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Research article

SYNTHESIS AND EVALUATION OF ANTIMICROBIAL AND *IN-VITRO* ANTI-INFLAMMATORY ACTIVITYOF SOME PYRIMIDINE DERIVATIVES FROM CHALCONES

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ABSTRACT : In this present study, a series of some new pyrimidine derivatives were synthesized via the condensed of substituted 2-hydroxy acetophenones**(1a-g)**with 3,4,5-trimethoxybenzaldehyde**(2)**in ethanolic solution of sodium hydroxide to yield1-(2-hydroxy-substituted-phenyl)-3-(3,4,5-trimethoxy phenyl)prop-2-en-1-one**(3a-g)** (chalcones), these chalcones were further reacted with urea, thiourea in the presence of HCl in ethanol, which led to the formation of pyrimidine derivatives**(4a-g) & (5a-g)** respectively. The structures of newly synthesized compounds were confirmed by IR, ^{1}H NMR, mass and elemental analysis. All the synthesized compounds were evaluated for anti-inflammatory (*in-vitro*) and antimicrobial activity.
Key words: Chalcones, Pyrimidine derivatives, anti-inflammatory (*in-vitro*), antibacterial, antifungal activity.

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INTRODUCTION

Nitrogen containing heterocycles play an important role in medicinal chemistry and also contribute to the society by helping in different life processes. Pyrimidine is also nitrogen containing heterocyclic compound, it is six-membered heterocyclic compound consist of two nitrogen atoms at 1 and 3 positions in heterocyclic ring. Pyrimidine moiety is of great interest because they constitute an important class of natural and non-natural products, many of which exhibit useful biological activities. Pyrimidine derivatives form a component in a number of useful drugs and are associated with many biological and clinical applications (D. J. Brown et. al., 1984;R. C. Elderfield et. al., 1957).Pyrimidine derivatives generally studied are 2-hydroxy pyrimidine, 2-mercapto pyrimidine and 2-amino pyrimidine (Shailesh P. Prajapati et. al., 2012). Many derivatives of pyrimidine have displayed diverse biological activities such as antibacterial (Deshmukh M Bet. al., 2009;Roth B et. al., 1980), antifungal (Ingaral N et. al, 2007),antiviral (Amr A E, et. al, 2007),anti-inflammatory (Sondhi S M, et. al., 2009), anticancer (Xie F, et. al., 2009),anti-depressive (Bernier J. L, et. al,1980), antihistaminic (Rahaman S A, et. al., 2009) and analgesic (El-Gazzar A B A,et. al., 2008).

Owing to the biological significance of these classes of compounds and in continuation of our ongoing study on heterocyclic compounds and anti-inflammatory, antimicrobial agents(Satish Babulal Jadhav, et. al.,2015), we planned to synthesize a series of some novelpyrimidine derivatives. In this present study various1-(2-hydroxy-substitutedphenyl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one(3a-g) (Chalcones), were prepared by Claisen-Schmidt condensation of Substituted 2-hydroxy acetophenones with3,4,5-trimethoxybenzaldehyde in presence of ethanol and NaOH.

The Chalcones were subjected to condensation reaction with urea, thiourea in the presence of HCl and ethanol as solvent to produce 4-(2-hydroxy-substitutedphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-ol(4a-g)and4-(2-hydroxy-substitutedphenyl)-6-(3,4,5-trimethoxy phenyl) pyrimidin-2-thiol(5a-g)respectively (Scheme-I). The structures of all synthesizedcompounds were assigned on the basis of IR, Mass, ^{1}H NMR spectral data and elemental analysis. Further these compounds were subjected for anti-inflammatory (*in-vitro*), antifungal and antibacterial activity.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded using Perkin –Elmer spectrometer.^{1}H NMR spectra were recorded on Brucker Advance II 400 spectrometer in DMSO by using TMS as internal standard. Thin layer chromatography was performed with E. Merck precoated TLC plates, silica gel $60F_{254}$ with thickness of 0.25mm and spots were visualized by irradiation with ultraviolet light (254 nm). Physical constants and analytical data of all the compounds reported in this paper are summarized in Table 1.

Synthesis of 1-(2-hydroxy-substitutedphenyl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (Chalcones) from substituted 2-hydroxy acetophenones and 3,4,5-trimethoxybenzaldehyde(3a-g)

A mixture of substituted 2-hydroxy acetophenones **(1a-g)**(0.01 mol) and3,4,5-trimethoxybenzaldehyde(**2**)(0.01 mol) was stirred in ethanol (30 mL) and thensodiumhydroxide solution (15 ml, 0.02 mol) was added to it. The reaction mixture was kept overnight at room temperature and then it was poured on crushed ice and acidified with dilute hydrochloric acid. The Chalcones derivative precipitates out as solid. Then it was filtered and purified by recrystallization from acetic acid.

