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Synthesis, characterization and biological evaluations of 2-(4-hydroxyaryl)–N'-[{5'-(substituted aryl)-furan-2'-yl}-methylidene]-ketohydrazides Schiff bases

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ABSTARCT

*A novel series of 2-(4-hydroxyaryl)-N'-[{5'-(substituted aryl)-furan-2'-yl}-methylidene]-ketohydrazides have been designed and synthesized from the reaction of methyl-p-hydroxybenzoate **1**, with hydraziane hydrate in anhydrous condition yielded 4-hydroxyphenyl-1-ketohydrazide **2**, Further the resultant compound (2) was treated with different aromatic furfural aldehydes to yield substituted 2-(4-hydroxyaryl)-N'-[{5'-(substituted aryl)-furan-2'-yl}-methylidene]-ketohydrazides **(3a-k)** Schiff bases. The structures of these compounds were elucidated by IR, ^{1}HNMR, Mass spectral data and CHN analysis. The title compounds **3a-k**, have been evaluated in vitro antibacterial screening against Gram positive bacterial strains S. aureus, B. cereus , E. faecalis and S. epidermidis and Gram negative bacteria strains E. coli , S. typhi, S. dysenteriae and K. pneumoniae. The synthesized Schiff bases also showed significant anthelmintic activity against two species of earthworms (Pheritima posthuma and Perionyx excavates).*

Keywords: Methyl-*p*-hydroxybenzoate, Schiff bases, Antimicrobial activity, Anthelmintic activity

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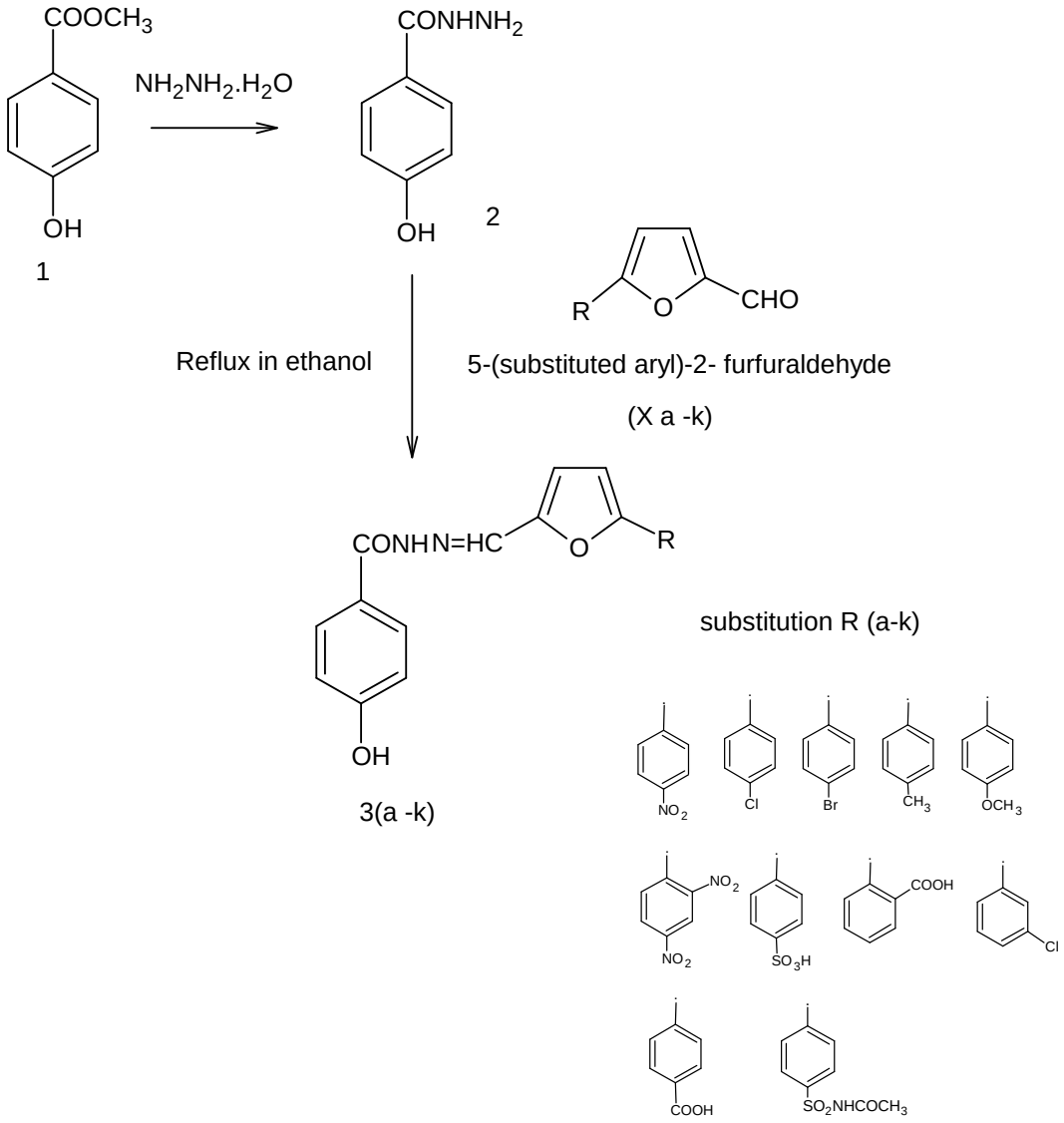
INTRODUCTION

