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Discovery of New Imidazolinones Derivatives as Potential Microbial Agents

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ABSTRACT: A series of imidazolinone were prepared by heating the hippuric acid in presence of acetic anhydride and sodium acetate with different aromatic aldehydes gave 5-oxazolone derivatives which reacting with *N*-amino-2,3,4,5,6-pentafluoro benzamide in pyridine gave imidazolinone. All the synthesized compounds have been characterized on the basis of elemental analysis, IR, ^{1}H-NMR and ^{13}C-NMR spectral data. All the synthesized compounds have been screened against four different bacterial strains *S. aureus, S. paratyphi-A, E. coli* and *B. subtilis* and fungal strain *F. molaniforme* and *A. niger*. Some of the compound was endowed with a remarkable antibacterial as well as antifungal activity.

KEYWORDS: Imidazolinone; Oxazolone; Antibacterial; Antifungal

Introduction

The synthesis of heterocyclic compounds has always drawn the attention of chemists over the years mainly because of their important biological properties. Imidazolinone have been reported to possess different biological activities such as antimicrobial[1-4], anticancer[5] and antitumor[6]. In present claim, imidazolinone have been synthesized by codensation of *N*-amino-2, 3,4,5,6-pentafluoro benzidine with 2-phenyl-4-arylidene-5-oxazolones (Azalactones). These azlactone derivatives are prepared by well known Erlenmeyer condensation of hippuric acid with different aromatic aldehydes in presence of sodium acetate and acetic anhydride[7]. The structures of the various synthesized compounds were assigned on the basis of elemental analyses, IR, ^{1}H NMR and ^{13}CNMR spectral data. These compounds were also screened for antibacterial and antifungal activity. During this study, we observed that several compounds displayed promising antibacterial and antifungal activity. This article showed the biological significance of some of the most important imidazolinone derivatives.

Result and Discussion

Chemistry

The synthesis of imidazolinone was performed by the following steps shown in Scheme-1. In the initial step, oxazolone derivatives **4-23** were synthesized from the condensation of hippuric acid and different substituted aromatic aldehydes in the presence of sodium acetate and acetic anhydride solution. Compounds **24-43** were prepared from the reaction between oxazolone derivative and 2,3,4,5,6-pentafluoro benzohydrazide (which was prepared from esterification of pentafluoro benzoic acid and further ester react with hydrazine hydrate to get the benzamide). The purity of the compounds was determined by TLC and elemental analysis. Spectral data (IR, ^{1}H NMR & ^{13}CNMR) of all the newly synthesized compounds were in full agreement with the proposed structures. (Scheme-1 & 2)

The synthesized compounds **4-23** were confirmed by IR and NMR spectra. A typical sharp characteristic absorption band for -C=O were observed at ν_{max} 1696. The band of -C=N of oxazolone derivatives clearly appeared at 1632 cm^{-1}. In ^{1}H NMR, a singlet at δ 7.55 attributed to the -CH- protons while in the ^{13}C NMR spectra, the high δ value at 164.5 ppm attributed to the carbonyl group present in oxazolone. Another carbon value of –CH- group present in the structure observed at 113.0 ppm. The structures of compounds **24-43** were also established by IR and NMR spectra. In IR spectra of **24-43**, -C=O group of amide and imidazolinone derivatives observed at 1682 and 1672 cm^{-1} respectively and 1631 cm^{-1} band of -C=N- group present in the imidazolinone. A signal found in ^{1}H NMR at δ 7.55 for –CH of group present in the structure and also singlet at 13.45 for –NH- group; In ^{13}C NMR spectra, amidic carbon of -C=O- group observed at δ 164.2 and signal at δ 163.8 attributed to carbon of imidazolinone derivatives.

