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Original Article

Synthesis, characterization and antimicrobial activity of pyrimidine based derivatives

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ABSTRACT

Aim: Pyrimidine and their derivatives play the vital role in the field of drugs and agricultural chemicals. In recent decades, a large no. of pharmacological studies has been done on Pyrimidine and their derivatives. But still more research is required in order to necessity of biological compounds. "The Chalcone is an aromatic compound that forms the central core for different necessity of biological compounds. The Chalcone is synthesized by an aldol, condensation of 4-methoxy acetophenone with m-phenoxy benzaldehydes in the presence of a catalyst that is treated with thiourea to provide Pyrimidine. The Pyrimidine treated with substituted *N*-1,3-benzothiazole-2-yl-2-chloro amide gives a compound".

Methods: Elemental analysis, IR, H NMR, C NMR melting point, Thin layer chromatography (TLC) plates (silica gel G) is used to determine the purity of the compounds.

Result: **Antimicrobial activity:** All the synthesized compounds screened against four different strains, viz two Gram +ve bacteria (*Staphylococcus aureus* & *Streptococcus pyogenes*) and two Gram −ve bacteria (*Escherichia coli* & *Pseudomonas aeruginosa*), analyzed with standard drugs ampicillin, chloramphenicol, ciprofloxacin, & norfloxacin. **Antifungal activities:** All the synthesized compounds screened against *Candida albicans*, and *Aspergillus niger* organisms, analyzed with standard drugs nystatin and griseofulvin.

Conclusion: In this paper we focused on the reactions, synthesis, spectral analysis and Microbial activities of Pyrimidine based benzothiazole derivatives. The method gives excellent than previously reported literature. Some of the compounds were effective as antimicrobial and antifungal agents.

1. Introduction

Heterocyclic compounds containing nitrogen and sulphur have considerably a lot of attention due to wide application of pharmacological activity. Pyrimidine and their derivatives play the vital role in the field of drugs and agricultural chemicals. Pyrimidine could be a basic nucleus in DNA & RNA; it is associated with various biological activities.[1] The synthesis of substituted Pyrimidine and lot of review has reported.[2,3]

"Pyrimidine" and their derivatives are popular in inorganic synthetic chemistry. Pyrimidine does not exist in nature

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however with in the form of its different derivatives, and are widely distributed. Pyrimidine derivatives are of interest due to their pharmacological properties such as antitumor,[4–7] antiviral,[8] antifungal, anticancer,[9] antibcteria,[10] anti-inflammator,[11–14] analgesic,[15] antagonist,[16,17] antifolate,[18] antimicrobial,[19] anti-HIV,[20] atiproliferative,[21] antiplatelet,[22] antithrombotic,[22] antifilarial[23] activities, etc.

Moreover benzothiazole[24–26] is alternative vital pharmacodynamic heterocyclic nuclei that once incorporated in several heterocyclic templates have currently been possess wide spectrum of activities.

The literature study reveals that both Pyrimidine and benzothiazole are a significant pharmacophore and exhibits outstanding biological activities. Encourage by these observation, we synthesized a new series of Pyrimidine derivatives by incorporating the benzothiazole moiety with the hope of obtaining better antimicrobial activity agent. All the synthesized compounds have been screened for their antimicrobial activities.

2. Experimental

2.1. General procedures

Laboratory chemicals were provided by Rankem India Ltd. and Ficher Scientific Ltd. Melting points were determined by the open tube capillary method and are not correct. The purity of the compounds was determined by thin layer chromatography (TLC) plates (silica gel G) in the solvent system toluene:ethyl acetate (7.5:2.5). The spots were observed by exposure to iodine Vapours or by UV light. The IR spectra were received by Perkin–Elmer 1720 FT-IR spectrometer (KBr pellets). The H NMR &[13] C NMR spectra were obtained by Bruker Advance II 400 spectrometer using TMS because the internal standard in $CDCl_3$. Elemental analysis of the new synthesized compounds were obtained by Carlo Erba 1108 analyzer.

The synthesis of the compounds as per the following Scheme 1 given below.

2.2. Step-1

2.2.1. Synthesis of 1-(4-methoxyphenyl)-3-(3-phenoxyphenyl) prop-2-en-1-one

The solution of 3-phenoxy benzaldehyde (0.01 mol.) and 4-methoxyacetophenone (0.01 mol.) in ethyl alcohol (25 ml) Cooled at 5–10 °C and was mixed with aqueous sodium _hydroxide (70%, 5 ml) drop wise with continuous stirring. The reaction mixture was again stirred for 2 h. and left all night. The mixture was neutralized with concentrated hydrochloric acid, so the solid separated was collected and crystallized from suitable solvent to obtain the chalcone derivatives with 85–90% yield. mp. 178–180 °C, IR (KBr): 1511, 1649, 2840, 2917, ^{1}H NMR ($CDCl_3$) δ ppm; 3.82 (s, 3H, $-OCH_3$), 6.63–6.65 (d, 1H, –CO-CH), 7.38–7.41 (d, 1H, =CH–Ar) 7.02–8.32 (m, 13H, Ar–H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 54.43, 113.83, 114.50, 116.32, 118.17, 118.63, 121.54, 121.90, 128.37, 128.69, 130.63, 131.78, 133.89, 143.48, 157.02, 159.38, 165.36, 189.14. Mass (*m*/*z*): 333. Anal. (%) for $C_{22}H_{18}O_3$, Calcd. C, 79.95; H, 5.45; Found: C, 79.93; H, 5.80.

