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Synthesis and biological activities of some new pyrimidine derivatives from chalcones

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ABSTRACT

Chalcones have been reported to present various biological activities such as anti-inflammatory, antioxidant, antitubercular, antibacterial activities. It is a basic moiety of many heterocyclic systems containing oxygen, sulphur and nitrogen. Nitrogen containing heterocyclic derivatives synthesized from chalcones have exhibited anti-inflammatory, antioxidant, antitubercular, antibacterial activities. An attempt has been made to synthesize chalcones by the reaction of 4-acetylpyridine with various aromatic and heteroaromatic aldehydes. Further, chalcones derivatives were cyclised to pyrimidine analogs by using thiourea, urea and guanidine hydrochloride. The newly synthesized pyrimidine derivatives have been characterized by UV, IR, ^{1}HNMR, ^{13}CNMR, Mass spectra and elemental analysis and evaluated for their anti-inflammatory, antioxidant, antitubercular and antibacterial activities. It was found that 2-amino pyrimidine analog bearing 4-fluoro substitution on phenyl ring (3d) has exhibited excellent antitubercular activity at lowest concentration in the series moreover it has also exhibited good anti-inflammatory and antioxidant activities.

Keywords: Chalcones, pyrimidine, antitubercular activity, anti-inflammatory activity, antioxidant activity, antibacterial activity.

INTRODUCTION

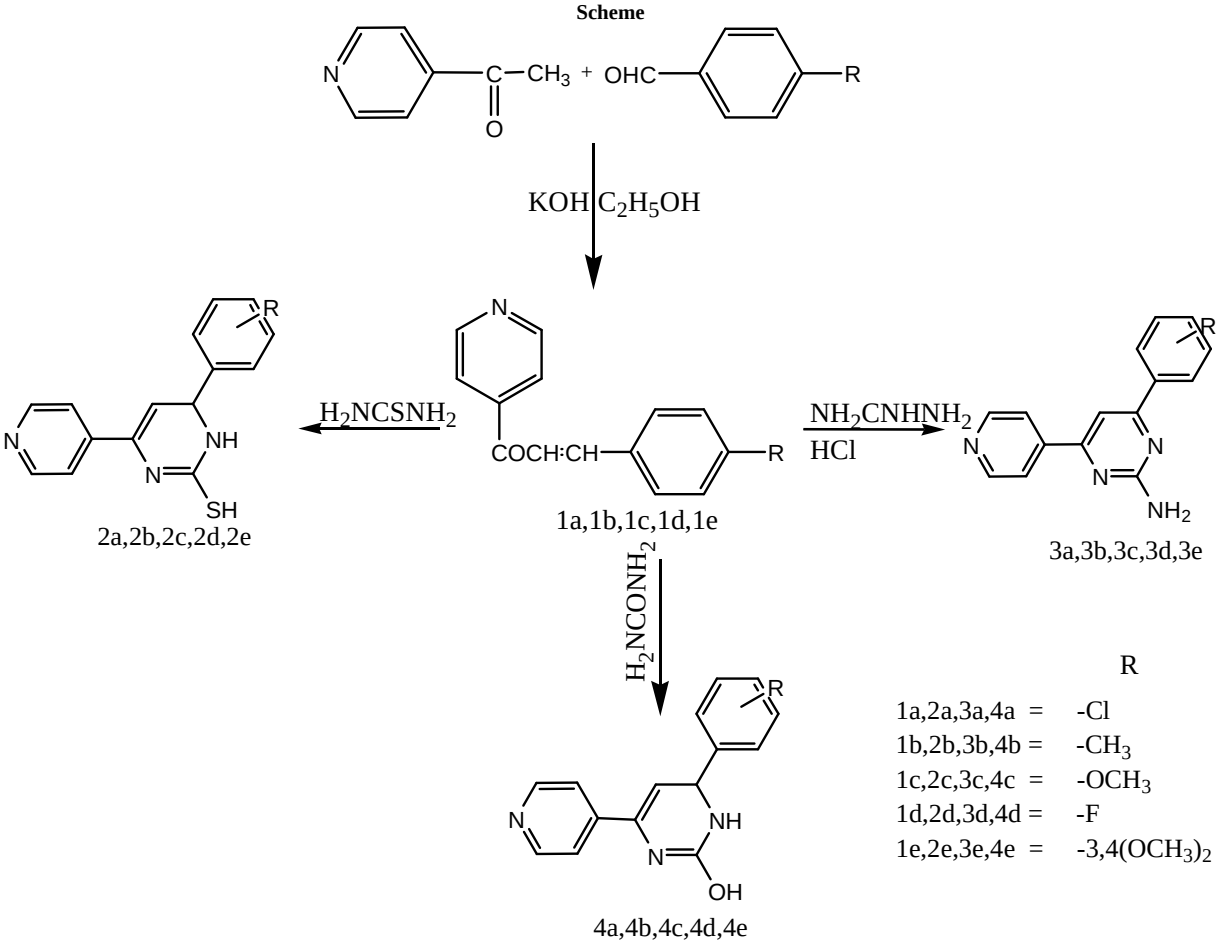
Heterocyclic compounds are abundant in nature and are of great significance to life because their structural subunits exist in many natural products such as vitamins, hormones, antibiotics etc. A practical method for the synthesis of such compounds is of great interest in synthetic organic chemistry [1]. Nitrogen containing heterocyclics play an important role in medicinal chemistry and also contribute to the society by helping in different life processes. Pyrimidine is a six-member heterocyclic compound that contains two nitrogen atoms at positions 1 and 3. The structure of the pyrimidine ring is similar to benzene and pyridine [2]. The key role pyrimidines play in cellular processes has made them valuable leads for drug discovery [3]. Pyrimidine derivatives are known to be biologically active compounds and substituted pyrimidines have shown wide range of biological activities like antitubercular [4-8], antibacterial [4,7, 9-11], antioxidant[4,9], anti-inflammatory [12] activity.