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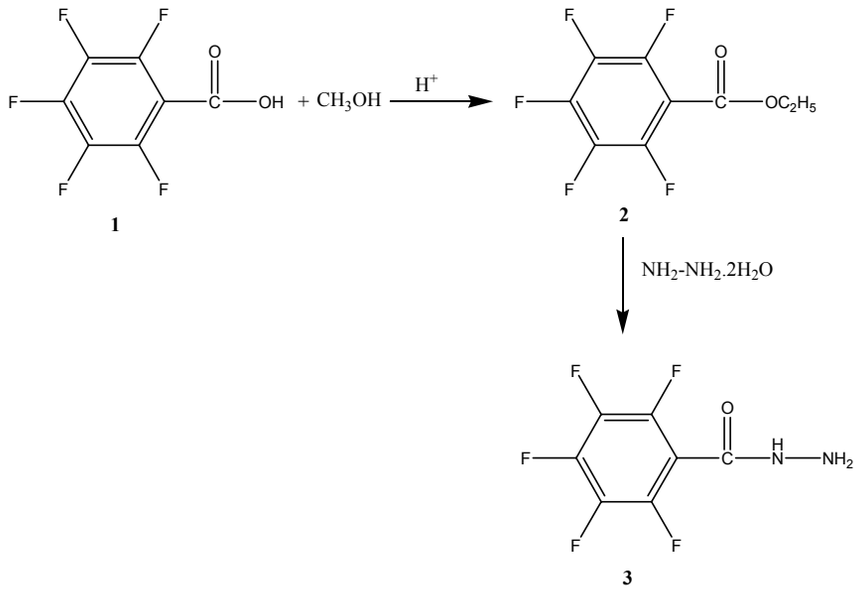
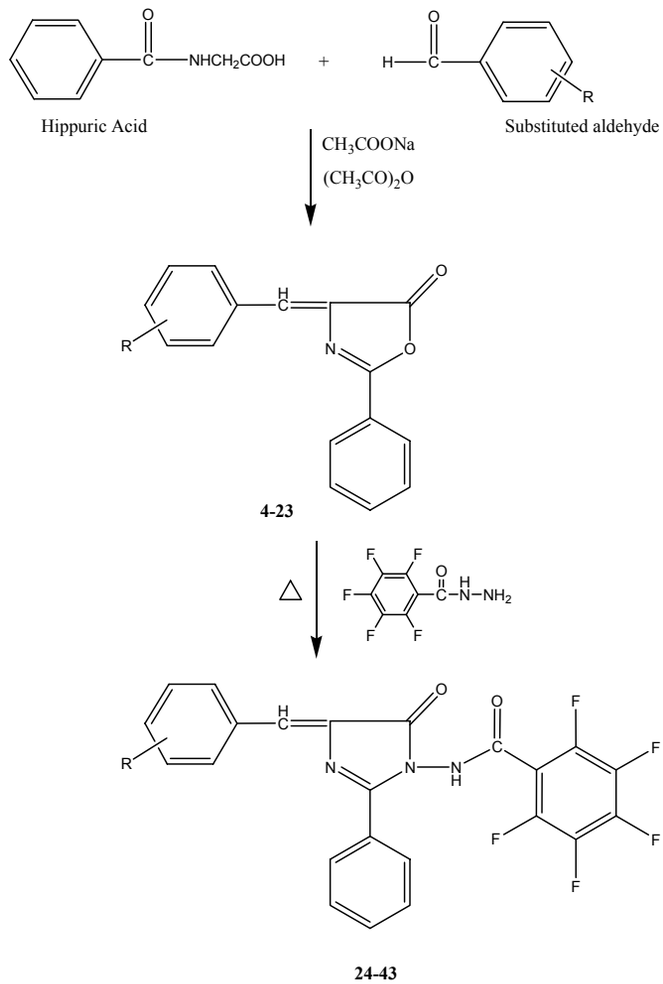


Scheme 1



Scheme 2

On the basis of the above spectral data, it was confirmed that compounds **4-23** and **24-43** have been synthesized. (Table-1-4)

Antimicrobial activity

All the synthesized compounds have been screened against four different bacterial strains *S. aureus, S. paratyphi-A, E. coli* and *B. subtilis* and fungal strain are *F. molaniforme* and *A. niger*. (Table-5)

Table 1 Characterization data of compounds 24-43

Compd.	R	M.P (°C)	Yield (%)	Crystalization solvent	Mol. Formula	Found (Calcd) %	
						C	N
24	-H	190-191	70.21	Ethanol	$C_{23}H_{12}F_5N_3O_2$	60.31 60.41	9.12 9.18
25	2-Cl	127-128	78.35	Ethanol	$C_{23}H_{11}ClF_5N_3O_2$	56.08 56.17	8.51 8.54
26	3-Cl	200-201	87.21	Ethanol	$C_{23}H_{11}ClF_5N_3O_2$	56.09 56.17	8.53 8.54
27	4-Cl	201-202	45.25	Ethanol	$C_{23}H_{11}ClF_5N_3O_2$	56.08 56.17	8.52 8.54
28	4-F	155-156	53.21	Ethanol	$C_{23}H_{11}F_6N_3O_2$	58.10 58.11	8.80 8.84
29	3-Br	183-184	55.65	Ethanol	$C_{23}H_{11}BrF_5N_3O_2$	51.48 51.51	7.80 7.83
30	2,3-Cl	89-90	45.36	Ethanol	$C_{23}H_{10}Cl_2F_5N_3O_2$	52.44 52.49	7.93 7.98
31	2-NO_2	211-212	77.34	Ethanol	$C_{23}H_{11}F_5N_4O_4$	54.85 54.99	11.10 11.15
32	4-NO_2	233-234	71.34	Ethanol	$C_{23}H_{11}F_5N_4O_4$	54.86 54.99	11.11 11.15
33	4-OCH_3	229-230	68.21	Ethanol	$C_{24}H_{14}F_5N_3O_3$	59.10 59.14	8.60 8.62
34	3,4- OCH_3	186-187	55.32	Ethanol	$C_{25}H_{16}F_5N_3O_4$	57.99 58.03	8.09 8.12
35	3,4,5-OCH_3	135-136	45.32	Ethanol	$C_{26}H_{18}F_8N_3O_5$	56.89 57.04	7.65 7.67
36	3-O-Ph	171-172	71.52	Ethanol	$C_{29}H_{16}F_5N_3O_3$	63.41 63.39	7.66 7.64
37	4-OC_2H_5	232-233	74.65	Ethanol	$C_{25}H_{16}F_5N_3O_3$	59.84 59.88	8.36 8.38
38	2,5- OC_2H_5	225-226	53.64	Ethanol	$C_{27}H_{20}F_5N_3O_4$	59.44 59.45	7.72 7.70
39	4- OH-3-OCH_3	121-122	79.89	Ethanol	$C_{24}H_{14}F_5N_3O_4$	57.30 57.26	8.32 8.34
40	3-Br-4-OH, 5-OCH_3	220-221	65.24	Ethanol	$C_{24}H_{13}BrF_5N_3O_4$	49.44 49.50	7.18 7.21
41	4-N-$(CH_3)_2$	114-115	75.46	Ethanol	$C_{25}H_{17}F_5N_4O_2$	59.88 60.00	11.14 11.19
42	2-pyridyl	196-197	65.87	Ethanol	$C_{22}H_{11}F_5N_4O_2$	57.66 57.56	12.21 12.22
43	3-furfuryl	195-196	75.68	Ethanol	$C_{21}H_{10}F_5N_3O_3$	56.33 56.38	9.34 9.39

