet, C-H of isopropyl), 3.545 (3H, singlet, -$COOCH_3$), 3.828 (6H, singlet, -OCH_3), 5.885 (2H, singlet, -OCH_2), 7.089 (1H, singlet, Ar-CH), 7.135 (^{1}H, doublet, Ar-CH), 7.283 (1H, doublet, Ar-CH), 7.564 (^{3}H, multiplet, Ar-CH), 8.056 (2H, doublet, Ar-CH), ***MS: (m/z)*** = 450.

RPD-6

IR (cm^{-1}): 1722.43 (carbonyl str. in COOCH3), 1695.43 (Acyclic carbonyl str.), 1598.99 (Ar-C=C str.), 1390.68 (alkane C-H bending), 1334.78 (C-O str. of ester), 1066.64 (C-O str. of ether), 850.61 (p-di substituted aromatic ring), ***^{1}H NMR (DMSO-d6) δ(ppm) :***1.250 (6H, doublet, -CH3 of isopropyl), 3.12 (^{1}H, multiplet, C-H of isopropyl), 3.715 (^{3}H, singlet, -$COOCH_3$), 5.983 (2H, singlet, -OCH_2), 7.017 (2H, doublet, Ar-CH), 7.520 (2H, doublet, Ar-CH), 7.600 (2H, triplet, Ar-CH),7.744 (1H, triplet, Ar-CH) and 8.043 (2H, doublet, Ar-CH), ***MS: (m/z)*** = 408.

RPD-7

IR (cm-^{1}): 1722.43 (carbonyl str. in COOCH3), 1695.43 (Acyclic carbonyl str.), 1546.91 (Ar-C=C str.), 1390.68 (alkane C-H bending), 1334.74 (C-O str. of ester), 1066.64 (C-O str. of ether), 850.61 (p-di substituted aromatic ring), ***^{1}H NMR (DMSO-d6) δ(ppm)*** :1.258 (6H, doublet, -CH_3 of isopropyl), 3.129 (1H, multiplet, C-H of isopropyl), 3.716 (^{3}H, singlet, -$COOCH_3$), 5.985 (^{2}H, singlet, -OCH_2), 7.019 (2H, doublet, Ar-CH), 7.528 (2H, doublet, Ar-CH),7.609 (2H, triplet, Ar-CH),7.746 (1H, triplet, Ar-CH) and 8.048 (2H, doublet, Ar-CH), ***MS: (m/z)*** = 469.

RPD-8

IR (cm^{-1}): 1722.43 (carbonyl str. in COOCH3), 1695.43 (Acyclic carbonyl str.), 1546.91 (Ar-C=C str.), 1390.68 (alkane C-H bending), 1334.74 (C-O str. of ester), 1008.77 (C-O str. of ether).

^{1}H NMR (DMSO-d6) δ(ppm) : 1.261 (^{6}H, doublet, -CH3 of isopropyl), 3.026 (^{1}H, multiplet, C-H of isopropyl), 3.546 (^{3}H, singlet, -COOCH3), 3.827 (^{6}H, singlet, -OCH_3), 5.885 (^{2}H, singlet, -OCH_2), 7.014 (1H, doublet, Ar-CH), 7.115 (1H, doublet, Ar-CH), 7.214 (1H, singlet, Ar-CH), 7.598 (^{2}H, triplet, Ar-CH), 7.740 (1H, triplet, Ar-CH), 8.040 (2H, doublet, Ar-CH). ***MS: (m/z)*** = 450.

RPD-9

IR (cm^{-1}): 1750.00 (carbonyl str. in -$COOCH_3$), 1541.12 (Acyclic carbonyl str.), 1446.61 (Ar-C=C str.), 1365.60 (alkane C-H bending),

1284.59 (C-O str. of ester), 1026.16 (C-O str. of ether), 840.99 (p-di substituted aromatic ring). 792.77 (m-di-substituted aromatic ring), ***^{1}H NMR (DMSO-d_6) δ(ppm)*** :1.260 (^{6}H, doublet, -CH_3 of isopropyl), 3.024 (^{1}H, multiplet, C-H of isopropyl), 3.536 (^{3}H, singlet, -$COOCH_3$), 3.820 (1H, singlet, -OCH_3), 5.861 (2H, singlet, -OCH_2), 7.570 (7H, multiplet, Ar-CH) and 8.062 (2H, doublet, Ar-CH), ***MS: (m/z)*** = 420.

