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Original article

Synthesis and antimicrobial activity of 7-(2-substituted phenylthiazolidinyl)-benzopyran-2-one derivatives

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ABSTRACT

A series of 7-(2-substituted phenylthiazolidinyl)-benzopyran-2-one derivatives have been synthesized by reaction of 7-amino-4-methyl-benzopyran-2-one (1) with an appropriate substituted aldehydes to obtain various Schiff bases (3a–k) which on treatment with thioglycolic acid afforded the title compounds (4a–k). Purity of the compounds has been confirmed by TLC. Structure of these compounds were established on the bases IR, ¹H NMR, ¹³C NMR and Mass spectral data. Schiff bases and title compounds were evaluated for antibacterial and antifungal activities against various bacterial and fungal strains. The results showed that compounds 3d, 3f, 4d, 4f and 4i (100 µg/ml) exhibited good antibacterial and antifungal activity as that of standard antibiotics Ciprofloxacin and Griseofulvin.

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1. Introduction

Coumarin derivatives reported with diverse structural features and versatile biological properties such as anti-inflammatory [1–3], antioxidant [4], vasorelaxant [5], cytotoxic [6], anti-HIV [7], antitubercular [8] and antimicrobial [9]. The literature survey revealed that compounds with thiazolidinone ring have been reported to demonstrate a wide range of pharmacological activities; which include antibacterial [10], antifungal [11,12], anticonvulsant [13]. The emergence of multidrug-resistant gram-positive bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA) have made treatment of infectious diseases difficult and over the last decades, became a serious medical problem. As pathogenic bacteria continuously evolve resistance to currently used antibacterial agents, so the discovery of novel and potent antibacterial agents is the best way to overcome bacterial resistance and develop effective therapies [14].

The molecular manipulation of promising lead compounds is still a major line of approach to develop new drugs. It involves an effort to combine the separate pharmacophoric groups of similar activity into one compound, thus making structural changes in the

biological activity. As reported earlier the thiazolidinone ring present in a large number of biologically active molecules of different pharmacological classes exhibited different activities. The historical importance of thiazolidine derivative was emphasized during the period 1941–1945, i.e. the development of penicillin which shows the presence of thiazoline ring.

The development of novel 7-amino-4-methylcoumarin is one of the most fascinating and useful areas in medicinal chemistry. The discovery of coumarin as therapeutic agents in early 1820's was the beginning of the coumarin drug development. The coumarin have a relatively broad spectrum with high activity profile against various bacteria and fungi [8,9].

Due to the diversified nature of coumarin and thiazolidinone which render them useful substances in drug research. In continuation of our search for novel biologically active coumarinyl heterocycles [1–3], in this paper we report the synthesis and antibacterial activity of a novel series of Schiff bases of 7-amino-4-methylcoumarin and its derivatives 3-(4-methyl-2-oxo-2H-chromen-7-yl)-2-phenylthiazolidin-4-one.

2. Chemistry

The synthesis of 7-amino-4-methylcoumarin (1) was carried out by the condensation of 3-amino phenol with ethylchloroformate

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by earlier reported methods [15,16]. The various substituted schiff's base of 7-amino-4-methylcoumarin (**3a–k**) was prepared by reacting 7-amino-4-methylcoumarin with substituted aromatic aldehydes (**2a–k**). Thus obtained Schiff base was further converted into thiazolidinyl coumarin derivatives (**4a–k**) on treatment with thioglycolic acid as shown in [scheme-1](#). The purity of compounds was confirmed by TLC using precoated silica gel as stationary phase, using appropriate solvent system as mobile phase and iodine vapors as visualizing agent. Structure of the title compounds were confirmed by IR, NMR and Mass spectral studies.