Drug resistant microbial pathogens leads by extensive use of antibiotics agents that become a major global problem, necessitating the need for research for new antimicrobial agents with reduce resistant to pathogens and for diverse biological activity. On the other hand, Helminthiasis or worm infestations, is one of the most leading disease and one of the most serious public health problem exist globally and increased worldwide with immigration from the developing countries. According to extensive literature survey, phenolic rings are associated with anthelmintic and anti-intestinal nematode activity [1] antioxidant activity [2] and antibacterial activity [3]. Schiff bases have gained importance because of diverse biological and pharmacological activities associated with anti-inflammatory [4], antibacterial [5], anticonvulsant [6], antioxidant [2], antimycobacterial [7] and anthelmintic [8] activities. In the present work, antimicrobial and anthelmintic activities are associated with substituted furfuraldehyde and phenolic moiety encouraged us to synthesized newer Schiff bases with an objective to obtained enhanced biological activities, as potent antimicrobial and anthelmintic agents by converting 4-hydroxy benzoate moiety in to the 2-(4-hydroxyaryl)-N'-[{5'-(substituted aryl)-furan-2'-yl}-methylidene]-ketohydrazides **(3a-k)** via synthesis of 4-hydroxyphenyl-1-ketohydrazide **2** with different aromatic furfural aldehydes. The novel Schiff bases were further characterized and screened for their antimicrobial and anthelmintic activities.

MATERIALS AND METHODS

A novel series of 2-(4-hydroxyaryl)-N'-[{5'-(substituted aryl)-furan-2'-yl}-methylidene]-ketohydrazides (3a-k) have been synthesize from 4-hydroxyphenyl-1-ketohydrazide condensed with 5-(substituted aryl)-2-furfuraldehyde (Xa-k), in the presence of ethanol as solvent. All the synthesized compounds were characterized by IR, 1H NMR, Mass spectroscopy and CHN analysis. The IR spectra were recorded on Bruker, alpha E ATR FTIR spectrophotometer. ^{1}HNMR spectra were recorded at 300 MHz by using DMSO-d_6 as solvents. Splitting patterns were assigned as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet (chemical shifts d ppm). ^{1}H NMR were reported as parts per million (ppm) downfield from TMS (Me_4Si). Mass spectra were scanned on Bruckers microOTOF-QII, ESI Mass spectrophotometer. Elemental analyses (C, H, and N) were done on a CHN rapid analyzer. All the compounds gave C, H and N analysis within ±0.05% of the theoretical values. Purity of synthesized compounds was determined by thin layer chromatography (TLC) on Merk silica gel 60 F_{254} precoated sheet in chloroform/methanol mixture and spots were detected by using ultraviolet light (λ=254 nm for few seconds). Melting points were determined by using the capillary method. The solvents and reagents were used without further purification.