RPD-10

IR (cm^{-1}): 1730.21 (carbonyl str. in $COOCH_3$), 1670.00 (Acyclic carbonyl str.), 1554.68 (Ar-C=C str.), 1383.01 (alkane C-H bending), 1334.78 (C-O str. of ester), 1082.10(C-O str. of ether), 721.40 and 792.77 (m-di-substituted aromatic ring), ***^{1}H NMR (DMSO-d_6) δ(ppm) :***1.255 (6H, doublet, -CH3 of isopropyl), 3.125 (1H, multiplet, C-H of isopropyl), 3.715 (3H, singlet, -$COOCH_3$), 5.984 (2H, singlet, -OCH_2), 7.018 (^{2}H, doublet, Ar-CH), 7.524 (^{2}H, doublet, Ar-CH),7.608 (^{2}H, triplet, Ar-CH),7.745 (^{1}H, triplet, Ar-CH) and 8.047 (^{2}H, doublet, Ar-CH), ***MS: (m/z)*** = 424.

Antimicrobial Activity

Figure 5 shows the zone of inhibition for the studied compounds against Gram positive bacteria in DMF and DMSO. Against BC, all the four selected Gram positive bacteria, RPD-5 exhibited inhibition. Against BC, maximum inhibition is observed by RPD-10 and minimum for RPD-8. RPD-4 and RPD-5 exhibited intermediate inhibition. Rest of the compounds had no effect on this bacterial strain. Against SA, only RPD-5 exhibited inhibition. For CR, again RPD-10 showed maximum inhibition which is followed by RPD-3 and RPD-5. Rest of the compounds could not inhibit CR. Only RPD-2, RPD-3, RPD-5, RPD-7 and RPD-9 exhibited inhibition against LM. Thus, comparison of inhibition by studied compounds against these four selected bacterial strains suggests that in DMF, LM is most susceptible strain whereas SA is most resistant. Figure 5[B] shows that in DMSO, against BC RPD-3, RPD-4, RPD-5, RPD-8 and RPD-9 exhibit inhibition. For SA only RPD-2, RPD-5, RPD-7 and RPD-8 showed inhibition. Only RPD-6 and RPD-9 could inhibit CR whereas there is no effect of studied compounds on LM. Thus, in DMSO, CM is most resistant and BC is most susceptible bacteria.