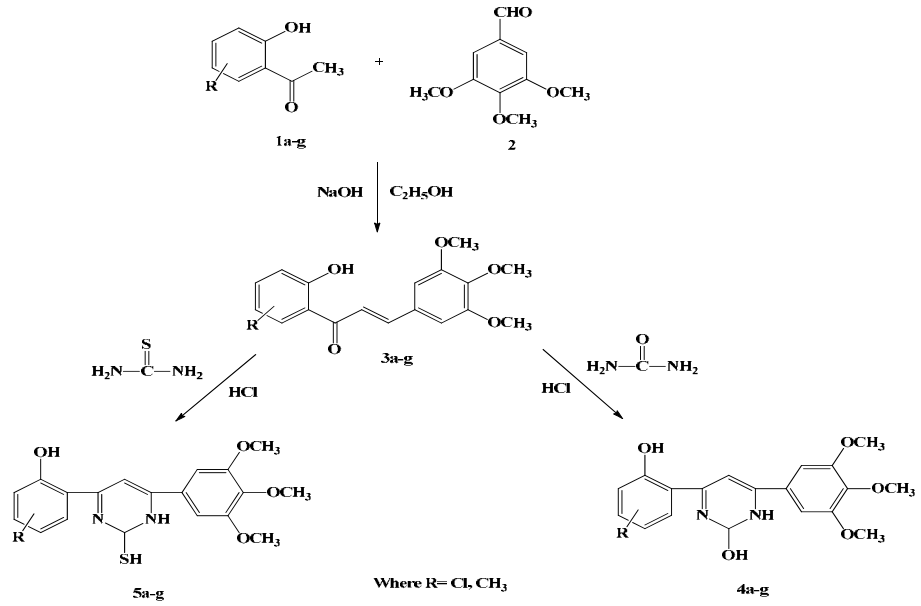
Synthesis of 4-(2-hydroxy-Substituted-phenyl)-6-(3, 4, 5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-ol (Dhaval M. Patel, et. al., 2009)(4a-g)

To a reaction mixture 1-(2-hydroxy-substitutedphenyl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (Chalcones) **(3a-g)**(0.02 mol) with urea (0.02 mole) in 100ml round bottom flask, hydrochloric acid 2-4 drops in 10 ml of alcohol was added. The reaction mixture was refluxed for 8-10 hr, after completion of reaction; it was poured into 250 ml of ice cold water kept for some time, where yellow color precipitate separated out. The so formed precipitate was filtered, and the product was recrystallized from ethanol.

Synthesis of 4-(2-hydroxy-Substituted-phenyl)-6-(3,4,5-trimethoxyphenyl))-1,2-dihydropyrimidin-2-thiol (Dhaval M. Patel, et. al., 2009) (5a-g)

To a reaction mixture 1-(2-hydroxy-substitutedphenyl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (Chalcones) **(3a-g)**(0.02 mol) with thiourea (0.02 mole) in 100ml round bottom flask, hydrochloric acid 2-4 drops in 10 ml of alcohol was added. The reaction mixture was refluxed for 8-10 hr, after completion of reaction; it was poured into 250 ml of ice cold water kept for some time, where yellow color precipitate separated out. The so formed precipitate was filtered, and the product was recrystallized from ethanol.

Scheme-I



RESULT AND DISCUSSION

Literature survey reveals that synthesis of 4-(2-hydroxy-Substituted-phenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-ol derivatives (4a-g) and of 4-(2-hydroxy-Substituted-phenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-thiol derivatives (5a-g)were not reported. Hence it was thought worthwhile to synthesize these compounds. The structures of the synthesized compounds (4a-g) and (5a-g) were confirmed on the basis of spectral and elemental analysis. Selected diagnostic band of the IR spectra of (4a-g) showed useful information about the structure of the compounds. It showed 1690.53 cm-^{1} (C=N str) and 3423.16 cm-1 (NH) because of ring closure. Further, in their ^{1}H NMR (DMSO) spectrums, the appearance of a signal at δ6.84 (s, 1H, -CH- pyrimidine), 3.36 (s, 1H, pyrimidine -OH) and 2.51 (s, 1H, pyrimidine NH) confirms the presence of1,2-dihydropyrimidin-2-ol ring.

Similarly, the structures of compounds 5a-gwere confirmed on the basis of spectral and elemental analysis. The IR spectrum of 5a-gexhibited a band due to 2843.80 cm^{-1} (SH), 1697.20 cm^{-1} (C=N str), which indicates the presence of 1,2-dihydropyrimidin-2-thiol.Further, in their 1H NMR (DMSO) spectrums, the appearance of a signal at5.55 (d, 1H, -CH- pyrimidine), 2.85-2.84 (d, 1H,pyrimidine NH), 2.51 (s, 1H,pyrimidine -SH) confirms the presence of 1,2-dihydropyrimidin-2-thiol ring. The synthetic pathway followed for the synthesis of the title compounds is described in Scheme-I.