SCHEME



General Synthesis of 4-hydroxyphenyl-1-ketohydrazide (2)

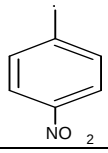
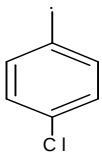
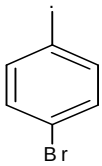
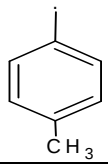
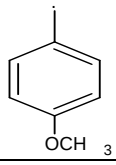
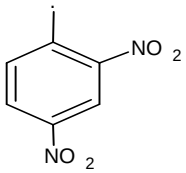
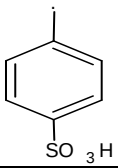
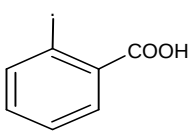
A mixture of methyl-*p*-hydroxybenzoate (0.05M) and hydrazine hydrate (0.075M) was refluxed on water bath for 4-5 hrs. After completion of reaction, the solution was allowed to cool and separated the solid crystals and washed, finally the product thus obtained and recrystallized with ethanol. mw 152; m.p 240^{o}C; yield, 75%; IR ($\nu_{max,}$ cm^{-1}): 3195 (N-H of CONH), 1467.10 (Ar-OH), ^{1}H-NMR: (DMSO-$d_{6),}$ δ, ppm, 4.26 (1H, s, Ar-OH), 9.52 (1H, s, CONH),

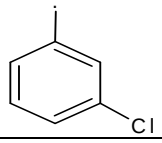
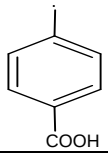
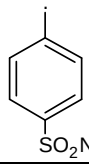
4.81 6.77-7.81 (m, Ar-H), Anal. Calcd for $C_7H_8N_2O_2$ (%): C, 55.26; H, 5.30, N, 18.41. Found: C, 55.21; H, 5.35, N, 18.40.

General Synthetic approach of 2-(4-hydroxyaryl)-N'-[{5'-(substituted aryl)-furan-2'-yl}-methylidene]-ketohydrazides (3a-k) Schiff bases.

A mixture of 4-hydroxyphenyl-1-ketohydrazide (0.1 mol) and 5-(phenyl substituted)-2- furfuraldehyde (0.05 mol) was refluxed on water bath for 7-8 hrs in ethanol as solvent, in the presence of few drops of sulfuric acid as catalyst. The progress of the reaction was monitored by thin layer chromatography (*vide* TLC). After completion of reaction, the solution was allowed to cool and separated the brown solid crystals, washed and finally the product thus obtained was recrystallized with ethanol.

Table 1: Physical data of compounds (3a-k)

Product code	R	M.F	M.P (0^oC)	M.W	Physical State	% Yield
3a		$C_{18}H_{13}N_3O_5$	190	351	Pale brown crystals	39
3b		$C_{18}H_{13}ClN_2O_3$	167	340	Brown crystals	23
3c		$C_{18}H_{13}BrN_2O_3$	190	385	Brown crystals	56
3d		$C_{19}H_{16}N_2O_3$	194	320	Pale brown crystals	77
3e		$C_{19}H_{16}N_2O_4$	165	336	Dark brown crystals	73
3f		$C_{18}H_{12}N_4O_7$	150	396	Dark brown crystals	70
3g		$C_{18}H_{14}N_2O_6S$	185	386	Brown crystals	70
3h		$C_{19}H_{14}N_2O_5$	180	350	Brown crystals	70

3i		$C_{18}H_{13}ClN_2O_3$	178	328	Dark brown crystals	84
3j		$C_{19}H_{14}N_2O_5$	160	350	Dark brown crystals	73
3k		$C_{20}H_{17}N_3O_7S$	185	443	Dark brown crystals	69

Spectral analysis of compounds (3a-k)