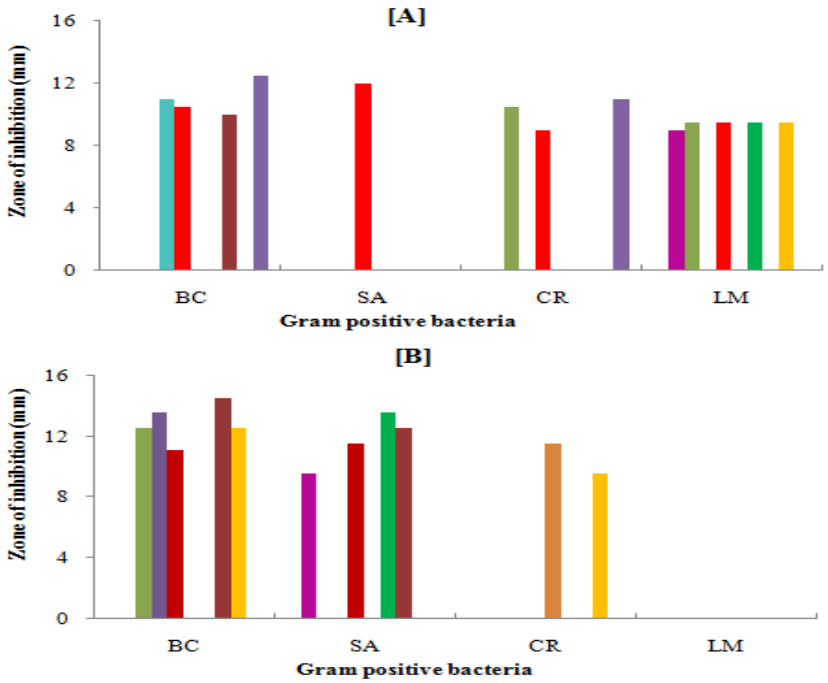

Figure 5: Antimicrobial activity of RPD-1 to RPD-10 against Gram positive bacteria in [A] DMF and [B] DMSO. RPD-1, (▪); RPD-2, (▪); RPD-3, (▪); RPD-4, (▪); RPD-5, (▪); RPD-6, (▪); RPD-7, (▪); RPD-8, (▪); RPD-9, (▪); RPD-10, (▪)

Comparison of Figure 5[A] and Figure 5[B] shows that inhibition is higher in DMF than that in DMSO. Thus, inhibition depends on solvent, bacterial strain and structure of compound. For the studied compounds, DMF is found to be better solvent against selected Gram positive bacterial strains. In all the studied compound, central moiety is same but different substitutions. Table 1 shows that RPD-5 contains 2, 5-di-OCH3 group which is found to effective against all the four Gram positive bacteria. RPD-10 contains 4-chloro group which causes maximum inhibition against BC and CR. SA is inhibited by only RPD-5 containing 2, 5-di-OCH3 group. For CR, hydrogen (as in RPD-3) and 2, 5-di- OCH3 (as in RPD-5) groups are also effective. Against LM 4-CH3 (as in RPD-2), H (as in RPD-3), 4-Br (as in RPD-7) and 3-OCH3 (as in RPD-9) are found to effective. In DMSO, the compound RPD-8 containing 3,4-di-OCH3 showed maximum inhibition against BC whereas against SA, 4-Br group present in RPD-7 is most effective. The 4-F group present in RPD-6 and 3-OCH3 (present in RPD-9) causes inhibition in CR whereas LM is not affected at all by any of the compounds. This finding also suggests that the position of group also plays an important role in inhibition of strains in different solvents.

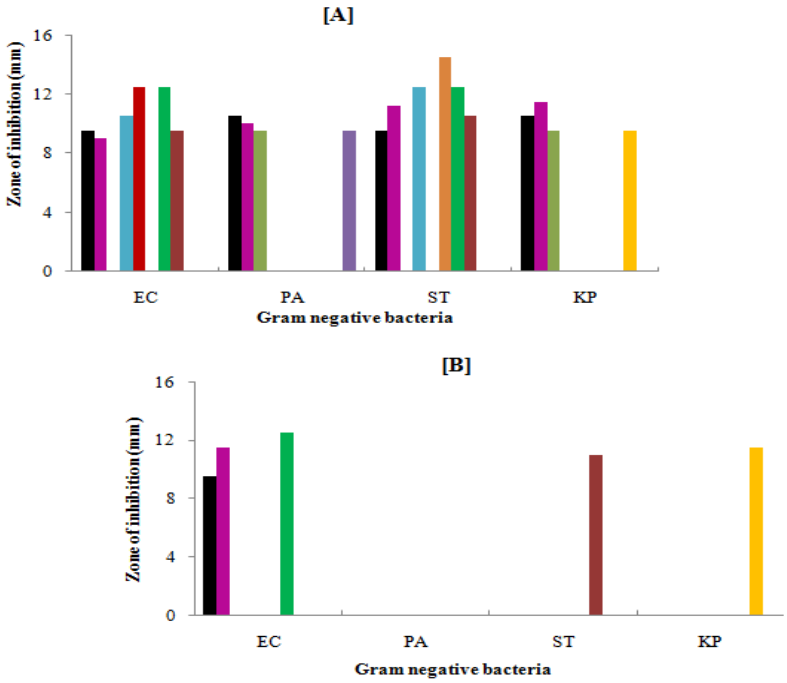

Figure 6: Antimicrobial activity of RPD-1 to RPD-10 against Gram negative bacteria in [A] DMF and [B] DMSO. RPD-1, (▪); RPD-2, (▪); RPD-3, (▪); RPD-4, (▪); RPD-5, (▪); RPD-6, (▪); RPD-7, (▪); RPD-8, (▪); RPD-9, (▪); RPD-10, (▪)