3. Result and discussion

Eleven derivatives of both Schiff bases and its phenyl-thiazolidinyl coumarin derivatives were reported. Structure of the synthesized compounds was established on the basis of IR, ^1H NMR, ^{13}C NMR and Mass spectral data. The general spectral characters of **3a–k** showed absorption bands ranging from $1555\text{--}1610\text{ cm}^{-1}$ for imine (>C=N-) formation and $1680\text{--}1710\text{ cm}^{-1}$ for (>C=O) of coumarin. Similarly compounds **4a–k** have showed absence of absorption band at $1555\text{--}1610\text{ cm}^{-1}$ and two sharp bands at $1680\text{--}1730\text{ cm}^{-1}$ gave conformation of >C=O in both thiazolidinone and coumarin ring in their respective spectra.

In particular, it must be pointed out that ^1H NMR of compounds **3a–k** showed presence of a singlet between δ 8.4–8.9 ppm indicated the formation of imine (>CH=N-) by simple condensation process. Further characteristic peaks at δ 2.4 ppm indicated the presence of 4- CH_3 group of coumarin ring in their structure. The compounds **3a–k** showed prominent singlet at δ 6.2–6.3 ppm for 3rd proton of coumarin and multiplet at δ 6.9–8.3 ppm for aromatic protons.

Title compound **4a–k** has shown singlet at δ 3.7–4.0 ppm ($-\text{CH}_2$ of thiazolidinone) and the absence of peak at δ 8.4–8.9 ppm confirmed the formation of thiazolidinone. ^{13}C NMR spectral data for the title compounds most characteristic peak around δ 53.0 and 63.0 ppm ($-\text{CH}_2$) indicated the formation thiazolidinone ring. Electron impact mass spectra showed an accurate molecular ion peak at m/z 337.4, 353.4, 367.4, 382.4, 406.2, 367.4, 327.6, 380.4, 355.3, 351.4 and 353.4 for title compounds **4a–k** respectively.

The synthesized compounds were evaluated for in vitro antibacterial and antifungal activity against various gram-positive, gram-negative bacteria and fungal strains using agar cup plate method. The results are shown in [table-1](#) and [2](#).

The results showed that compounds **3d**, **3f**, **4d**, **4f** and **4i** exhibited good antibacterial and antifungal activity at a concentration of $100\text{ }\mu\text{g/ml}$ as that of standard antibiotics Ciprofloxacin and Griseofulvin.

The activity is considerably affected by substituents of para position of phenyl ring of thiazolidinone. It has been observed that having furan group instead of phenyl showed moderate activity. It was also noted that the effect of imine and thiazolidinone ring on the antibacterial and antifungal activity. It was observed that the Schiff bases are less active than thiazolidinone derivatives.

4. Conclusion

In this paper we report the synthesis and antimicrobial activity of novel series of Schiff base (**3a–k**) and 7-(2-substituted-phenyl-thiazolidinyl)-coumarin derivatives (**4a–k**). The derivatives were prepared by condensation between 7-amino-4-methylcoumarin with various substituted aromatic aldehydes to obtain schiff bases, further it was condensed with thioglycolic acid to obtain title compounds (**4a–k**).

The preliminary in vitro antimicrobial activity of these novel series of derivative has evidenced that thiazolidinone derivatives are more active than that of schiff bases. Further studies are required for the detailed mechanism of action of these derivatives.