3a: 2-(4-hydroxyaryl)-N'-[{5'-(4-nitrophenyl)-furan-2'-yl}-methylidene]-ketohydrazide.
IR ($\nu_{max,}$ cm^{-1}): 1656 (CO of CONH), 1619, 3332 (NH of CONH), 1551, 1457, 1217, 1191, 1067, 913, 727 (C=C and C-H of aromatic ring), ^{1}H NMR: (DMSO-d_6), δ, ppm, 6.76-7.82 (10H, m, Ar), 9.91 (1H, s, CONH), 9.48 (1H, s, N=CH), 4.51 (1H, s, OH), EI-MS (*m/z*, %); 351 [M+1, 100]. Anal. Calcd for $C_{18}H_{13}N_3O_5$ (%): C, 61.54; H, 3.73, N, 11.75. Found: C, 61.50; H, 3.75, N, 11.80.

3b: 2-(4-hydroxyaryl)-N'-[{5'-(4-cholrophenyl)-furan-2'-yl}-methylidene]-ketohydrazide. IR ($\nu_{max,}$ cm^{-1}): 1655 (CO of CONH), 1623, 3312 (NH of CONH), 1548, 1459, 1216, 1158, 1064, 986, 718 (C=C and C-H of aromatic ring), ^{1}H NMR: (DMSO-d_6), δ, ppm, 6.82-7.79 (10H, m, Ar), 9.91 (1H, s, CONH), 10.14 (1H, s, N=CH), 4.23 (1H, s, OH), EI-MS (*m/z*, %); 340 [M+1, 100]. Anal. Calcd for $C_{18}H_{13}ClN_2O_3$ (%): C, 63.54; H, 3.85, N, 10.40. Found: C, 63.58; H, 3.86, N, 10.43.

3c: 2-(4-hydroxyaryl)-N'-[{5'-(4-bromophenyl)-furan-2'-yl}-methylidene]-ketohydrazide. IR ($\nu_{max,}$ cm^{-1}): 1650 (CO of CONH), 1604, 3332 (NH of CONH), 1546, 1447, 1228, 1151, 1022, 931, 737 (C=C and C-H of aromatic ring), ^{1}H NMR: (DMSO-d_6), δ, ppm, 6.77-7.82 (10H, m, Ar), 9.77 (1H, s, CONH), 9.69 (1H, s, N=CH), 4.00 (1H, s, OH), EI-MS (*m/z*, %); 385 [M+1, 100]. Anal. Calcd for $C_{18}H_{13}BrN_2O_3$ (%): C, 56.12; H, 3.40, N, 7.27. Found: C, 56.17; H, 3.43, N, 7.26

3d: 2-(4-hydroxyaryl)-N'-[{5'-(4-methylphenyl)-furan-2'-yl}-methylidene]-ketohydrazide. IR ($\nu_{max,}$ cm^{-1}): 1639 (CO of CONH), 1639, 3342 (NH of CONH), 1542, 1456, 1237, 1164, 1075, 956, 749 (C=C and C-H of aromatic ring), ^{1}H NMR: (DMSO-d_6), δ, ppm, 6.77-7.80 (10H, m, Ar), 9.93 (1H, s, CONH), 9.59 (1H, s, N=CH), 4.35 (1H, s, OH), 3.17 (3H, s, CH_3), EI-MS (*m/z*, %); 320 [M+1, 100]. Anal. Calcd for $C_{19}H_{16}N_2O_3$ (%): C, 71.24; H, 5.03, N, 8.04. Found: C, 71.29; H, 5.05, N, 8.07.

3e: 2-(4-hydroxyaryl)-N'-[{5'-(4-methoxyphenyl)-furan-2'-yl}-methylidene]-ketohydrazide. IR ($\nu_{max,}$ cm^{-1}): 1650 (CO of CONH), 1607, 3316 (NH of CONH), 1282 (C-O-C of Ar-OCH_3), 1545, 1424, 1227, 1167, 1054, 940, 745 (C=C and C-H of aromatic ring), ^{1}H NMR: (DMSO-d_6), δ, ppm, 6.83-7.79 (10H, m, Ar), 10.24 (1H, s, CONH), 9.94 (1H, s, N=CH), 4.23 (1H, s, OH), EI-MS (*m/z*, %); 336 [M+1, 100]. Anal. Calcd for $C_{19}H_{16}N_2O_4$ (%): C, 67.85; H, 4.79, N, 8.33. Found: C, 67.83; H, 4.75, N, 8.28.