Figure 6 shows the zone of inhibition for the studied compounds against Gram negative bacteria in DMF and DMSO. It is evident from Figure 6 [A] that in DMF, RPD-1 and RPD-2 having 4-OCH3 and 4-CH3 groups respectively are more effective against all gram negative bacteria. ECis inhibited by RPD-1, RPD-2, RPD-4, RPD-5, RPD-7 and RPD-8 while PA is inhibited by RPD-1, RPD-2, RPD-3 and RPD-10. ST is inhibited by some of the compounds and maximum inhibition is shown by RPD-6 whereas KP is inhibited by RPD-1, RPD-2, RPD-3 and RPD-9. In, DMSO, EC is inhibited by RPD-1, RPD-2 and RPD-7 and maximum for RPD-7 having -4-Br group. PA is most resistant bacteria. ST is inhibited by only RPD-8 having -3, 4-di- OCH3 group similarly KP is inhibited by only RPD-9 having 3-OCH3 group.Thus, DMF is good solvent for the studied compounds against these Gram negative bacteria.

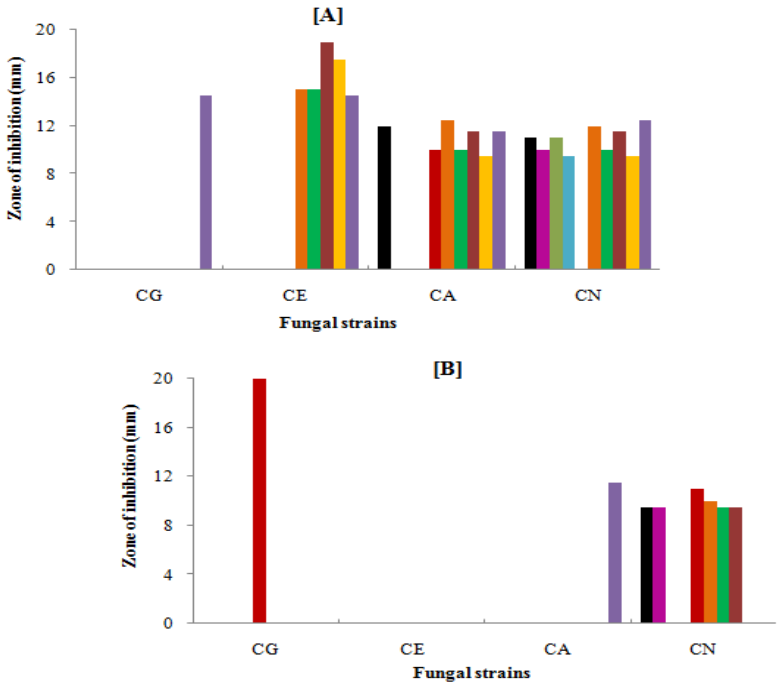

Figure 7: Antimicrobial activity of RPD-1 to RPD-10 against fungal strains in [A] DMF and [B] DMSO. RPD-1, (▪); RPD-2, (▪); RPD-3, (▪); RPD-4, (▪); RPD-5, (▪); RPD-6, (▪); RPD-7, (▪); RPD-8, (▪); RPD-9, (▪); RPD-10, (▪)

Figure 7 shows the zone of inhibition for the studied compounds against fungal strains in DMF and DMSO. It is evident from Figure 7 that RPD-10 having -4-Cl group shows better activity against all four fungal strains. Against CG, only RPD-10 is effective. CE is inhibited by RPD-6, RPD-7, RPD-8 and RPD-9 while CA is inhibited by RPD-1, RPD-5, RPD-6, RPD-7, RPD-8 and RPD-9. In DMSO, CG is inhibited by only RPD-5. CE is most resistant fungal strain. CA is inhibited by only RPD-10 and CN is inhibited by RPD-1, RPD-2, RPD-5, RPD-6, RPD-7 and RPD-8. CN is most powerful fungal strain which is inhibited by all the compounds except RPD-5 having -2, 5-OCH3 group. SO, again DMF is better solvent than DMSO against fungal strains.