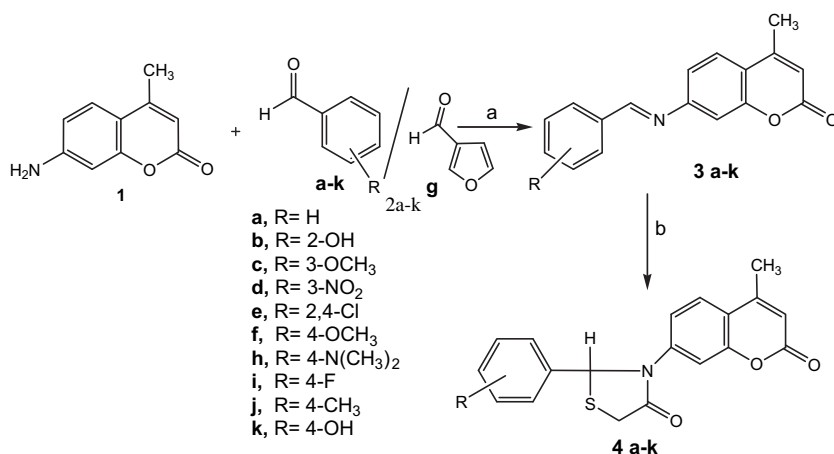
5. Experimental section

Melting points were determined in ThermoNik melting point apparatus and are uncorrected. IR spectrum was recorded on Thermo Nicolet FTIR 200 spectrophotometer by using KBr pellet values are expressed in cm^{-1} . NMR spectra were recorded in $\text{DMSO-}d_6$ using Varian 400 mHz mercury plus and chemical shift are reported in δ (ppm). Mass spectra were recorded on Shimadzu 2010 and mass values are reported in m/z .

Microbial strains obtained from NCL Pune, Maharashtra, India- *S aureus* NCIM 2602; *Bacillus subtilis* NCIM 2613; *Escherichia coli* NCIM 2666; *Pseudomonas desmolyticum* NCIM 2028; *Penicillium roquefortii* NCIM 712; *Aspergillus niger* NCIM 813.

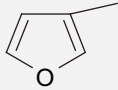
5.1. General procedure for the preparation of schiff's bases of coumarin: (**3a–k**)

A mixture of 7-amino-4-methylcoumarin (**1**) (1.5 g, 0.0085 mmol) and substituted aromatic aldehyde (**a–k**) (0.017 mmol) in 25 ml of



Scheme 1. Synthesis of 7-(2-substituted-phenylthiazolidinyl)-benzopyran-2-one derivatives (**4a–k**). Reagents and Reaction Conditions. (a) Acetic anhydride, Ethanol, Reflux, 6 h. (b) Thioglycolic acid, Dioxan, anhydrous ZnCl_2 , Reflux 4–6 h.

Table 1Antibacterial and antifungal activity of synthesized novel series of 7-(substituted benzylideneamino)-4-methylcoumarin derivatives (**3a–k**)*.

Zone of inhibition in mm							
Compound	R	<i>B. subtilis</i>	<i>S. aureus</i>	<i>E. coli</i>	<i>P. desmolyticum</i>	<i>P. roquefortii</i>	<i>A. niger</i>
3a	H	10(±0.89)	11(±1.07)	13(±1.31)	10(±1.37)	11(±1.07)	9(±1.29)
3b	2-OH	7(±1.32)	3(±0.58)	NA	NA	10(±0.89)	6(±0.89)
3c	3-OCH ₃	13(±0.97)	9(±1.29)	11(±1.16)	8(±0.97)	13(±1.32)	11(±1.06)
3d	3-NO ₂	20(±0.72)	15(±1.81)	9(±1.24)	10(±0.89)	4(±0.73)	NA
3e	2,4-Cl	12(±0.58)	5(±1.07)	14(±0.97)	13(±1.24)	9(±1.29)	7(±1.07)
3f	4-OCH ₃	21(±0.52)	13(±1.32)	7(±1.07)	NA	14(±0.97)	9(±0.97)
3g		11(±1.07)	7(±1.07)	12(±0.58)	7(±1.32)	6(±0.89)	NA
3h	4-N(CH ₃) ₂	14(±0.97)	6(±0.89)	8(±0.97)	8(±0.97)	NA	NA
3i	4-F	17(±1.07)	16(±0.68)	14(±0.97)	12(±0.73)	5(±1.07)	NA
3j	4-CH ₃	9(±1.65)	7(±1.07)	10(±1.37)	11(±1.16)	7(±1.07)	3(±0.58)
3k	4-OH	10(±1.37)	4(±1.03)	NA	NA	8(±1.16)	6(±0.89)
Ciprofloxacin		25(±0.87)	18(±0.63)	30(±0.58)	18(±0.73)	–	–
Gresiofulvin		–	–	–	–	2(±0.78)	17(±0.86)