3f: 2-(4-hydroxyaryl)-N'-[{5'-(2,4-dinitrophenyl)-furan-2'-yl}-methylidene]-ketohydrazide. IR ($\nu_{max,}$ cm^{-1}): 1649 (CO of CONH), 1541, 3389 (NH of CONH), 1512, 1457, 1232, 1108, 1067, 992, 746 (C=C and C-H of aromatic ring), ^{1}H NMR: (DMSO-d_6), δ, ppm, 6.79-8.89 (10H, m, Ar), 9.95 (1H, s, CONH), 9.82 (1H, s, N=CH), 3.78 (1H, s, OH), EI-MS (*m/z*, %); 396 [M+1, 100]. Anal. Calcd for $C_{18}H_{12}N_4O_7$ (%): C, 54.55; H, 3.05, N, 14.14. Found: C, 54.53; H, 3.10, N, 14.17.

3g: 2-(4-hydroxyaryl)-N'-[{5'-(4-sulfoxyphenyl)-furan-2'-yl}-methylidene]-ketohydrazide. IR ($\nu_{max,}$ cm^{-1}): 1650 (CO of CONH), 1544, 3335 (NH of CONH), 1544, 1457, 1239, 1152, 1055, 989, 751 (C=C and C-H of aromatic ring), ^{1}H NMR: (DMSO-d_6), δ, ppm, 5.00-7.83 (10H, m, Ar), 10.08 (1H, s, CONH), 9.86 (1H, s, N=CH), 4.72 (1H, s, OH), EI-MS (*m/z*, %); 386 [M+1, 100]. Anal. Calcd for $C_{18}H_{14}N_2O_6S$ (%): C, 55.95; H, 3.65, N, 7.25. Found: C, 55.93; H, 3.66, N, 7.21.

3h: 2-(4-hydroxyaryl)-N'-[{5'-(2-carboxyphenyl)-furan-2'-yl}-methylidene]-ketohydrazide. IR ($\nu_{max,}$ cm^{-1}): 1701 (CO of CONH), 1649, 3385 (NH of CONH), 1742 (CO of COOH), 1514, 1455, 1227, 1171, 1068, 939, 753 (C=C and C-H of aromatic ring), ^{1}H NMR: (DMSO-d_6), δ, ppm, 6.78-8.39 (10H, m, Ar), 10.07 (1H, s, CONH), 9.87 (1H, s, N=CH), 4.88 (1H, s, OH), EI-MS (*m/z*, %); 350 [M+1, 100]. Anal. Calcd for $C_{19}H_{14}N_2O_5$ (%): C, 65.14; H, 4.03, N, 8.00. Found: C, 65.12; H, 4.05, N, 7.96.

3i: 2-(4-hydroxyaryl)-N'-[{5'-(3-chlorophenyl)-furan-2'-yl}-methylidene]-ketohydrazide. IR ($\nu_{max,}$ cm^{-1}): 1697 (CO of CONH), 1648, 3365 (NH of CONH), 1547, 1456, 1237, 1145, 1064, 930, 753 (C=C and C-H of aromatic ring), ^{1}H NMR: (DMSO-d_6), δ, ppm, 6.78-8.38 (10H, m, Ar), 10.06 (1H, s, CONH), 9.87 (1H, s, N=CH), 4.85 (1H, s, OH), EI-MS (*m/z*, %); 328 [M+1, 100]. Anal. Calcd for $C_{18}H_{13}ClN_2O_3$ (%): C, 63.54; H, 3.85, N, 10.40. Found: C, 63.53; H, 3.85, N, 10.37.