Spectral data of compounds

4-(3-chloro-2-hydroxyphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-ol (4a):

Yield 85%; m.p. 120^{o}C: Elemental analysis Calcd for ($C_{19}H_{19}ClN_2O_5$); C, 58.39; H, 4.90; N, 7.17; found: C, 58.30; H, 4.79; N, 6.95;IR (KBr pellets Cm^{-1}): 3390 cm^{-1}(OH), 3095.13 cm^{-1} (Ar-C-H str.), 1692.45 cm^{-1}(C=N str), 1584.25 cm^{-1} (Ar C=C), 3420.12 cm^{-1}(NH) and 768.58 cm^{-1} (C-Cl str.); ^{1}H NMR (DMSO, 400 MHz), δ12.65 (s, 1H, Ar-OH), 7.78-6.50 (m, 5H, Ar-H), 6.82 (s, 1H, -CH- pyrimidine), 5.50-5.48 (d, 1H,pyrimidine), 3.78 (s, 6H, 2x -OCH_3), 3.70 (s, 3H, -OCH_3), 3.35 (s, 1H,pyrimidine -OH), 2.53 (s, 1H,pyrimidine NH).

4-(5-chloro-2-hydroxyphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-ol (4b):

Yield 82%; m.p. 160^{o}C: Elemental analysis Calcd for ($C_{19}H_{19}ClN_2O_5$);C, 58.39; H, 4.90; N, 7.17; found: C, 58.34; H, 4.90; N, 7.12; IR (KBr pellets Cm^{-1}): 3425.12 cm^{-1}(OH), 3100.00 cm^{-1} (Ar-C-H str.), 1685.15 cm^{-1} (C=N str), 1590.22 cm^{-1} (Ar C=C), 3440.30 cm^{-1}(NH) and 765.18 cm^{-1} (C-Cl str.);^{1}H NMR (DMSO, 400 MHz), δ12.61 (s, 1H, Ar-OH), 7.75-6.50 (m, 5H, Ar-H), 6.80 (s, 1H, -CH- pyrimidine), 5.50-5.48 (d, 1H,pyrimidine), 3.75 (s, 6H, 2x -OCH_3), 3.68 (s, 3H, -OCH_3), 3.37 (s, 1H,pyrimidine -OH), 2.55 (s, 1H,pyrimidine NH).

4-(3,5-dichloro-2-hydroxyphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-ol (4c):

Yield 88%; m.p. 138^{o}C: Elemental analysis Calcd for ($C_{19}H_{18}Cl_2N_2O_5$);C, 53.66; H, 4.27; N, 6.59; found: C, 53.60; H, 4.25; N, 6.49; IR (KBr pellets Cm^{-1}): 3400.18 cm^{-1}(OH), 3110.18 cm^{-1} (Ar-C-H str.), 1690.53 cm^{-1} (C=N str), 1570.48 cm^{-1} (Ar C=C), 3430.36 cm^{-1}(NH) and 770.58 cm-1 (C-Cl str.);^{1}H NMR (DMSO, 400 MHz), δ12.60 (s, 1H, Ar-OH), 7.77-6.50 (m, 5H, Ar-H), 6.78 (s, 1H, -CH- pyrimidine), 5.51-5.50 (d, 1H,pyrimidine), 3.76 (s, 6H, 2x -OCH_3), 3.70 (s, 3H, -OCH_3), 3.34 (s, 1H,pyrimidine -OH), 2.50 (s, 1H,pyrimidine NH).

4-(5-chloro-2-hydroxy-4-methylphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-ol (4d):

Yield 83%; m.p. 142^{o}C: Elemental analysis Calcd for ($C_{20}H_{21}ClN_2O_5$);C, 59.33; H, 5.23; N, 6.92; found: C, 59.25; H, 5.20; N, 6.80;IR (KBr pellets Cm^{-1}): 3400 cm-1 (OH), 3100.00 cm-1 (Ar-C-H str.), 1690.53 cm-1 (C=N str), 1594.25 cm-1 (Ar C=C), 3423.16 cm-1 (NH) and 770.58 cm-1 (C-Cl str.); ^{1}H NMR (DMSO, 400 MHz), δ12.68 (s, 1H, Ar-OH), 7.69-6.99 (m, 4H, Ar-H), 6.84 (s, 1H, -CH- pyrimidine), 5.52-5.51 (d, 1H,pyrimidine), 3.80 (s, 6H, 2x -OCH_3), 3.68 (s, 3H, -OCH_3), 3.36 (s, 1H,pyrimidine -OH), 2.51 (s, 1H,pyrimidine NH), 2.35 (s, 3H, -CH_3).