Gram-positive bacterial strains: *B. subtilis*-*Bacillus subtilis*; *S. aureus*-*Staphylococcus aureus* Gram-negative bacterial strains: *E. coli*-*Escherichia coli*; *P. aeruginosa*-*Pseudomonas desmolyticum*. Fungal strains *P. roquefortii*-*Penicillium roquefortii*; *A. niger*-*Aspergillus niger*. The concentration of test compounds was 100 µg/ml. Solvent used DMF. NA = Not active. * mean value (SEM).

absolute alcohol and 0.5 ml of acetic anhydride were refluxed for 6 h and the solvent was removed under reduced pressure. The resulting crude compound was washed with cold water and recrystallized by using appropriate solvents. The purity of the compounds was confirmed by TLC using silica gel G as stationary phase, ethylacetate: cyclohexane (1:2) as mobile phase and iodine vapors as visualizing agent. The structure of the compounds was confirmed by spectroscopic data¹.

5.2. General procedure for the preparation of 7-(2-substituted-phenylthiazolidinyl)-benzopyran-2-one derivatives: (**4a–k**)

Schiff's bases (**3a–k**) (0.001 mmol) treated with mercaptoacetic acid (0.001 mmol) in dioxan (25 ml) in presence of anhydrous ZnCl₂ and reaction mixture was refluxed for 4–6 h (monitored by TLC), after cooling the reaction mixture was poured on crushed ice with stirring. Thus separated solid was then filtered, washed with sodium bicarbonate to remove the unreacted thioglycolic acid and recrystallized from ethanol. The purity of the compounds was confirmed

by TLC using silica gel G as stationary phase, ethylacetate: cyclohexane (1:2) as mobile phase and iodine vapors as visualizing agent

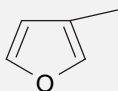
5.2.1. 7-(2-phenyl thiazolidinyl)-4-methyl-benzopyran-2-one (**4a**)

m.p.: 270–272; % yield: 75; IR (KBr) cm⁻¹: 1717 (C=O of α-pyrone and thiazolidone), 1631 (C=C stretching), 1377 (C–N stretching), 1253 (C=O stretching, 1135(C–O)), 651 (C–S–C); ¹H NMR (400 Mz, CDCl₃) δ ppm: 7.7–7.4 (m, 8H, Ar–H), 6.2 (s, 1H, 2-CH), 3.4, 3.3 (s, 2H, CH₂–S), 2.4 (s, 3H, CH₃); ¹³C NMR (400 Mz, CDCl₃) δ ppm: 170.3 (C=O of thiazolidone), 160.9 (C=O of α-pyrone), 153.6–116.5 (12C, Ar), 112.5 (C₃ of α-pyrone), 63.7 (C₂ of thiazolidone), 32.7 (C₄ of thiazolidone), 21.3 (C₄–CH₃ of α-pyrone). DIPMS m/z: 336.03 M⁺ and HRMS calcd for C₁₉H₁₅NO₃S: 337.0773 found 337.0769

5.2.2. 7-(2-(p-hydroxy)phenyl thiazolidinyl)-4-methyl-benzopyran-2-one (**4b**)

m.p.: 276–278; % yield: 70; IR (KBr) cm⁻¹: 3348 (–OH stretching), 2922 (C–H), 1719 (C=O of α-pyrone and

Table 2Antibacterial and antifungal activity of synthesized novel series of 7-(2-substituted phenyl thiazolidinyl)-benzopyran-2-one derivatives (**4a–k**)*