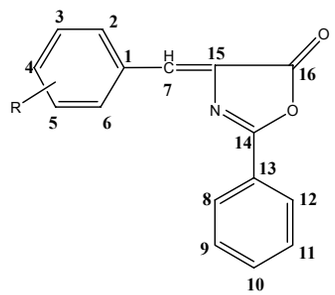
Table 2 IR Spectral data of 4-23 and 24-43

Compd.	IR Spectral data
4	1696 (C=O of Azalctones), 1632 (C=N), 1613 (C=C), 1347 (C-N)
5	1694 (C=O of Azalctones), 1629 (C=N), 1617 (C=C), 1342 (C-N), 770 (C-Cl)
6	1689 (C=O of Azalctones), 1637 (C=N), 1612 (C=C), 1348 (C-N), 778 (C-Cl)
7	1690 (C=O of Azalctones), 1635 (C=N), 1615 (C=C), 1347 (C-N), 773 (C-Cl)
8	1696 (C=O of Azalctones), 1630 (C=N), 1617 (C=C), 1345 (C-N), 954 (C-F)
9	1692 (C=O of Azalctones), 1628 (C=N), 1619 (C=C), 1347 (C-N), 622 (C-Br)
10	1691 (C=O of Azalctones), 1634 (C=N), 1615 (C=C), 1345 (C-N), 775 (C-Cl)
11	1693 (C=O of Azalctones), 1631 (C=N), 1613 (C=C), 1548, 1360 (N=O), 1348 (C-N)
12	1690 (C=O of Azalctones), 1629 (C=N), 1617 (C=C), 1546, 1363 (N=O), 1345 (C-N)
13	1697 (C=O of Azalctones), 1634 (C=N), 1612 (C=C), 1364, 1202 (C-O-C), 1342 (C-N)
14	1693 (C=O of Azalctones), 1634 (C=N), 1618 (C=C), 1363, 1203 (C-O-C), 1347 (C-N)
15	1690 (C=O of Azalctones), 1630 (C=N), 1612 (C=C), 1360, 1200 (C-O-C), 1342 (C-N)
16	1694 (C=O of Azalctones), 1633 (C=N), 1610 (C=C), 1365, 1204 (C-O-C), 1340 (C-N)
17	1692 (C=O of Azalctones), 1630 (C=N), 1614 (C=C), 1362, 1207 (C-O-C), 1346 (C-N)
18	1693 (C=O of Azalctones), 1635 (C=N), 1616 (C=C), 1360, 1202 (C-O-C), 1345 (C-N)
19	3254 (OH), 1693 (C=O of Azalctones), 1628 (C=N), 1611 (C=C), 1364, 1203 (C-O-C), 1343 (C-N)
20	3252 (OH), 1693 (C=O of Azalctones), 1634 (C=N), 1612 (C=C), 1358, 1202 (C-O-C), 1343 (C-N), 620 (C-Br)
21	1696 (C=O of Azalctones), 1634 (C=N), 1613 (C=C), 1344 (C-N)
22	1692 (C=O of Azalctones), 1628 (C=N), 1610 (C=C), 1342 (C-N)
23	1696 (C=O of Azalctones), 1630 (C=N), 1614 (C=C), 1360, 1204 (C-O-C), 1347 (C-N)
24	3405 (NH), 1695 (C=O of Azalctones), 1681 (C=O of Amide), 1635 (C=N), 1612 (C=C), 1345 (C-N), 955 (C-F)
25	3408 (NH), 1692 (C=O of Azalctones), 1681 (C=O of Amide), 1625 (C=N), 1618 (C=C), 1345 (C-N), 957 (C-F), 775 (C-Cl)
26	3410 (NH), 1685 (C=O of Azalctones), 1683 (C=O of Amide), 1635 (C=N), 1614 (C=C), 1345 (C-N), 955 (C-F), 777 (C-Cl)
27	3405 (NH), 1692 (C=O of Azalctones), 1685 (C=O of Amide), 1630 (C=N), 1614 (C=C), 1345 (C-N), 957 (C-F), 772 (C-Cl)
28	3408 (NH), 1694 (C=O of Azalctones), 1683 (C=O of Amide), 1633 (C=N), 1615 (C=C), 1347 (C-N), 956 (C-F)
29	3412 (NH), 1690 (C=O of Azalctones), 1685 (C=O of Amide), 1627 (C=N), 1620 (C=C), 1345 (C-N), 956 (C-F), 625 (C-Br)
30	3409 (NH), 1694 (C=O of Azalctones), 1683 (C=O of Amide), 1635 (C=N), 1614 (C=C), 1344 (C-N), 957 (C-F), 772 (C-Cl)
31	3410 (NH), 1694 (C=O of Azalctones), 1684 (C=O of Amide), 1632 (C=N), 1615 (C=C), 1545, 1362 (N=O), 1345 (C-N), 957 (C-F),
32	3414 (NH), 1692 (C=O of Azalctones), 1685 (C=O of Amide), 1630 (C=N), 1615 (C=C), 1547, 1364 (N=O), 1346 (C-N), 957 (C-F)
33	3403 (NH), 1694 (C=O of Azalctones), 1687 (C=O of Amide), 1636 (C=N), 1617 (C=C), 1364, 1208 (C-O-C), 1345 (C-N), 954 (C-F)
34	3404 (NH), 1690 (C=O of Azalctones), 1684 (C=O of Amide), 1630 (C=N), 1615 (C=C), 1360, 1204 (C-O-C), 1347 (C-N), 957 (C-F)