4-(2-hydroxy-3-methylphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-ol (4e):

Yield 80%; m.p. 133^{o}C: Elemental analysis Calcd for ($C_{20}H_{22}N_2O_5$);C, 64.85; H, 5.99; N, 7.56; found: C, 64.78; H, 5.90; N, 7.50; IR (KBr pellets Cm^{-1}): 3390.52 cm^{-1}(OH), 3080.18 cm^{-1} (Ar-C-H str.), 1675.13 cm^{-1}(C=N str), 1574.15 cm.$_{1}$ (Ar C=C), 3413.36 cm^{-1}(NH);^{1}H NMR (DMSO, 400 MHz), δ12.72 (s, 1H, Ar-OH), 7.65-6.95 (m, 5H, Ar-H), 6.81 (s, 1H, -CH- pyrimidine), 5.50-5.51 (d, 1H,pyrimidine), 3.82 (s, 6H, 2x -OCH_3), 3.68 (s, 3H, -OCH_3), 3.38 (s, 1H,pyrimidine -OH), 2.48 (s, 1H,pyrimidine NH), 2.30 (s, 3H, -CH_3).

4-(2-hydroxy-4-methylphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-ol (4f):

Yield 82%; m.p. 153^{o}C: Elemental analysis Calcd for ($C_{20}H_{22}N_2O_5$);C, 64.85; H, 5.99; N, 7.56; found:C, 64.80; H, 5.92; N, 7.55; IR (KBr pellets Cm^{-1}): 3400.15 cm^{-1}(OH), 3100.00 cm^{-1} (Ar-C-H str.), 1692.13 cm^{-1}(C=N str), 1592.15 cm^{-1} (Ar C=C), 3420.10 cm^{-1}(NH);^{1}H NMR (DMSO, 400 MHz), δ12.70 (s, 1H, Ar-OH), 7.63-6.95 (m, 5H, Ar-H), 6.78 (s, 1H, -CH- pyrimidine), 5.49-5.51 (d, 1H,pyrimidine), 3.87 (s, 6H, 2x -OCH_3), 3.65 (s, 3H, -OCH_3), 3.35 (s, 1H,pyrimidine -OH), 2.55 (s, 1H,pyrimidine NH), 2.38 (s, 3H, -CH_3).

4-(2-hydroxy-5-methylphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-ol (4g):
Yield 70%; m.p. 147°C: Elemental analysis Calcd for ($C_{20}H_{22}N_2O_5$);C, 64.85; H, 5.99; N, 7.56; found: C, 64.82; H, 5.00; N, 7.48;IR (KBr pellets Cm^{-1}): 3380.26 cm^{-1}(OH), 3080.10 cm^{-1} (Ar-C-H str.), 1600.50 cm^{-1}(C=N str), 1574.20 cm^{-1} (Ar C=C), 3415.10 cm^{-1}(NH); ^{1}H NMR (DMSO, 400 MHz), δ12.65 (s, 1H, Ar-OH), 7.60-6.90 (m, 5H, Ar-H), 6.71 (s, 1H, -CH- pyrimidine), 5.51-5.49 (d, 1H,pyrimidine), 3.85 (s, 6H, 2x -OCH_3), 3.65 (s, 3H, -OCH_3), 3.30 (s, 1H,pyrimidine -OH), 2.51 (s, 1H,pyrimidine NH), 2.35 (s, 3H, -CH_3).

4-(3-chloro-2-hydroxyphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-thiol (5a):
Yield 78%; m.p. 135°C: Elemental analysis Calcd for ($C_{19}H_{19}ClN_2O_4S$);C, 56.09; H, 4.71; N, 6.88; found: C, 55.95; H, 4.65; N, 6.82;3100.20 cm^{-1}(Ar C-H str.),2880.35 cm^{-1} (SH),1690.10 cm^{-1}(C=N str), 1595.35 cm^{-1}(Ar C=C) and 765.65 cm^{-1} (C-Cl str.); ^{1}H NMR (DMSO, 400 MHz), δ8.25 (s, 1H, Ar-OH), 7.70-6.84 (m, 5H, Ar-H), 5.54 (d, 1H, -CH- pyrimidine), 5.51-5.49 (d, 1H,pyrimidine), 3.81 (s, 6H, 2x -OCH_3), 3.65 (s, 3H, -OCH_3), 2.85-2.84 (d, 1H,pyrimidine NH), 2.50 (s, 1H,pyrimidine -SH).