MATERIALS AND METHODS

All the melting points were determined in a Thermonik melting point apparatus and are uncorrected. The IR spectra of the synthesized compounds was recorded on a Fourier Transform IR spectrometer (model Shimadzu 8700) in the range of 400 -4000 using KBr pellets and the value of λmax were reported in cm^{-1}. ^{1}HNMR spectra was recorded on

Amx - 400 MHz NMR spectrometer using $CDCl_3$ and the chemical shifts (δ) reported are in parts per million downfield using tetramethylsilane (TMS) as internal reference. ^{13}CNMR spectra was recorded on Amx - 400 MHz NMR spectrometer using $CDCl_3$ and the chemical shifts (δ) reported are in parts per million downfield using tetramethylsilane (TMS) as an internal reference. A mass spectrum was recorded on Mass spectrophotometer (model Shimadzu) by LC-MS 2010A. The purity of the compounds was checked by thin-layer chromatography on silica gel G plates of 0.5mm thickness as stationary phase and combination of n-hexane: ethyl acetate in different ratios as mobile phase. The UV spectra of the synthesized compounds were recorded on UV–Visible spectrophotometer (model Shimadzu 1601) using methanol and the values of wave length (λ max) were reported in nm. Elemental analysis were analysed by Thermo Finnigan Flash EA 1112 Series.

Scheme



Preparation of 3-(4-substitutedphenyl)-1-(pyridin-4-yl) prop-2-en-1-one (1a-1e)

A mixture of 4-acetylpyridine (0.01 mol) and substituted benzaldehydes (0.01 mol) was stirred in ethanol (40 ml) and an aqueous solution of KOH (15 ml) was added to it. The stirring was continued for 6 hr and the mixture was kept overnight at room temperature. The mixture was then poured into crushed ice, acidified with HCl. The solid separated was filtered and recrystallized from ethanol.