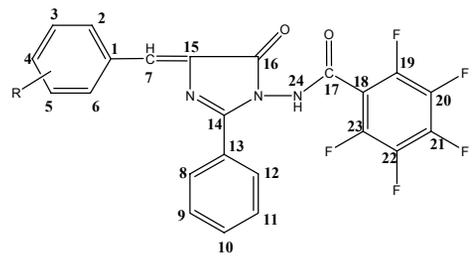
Table 2 *Contd…*

Compd.	IR Spectral data
35	3401 (NH), 1692 (C=O of Azalctones), 1680 (C=O of Amide), 1632 (C=N), 1614 (C=C), 1363, 1204 (C-O-C), 1346 (C-N), 950 (C-F)
36	3406 (NH), 1697 (C=O of Azalctones), 1685 (C=O of Amide), 1634 (C=N), 1612 (C=C), 1360, 1205 (C-O-C), 1342 (C-N), 953 (C-F)
37	3414 (NH), 1690 (C=O of Azalctones), 1686 (C=O of Amide), 1632 (C=N), 1612 (C=C), 1364, 1208 (C-O-C), 1343 (C-N), 958 (C-F)
38	3405 (NH), 1690 (C=O of Azalctones), 1684 (C=O of Amide), 1630 (C=N), 1610 (C=C), 1360, 1204 (C-O-C), 1346 (C-N), 950 (C-F)
39	3409 (NH), 3250 (OH), 1694 (C=O of Azalctones), 1685 (C=O of Amide), 1627 (C=N), 1612 (C=C), 1360, 1204 (C-O-C), 1344 (C-N), 956 (C-F)
40	3402 (NH), 3250 (OH), 1695 (C=O of Azalctones) 1683 (C=O of Amide), 1635 (C=N), 1614 (C=C), 1358, 1209 (C-O-C), 1343 (C-N), 958 (C-F), 623 (C-Br)
41	3405 (NH), 1693 (C=O of Azalctones), 1684 (C=O of Amide), 1637 (C=N), 1617 (C=C), 1345 (C-N), 950 (C-F)
42	3412 (NH), 1690 (C=O of Azalctones), 1685 (C=O of Amide), 1625 (C=N), 1614 (C=C), 1345 (C-N), 955 (C-F)
43	3408 (NH), 1695 (C=O of Azalctones), 1680 (C=O of Amide), 1632 (C=N), 1612 (C=C), 1361, 1207 (C-O-C), 1344 (C-N), 952 (C-F)

Table 3 ^{1}H-NMR Spectral data of 4-23 and 24-43



4-23



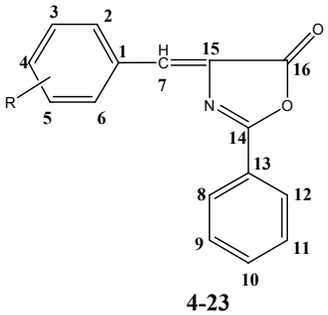
24-43

Compd.	^{1}*H*-NMR Spectral data
4	7.32-7.95 (10H, m, Ar-H), 7.52 (1H, s, -CH=)
5	7.00-7.92 (9H, m, Ar-H), 7.59 (1H, s, -CH=)
6	7.08-7.97 (9H, m, Ar-H), 7.55 (1H, s, -CH=)
7	7.10-7.93 (9H, m, Ar-H), 7.54 (1H, s, -CH=)
8	6.95-7.97 (9H, m, Ar-H), 7.85 (1H, s, -CH=)
9	7.00-7.35 (9H, m, Ar-H), 7.80 (1H, s, -CH=)
10	7.04-7.92 (8H, m, Ar-H), 7.80 (1H, s, -CH=)
11	7.52-8.25 (9H, m, Ar-H), 7.98 (1H, s, -CH=)
12	7.50-8.15 (9H, m, Ar-H), 7.88 (1H, s, -CH=)
13	3.84 (3H, s, -OCH_3), 7.50-8.15 (9H, m, Ar-H), 7.88 (1H, s, -CH=)
14	3.86 (3H, s, -OCH_3), 6.78-7.90 (8H, m, Ar-H), 7.65 (1H, s, -CH=)
15	3.85 (3H, s, -OCH_3), 6.78-7.95 (7H, m, Ar-H), 7.64 (1H, s, -CH=)