Zone of inhibition in mm							
Compound	R	<i>B. subtilis</i>	<i>S. aureus</i>	<i>E. coli</i>	<i>P. desmolyticum</i>	<i>P. roquefortii</i>	<i>A. niger</i>
4a	H	19(±0.97)	12(±0.73)	2(±1.07)	14(±0.97)	13(±0.97)	8(±1.16)
4b	2-OH	8(±0.86)	4(±0.73)	NA	NA	11(±1.07)	7(±1.07)
4c	3-OCH ₃	17(±1.07)	10(±0.89)	12(±0.58)	9(±1.07)	20(±1.16)	13(±1.07)
4d	3-NO ₂	27(±0.58)	19(±1.03)	10(±0.73)	9(±1.24)	3(±0.87)	NA
4e	2,4-Cl	10(±0.89)	7(±0.93)	15(±1.07)	11(±1.16)	8(±0.96)	6(±0.89)
4f	4-OCH ₃	21(±0.52)	16(±0.68)	8(±0.97)	NA	17(±0.73)	11(±1.06)
4g		10(±1.37)	8(±1.16)	13(±1.32)	6(±0.89)	5(±1.07)	NA
4h	4-N(CH ₃) ₂	13(±1.24)	5(±0.93)	10(±0.73)	7(±1.32)	NA	NA
4i	4-F	28(±0.73)	20(±0.82)	18(±0.58)	13(±0.97)	19(±0.73)	13(±0.58)
4j	4-CH ₃	8(±0.97)	6(±1.07)	20(±0.71)	15(±1.81)	6(±0.89)	3(±0.58)
4k	4-OH	9(±1.65)	4(±1.03)	NA	NA	9(±1.29)	5(±1.07)
Ciprofloxacin		25(±0.87)	18(±0.63)	30(±0.58)	18(±0.73)	–	–
Gresiofulvin		–	–	–	–	2(±0.78)	17(±0.86)

Gram-positive bacterial strains: *B. subtilis*-*Bacillus subtilis*; *S. aureus*-*Staphylococcus aureus* Gram-negative bacterial strains: *E. coli*-*Escherichia coli*; *P. aeruginosa*-*Pseudomonas desmolyticum*. Fungal strains *P. roquefortii*-*Penicillium roquefortii*; *A. niger*-*Aspergillus niger*. The concentration of test compounds was 100 µg/ml. Solvent used DMF. NA = Not active. * mean value(SEM).

thiazolidone), 1611 (C=C stretching), 1396 (C–N stretching), 1263 (>C=O stretching, 1155 (>C-O), 701 (C–S–C)); $^1\text{H NMR}$ (400 Mz, CDCl_3) δ ppm: 10.7 (s, 1H, OH), 7.8–7.3 (m, 7H, Ar–H), 6.2 (s, 1H, 3-CH), 3.3 (s, 2H, $\text{CH}_2\text{-S}$), 2.4 (s, 3H, CH_3). $^{13}\text{C NMR}$ (400 Mz, CDCl_3), δ ppm: 171.3 (>C=O of thiazolidone), 160.9 (<C=O of α -pyrone), 153.1–115.9 (12C, Ar), 112.7 (C_3 of α -pyrone), 55.7 (C_2 of thiazolidone), 33.7 (C_4 of thiazolidone), 21.3 ($\text{C}_4\text{-CH}_3$ of α -pyrone). DIPMS m/z : 353.07 M^+ and HRMS calcd for $\text{C}_{19}\text{H}_{15}\text{NO}_4\text{S}$: 353.0722 found 353.0700.

5.2.3. 7-(2-(*m*-methoxy)-phenyl thiazolidinyl)-4-methyl-benzopyran-2-one (**4c**)

m.p.: 258–260; % yield: 55; IR (KBr) cm^{-1} : 2927 (>C-H), 1727 (>C=O of α -pyrone and thiazolidone), 1610 (C=C stretching), 1356 (C–N stretching), 1260 (>C=O stretching, 1145 (>C-O), 697 (C–S–C)); $^1\text{H NMR}$ (CDCl_3) δ ppm: 8.3–7.4 (m, 7H, Ar–H), 6.23 (s, 1H, 2-CH), 3.8 (s, 2H, $\text{CH}_2\text{-S}$), 3.6 (s, 3H, OCH_3), 2.4 (s, 3H, CH_3). $^{13}\text{C NMR}$ (400 Mz, CDCl_3), δ ppm: 171.3 (>C=O of thiazolidone), 160.9 (<C=O of α -pyrone), 160.5–115.9 (12C, Ar), 112.7 (C_3 of α -pyrone), 65.7 (C_2 of thiazolidone), 33.7 (C_4 of thiazolidone), 21.1 ($\text{C}_4\text{-CH}_3$ of α -pyrone). DIPMS m/z : 367.09 M^+ and HRMS calcd for $\text{C}_{20}\text{H}_{17}\text{NO}_4\text{S}$: 367.0878 found 367.0870.