3j: 2-(4-hydroxyaryl)-N'-[{5'-(4-carboxyphenyl)-furan-2'-yl}-methylidene]-ketohydrazide. IR ($\nu_{max,}$ cm^{-1}): 1697 (CO of CONH), 1640, 3315 (NH of CONH), 1701 (CO of COOH), 1524, 1451, 1222, 1171, 1064, 936, 751 (C=C and C-H of aromatic ring), ^{1}H NMR: (DMSO-d_6), δ, ppm, 6.68-8.39 (10H, m, Ar), 10.02 (1H, s, CONH), 9.57 (1H, s, N=CH), 4.88 (1H, s, OH), EI-MS (*m/z*, %); 350 [M+1, 100]. Anal. Calcd for $C_{19}H_{14}N_2O_5$ (%): C, 65.14; H, 4.03, N, 8.00. Found: C, 65.13; H, 4.05, N, 8.03.

3k: 2-(4-hydroxyaryl)-N'-[{5'-(4-sulfacetamidophenyl)-furan-2'-yl}-methylidene]-ketohydrazide. IR ($\nu_{max,}$ cm^{-1}): 1654 (CO of CONH), 1617, 3343 (NH of CONH), 1514, 1443, 1227, 1170, 1043, 940, 751 (C=C and C-H of aromatic ring), ^{1}H NMR: (DMSO-d_6), δ, ppm, 6.70-8.49 (10H, m, Ar), 9.95 (1H, s, CONH), 9.54 (1H, s, N=CH), 4.88 (1H, s, OH), 3.65 (2H, s, NHCOCH_3), EI-MS (*m/z*, %); 443 [M+1, 100]. Anal. Calcd for $C_{20}H_{17}N_3O_7S$ (%): C, 54.17; H, 3.85, N, 9.48. Found: C, 54.13; H, 3.88, N, 9.47.

BIOLOGICAL STUDIES

Antimicrobial activity

Antibacterial bioassay was evaluated against gram positive bacterial strains, *S. aureus*, *B. cereus*, *E. faecalis* and *S. epidermidis*, gram negative bacterial strains, *E. coli*, *S. typhi*, *S. dysenteriae* and *K. pneumoniae* by disc diffusion method [10,11]. Standard inoculums (1ml/100 ml of medium) with suspension (10^5cfu/ml) were introduced onto the surface of sterile agar plates, and a sterile bent glass spreader was used for even distribution of the inoculums. The discs measuring 6 mm in diameter and 2 mm thickness were prepared from Whatman (grade no. 1) filter paper and sterilized by dry heat for 1 h. Three discs of test samples were placed on three portion together with one disc with reference drug Ampicillin and disc impregnated with solvent (DMF) as negative control. The sterile discs previously soaked in a known concentration (25µg/ml in dimethyl formamide) of the test compounds (3a-k) were placed in nutrient agar medium. Ampicillin (20µg/disc) was used as positive control for bacteria. Plates were inverted and incubated for 24 h at 37±2^{0}C. Diameters of zone of inhibition (mm) were determined and average diameter of test samples were calculated in triplicate sets. Zone of inhibition of test compounds were compared with that produced by standard.

Anthelmintic Studies

Anthelmintic activity studies were carried out against two different species *Pheritima posthuma* and *Perionyx excavates*, at 2 mg/ml concentration. Collected earthworms were washed with normal saline water to remove soil and fecal matter. Suspensions of samples were prepared by triturating synthesized compounds (100 mg) with Tween 80 (0.5%) and normal saline solution (9%). and the resulting mixtures were stirred for 30 min. The suspensions were diluted to contain 0.2% w/v of the test samples [8, 12]. Suspension of reference drug, Albendazole, was prepared with the same concentration (0.2% w/v) in a similar way. Three sets of five earthworms of almost similar sizes (2 inch in length) were placed in Petri plates of 4 inch diameter containing 50 ml of suspension of test sample and reference drug. Another set of five earthworms was kept as control in 50 ml suspension of distilled water and Tween 80 (0.5%). The paralyzing and death times were noted and their mean was calculated for triplicate sets. The death time was ascertained by placing the earthworms in warm water (50 °C) which stimulated the movement, if the worm was alive.