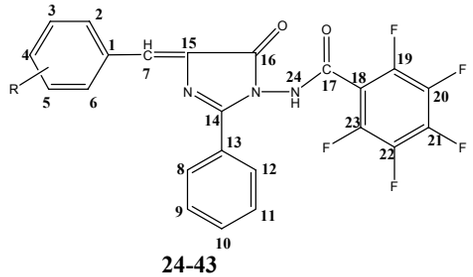
Table 3 *Contd…*

Compd.	^{1}H-NMR Spectral data
16	6.85-7.95 (14H, m, Ar-H), 7.68 (1H, s, -CH=)
17	1.30 (3H, s, $-CH_3$), 4.15 (2H, s, $-CH_2$), 7.00-7.95 (9H, m, Ar-H), 7.68 (1H, s, -CH=)
18	1.36 (3H, s, $-CH_3$), 4.18 (2H, s, $-CH_2$), 6.54-7.92 (8H, m, Ar-H), 7.62 (1H, s, -CH=)
19	3.86 (3H, s, $-OCH_3$), 7.15-7.90 (6H, m, Ar-H), 7.64 (1H, s, -CH=), 9.52 (1H, s, -OH)
20	3.86 (3H, s, $-OCH_3$), 7.15-7.90 (6H, m, Ar-H), 7.64 (1H, s, -CH=), 9.52 (1H, s, -OH)
21	3.34 (3H, s, $-CH_3$), 6.75-7.95 (9H, m, Ar-H), 7.68 (1H, s, -CH=)
22	7.55-8.64 (9H, m, Ar-H), 7.88 (1H, s, -CH=)
23	7.52-8.68 (8H, m, Ar-H), 7.68 (1H, s, -CH=)
24	7.32-7.58 (10H, m, Ar-H), 7.65 (1H, s, -CH=), 13.75 (1H, s, -NH-)
25	7.02-7.58 (9H, m, Ar-H), 7.85 (1H, s, -CH=), 13.70 (1H, s, -NH-)
26	7.12-7.54 (9H, m, Ar-H), 7.80 (1H, s, -CH=), 13.67 (1H, s, -NH-)
27	7.22-7.64 (9H, m, Ar-H), 7.60 (1H, s, -CH=), 13.70 (1H, s, -NH-)
28	7.25-7.60 (9H, m, Ar-H), 7.64 (1H, s, -CH=), 13.72 (1H, s, -NH-)
29	7.15-7.61 (9H, m, Ar-H), 7.63 (1H, s, -CH=), 13.76 (1H, s, -NH-)
30	7.04-7.65 (8H, m, Ar-H), 7.62 (1H, s, -CH=), 13.78 (1H, s, -NH-)
31	7.44-8.25 (9H, m, Ar-H), 7.99 (1H, s, -CH=), 13.75 (1H, s, -NH-)
32	7.45-8.34 (9H, m, Ar-H), 7.79 (1H, s, -CH=), 13.70 (1H, s, -NH-)
33	3.84 (3H, s, $-OCH_3$), 7.05-7.64 (9H, m, Ar-H), 7.69 (1H, s, -CH=), 13.78 (1H, s, -NH-)
34	3.85 (3H, s, $-OCH_3$), 6.75-7.62 (8H, m, Ar-H), 7.60 (1H, s, -CH=), 13.72 (1H, s, -NH-)
35	3.83 (3H, s, $-OCH_3$), 6.73-7.60 (7H, m, Ar-H), 7.62 (1H, s, -CH=), 13.78 (1H, s, -NH-)
36	6.83-7.40 (14H, m, Ar-H), 7.64 (1H, s, -CH=), 13.73 (1H, s, -NH-)
37	1.35 (3H, s, $-CH_3$), 4.10 (2H, s, $-CH_2$), 6.63-7.60 (9H, m, Ar-H), 7.64 (1H, s, -CH=), 13.75 (1H, s, -NH-)
38	1.32 (3H, s, $-CH_3$), 4.15 (2H, s, $-CH_2$), 6.53-7.67 (8H, m, Ar-H), 7.60 (1H, s, -CH=), 13.70 (1H, s, -NH-)
39	3.80 (3H, s, $-OCH_3$), 6.63-7.62 (8H, m, Ar-H), 7.61 (1H, s, -CH=), 13.74 (1H, s, -NH-), 9.80 (1H, s, -OH)
40	3.75 (3H, s, $-OCH_3$), 7.12-7.64 (7H, m, Ar-H), 7.62 (1H, s, -CH=), 13.73 (1H, s, -NH-), 9.81 (1H, s, -OH)
41	3.15 (3H, s, $-CH_3$), 6.73-7.62 (9H, m, Ar-H), 7.65 (1H, s, -CH=), 13.78 (1H, s, -NH-)
42	7.33-8.62 (9H, m, Ar-H), 7.85 (1H, s, -CH=), 13.71 (1H, s, -NH-)
43	7.43-7.65 (9H, m, Ar-H), 7.65 (1H, s, -CH=), 13.72 (1H, s, -NH-)

Table 4 ^{13}C-NMR Spectral data of 4-23 and 24-43



4-23



24-43

Compd.	^{13}C-NMR Spectral data
4	C_7 (112.00), C_{15} (130.15), C_1-C_6 (126.02-135.15), C_8-C_{13} (128.22-131.15), C_{14} (160.50), C_{16} (165.15)
5	C_7 (113.05), C_{15} (130.10), C_1-C_6 (126.02-133.10), C_8-C_{13} (128.24-131.14), C_{14} (160.55), C_{16} (165.10)
6	C_7 (113.08), C_{15} (131.12), C_1-C_6 (126.08-132.15), C_8-C_{13} (127.23-131.16), C_{14} (160.50), C_{16} (165.12)