Preparation of 6-(4-substitutedphenyl)-4-pyridin-4-yl-1,6-dihydropyrimidine-2-thiol (2a 2e)

A mixture of 3-(4-substitutedphenyl)-1-(pyridine-4-yl) prop-2-en-1-one (0.01 mol) and thiourea (0.01 mol) was refluxed for 22 h in 25 ml of ethanolic KOH solution. The reaction mixture was cooled to room temperature and kept overnight. The mixture was acidified with acetic acid and the solid product obtained was filtered and recrystallized from ethanol.

Preparation of 4-(4-substitutedphenyl)-6-pyridin-4-yl-pyrimidin-2-ylamine (3a-3e)
A mixture of 3-(4-substitutedphenyl)-1-(pyridine-4-yl) prop-2-en-1-one (0.01 mol) dissolved in alcohol (25 ml) , guanidine hydrochloride (0.01 mol) and solution of KOH (5 ml) was added and refluxed for 10 hours. The reaction mixture was cooled, poured into crushed ice. The product obtained was filtered, washed with water, dried and recrystallized from ethanol.

Preparation of 6-(4-substitutedphenyl)-4-pyridin-4-yl-1,6-dihydropyrimidin-2-ol (4a-4e)
3-(4-substitutedphenyl)-1-(pyridine-4-yl) prop-2-en-1-one (0.01 mol) was reacted with urea (0.01 mol) using ethanol as solvent in a round bottom flask. The reaction mixture was refluxed for 3 to 4 hrs with 10 ml NaOH. The content were cooled and poured into beaker containing crushed ice, the solid obtained was filtered, washed with water and recrystallized from ethanol.

3-(4-Chlorophenyl)-1-(pyridin-4-yl)prop-2-en-1-one ***1a****:*
Buff green solid; m.p.138-145ºC; Yield: 69.5%; λmax= 204.40; IR (KBr) cm^{-1}: 1682.96 cm^{-1} (C=O of α,β unsaturated ketone) , 1688.75 cm^{-1} (C=N str),1597.13 cm^{-1} (Ar C=C) and 750.69 cm^{-1}(C-Cl str.).

1-(Pyridin-4-yl)-3-tolyl prop-2-en-1-one ***1b:***
Light brown solid; m.p. 195-207ºC; Yield: 66.17 %; λmax= 203.00; IR (KBr) cm^{-1}: 3115.17 cm^{-1} (Ar C-H str.), 2876.95 cm^{-1} (Al C-H str.), 1678.36 cm^{-1} (C=O of α,β unsaturated ketone) , 1687.36 cm^{-1} (C=N str) and 1570.12 cm^{-1} (Ar C=C) .

3-(4-Methoxyphenyl)-1-(pyridin-4-yl) prop-2-en-1-one ***1c:***
Light green solid; m.p. 180-190ºC; Yield: 62.92%; λmax= 202.80; IR (KBr) cm^{-1}: 2842.23 cm^{-1} (Al C-H str.), 1679.11 cm^{-1} (C=O of α,β unsaturated ketone) , 1688.75 cm^{-1} (C=N str.), 1605.81 cm^{-1} (Ar C=C) and 1188.20 cm^{-1} [C-O-C(-OCH_3)] .

3-(4-Fluorophenyl)-1-(pyridin-4-yl) prop-2-en-1-one ***1d:***
Yellow solid; m.p. 204-210°C; Yield: 53.88 %; λmax= 203.60; IR (KBr) cm^{-1}: 2914.57 cm^{-1} (Al C-H str.), 1679.11 cm^{-1} (C=O of α,β unsaturated ketone) , 1688.75 cm^{-1} (C=N str.), 1605.81 cm^{-1} (Ar C=C) and 1288.50 cm^{-1} [C-F str.].