Prediction of Molecular Descriptors and Bioactivity Score

Mol inspiration software was used for calculation of molecular properties such as lipophilicity (Log P), total polar surface area, number of hydrogen bond doners and acceptors, number of atoms, number of rotatable bonds etc. Further, prediction of bioactivity score for drug targets such as G-protein coupled receptor (GPCR) ligands, kinase inhibitors, ion channel modulators, enzymes and nuclear receptors etc.To determine drug likeness of compounds, Lipinski's rule [14] is applied. It is a thumb rule of five to determine if a compound has properties that would make it likely to be drug. Lipinski's rule states that absorption or permeation of a molecule is more likely when the molecular mass less than 500 daltons, the octanol-water partition coefficient (log P) is not greater than 5 and the molecule has not more than 5 hydrogen bond donors (nitrogen or oxygen atoms with one or more hydrogen atoms) and not more than 10 hydrogen bond acceptors (nitrogen or oxygen atoms). Further, the probability of organic molecules to be drug like can also be predicted by their bioactivity score [15]. If the bioactivity score is greater than zero, compound is active, if score is in the range 0.0 to -5.0 then compound is moderately active but less than -5.0 score suggests inactive compound.

Drug Likeness Calculation Based on Lipinski Rule

The molecular properties and bioactivity score of all synthesized compound calculated by mol inspiration software are given in Tables 2 and 3 respectively.

All the synthesized compounds RPD-1 to RPD-10 obeyed Lipinski's rule except RPD-4, RPD-7 and RPD-10. These compounds showed good permeability across cell membrane as miLog values were found below 5 except RPD-4, RPD-7 and RPD-10. TPSA of these compounds were found in the range of 78.39-96.86. Molecular weights of all the compounds were found to be less than 500. Number of hydrogen bond donors and hydrogen bond acceptors are 0 and <9 respectively for all the compounds. n violations is zero and one suggesting thereby that these compounds can be easily binded to receptor.

Table 2: Drug likeness score for compounds

Comp. Code	miLogP	TPSA	nAtoms	nON	nOHNH	n violation	N rotb.	volume
RPD-1	4.52	87.63	31	7	0	0	9	383.34
RPD-2	4.92	78.39	30	6	0	0	8	374.36
RPD-3	4.47	78.39	29	6	0	0	8	357.80
RPD-4	5.12	78.39	30	6	0	1	8	371.33
RPD-5	4.51	96.86	33	8	0	0	10	408.89
PDR-6	4.63	78.39	30	6	0	0	8	362.73
RPD-7	5.28	78.39	30	6	0	1	8	375.68
RPD-8	4.11	96.86	33	8	0	0	10	408.89
RPD-9	4.50	87.63	31	7	0	0	9	383.34
RPD-10	5.14	78.39	30	6	0	1	8	371.33

Table 3: Bioactivity score of the compounds

Comp. Code	GPCR ligand	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease Inhibitor	Enzyme inhibitor
RPD-1	-0.07	-0.07	-0.13	-0.19	-0.33	0.02
RPD-2	-0.08	-0.09	-0.14	-0.22	-0.36	0.00
RPD-3	-0.05	-0.03	-0.11	-0.20	-0.32	0.05
RPD-4	-0.05	-0.04	-0.12	-0.19	-0.36	0.02
RPD-5	-0.07	-0.09	-0.12	-0.17	-0.34	0.02
RPD-6	-0.04	-0.04	-0.08	-0.18	-0.33	0.03
RPD-7	-0.13	-0.09	-0.14	-0.29	-0.41	-0.02
RPD-8	-0.08	-0.07	-0.09	-0.21	-0.34	0.02
RPD-9	-0.07	-0.07	-0.10	-0.19	-0.34	0.03
RPD-10	-0.05	-0.03	-0.12	-0.21	-0.34	0.02

Table 3 shows that all the parameters i.e., GPCR ligand, ion channel modulator, kinase inhibitor, nuclear receptor ligand, protease inhibitor, enzyme inhibitor are in the range (0.05 to -0.41). This suggests that the synthesized compounds are moderately bioactive.