Table 4 *Contd…*

Compd.	^{13}C-NMR Spectral data
7	C_7 (113.10), C_{15} (130.12), C_1-C_6 (126.05-133.14), C_8-C_{13} (128.25-132.15), C_{14} (160.50), C_{16} (165.14)
8	C_7 (113.14), C_{15} (130.19), C_1-C_6 (115.05-156.15), C_8-C_{13} (127.25-132.19), C_{14} (161.50), C_{16} (166.15)
9	C_7 (112.13), C_{15} (130.15), C_1-C_6 (118.05-135.14), C_8-C_{13} (127.20-132.15), C_{14} (162.54), C_{16} (166.10)
10	C_7 (112.18), C_{15} (130.10), C_1-C_6 (125.06-133.15), C_8-C_{13} (127.27-131.16), C_{14} (163.00), C_{16} (166.12)
11	C_7 (113.15), C_{15} (131.12), C_1-C_6 (127.06-145.10), C_8-C_{13} (127.25-131.13), C_{14} (163.15), C_{16} (166.15)
12	C_7 (113.15), C_{15} (131.12), C_1-C_6 (123.06-147.15), C_8-C_{13} (127.25-131.13), C_{14} (163.15), C_{16} (166.15)
13	C_7 (113.12), C_{15} (131.10), C_1-C_6 (114.02-160.12), C_8-C_{13} (127.25-131.10), C_{14} (163.10), C_{16} (166.10)
14	C_7 (113.19), C_{15} (131.15), C_1-C_6 (111.02-150.15), C_8-C_{13} (126.27-131.15), C_{14} (163.15), C_{16} (166.15)
15	C_7 (112.95), C_{15} (131.14), C_1-C_6 (103.02-150.18), C_8-C_{13} (126.25-131.14), C_{14} (163.14), C_{16} (166.17)
16	C_7 (112.90), C_{15} (131.12), C_1-C_6 (113.04-156.17), C_8-C_{13} (126.20-131.10), C_{14} (163.12), C_{16} (166.10)
17	C_7 (112.88), C_{15} (131.18), C_1-C_6 (114.07-156.19), C_8-C_{13} (126.28-131.13), C_{14} (163.18), C_{16} (166.15)
18	C_7 (112.78), C_{15} (132.17), C_1-C_6 (111.09-151.15), C_8-C_{13} (126.29-131.12), C_{14} (164.15), C_{16} (166.18)
19	C_7 (112.71), C_{15} (132.15), C_1-C_6 (112.82-151.10), C_8-C_{13}(126.28-131.10), C_{14} (164.15), C_{16} (166.00)
20	C_7 (113.70), C_{15} (132.16), C_1-C_6 (111.08-152.18), C_8-C_{13}(126.32-131.19), C_{14} (164.85), C_{16} (166.78)
21	C_7 (113.70), C_{15} (132.16), C_1-C_6 (115.18-150.15), C_8-C_{13}(126.32-131.10), C_{14} (164.80), C_{16} (166.70)
22	C_7 (113.75), C_{15} (132.10), C_1-C_6 (120.28-154.19), C_8-C_{13} (126.34-131.16), C_{14} (164.85), C_{16} (166.74)
23	C_7 (114.70), C_{15} (132.15), C_1-C_6 (116.27-155.18), C_8-C_{13} (125.34-132.15), C_{14} (164.81), C_{16} (166.70)
24	C_7 (108.70), C_{18}-C_{23} (113.05-146.15), C_{15} (130.16), C_1-C_6 (126.08-135.18), C_8-C_{13} (126.30-130.19), C_{14} (144.85), C_{17} (164.85) C_{16} (166.58)
25	C_7 (108.75), C_{18}-C_{23} (113.05-146.25), C_{15} (130.76), C_1-C_6 (126.00-133.28), C_8-C_{13} (127.32-130.29), C_{14} (144.80), C_{17} (164.81) C_{16} (166.52)
26	C_7 (108.86), C_{18}-C_{23} (113.15-146.85), C_{15} (131.79), C_1-C_6 (124.05-136.19), C_8-C_{13} (127.42-130.32), C_{14} (144.82), C_{17} (164.84) C_{16} (166.50)
27	C_7 (109.06), C_{18}-C_{23} (112.19-146.80), C_{15} (131.59), C_1-C_6 (127.18-135.12), C_8-C_{13} (127.40-130.34), C_{14} (143.84), C_{17} (165.80) C_{16} (166.42)
28	C_7 (109.10), C_{18}-C_{23} (112.00-144.81), C_{15} (131.54), C_1-C_6 (115.28-162.24), C_8-C_{13} (127.42-130.30), C_{14} (143.81), C_{17} (165.79) C_{16} (166.12)
29	C_7 (108.55), C_{18}-C_{23} (113.10-144.80), C_{15} (131.50), C_1-C_6 (123.19-137.54), C_8-C_{13} (127.45-130.31), C_{14} (143.85), C_{17} (165.75) C_{16} (166.10)
30	C_7 (108.22), C_{18}-C_{23} (113.18-144.82), C_{15} (131.54), C_1-C_6 (125.13-134.59), C_8-C_{13} (127.40-130.21), C_{14} (143.78), C_{17} (165.70) C_{16} (166.78)
31	C_7 (108.28), C_{18}-C_{23} (112.88-144.85), C_{15} (131.52), C_1-C_6 (123.23-145.24), C_8-C_{13} (127.38-130.29), C_{14} (143.88), C_{17} (165.72) C_{16} (166.74)
32	C_7 (109.18), C_{18}-C_{23} (113.48-145.83), C_{15} (131.54), C_1-C_6 (123.34-147.45), C_8-C_{13} (127.45-130.59), C_{14} (143.68), C_{17} (165.78) C_{16} (166.84)
33	C_7 (109.45), C_{18}-C_{23} (113.45-145.25), C_{15} (131.14), C_1-C_6 (114.24-159.34), C_8-C_{13} (127.41-130.33), C_{14} (143.56), C_{17} (165.73) C_{16} (166.82)
34	C_7 (109.41), C_{18}-C_{23} (113.40-145.45), C_{15} (131.24), C_1-C_6 (111.34-149.23), C_8-C_{13} (127.43-130.35), C_{14} (143.36), C_{17} (165.70) C_{16} (166.81)
35	C_7 (109.45), C_{18}-C_{23} (113.43-145.48), C_{15} (131.54), C_1-C_6 (85.34-156.43), C_8-C_{13} (127.48-130.45), C_{14} (143.26), C_{17} (165.72) C_{16} (166.78)
36	C_7 (109.35), C_{18}-C_{23} (113.48-145.41), C_{15} (131.50), C_1-C_6 (113.45-156.42), C_8-C_{13} (127.44-130.55), C_{14} (143.21), C_{17} (165.73) C_{16} (166.88)
37	C_7 (109.15), C_{18}-C_{23} (113.38-145.44), C_{15} (131.52), C_1-C_6 (110.55-115.45), C_8-C_{13} (127.40-130.51), C_{14} (143.41), C_{17} (165.70) C_{16} (166.81)