4-(5-chloro-2-hydroxyphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-thiol (5b):
Yield 85%; m.p. 142°C: Elemental analysis Calcd for ($C_{19}H_{19}ClN_2O_4S$);C, 56.09; H, 4.75; N, 6.88;found; C, 56.00; H, 4.70; N, 6.80; IR (KBr) cm^{-1}: 3081.30 cm^{-1}(Ar C-H str.),2843.80 cm^{-1} (SH),1697.20 cm^{-1}(C=N str),1598.16 cm^{-1}(Ar C=C) and 767.69 cm^{-1} (C-Cl str.).^{1}H NMR (DMSO, 400 MHz), δ8.18 (s, 1H, Ar-OH), 7.72-6.82 (m, 5H, Ar-H), 5.55 (d, 1H, -CH- pyrimidine), 5.52-5.51 (d, 1H,pyrimidine), 3.80 (s, 6H, 2x -OCH_3), 3.69 (s, 3H, -OCH_3),2.85-2.84 (d, 1H,pyrimidine NH), 2.51 (s, 1H,pyrimidine -SH).

4-(3,5-dichloro-2-hydroxyphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-thiol (5c):
Yield 75%; m.p. 136°C: Elemental analysis Calcd for ($C_{19}H_{18}Cl_2N_2O_4S$);C, 51.71; H, 16.07; N, 6.35;found: C, 51.70; H, 15.90; N, 6.35;IR (KBr) cm^{-1}: 3025.15 cm^{-1}(Ar C-H str.),2833.30 cm^{-1} (SH),1697.20 cm^{-1}(C=N str),1595.25 cm^{-1}(Ar C=C) and 770.65 cm^{-1} (C-Cl str.);^{1}H NMR (DMSO, 400 MHz), δ8.52 (s, 1H, Ar-OH), 7.70-6.80 (m, 4H, Ar-H), 5.53(d, 1H, -CH- pyrimidine), 5.45-5.44 (d, 1H,pyrimidine), 3.85 (s, 6H, 2x -OCH_3), 3.65 (s, 3H, -OCH_3), 2.88-2.87 (d, 1H,pyrimidine NH), 2.50 (s, 1H,pyrimidine -SH).

4-(5-chloro-2-hydroxy-4-methylphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-thiol (5d):
Yield 82%; m.p. 150°C: Elemental analysis Calcd for ($C_{20}H_{21}ClN_2O_4S$);C, 57.07; H, 5.03; N, 6.66; found: C, 56.90; H, 5.00; N, 6.60; IR (KBr) cm^{-1}: 3075.20 cm^{-1}(Ar C-H str.),2823.80 cm^{-1} (SH),1660.30 cm^{-1}(C=N str),1560.26 cm^{-1}(Ar C=C) and 765.19 cm^{-1} (C-Cl str.); ^{1}H NMR (DMSO, 400 MHz), δ8.50 (s, 1H, Ar-OH), 7.72-6.80 (m, 4H, Ar-H), 5.53(d, 1H, -CH- pyrimidine), 5.48-5.47 (d, 1H,pyrimidine), 3.88 (s, 6H, 2x -OCH_3), 3.65 (s, 3H, -OCH_3), 2.85-2.84 (d, 1H,pyrimidine NH), 2.51 (s, 1H,pyrimidine -SH), 2.38 (s, 3H, -CH_3).

4-(2-hydroxy-3-methylphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-thiol (5e):
Yield 85%; m.p. 163°C: Elemental analysis Calcd for ($C_{20}H_{22}N_2O_4S$);C, 62.16; H, 5.74; N, 7.25; found:C, 62.00; H, 5.70; N, 7.15;IR (KBr) cm^{-1}: 3100.20 cm^{-1}(Ar C-H str.),2873.30 cm^{-1} (SH),1687.20 cm^{-1}(C=N str),1578.25 cm^{-1}(Ar C=C);^{1}H NMR (DMSO, 400 MHz), δ8.52 (s, 1H, Ar-OH), 7.70-6.80 (m, 5H, Ar-H), 5.53(d, 1H, -CH- pyrimidine), 5.46-5.47 (d, 1H,pyrimidine), 3.88 (s, 6H, 2x -OCH_3), 3.63 (s, 3H, -OCH_3), 2.85-2.84 (d, 1H,pyrimidine NH), 2.48 (s, 1H,pyrimidine -SH), 2.15 (s, 3H, -CH_3).