Conclusion

It is concluded that LM is most resistant Gram positive bacteria. PA is most resistant Gram negative bacteria while CE and CA are most resistant fungal strains in DMSO. For studied antimicrobial activity, DMF is found to be good solvent. Inhibition depends on solvent, structure and strain. Further, position of different groups also affects inhibition. All these compounds are moderately bioactive as GPCR ligand, ion channel modulator, kinase inhibitor, nuclear receptor ligand, protease inhibitor, enzyme inhibitor.

Acknowledgments

Authors are thankful to Heads of Chemistry and Biosciences Department for providing for providing necessary facilities to carry out this work.

References

1. Lerner SA (1998) Clinical impact of antibiotic resistance, Advances in Experimental Medicine and Biology 456: 71-98.

2. Garcia-Valverde M, Torroba T (2005) Special issue: sulfur-nitrogen heterocycles, Molecules, 10(2): 318-320.

3. Kappe CO (1993) 100 years of the biginellidihydropyrimidine synthesis, Tetrahedron 49(32): 6937-6963.

4. Amr AG, Mohamed AM, Mohamed SF, Abdel-Hafez NA, Hammam Ael-F (2006) Anticancer activities of some newly synthesized pyridine, pyrane, and pyrimidine-5-carboxylate derivatives, Bioorg. Med. Chem 14(16): 5481-5488.

5. Mai A, Rotili D, Massa S, Brosch G, Simonetti G (2007) Discovery of uracil-based histone deacetylase inhibitors able to reduce acquired antifungal resistance and trailing growth in Candida albicans, Bioorg. Med. Chem. Lett 17(5): 1221-1225.

6. Chaudhary A, Sharma PK, Verma P, Kumar N, Dudhe R (2012) Microwave assisted synthesis of novel pyrimidine-5-carboxylate derivatives and investigation of their analgesic and ulcerogenic activity, Med. Chem. Res 21(11): 3629-3645.

7. Shao H, Shi S, Foley DW, Lam F, Abbas AY, et al (2013). Synthesis, structure-activity relationship and biological evaluation of 2,4,5-trisubstituted pyrimidine-5-carboxylate CDK inhibitors as potential anti-tumour agents, Eur. J. Med. Chem 70: 447-55.

8. Gillespie RJ, Bamford SJ, Clay A, Gaur S, Haymes T, et al (2009). Antagonists of the human A(2A) receptor. Part 6: Further optimization of pyrimidine-5-carboxylate-4-carboxamides, Bioorg. Med. Chem 17 (18): 6590-6605.

9. Sekiya T, Hiranuma H, Hata S, Mizogami S, Hanazuka M (1983) Pyrimidine-5-carboxylate derivatives. 4.' Synthesis and antihypertensive activity of 4-amino-2-(4-cinnamoylpiperazino)-6,7-dimethoxyquinazoline derivatives, J. Med. Chem 26(3): 411-416.

10. Mallikarjunaswamy C, Bhadregowda DG, Malleshan L (2013) Synthesis and antimicrobial activity of pyrimidine-5-carboxylate salts with chloranilic and picric acids, J. Chemi 2013: 727182.

11. Sirichaiwat C, Intaraudom C, Kamchonwongpaisan S, Vanichtanankul J, Thebtaranonth Y (2004) Target guided synthesis of 5-benzyl-2,4-diamonopyrimidine-5-carboxylates: Their antimalarial activities and binding affinities to wild type and mutant dihydrofolate reductases from plasmodium falciparum, J. Med. Chem 47(2): 345-354.

12. Liu LJ, Hong JH (2009) Synthesis and anti-HIV activity of 4'-modified cyclopentenyl pyrimidine-5-carboxylate C-nucleosides, Nucleosides, Nucleotides & Nucleic acids, 28(4): 303-314.

13. Negi BS, Dave BP (2010) In vitro antimicrobial activity of acacia catechu and its phytochemical analysis, Indian J Microbiol 50(4): 369-374.

14. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ (2001) Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings, Adv Drug Deliv Rev 46(1-3): 3-26.

15. Valasani KR, Vangavaragu JR, Day VW, Yan SS (2014) Structure based design, synthesis, pharmacophore modeling, virtual screening, and molecular docking studies for identification of novel cyclophilin d inhibitors, J Chem Inf Model 54(3): 902-912.