Table 4 *Contd…*

Compd.	^{13}C-NMR Spectral data
38	C_7 (109.23), C_{18}-C_{23} (113.58-145.41), C_{15} (131.50), C_1-C_6 (111.12-148.32), C_8-C_{13} (127.45-130.54), C_{14} (143.47), C_{17} (165.62) C_{16} (166.72)
39	C_7 (109.45), C_{18}-C_{23} (113.28-145.47), C_{15} (131.52), C_1-C_6 (111.23-151.42), C_8-C_{13} (127.34-130.53), C_{14} (143.47), C_{17} (165.22) C_{16} (166.79)
40	C_7 (109.33), C_{18}-C_{23} (112.99-144.45), C_{15} (131.58), C_1-C_6 (110.44-153.25), C_8-C_{13} (127.31-130.43), C_{14} (143.56), C_{17} (165.26) C_{16} (166.80)
41	C_7 (108.88), C_{18}-C_{23} (113.39-144.40), C_{15} (131.48), C_1-C_6 (114.14-148.33), C_8-C_{13} (127.32-130.44), C_{14} (143.44), C_{17} (165.16) C_{16} (166.87)
42	C_7 (109.12), C_{18}-C_{23} (113.35-144.44), C_{15} (131.42), C_1-C_6 (120.54-154.12), C_8-C_{13} (127.34-130.34), C_{14} (143.54), C_{17} (165.23) C_{16} (166.77)
43	C_7 (109.22), C_{18}-C_{23} (113.45-144.44), C_{15} (131.45), C_1-C_6 (134.14-144.33), C_8-C_{13} (127.44-130.22), C_{14} (143.57), C_{17} (165.58) C_{16} (166.79)

Table 5 Antimicrobial data of compounds 24-43

Compounds No.	R	Antibacterial activity				Antifungal activity	
		Diameter of zone of inhibition in mm				% Inhibition	
		S. aureus	*S. paratyphi-A*	*E. coli*	*B. subtilis*	*A. niger*	*F. molaniforme*
24	Phenyl	10	12	13	11	35.51	36.21
25	2-Chlorophenyl	14	12	15	10	51.12	35.21
26	3-Chlorophenyl	15	14	17	13	48.20	30.12
27	4-Chlorophenyl	13	11	14	10	52.54	38.24
28	4-Fluorophenyl	19	17	15	14	55.21	41.23
29	3-Bromophenyl	14	11	14	10	49.68	24.24
30	2,3-Dichloro phenyl	16	16	19	14	58.20	34.32
31	2-Nitrophenyl	09	07	10	08	32.21	31.12
32	4-Nitrophenyl	10	06	09	11	37.86	29.54
33	4- methoxyphenyl	14	15	12	14	53.41	48.74
34	3,4- Dimethoxyphenyl	14	16	16	11	53.12	55.42
35	3,4,5- Trimethoxyphenyl	18	19	16	15	55.54	59.21
36	3-phenoxyphenyl	10	11	14	12	32.36	33.65
37	4-Ethoxy phenyl	12	15	17	11	33.25	36.54
38	2,5- Diethoxyphenyl	14	17	19	13	36.36	45.21
39	4- Hydroxy-3-methoxy phenyl	16	19	18	17	54.56	58.21
40	3-Bromo-4- Hydroxy-5-methoxy phenyl	21	19	18	19	47.31	54.58
41	4-N,N-dimethyl amino phenyl	09	14	10	12	31.36	28.25
42	2- Pyridyl	10	11	09	08	30.12	49.21
43	3-Furfuryl	09	08	06	07	29.25	34.24
	Ampicillin	**32**	**34**	**36**	**36**	**------**	**------**
	Penicillin-G	**33**	**30**	**31**	**34**	**---**	**-----**
	Griseofulvin					**87**	**82**
	Fungiguard	**---**	**----**	**---**	**---**	**79**	**78**

Antibacterial activity

Activity against S. aureus

The compounds were tested *in vitro* for antimicrobial activity against the test organisms *S. aureus*. The maximum activity was shown by the compounds **40** zone of inhibition is 21mm and the minimum activity was shown by the compound **41** the zone of inhibition is 09 mm. Compounds **28**, **35** and **40** positively acted. Among these **40** was found to be the more active, since this compound could inhibit the microbial growth maximum. It has been observed that compounds substituted with halogen and methoxy exhibits the good activity against *S. aureus.* When the comparison is made between the compounds **24**, **25**, **26**, **27**, **28** and **29**; it appear that antimicrobial activity is enhanced due to the presence of halogen group as a substituent on the ring. Furthermore, the comparison of compounds in pairs **28** and **25**, **26**, **27**, **29**, **30** indicates that the –F group as a constituent on the phenyl ring causes a substantial increase in antimicrobial activity. The compound **40** shown maximum activity, due to bromo, methoxy and hydroxy group. Means the combination of halogen and methoxy enhanced the activity.

Activity against S. paratyphi-A

The maximum activity was shown by the compounds **35**, **39** and **40** the zone of inhibition is 19mm and the minimum activity was shown by the compound **32** the zone of inhibition is 06mm. It has been observed that compounds which are substituted with fluoro and methoxy exhibits the good activity against *S. paratyphi-A.* When comparison is made between the compounds **24** and **28** it appear that antimicrobial activity is enhanced due to the presence of fluoro group as a substituent on the ring. Furthermore, the comparison of compounds in pairs **24, 32, 33**, **35** and **40** indicates that the methoxy group as a constituent on the phenyl ring causes a substantial increase in antimicrobial activity.