3-(3,4-Dimethoxyphenyl)-1-(pyridin-4-yl) prop-2-en-1-one ***1e:***
Brown solid; m.p. 186-191°C; Yield: 54.56 % ; λmax= 204.40; IR (KBr) cm^{-1}: 2909.74 cm^{-1} (Al C-H str.), 1672.36 cm^{-1} (C=O of α,β unsaturated ketone) , 1688.00 cm^{-1} (C=N str), 1606.77 cm^{-1} (Ar C=C) and 1160.23 cm^{-1} [C-O-C(-OCH_3)].

6-(4-Chlorophenyl)-4-pyridin-4-yl-1,6-dihydropyrimidine-2-thiol ***2a:***
Off white solid; m.p. 245-250ºC; Yield: 57.14 %; λmax= 203.60; IR (KBr) cm^{-1}: 3167.21 cm^{-1} (,Ar C-H str.), 1688.75 cm^{-1} (C=N str),1605.81 cm^{-1} (Ar C=C), 2266.46 cm^{-1} (SH) and 767.69 cm^{-1} (C-Cl str.).

4-Pyridin-4-yl-6-p-tolyl-1,6-dihydropyrimidine-2-thiol ***2b:***
Brown solid; m.p. 183-190ºC; Yield: 56.58 %; λmax= 203.60; IR (KBr) cm^{-1}: 3443.05 cm^{-1} (NH str.), 3101.64 cm^{-1} (Ar C-H str.), 2848.96 cm^{-1} (Al C-H str), 2267.42 cm^{-1} (SH), 1664.98 cm^{-1} (C=N str) and 1606.93 cm^{-1} (Ar C=C); ^{1}HNMR ($CDCl_3$, ppm): 7.81-7.83 [4H, (m, pyridyl)], 7.20-7.72 [4H, (m, Ar H)], 2.35 [1H, (s, pyrimidine NH], 4.36 [1H, (d, pyrimidine)], 1.27 [1H,(s,-SH)], 2.50 [3H,(s,-CH_3)]; ^{13}CNMR ($CDCl_3$, ppm): C (methyl)-21.1, C (benzene)-115.7-128.7, C (pyrimidine)-39.3-167.3, C (pyridine)-115.5-151.9; m/e 282 (Molecular ion), 267. 191, 92, 79; CHN: found C=68.12%, H=5.41% and N=14.85%. Calculated C=68.23%, H=5.33% and N=14.92%.

6-(4-Methoxyphenyl)-4-pyridin-4-yl-1,6-dihydropyrimidine-2-thiol ***2c:***
Brick red solid; m.p. 147-151ºC; Yield: 58.58 %; λmax= 203.40; IR (KBr) cm^{-1}: 3363.97 cm^{-1} (NH), 3167.22 cm^{-1} (Ar C-H str.), 2269.05 cm^{-1} (SH), 1683.93 cm^{-1} (C=N str) and 1608.70 cm^{-1} (Ar C=C).

6-(4-Fluorophenyl)-4-pyridin-4-yl-1,6-dihydropyrimidin-2-thiol ***2d:***
Buff yellow solid; m.p. 185-189ºC; Yield: 53.33 %; λmax= 203.00; IR (KBr) cm^{-1}: 3344.68 cm-1 (NH str.), 3067.91 cm^{-1} (Ar C-H str.), 2258.68 cm^{-1} (SH str.), 1683.93 cm^{-1} (C=N str), 1602.91 cm^{-1} (Ar C=C) and 1025.21 cm^{-1} (C-F str.); ^{1}HNMR($CDCl_3$, ppm): 7.90-8.18 [4H, (m, pyridyl)], 6.95-6.99 [4H, (m, Ar H)], 2.50 [1H,(s, pyrimidine NH)],

4.36 [1H, (d, pyrimidine)], 7.89 [1H, (d, pyrimidine)], 1.68 [1H,(s,-SH)]; ^{13}CNMR($CDCl_3$, ppm): C (pyridine)-125.8-142.6, C (pyrimidine)-40.02-164.9, C(benzene)- 113.3-131.15; m/e 286 (Molecular ion), 208, 190; CHN: found C=63.26%, H=4.18% and N=14.82% , Calculated C=63.08%, H=4.20% and N= 14.71%.