Statistical evaluation

The statistics i.e. one way ANOVA and *t*-test, were applied on the values of mean ± SEM of triplicates (n=3) zone of growth of inhibition. The Schiff bases were compared with standard drug Ampicillin and control as DMF (Dimethyl formamide). While Anthelmintic activity of newly Schiff base compounds were analyzed by mean± S.D (n=5) compared with standard drug Albendazole.

Table 2: Antibacterial-sensitivity testing of compounds 3a-k

Compounds	Antibacterial activity Zone of inhibition (mm)							
	Gram (+) bacteria				Gram (-) bacteria			
S.No	SA	BC	EF	SE	EC	ST	SD	KP
3a	9±0.45	11±0.43	21±0.72	12±0.66	8±0.56	13±0.78	19±0.23	17±0.16
3b	8±0.32	11±0.64	13±0.20	7±0.19	7±0.24	9±0.35	8±0.19	10±0.42
3c	11±0.14	15±0.27	16±0.31	19±0.64	17±0.17	21±0.70	23±0.30	12±0.31
3d	7±0.37	20±0.50	20±0.48	8±0.38	11±0.41	12±0.28	13±0.40	22±0.42
3e	17±0.19	11±0.30	16±0.22	14±0.56	7±0.28	13±0.72	9±0.16	15±0.24
3f	16±0.28	15±0.11	18±0.88	19±0.33	9±0.59	17±0.35	24±0.44	20±0.72
3g	8±0.19	21±0.14	22±0.27	11±0.38	18±0.67	14±0.36	17±0.48	24±0.30
3h	8±0.38	16±0.58	14±0.10	13±0.42	9±0.44	16±0.36	15±0.37	21±0.34
3i	11±0.22	21±0.61	11±0.48	17±0.17	16±0.44	14±0.37	19±0.54	14±0.62
3j	14±0.54	24±0.74	13±0.70	20±0.27	17±0.47	18±0.32	22±0.43	11±0.19
3k	23±0.32	11±0.27	22±0.31	21±0.19	17±0.28	25±0.52	22±0.34	27±0.39
Ampicillin	25±0.00	25±0.00	26±0.00	24±0.00	22±0.00	27±0.00	26±0.00	26±0.00
DMF	….	…..	…..	…..	…..	…..	…..	…..

- *All the values are expressed as mean ± SEM of tripl icates*
- *SA = Staphylococcus aureus (ATCC 11633)*
- *ST = Salmonella typhi (MTCC 733)*
- *SE = Staphylococcus epidermidis (ATCC 155)*
- *SD = Shigella dysenteriae (ATCC 13313)*
- *EC = Escherichia coli (ATCC10536)*
- *BC = Bacillus cereus (ATCC 11778)*
- *EF = Enterococccus faecalis (ATCC 14506)*
- *KP = Klebsiella pneumoniae (ATCC 10031)*
- *PA=Pseudomonas aeruginosa (ATCC 27853*

Table 3: Anthelmintic activity of compounds 3a-k

Compounds	Earthworms Species			
	Perionyx excavatus		*Pheritima posthuma*	
	Mean paralyzing time (min)[a]	Mean death time (min)[a]	Mean paralyzing time (min)[a]	Mean death time (min)[a]
3a	10.15±0.79	15.43±0.79	14.29±0.18	20.30±0.48
3b	11.52±0.70	17.49±0.72	11.32±0.32	17.29±0.81
3c	12.18±0.30	20.19±0.12	16.19±0.28	23.92±0.18
3d	13.82±0.68	25.49±0.36	14.36±0.63	24.19±0.49
3e	10.13±0.13	20.43±0.41	16.19±0.35	29.19±0.19
3f	9.10±0.12	23.40±0.36	13.24±0.38	22.19±0.22
3g	9.86±0.45	25.28±0.68	11.40±0.38	26.19±0.49
3h	14.32±0.38	26.82±0.60	13.35±0.40	25.41±0.69
3i	11.23±0.23	27.48±0.56	16.40±0.69	27.40±0.65
3j	10.34±0.86	28.80±0.63	16.19±0.35	26.41±0.43
3k	10.49±0.39	19.39±0.53	12.13±0.83	26.90±0.69
Albendazole	10.13±0.69	15.72±0.52	11.53±0.85	17.92±0.59
Controlled	---------	---------	--------	--------