Activity against E. coli

The maximum activity was shown by the compounds **30** and **38** the zone of inhibition was 19mm, and the minimum activity was shown by the compound **43** the zone of inhibition was 06mm. For compounds **24 25**, **26**, **27**, **28**, **29** and **30** antimicrobial activity is enhanced due to the presence of halogen group as a substituent on the ring. The comparison of compounds **24**, **34**, **35**, **37** and **38** indicates that the methoxy and ethoxy group as a constituent on the phenyl ring causes increase in antimicrobial activity.

Activity against B. subtilis

The maximum activity was shown by the compounds **40** the zone of inhibition is 19mm and the minimum activity was shown by the compound **43** the zone of inhibition is 07mm. When comparison is made between the compounds in pair **24 28**, **33**, **34**, **35**, **39** and **40** it appear that antimicrobial activity is enhanced due to the presence of fluoro and methoxy group as a substituent on the ring.

Antifungal activity

Against F. molaniforme

The maximum activity was shown by the compound **35** the inhibition was 59.21% and the minimum activity was shown by the compound **41** the zone of inhibition was 28.25%. Comparison of compounds **24**, **33**, **34**, **35**, **39** and **40** it appeared that introduction of methoxy group enhanced the antifungal activity against *F. molaniforme*.

Against A. niger

The maximum activity was shown by the compound **30**, the inhibition was 58.20% and the minimum activity was shown by the compound **43** the inhibition was 29.25%. When comparison is made between the compounds in pair **24 25**, **26**, **27**, **28**, **29**, **30** and **40** it appeared that antimicrobial activity against *A. niger* is enhanced due to the presence of halogen and methoxy group as a substituent on the ring. From the above antifungal activity data, it has been observed that compounds **25**, **27**, **28**, **29**, **35** and **40** possess good activity against *A. niger;* the compounds **34**, **35**, **39**, and **42** exhibited good activity against *F. molaniforme*. Remaining compounds exhibited moderate activity against *A. niger* and *F. molaniforme.*

Conclusions

In order to discover new and potent bactericides, the best way is to overcome bacterial resistance, molecular modeling was used to design a series of substituted imidazolinone. On basis of the inhibition values of these compounds, it can be concluded that compounds which substituted with fluoro, methoxy, hydroxyl and ethoxy in imidazolinone skeleton furnishes active antimicrobial activity, however, best antimicrobial activity can be obtained with methoxy, fluoro and hydroxy substitution. Thus, it appears that most potential antimicrobial activity of compound can be achieved with appropriate combination of heterocyclic moiety substitution with fluoro and methoxy group.

Experimental

General

All commercial reagents and solvents were used without further purification. Reactions were monitored by Thin layer chromatography (TLC). and was performed on silica gel plates (Merck); the spots were located by UV (254 nm) or iodine. Melting points (uncorrected) were measured in open capillary tubes on a Gallenkamp-5 apparatus. The IR spectra were recorded on NICOLET (NEXUS) 470 FT-IR spectrometer. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on BRUKER AVANCE II 400 NMR spectrometer in $CDCl_3$.

General procedure for the synthesis of *N*-amino -2, 3, 4, 5, 6-pentafluoro benzamide 3

2,3,4,5,6-Pentafluoro phenyl methyl ester (0.1 mol) was dissolved in methanol (100 ml) and cool up to 20°C under stirring, added 50% solution of hydrazine hydrate (0.1mol) then stirred the reaction mass for 2 h at 25°C. After then applied the vacuum to remove excess methanol (up to slurry formation observe). Filtered the mass under vacuum, solid product was obtained, then washed with chilled methanol (25 ml) and recrystalized from ethanol. Yield-65%, M.P.- 115 °C; IR (KBr):ν_{max} (cm^{-1}) 3315, 3178 (NH), 1686 (C=O), 1300 (C-N), 1087 (C-F); ^{1}H-NMR (chemical shift in δ ppm) 3.20 δ (s, 2H, -NH_2), 3.10 δ (s, 1H, -NH**)**

General procedure for the synthesis of 4-(2-substitutedbenzylidene)-2-phenyloxazol-5(4H)-one 4-23.

A mixture of 3,4,5-trimethoxy benzaldehyde (0.01 mol), hippuric acid (0.01 mol), acetic anhydride (0.04 mol) and sodium acetate (0.01 mol) in a round bottom flask (50 ml) was heated up to 100°C under constant stirring for the 2 h. Then cooled the flask at 50°C; added ethanol (10 ml) slowly and kept the mass at room temperature over night. After then filtered the reaction mass followed by hot water washing and recrystalized from ethanol. Similarly remaining compounds were prepared by same method.

General procedure for the synthesis of 1–(2,3,4,5, 6-pentafluoro benzamido)-2-phenyl-4-(3,4,5-trimethoxy phenyl)-5-imidazolone 24-43.

A mixture of 2-phenyl-4-(3,4,5-trimethoxy benzylidine)-5-oxazolone (0.01 mol) and *N*-amino-2,3,4,5,6-pentafluoro benzamide (0.01 mol) was taken in pyridine (25 ml), heated the reaction mass for 15 h at reflux temperature. After completion of reaction, excess pyridine was distilled under vacuum and poured it into crushed ice containing concentrated HCl. Product was filtered and recrystalised from ethanol. Similarly remaining compounds were prepared by same method.

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