4-(2-hydroxy-4-methylphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-thiol (5f):
Yield 85%; m.p. 158°C: Elemental analysis Calcd for ($C_{20}H_{22}N_2O_4S$);C, 62.16; H, 5.74; N, 7.25; found:C, 62.00; H, 5.68; N, 7.00;IR (KBr) cm^{-1}: 3080.20 cm^{-1}(Ar C-H str.),2863.20 cm^{-1} (SH),1685.35 cm^{-1}(C=N str), 1568.15 cm^{-1}(Ar C=C); ^{1}H NMR (DMSO, 400 MHz), 8.52 (s, 1H, Ar-OH), 7.70-6.82 (m, 5H, Ar-H), 5.56(d, 1H, -CH- pyrimidine), 5.48-5.45 (d, 1H,pyrimidine), 3.78 (s, 6H, 2x -OCH_3), 3.59 (s, 3H, -OCH_3), 2.85-2.84 (d, 1H,pyrimidine NH), 2.52 (s, 1H,pyrimidine -SH), 2.25 (s, 3H, -CH_3).

4-(2-hydroxy-5-methylphenyl)-6-(3,4,5-trimethoxyphenyl)-1,2-dihydropyrimidin-2-thiol (5g):
Yield 72%; m.p. 154°C: Elemental analysis Calcd for ($C_{20}H_{22}N_2O_4S$);C, 62.16; H, 5.74; N, 7.25; found:C, 62.10; H, 5.64; N, 7.00;IR (KBr) cm^{-1}: 3050.25 cm^{-1}(Ar C-H str.),2853.10 cm^{-1} (SH),1680.15 cm^{-1}(C=N str), 1560.25 cm^{-1}(Ar C=C);^{1}H NMR (DMSO, 400 MHz), δ 8.52 (s, 1H, Ar-OH), 7.65-6.80 (m, 5H, Ar-H), 5.55 (d, 1H, -CH- pyrimidine), 5.48-5.45 (d, 1H,pyrimidine), 3.78 (s, 6H, 2x -OCH_3), 3.55 (s, 3H, -OCH_3), 2.85-2.84 (d, 1H,pyrimidine NH), 2.50 (s, 1H,pyrimidine -SH), 2.15 (s, 3H, -CH_3).

Biological activity

In-vitro anti-inflammatory activity (Gelias M N et. al, 1988; Gajraj Sharma, et. al, 2008).

The standard drug and synthesized compounds (5a-h) was dissolve in minimum amount of dimethyl formamide (DMF) and diluted with phosphate buffer (0.2 M, pH 7.4). Final concentration of DMF in all solutions was less than 2.0%. Test solution (1 ml) containing different concentration of drugs was mixed with 1 ml of 1% mM albumin solution in phosphate buffer and incubated at 27±1^{0}C in BOD incubator for 15 min. Denaturation was induced by keeping the reaction mixture at 60±1 ^{0}C in water bath for 10 min. After cooling, the turbidity was measured at 660nm (UV-Visible Shimadzu Spectrophotometer). Percentage of inhibition of denaturation was calculated from control where no drug was added. Each experiment was done in triplicate and average was taken. The ibuprofen was used as standard drug. Results are tabulated in table no. 1

$$\% \text{ of inhibition} = \left(\frac{Vt}{Vc} - 1 \right) X\ 100$$

Where, Vt = Mean absorbance value of test group.
Vc = Mean absorbance value of control group

Table-1: Anti-inflammatory activity of synthesized compounds (5a-g)

S.No.	Compounds	Mean absorbance value ± SEM	Inhibition of denaturation (in %)
1	Control	0.0850	-
2	Ibuprofen	0.162 ± 0.008	90.58
3	5a	0.118 ± 0.006	38.82
4	5b	0.134 ± 0.002	57.64
5	5c	0.141 ± 0.007	65.88
6	5d	0.115 ± 0.002	35.29
7	5e	0.102 ± 0.002	20.00
8	5f	0.105 ± 0.003	23.52
9	5g	0.095± 0.005	11.75