6-(3,4-Dimethoxyphenyl)-4-pyridin-4-yl-1,6-dihydropyrimidine-2-thiol ***2e:***
Yellow solid; m.p. 140-150ºC; Yield: 60.85 %; λmax= 205.20; IR (KBr) cm^{-1}: 3337.69 cm^{-1} (NH str.), 3039.34 cm^{-1} (Ar C-H str.), 2262.08 cm^{-1} (SH), 2940.61 cm^{-1} (Al C-H str), 1679.77 cm^{-1} (C=N str),1605.81 cm^{-1} (Ar C=C) and 1171.81 cm^{-1} [C-O-C(-OCH_3)].

4-(4-Chlorophenyl)-6-pyridin-4-yl-pyrimidin-2-ylamine ***3a****:*
Light brown solid; m.p. 223-230°C; Yield: 52.83 %; λmax= 204.20; IR (KBr) cm^{-1}: 3340.82 cm^{-1} (NH str.), 3063.06 cm^{-1} (Ar C-H str.), 1681.98 cm^{-1} (C=N str), 1605.86 cm^{-1} (Ar C=C) and 759.98 cm^{-1} (C-Cl str.).

4-Pyridin-4-yl-6-p-tolyl-pyrimidin-2-ylamine ***3b****:*
Yellow solid; m.p. 170-185ºC; Yield: 61.68 %; λmax= 204.00; IR (KBr) cm^{-1}: 3362.04 cm^{-1} (NH), 3067.91 cm^{-1} (Ar C-H str.), 2900.10 cm^{-1} (Al C-H str), 1683.93 cm^{-1} (C=N str) and 1602.91 cm^{-1} (Ar C=C).

4-(4-Methoxyphenyl)-6-pyridin-4-yl-pyrimidin-2-ylamine ***3c:***
Reddish brown solid; m.p. 225-228ºC; Yield: 47.68 %; λmax= 204.00; IR (KBr) cm^{-1}: 3251.22 cm^{-1} (NH str.), 3064.06 cm^{-1} (Ar C-H str.), 2904.92 cm^{-1} (Al C-H str), 1688.32 cm^{-1} (C=N str),1601.95 cm^{-1} (Ar C=C) and 1031.96 cm^{-1} [C-O-C(-OCH_3)].

4-(4-Fluorophenyl)-6-pyridin-4-yl-pyrimidin-2-ylamine ***3d:***
Yellow solid; m.p. 138-145ºC; Yield: 59.02 %; λmax= 203.40; IR (KBr) cm^{-1}: 3144.50 cm^{-1} (NH str.), 3039.94 cm^{-1} (Ar C-H str.), 1672.36 cm^{-1} (C=N str), 1600.02 cm^{-1} (Ar C=C) and 1044.5 cm^{-1} (C-F str.).

4-(3,4-Dimethoxyphenyl)-6-pyridin-4-yl-pyrimidin-2-ylamine ***3e:***
yellow solid; m.p. 230-238ºC; Yield: 51.62 %; λmax= 206.00; IR (KBr) cm^{-1}: 3434.14 cm^{-1} (NH str.), 3064.06 cm^{-1} (Ar C-H str.), 2951.22 cm^{-1} (Al C-H str.), 1682.32 cm^{-1} (C=N str.), 1601.95 cm^{-1} (Ar C=C) and 1300.08 cm^{-1} [C-O-C(-OCH_3)].