5.2.4. 7-(2-(*m*-nitro)-phenyl thiazolidinyl)-4-methyl-benzopyran-2-one (**4d**)

m.p.: 249–251; % yield: 48; IR (KBr) cm^{-1} : 1728 (>C=O of α -pyrone and thiazolidone), 1613 (C=C stretching), 1359 (C–N stretching), 1250 (>C=O stretching), 631 (C–S–C); $^1\text{H NMR}$ (400 Mz, CDCl_3) δ ppm: 7.8–7.3 (m, 7H, Ar–H), 6.2 (s, 1H, 2-CH), 3.8 (s, 2H, $\text{CH}_2\text{-S}$), 2.4 (s, 3H, CH_3). $^{13}\text{C NMR}$ (400 Mz, CDCl_3), δ ppm: 171.1 (>C=O of thiazolidone), 160.9 (<C=O of α -pyrone), 153.1–116.9 (12C, Ar), 112.1 (C_3 of α -pyrone), 64.7 (C_2 of thiazolidone), 33.7 (C_4 of thiazolidone), 21.3 ($\text{C}_4\text{-CH}_3$ of α -pyrone). DIPMS m/z : 382.06 M^+ and HRMS calcd for $\text{C}_{19}\text{H}_{14}\text{N}_2\text{O}_5\text{S}$: 382.0623 found 382.0619.

5.2.5. 7-(2-(*o,p*-dichloro)-phenyl thiazolidinyl)-4-methyl-benzopyran-2-one (**4e**)

m.p.: 277–279; % yield: 60; IR (KBr) cm^{-1} : 1730 (>C=O of α -pyrone and thiazolidone), 1602 (C=C stretching), 1342 (C–N stretching), 1265 (>C=O stretching), 625 (C–S–C); $^1\text{H NMR}$ (400 Mz, CDCl_3) δ ppm: 7.4–6.8 (m, 8H, Ar–H), 6.2 (s, 1H, 2-CH), 5.8 (s, 1H, CH–S), 3.5 (s, 2H, $\text{CH}_2\text{-S}$), 2.4 (s, 3H, CH_3). $^{13}\text{C NMR}$ (400 Mz, CDCl_3), δ ppm: 171.3 (>C=O of thiazolidone), 160.9 (<C=O of α -pyrone), 152.9–116.9 (12C, Ar), 112.5 (C_3 of α -pyrone), 56.7 (C_2 of thiazolidone), 33.7 (C_4 of thiazolidone), 21.3 ($\text{C}_4\text{-CH}_3$ of α -pyrone). DIPMS m/z : 405.01 M^+ and HRMS calcd for $\text{C}_{19}\text{H}_{13}\text{Cl}_2\text{NO}_3\text{S}$: 404.9993 found 404.9990.

5.2.6. 7-(2-(*p*-methoxy)-phenyl thiazolidinyl)-4-methyl-benzopyran-2-one (**4f**)

m.p.: 267–269; % yield: 45; IR (KBr) cm^{-1} : 1735 (>C=O of α -pyrone and thiazolidone), 1596 (C=C stretching), 1362 (C–N stretching), 1257 (>C=O stretching), 639 (C–S–C); $^1\text{H NMR}$ (400 Mz, CDCl_3) δ ppm: 8.1–6.8 (m, 8H, Ar–H), 6.2 (s, 1H, 2-CH), 5.9 (s, 1H, CH–S), 3.5 (s, 2H, $\text{CH}_2\text{-S}$), 3.7 (s, 3H, OCH_3), 2.4 (s, 3H, CH_3). $^{13}\text{C NMR}$ (400 Mz, CDCl_3), δ ppm: 171.1 (>C=O of thiazolidone), 160.9 (<C=O of α -pyrone), 152.9–116.9 (12C, Ar), 112.5 (C_3 of α -pyrone), 65.7 (C_2 of thiazolidone), 58.5 (4- OCH_3), 33.7 (C_4 of thiazolidone), 21.3 ($\text{C}_4\text{-CH}_3$ of α -pyrone). DIPMS m/z : 367.06 M^+ and HRMS calcd for $\text{C}_{20}\text{H}_{17}\text{NO}_4\text{S}$: 367.0878 found 367.0870.