(a) Data are given as mean± S.D (n=5)

RESULTS AND DISCUSSION

Chemistry

The treatment of methyl-p-hydroxybenzoate **1** with hydrazine hydrate to yield 4-hydroxyphenyl-1-ketohydrazide **2**, it has been observed that in this hydrazination/amination reaction, the metoxy group of the resultant compound **1** was found to undergo replacement with hydrazide group of hydrazine hydrate. The resultant compound **2** was treated with different aromatic furfural aldehydes to yield substituted 2-(4-hydroxyaryl)-N'-[{5'-(substituted aryl)-furan-2'-yl}-methylidene]-ketohydrazides **(3a-k)** in the reaction of Schiff bases formation, the primary amine of compound **3** and aldehyde group of substituted aromatic aldehydes were found to undergo condensation to form imine group. All final compounds were pure and stable. Compounds were characterized by IR, ^{1}H NMR and Mass spectroscopy and CHN analysis. The IR spectral peaks of compound 3a-k, were recognized for C=O of CONH from 1649 to 1697; NH of CONH 1617-1649 and 3315-3389 cm^{-1}. In ^{1}H-NMR spectra of compounds 3a-k, showed the typical protons signals for OH, N=CH and CONH groups near 3.72-4.88, 9.54-9.87, 9.77-10.08 and 5.1-7.9 ppm δ range.

Biological studies

Newly synthesized novel Schiff bases were incorporated with chemotherapeutic pharmacophores and were screened

for their *in vitro* antibacterial activity by using standard drug Ampicillin. Antibacterial bioassay were done against gram positive bacterial strains, *S. aureus*, *B. cereus*, *E. faecalis* and *S. epidermidis* and gram negative bacterial strains, *E. coli*, *S. typhi*, *S. dysenteriae* and *K. pneumoniae*. Almost all the newly synthesized compounds **3a-k** showed good antibacterial activity. The results of antibacterial studies are presented in Table 2. While performing the antimicrobial studies by disk diffusion method, it was observed that, among tested compounds 3a-k**,** Some of the Compounds **3j, 3a, 3f, 3g, 3k** containing electron withdrawing groups (4-carboxylic, 4-bromo, 2,4-dinitro and 4-sulfoxy) phenyl substitution, were found to be equipotent against *B. cereus*, *S. dysenteriae*, *K. pneumonia*, *S. aureus*, *S. epidermidis* and *K. pneumoniae* when compared with Ampicillin as standard. Compound **3e** which containing electron donating group (4-methoxy) phenyl substitution also exhibited equipotent activity against *S. aureus* Compounds **3b, 3c, 3h, 3i** have shown moderate antibacterial activity when tested against strains of *S. aureus*, *B. cereus*, *E. faecalis*, and *S. epidermidis*, *E. coli*, *S. typhi*, *S. dysenteriae* and *K. pneumonia*.

On the other hand newly synthesized Schiff base derivatives 3a-k, also showed moderate to good anthelmintic activity at 2 $mgml^{-1}$ concentration. The results of anthelmintic activity revealed that Compounds were found to be most active possessing more activity against *Pheritima posthuma*, and *Perionyx excavates*, in respect of mean paralyzing and mean death time, in comparison to Albendazole as standard. The results of anthelmintic studies are tabulated in Table.3.

Structure activity relationship (SAR) studies from the result of antimicrobial and anthelmintic activities explained that substitution of aryl ring at C-5 position of furfuryl ring in the target compounds exhibited promising antibacterial and anthelmintic activities. From these results, it may be concluded that introduction of substituted aryl ring in the Schiff bases **3a-k** may contribute for enhanced antimicrobial and anthelmintic activities and also to evaluate the compounds for their broad spectrum of biological activities.

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