6-(4-Chlorophenyl)-4-pyridin-4-yl-1,6-dihydro-pyrimidin-2-ol ***4a****:*
Yellow solid; m.p. 180-197ºC; Yield: 56.58 %%; λmax= 203.40; IR (KBr) cm^{-1}: 3400 cm^{-1} (OH), 3101.64 cm^{-1} (Ar C-H str.), 1670.41 cm^{-1} (C=N str), 1604.81 cm^{-1} (Ar C=C), 3423.76 cm^{-1} (NH) and 771.58 cm^{-1} (C-Cl str.); ^{1}HNMR ($CDCl_3$, ppm): 8.11-8.12 [4H, (m, pyridyl)], 7.81-7.83 [4H, (m, Ar H)], 2.35 [1H, (s, pyrimidine NH)], 4.36 [1H, (d, pyrimidine)], 7.20-7.22 [1H, (d, pyrimidine)]; ^{13}CNMR($CDCl_3$, ppm): C (pyridine)-151.9-115.7, C (pyrimidine)-39.5-167.3, C (benzene)-125.8-132.7; m/e 286 (Molecular ion), 208, 192, 112, 80; CHN: Found C=63.15%, H=4.14% and N=14.62%. Calculated C=62.99%, H=4.19 and N= 14.69%.

4-Pyridin-4-yl-6-p-tolyl-1,6-dihydropyrimidin-2-ol ***4b****:*
Brick red solid; m.p. 164-175ºC; Yield: 52.07 %; λmax= 203.40; IR (KBr) cm^{-1}: 3462.34 cm^{-1} (NH str.), 3425.69 cm-1 (OH str.) 3152.22 cm^{-1} (Ar C-H str.), 2848.02 cm^{-1} (Al C-H str.), 1682.00 cm^{-1} (C=N str.) and 1602.91 cm^{-1} (Ar C=C).

6-(4-Methoxyphenyl)-4-pyridin-4-yl-1,6-dihydropyrimidin-2-ol ***4c:***
Brick red solid; m.p. 204-209ºC; Yield: 42.68 %; λmax= 201.00; IR (KBr) cm^{-1}: 3422.70 cm-1 (NH str.), 3288.64 cm^{-1} (OH str.), 3040.56 cm^{-1} (Ar C-H str.), 2836.45 cm^{-1} (Al C-H str), 1688.64 cm^{-1} (C=N str),1606.77 cm^{-1} (Ar C=C) and 1033.89 cm^{-1} [C-O-C(-OCH_3)].

6-(4-Fluorophenyl)-4-pyridin-4-yl-1,6-dihydropyrimidin-2-ol ***4d:***
Brown solid; m.p. 142-151ºC; Yield: 60.22 %; λmax= 204.60; IR (KBr) cm^{-1}: 3448.02 cm^{-1} (0H str.), 3344.44 cm^{-1} (NH), 3015.57 cm^{-1} (Ar C-H str.), 1683.02 cm^{-1} (C=N str), 1602.91 cm^{-1} (Ar C=C) and 1047.99 cm^{-1} (C-F str.)

6-(3,4-Dimethoxyphenyl)-4-pyridin-4-yl-1,6-dihydropyrimidin-2-ol ***4e****:*
Greenish yellow solid; m.p. 230-238ºC; Yield: 51.62 %; λmax= 203.40; IR (KBr) cm^{-1}: 3393.63 cm^{-1} (NH str.), 3091.06 cm^{-1} (Ar C-H str.), 2838.37 cm^{-1} (Al C-H str.), 1682.00 cm^{-1} (C=N str.), 1608.51 cm^{-1} (Ar C=C) and 1309.36 cm^{-1} [C-O-C(-OCH_3)].

Antitubercular Activity
The antitubercular activity of compounds was assessed against *M. tuberculosis* using Microplate Alamar Blue Assay (MABA). 200µl of sterile 96 wells plate was taken to minimize evaporation of medium in the test wells during incubation. The 96 wells plate received 100µl of the Middlebrook 7H9 broth and serial dilution of compounds were made directly on plate. The final drug concentrations tested were 100 to 0.2 µg/ml. Plates were covered and sealed with parafilm and incubated at 37°C for five days. After this time, 25µl of freshly prepared 1:1 mixture of Almar Blue reagent and 10% tween 80 was added to the plate and incubated for 24 hrs. A blue colour in the well was interpreted as no bacterial growth, and pink colour was scored as growth.