5.2.7. 7-(2-(*o*-furan)-phenyl thiazolidinyl)-4-methyl-benzopyran-2-one (**4g**)

m.p.: 280–282; % yield: 44; IR (KBr) cm^{-1} : 1723 (>C=O of α -pyrone and thiazolidone), 1580 (C=C stretching), 1378 (C–N

stretching), 1253 (>C=O stretching), 635 (C–S–C); $^{13}\text{C NMR}$ (400 Mz, CDCl_3), δ ppm: 171.3 (>C=O of thiazolidone), 160.9 (<C=O of α -pyrone), 155.1–115.7 (12C, Ar), 112.5 (C_3 of α -pyrone), 59.7 (C_2 of thiazolidone), 33.7 (C_4 of thiazolidone), 19.7 ($\text{C}_4\text{-CH}_3$ of α -pyrone). DIPMS m/z : 327.06 M^+ and HRMS calcd for $\text{C}_{17}\text{H}_{13}\text{NO}_4\text{S}$: 327.0565 found 327.0560.

5.2.8. 7-(2-(*N,N*-dimethyl)-phenyl thiazolidinyl)-4-methyl-benzopyran-2-one (**4h**)

m.p.: 268–270; % yield: 48; IR (KBr) cm^{-1} : 1723 (>C=O of α -pyrone and thiazolidone), 1600 (C=C stretching), 1385 (C–N stretching), 1262 (>C=O stretching), 695 (C–S–C); $^1\text{H NMR}$ (400 Mz, CDCl_3) δ ppm: 7.3–6.5 (m, 8H, Ar–H), 6.2 (s, 1H, 2-CH), 5.9 (s, 1H, CH–S), 3.5 (s, 2H, $\text{CH}_2\text{-S}$), 2.9 (s, 6H, $\text{N}(\text{CH}_3)_2$), 2.4 (s, 3H, CH_3). $^{13}\text{C NMR}$ (400 Mz, CDCl_3), δ ppm: 171.1 (>C=O of thiazolidone), 160.7 (<C=O of α -pyrone), 153.9–115.9 (12C, Ar), 112.3 (C_3 of α -pyrone), 65.7 (C_2 of thiazolidone), 41.3 (2C of $\text{N}(\text{CH}_3)_2$), 33.7 (C_4 of thiazolidone), 19.5 ($\text{C}_4\text{-CH}_3$ of α -pyrone). DIPMS m/z : 380.10 M^+ and HRMS calcd for $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_3\text{S}$: 380.1196 found 380.1190.

5.2.9. 7-(2-(*p*-fluoro)-phenyl thiazolidinyl)-4-methyl-benzopyran-2-one (**4i**)

m.p.: 257–259; % yield: 68; IR (KBr) cm^{-1} : 1727 (>C=O of α -pyrone and thiazolidone), 1597 (C=C stretching), 1385 (C–N stretching), 1143 (>C=O stretching), 659 (C–S–C); $^1\text{H NMR}$ (400 Mz, CDCl_3) δ ppm: 7.3–6.8 (m, 8H, Ar–H), 6.2 (s, 1H, 2-CH), 5.9 (s, 1H, CH–S), 3.5 (s, 2H, $\text{CH}_2\text{-S}$), 2.4 (s, 3H, CH_3). $^{13}\text{C NMR}$ (400 Mz, CDCl_3), δ ppm: 171.3 (>C=O of thiazolidone), 160.9 (<C=O of α -pyrone), 152.9–115.1 (12C, Ar), 112.5 (C_3 of α -pyrone), 65.7 (C_2 of thiazolidone), 33.7 (C_4 of thiazolidone), 19.3 ($\text{C}_4\text{-CH}_3$ of α -pyrone). DIPMS m/z : 355.01 M^+ and HRMS calcd for $\text{C}_{19}\text{H}_{14}\text{FNO}_3\text{S}$: 355.0678 found 355.0671.