2.2.2. Synthesis of 4-(4-methoxyphenyl)-6-(3-phenoxy phenyl) pyrimidine-2-thiol

A mixture of 1-(4-methoxyphenyl)-3-(3-phenoxyphenyl) prop-2-en-1-one (0.01 mol), thiourea (0.01 mol) and sodium hydroxide (0.01 mol) in methyl alcohol (25 ml) was refluxed for 8 h. when the completion of reaction, the resultant mixture was cool to room temperature. The compound was separated, filtered, washed with water, dried and crystallized with methyl alcohol get titled compound with 82% yield. mp. 160–162 °C, IR (KBr): 1175, 1625, 2846, 2928, ^{1}H NMR ($CDCl_3$) δ ppm; 8.83 (s, 1H, NH), 3.81 (s, 3H, $-OCH_3$), 7.08–8.11 (m, 14H, Ar–H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 55.13, 113.83, 14.50, 109.76, 116.63, 118.48, 118.87, 121.54, 121.89, 128.37, 128.69, 129.63,, 136.09, 157.80,165.64, 160.58, 164. 63, 181.14. Mass (*m*/*z*): 386. Anal. (%) for $C_{23}H_{18}N_2O_2S$, Calcd. C, 71.46; H 4.67; N 7.23; Found: C, 71.53; H, 4.81; N 7.41.

2.3. Step-2

2.3.1. General method for the preparation of N-(benzo[d] thiazol-2-yl)-2-chloroacetamide (3a–j)

In conical flask take 0.01 mol substituted benzothiazole in 25 ml benzene and mixed up to 30 min in ice-bath until temp below 0–5 °C then add drop by drop 0.01 mol chloroacetyl chloride in conical flask at intervals of 2 h. After complete addition reflux it for 2 h in water bath then cool it and evaporate it and collect compound. Recrystallization from alcohol afforded yield 88% of yellow needles, IR (KBr): 752, 1728, 3345, ^{1}H NMR ($CDCl_3$) δ ppm 9.20 (s, 1H, NH), 7.53–8.26 (m, 4H, Ar–H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 43.67, 118.31, 121.89, 124.53, 125.32,130.67, 153.41, 165.42, 174.47. Mass (*m*/*z*): 226. Anal. (%) for $C_{23}H_{18}N_2O_2S$, Calcd. C, 47.67; H 3.10; N 12.34; Found: C, 47.53; H, 3.16; N 12.41.

2.4. Step-3

2.4.1. General method for synthesis of 2-(4-(4-methoxyphenyl)-6-(3-phenoxyphenyl) pyrimidin-2-ylthio)-N-(substituted benzo[d]thiazol-2-yl) acetamide(4a–j)

In R.B.F take 0.01 mol 4-(4-methoxyphenyl)-6-(3-phenoxyphenyl) pyrimidine-2-thiol in 25 ml acetone then add 0.01 mol substituted *N*-(1,3-benzothiazole-2yl)-2-chloro acetamide and add 2–3 drop TEA as a catalyst and reflux it for 3 h then cool it and fall out in ice precipitate come out filter it and recrystallization from alcohol.

2.4.2. N-(6-chlorobenzo[d]thiazol-2-yl)-2-(4-(4-methoxy phenyl)-6-(3-phenoxyphenyl) pyrimidin 2-ylthio)acetamide (4a)

Yield 70%, mp. 110–113 °C, IR (KBr): 3175, 2917, 2840, 1690, 1602, 1530, 745, 695. ^{1}H NMR ($CDCl_3$) δ ppm; 9.44 (s, 1H, –NH), 3.78 (s, 3H, $-OCH_3$), 4.65 (s, 2H, $-CH_2$), 6.70–8.10 (m, 17H, Ar–H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 38.82, 55.87, 107.33, 114.35, 115.14, 116.49, 118.31, 118.96, 119.37, 120.39, 121.62, 123.64, 124.28, 125.48, 126.15, 127.74, 128.21, 128.58, 129.28, 130.18, 131.38, 132.83, 136.46, 151.33, 157.70, 159.35, 160.16, 164.71, 165.86, 168.24, 172.63, 174.95.Mass (*m*/*z*): 610. Anal. (%) for $C_{33}H_{24}N_3O_3S_2$, Calcd. C, 64.96; H, 3.96; N, 6.89; Found: C, 64.95; H, 3.91; N, 6.83.