Antibacterial Activity
Microbial growth inhibitory properties of test substances were determined by cup plate method. The drugs were initially dissolved in H_2O_2/DMSO and tested at concentrations of 100µg/ml against all the microorganisms.

Sterile nutrient agar plates were prepared and 0.1 ml of the innoculum from standardized culture of test organism was spread uniformly. Wells were prepared by using a sterile borer of diameter 10 mm and 100µl of the test substance, standard antibiotic and the solvent control were added in each well separately. Standard antibiotic, ampicillin was tested against gram negative, gram positive bacteria respectively. The plates were placed at 4ºC for 1 h to allow the diffusion of test solution into the medium and plates were incubated at a temperature optimal for the test organism and for a period of time sufficient for the growth of at least 10 to 15 generations (usually 24 h at 37ºC). The zone of inhibitions of microbial growth around the well was measured in mm.

Anti-Inflammatory Activity
A solution of 0.2% w/v of BSA was prepared in tris buffer saline and pH was adjusted to 6.8 using glacial acetic acid. Stock solutions of 1000µg/ml of all test samples were prepared by using methanol as a solvent. From the stock solutions two different concentrations of 100µg/ml and 200µg/ml were prepared by using methanol as a solvent. 100µg/ml (0.1ml) of each test sample was transferred to volumetric flask (10ml) using 1ml micropipette. 5ml of 0.2% BSA was added to all of the above flasks. The control consists of 5ml 0.2% w/v BSA solution with 0.1ml methanol. The 0.1ml standard consists 100µg/ml of indomethacin in methanol with 5ml 0.2% w/v BSA solution. The volumetric flasks were heated at 72˚C for five minutes and then cooled for 10 min. the absorbance of these solutions was determined by using spectrophotometer at a wavelength of 660 nm. The % denaturation of the protein (% inhibition) was determined.

$$\% \text{ inhibition} = \frac{\text{Absorbance of Control} - \text{Absorbance of Test}}{\text{Absorbance of Control}} \times 100$$

Antioxidant Activity
2, 2-diphenyl-1-picryl hydrazine (DPPH method):
10 mg of standard ascorbic acid was dissolved in methanol. From this stock solution dilutions were made to obtain concentrations of 10 to 40 µg/ ml. 1 ml from each of these solutions was taken in different volumetric flasks to which 1 ml of DPPH solution was added and volume was made up to 10 ml. The test solution were prepared in similar manner as that of standard ascorbic acid and the absorbance were recorded at 516 nm after duration of 30 min.

$$\% \text{ inhibition} = \frac{\text{Absorbance of Control} - \text{Absorbance of Test}}{\text{Absorbance of Control}} \times 100$$

RESULTS AND DISSCUSSION

Antitubercular activity:
All the synthesized compounds were screened for *in-vitro* antitubercular activity by MABA method. It was evidenced by the observation that the compound 4-(4-Fluoro-phenyl)-6-pyridin-4-yl-pyrimidin-2-ylamine **(3d)** exhibited excellent anti-tubercular activity at conc. of 3.12 µg/ml whereas all other pyrimidine analogs exhibited antitubercular activity at conc. above 25 µg/ml.

Antibacterial activity:
Compounds 3c and 3b exhibited good antibacterial activity towards the both gram negative bacteria (*Escherichia coli* and *Klebsiella pneumonia*). Compounds 3c and 3b have also exhibited good antibacterial activity towards gram positive bacteria *Bacillus subtilus* and *Staphylococcus aureus* respectively.