5.2.10. 7-(2-(*p*-methyl)-phenyl thiazolidinyl)-4-methyl-benzopyran-2-one (**4j**)

m.p.: 254–256; % yield: 58; IR (KBr) cm^{-1} : 1735 (>C=O of α -pyrone and thiazolidone), 1596 (C=C stretching), 1383 (C–N stretching), 1257 (>C=O stretching), 709 (C–S–C); $^1\text{H NMR}$ (400 Mz, CDCl_3) δ ppm: 8.1–7.2 (m, 8H, Ar–H), 6.5 (s, 2H, CH_2), 6.2 (s, 1H, 2-CH), 3.5 (s, 2H, $\text{CH}_2\text{-S}$), 2.4 (s, 3H, CH_3). $^{13}\text{C NMR}$ (400 Mz, CDCl_3), δ ppm: 171.3 (>C=O of thiazolidone), 160.9 (<C=O of α -pyrone), 154.9–115.3 (12C, Ar), 112.5 (C_3 of α -pyrone), 65.7 (C_2 of thiazolidone), 33.3 (C_4 of thiazolidone), 21.3 (p-CH_3), 19.3 ($\text{C}_4\text{-CH}_3$ of α -pyrone). DIPMS m/z : 351.10 M^+ and HRMS calcd for $\text{C}_{20}\text{H}_{17}\text{NO}_3\text{S}$: 351.0929 found 351.0920.

5.2.11. 7-(2-(*p*-hydroxy)-phenyl thiazolidinyl)-4-methyl-benzopyran-2-one (**4k**)

m.p.: 277–278; % yield: 42; IR (KBr) cm^{-1} : 3400 (-OH stretching), 1723 (α -pyrone), 1600 (C=C stretching), 1375 (C–N stretching), 1255 (>C=O stretching), 635 (C–S–C); $^1\text{H NMR}$ (400 Mz, CDCl_3) δ ppm: 11.5 (b, 1H, OH), 7.3–6.6 (m, 8H, Ar–H), 6.2 (s, 1H, 2-CH), 5.9 (s, 1H, CH–S), 3.5 (s, 2H, $\text{CH}_2\text{-S}$), 2.4 (s, 3H, CH_3). $^{13}\text{C NMR}$ (400 Mz, CDCl_3), δ ppm: 171.3 (>C=O of thiazolidone), 160.7 (<C=O of α -pyrone), 156.9–115.9 (12C, Ar), 112.5 (C_3 of α -pyrone), 65.7 (C_2 of thiazolidone), 33.5 (C_4 of thiazolidone), 19.5 ($\text{C}_4\text{-CH}_3$ of α -pyrone). DIPMS m/z : 353.07 M^+ and HRMS calcd for $\text{C}_{19}\text{H}_{15}\text{NO}_4\text{S}$: 353.0722 found 353.0719.

6. Biological activity

The synthesized compounds were screened for antibacterial and antifungal activity using agar cup plate method [17–19]. Ciprofloxacin and Grisofulvin were used as standard drug for the antibacterial and antifungal activity respectively at a concentration of 50 $\mu\text{g/ml}$ and zone of inhibition of all newly synthesized compounds **3a–k** and **4a–k** was measured against various strains

(Table 1 and 2). The microbial strains used are *S aureus* NCIM 2602; *B subtilis* NCIM 2613; *E coli* NCIM 2666; *P desmolyticum* NCIM 2028; *P roquefortii* NCIM 712; *A niger* NCIM 813.

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