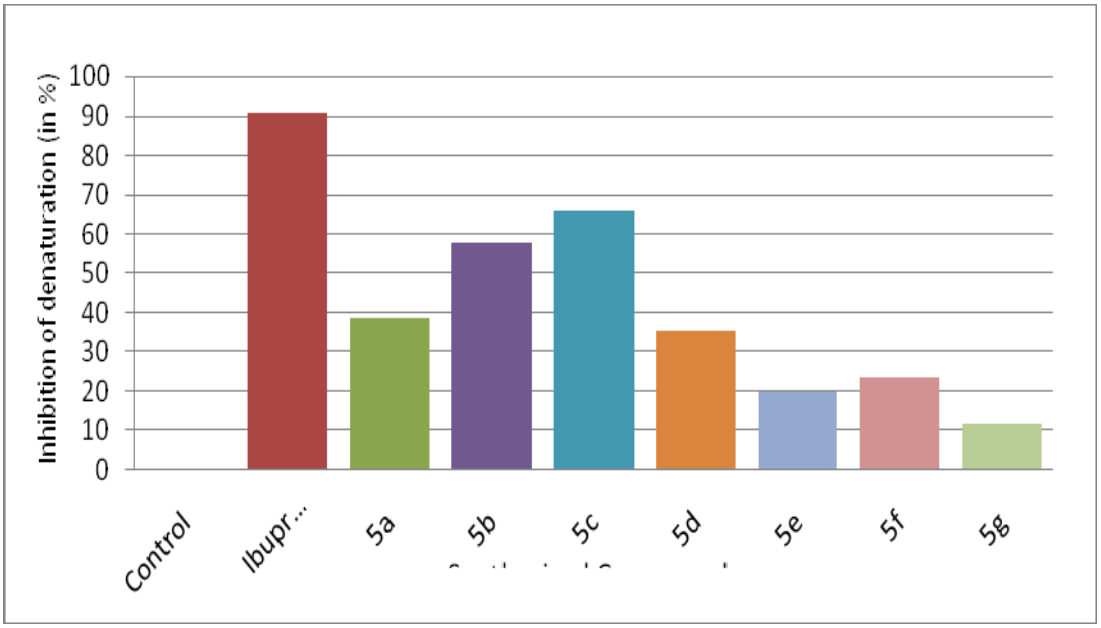


Fig. 1 Anti-inflammatory activity of the synthesized compounds

Antimicrobial activity

The newly synthesized compounds were screened for their antibacterial activity against *E.coli, Salmonella typhi, Staphylococcus aureus* and *Bacillus subtilis* by disc diffusion method(Cruickshank R, Duguid et. al., 1975; Collins A H, (Ed) et. al., 1976,21,22)using penicillin as standard and antifungal activity against *Aspergillus niger, Aspergillus flavus penicillium chrysogenum, Fusarium moneliforme,* by poison plate method (Cruickshank R, Duguid et. al., 1975) using Griseofulvin as reference standard and DMSO as control solvent. The investigation of antibacterial screening results indicates that few of the compounds shows significant property and some of the compounds are moderately active. The investigation of antifungal activity data revealed that some compounds have promising and some showed no antifungal activity. The results are shown in Table 2 and 3 respectively.

Table 2-Antibacterial screening results of the compounds 4a-g and 5a-g

S.No.	Compounds	*E.coli*	*Salmonella typhi*	*Staphylococcus aureus*	*Bacillus subtilis*
1	4a	12	11	14	13
2	4b	14	14	16	18
3	4c	17	19	24	20
4	4d	16	16	20	18
5	4e	08	14	11	11
6	4f	11	11	11	15
7	4g	04	03	14	10
8	5a	14	09	10	12
9	5b	14	13	16	18
10	5c	20	16	26	22
11	5d	12	10	218	14
12	5e	10	14	13	11
13	5f	09	12	11	15
14	5g	11	08	11	10
15	Penicillium	22	25	35	38
16	DMSO	-ve	-ve	-ve	-ve
	-ve no antibacterial activity				

Table-3: Antifungal screening results of the compounds 4a-gand 5a-g

S. No.	Compounds	*Aspergillus niger*	*Aspergillus flavus*	*Penicillum chrysogenum*	*Fusarium moneliforme*
1	4a	-ve	+ve	-ve	-ve
2	4b	-ve	-ve	RG	-ve
3	4c	-ve	-ve	-ve	-ve
4	4d	-RG	-ve	+ve	-ve
5	4e	-ve	+ve	RG	RG
6	4f	-ve	RG	-ve	-ve
7	4g	-ve	+ve	-ve	RG
8	5a	-ve	+ve	-ve	+ve
9	5b	+ve	+ve	+ve	RG
10	5c	-ve	-ve	-ve	-ve
11	5d	+ve	-ve	-ve	+ve
12	5e	-ve	RG	-ve	RG
13	5f	-ve	-ve	-ve	+ve
14	5g	-ve	-ve	RG	-ve
15	Griseofulvin	-ve	-ve	-ve	-ve
16	DMSO	+ve	+ve	+ve	+ve
	-ve No growth Antifungal activity present +ve Growth Antifungal activity absent RG Reduced growth				

CONCLUSION

In summary, Chalcone derivatives were cyclized by using urea and thiourea to obtain pyrimidine derivatives. All the pyrimidine derivatives were evaluated for antibacterial and (*in-vitro*) anti-inflammatory. All the synthesized compounds gave satisfactory spectral and analytical data. The screening of antimicrobial data revealed that most of the compounds show good antimicrobial activity, some compounds also exhibited good anti-inflammatory.