		Anti-bacterial activity (Zone of inhibition in mm)			
S.N.	**Compound code**	***E.coli***	***K.pneumonia***	***B.subtilis***	***S.aureus***
1	2a	-	10	13	11
2.	3a	12	11	16	13
3.	4a	14	12	-	13
4.	2b	9	16	-	6
5.	3b	14	16	12	13
6.	4b	7	10	7	8
7.	2c	12	14	14	-
8.	3c	14	16	18	9
9.	4c	7	9	8	-
10.	2d	10	7	9	-
11.	3d	12	16	14	10
12.	4d	14	12	16	13
13.	2e	8	9	10	13
14.	3e	12	11	10	8
15.	4e	10	9	12	10
	Ampicillin	17	19	20	16

Anti-inflammatory activity:
4-Pyridin-4-yl-6-p-tolyl-1,6-dihydropyrimidine-2-thiol (2b), 6-(4-Fluorophenyl)-4-pyridin-4-yl-1,6-dihydro pyrimidin-2-thiol (2d), 6-(3,4-Dimethoxyphenyl)-4-pyridin-4-yl-1,6-dihydropyrimidine-2-thiol (2e), 4-(4-Methoxyphenyl)-6-pyridin-4-yl-pyrimidin-2-ylamine (3c) and 4-(4-Fluorophenyl)-6-pyridin-4-yl-pyrimidin-2-ylamine (3d), 6-(4-Methoxyphenyl)-4-pyridin-4-yl-1,6-dihydropyrimidin-2-ol (4c), exhibited good *in vitro* anti-inflammatory activity as compared to standard indomethacin at 200µg/ml.

S. N.	**Compound code**	**% Inhibition**	
		100µg/ml	**200µg/ml**
1	2a	58.18	66.36
2.	3a	19.09	42.63
3.	4a	48.18	62.72
4.	2b	64.54	76.36
5.	3b	29.09	53.63
6.	4b	39.09	57.27
7.	2c	49.10	59.09
8.	3c	67.27	74.54
9.	4c	60.90	73.63
10.	2d	75.45	81.81
11.	3d	77.27	80.90
12.	4d	27.29	50
13.	2e	76.36	82.20
14.	3e	38.18	57.27
15.	4e	32.72	47.27
	Indomethacin	90%	91.81%

Antioxidant activity:
6-(4-Fluorophenyl)-4-pyridin-4-yl-1,6-dihydropyrimidin-2-thiol (2d), 4-(4-Fluorophenyl)-6-pyridin-4-yl-pyrimidin-2-ylamine (3d) exhibited good activity as compared to standard ascorbic acid at 10µg/ml.

		% Inhibition			
S.No	**Compound code**	**10 µg/ml**	**20 µg/ml**	**30 µg/ml**	**40 µg/ml**
1	2a	34.77	31.99	9.51	18.98
2.	3a	50.25	52.32	53.25	56.55
3.	4a	50.36	53.04	52.21	54.38
4.	2b	51.26	53.45	55.52	57.37
5.	3b	29.30	31.16	33.74	34.26
6.	4b	49.94	52.21	52.83	53.97
7.	2c	39.2	41.48	43.96	45.20
8.	3c	40.35	42.10	43.03	43.96
9.	4c	38.39	40.04	41.89	43.55
10.	2d	53.04	56.34	58.41	59.64
11.	3d	57.79	58.61	59.02	60.26
12.	4d	42.10	43.75	46.02	48.29
13.	2e	48.60	50.46	53.45	55.41
14.	3e	28.07	29.72	30.95	32.81
15.	4e	30.03	32.81	34.57	36.11
	Ascorbic acid	92.3	92.2	92	91.9

CONCLUSION

Chalcone derivatives were cyclised by using thiourea, guanidine hydrochloride and urea to obtain pyrimidine derivatives. All the pyrimidine derivatives were evaluated for antitubercular, antibacterial, anti-inflammatory and antioxidant activities. 4-(4-Fluorophenyl)-6-pyridin-4-yl-pyrimidin-2-ylamine (3d) has exhibited excellent antitubercular activity at the concentration of 3.12 µg/ml, moreover it has also exhibited good anti-inflammatory and antioxidant activities.

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