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REFERENCES

Amr A E, Nermien M S, Abdulla M M (2007). Synthesis, reactions and anti-inflammatory activity of heterocyclic systems fused to a thiophene moiety using citrazinic acid as synthon. Monatsh. Chem, Vol.138, 699-707.

Bernier J. L, Henichart J. P, Warin V, Baert. (1980). Synthesis and structure–activity relationship of a pyrimido [4,5-*d*]pyrimidine derivative with antidepressant activity. F. J. Pharm. Sci Vol. 69, 1343-1345.

Brown D. J. (1984). Comprehensive Heterocyclic Chemistry, Vol. 14, Pergamon Press, Oxford, UK.

Collins A H, (Ed) (1976). Microbiological Method, Second ed. Butter worth, London.

Cruickshank R, Duguid J P, Marion B P, Swain R H A (1975).Twelfth ed. Medicinal Microbiology, vol. II Churchill Livingstone, London, pp. 196-202

Deshmukh MB, Salunkhe SM, Patil DR, Anbhule P V, (2009). A noveland efficient one step synthesis of 2-amino-5-cyano-6-hydroxy-4-arylpyrimidines and their anti bacterial activity. Eur. J. Med. Chem., Vol. 44, 2651–2654.

Dhaval M. Patel, Dr. Dhrubo Jyoti Sen, (2009). Synthesis and Antimicrobial Screening By SAR Studies of Synthesized Chalocone Derivatives Having Heterocyclic ring International Journal Pharmaceutical Sciences, Vol. 1, 1, 35-41.

El-Gazzar Abed-Rahman B A, Mervat M. El-Enany, Mahmoud N. Mahmoud, (2008). Synthesis, analgesic, anti-inflammatory, and antimicrobial activity of some novel pyrimido[4,5-*b*]quinolin-4-ones Bioorg. Med.Chem, Vol. 16, 3261-3273.

Elias G, Rao MNA, (1998). Inhibition of albumin Denaturation and anti-inflammatory activity of dehydrozingerone and its analogs. Indian Journal Experimental Biology, vol.26, 540-42.

Gajraj Sharma, Jayachandran E, Sreenivasa G M, (2008). Synthesis of Bioactive molecule Fluoro Benzothiazole Comprising Quinazolylinyl Oxadiazole Derivatives For Biological and Pharmacological Screening Ultra Chemistry, Vol. 4, 1, 103, 144.

Ingaral N, Saravanan G, Amutha P, Nagarajan S (2007). Synthesis, in vitroantibacterial and antifungal evaluations of 2-amino-4-(1-naphthyl)-6-arylpyrimidines. Eur. J. Med. Chem., Vol. 42, 517-520.

Rahaman SA, Pasad YR, Kumar P, Kumar B (2009). Synthesis and anti-histaminic activity of some novel pyrimidines. Saudi Pharmaceutical Journal, Vol. 17: 255-258.

Roth B, Strelitz JZ, Rauckman BS, (1980). 2, 4-Diamino-5-benzylpyrimidines and analogs as antibacterial agents. 2. CAlkylation of pyrimidines with Mannich bases and application to the synthesis of trimethoprim and analogs. J. Med. Chem, Vol. 23,3, 379-384.

Satish Babulal Jadhav, Shantilal D. Rathod (2015). Design, Synthesis and *In-Vitro* Anti-Inflammatory, Antimicrobial Activities of Some Novel 2-(6-methoxynaphthalen-5-yl)-3-phenylthiazolidin-4-one derivatives, World Journal Of Chemistry And Pharmaceutical Science, Vol. 4, 09, 1288-1297.

Shailesh P. Prajapati, Dasharath P. Patel, Pankaj S. Patel, (2012). Synthesis, spectral and microbial studies of 4-(substitutedphenyl)-1-(2,4-dinitrophenyl)-3-methyl-4,5-dihydro-pyrazolo[3,4-*d*]pyrimidin-6-ol, Der Chemica Sinica, Vol. 3,4, 830-833.

Sondhi SM, Dinodia M, Rani R, Shukla R, Raghubir R (2009). Synthesis, antiinflammatory and analgesic activity evaluation of some pyrimidine derivatives. Ind J Chem., Vol. 49B:273-81.

Satish Babulal Jadhav, Shantilal D. Rathod (2015). Synthesis, characterization and *in-vitro* anti-inflammatory, antimicrobialctivities of some novel2, 4-disubstituted-1,5-benzothiazepine derivatives,Der Chemica Sinica, Vol. 6, 10,13-18.

Xie F, Zhao HB, Zhao L, Luo L, Hu Y (2009). Synthesis and biological evaluation of novel 2, 4, 5-substituted pyrimidine derivatives for anticancer activity. Bio org. Med. Chem. Lett.,Vol. 19, 275-278.

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