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Conventional and Microwave assisted synthesis of pyrimidine derivatives and their cytotoxic, antioxidant and antimicrobial activity

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ABSTRACT:
Pyrimidine is the parent substance of a large group of heterocyclic compounds and plays a vital role in many biological activities.Chemo protection by pyrimidines may be a consequence of their antioxidant properties, mediated via inhibition or induction of metabolic enzymes, by an anti- invasive effect reduction in nitric oxide production. Free Radicals areformed constantly in human system either as products during Metabolism or deliberately during the process of phagocytosis; or due to environmental Pollutants, ionizing radiation ozone heavy metal poisoning etc.The synthesized compound were purified by re crystallization or by chromatography and are characterized by 1H NMR,13c NMR and IR analysis.The microwave irradiation method Is proved to be advantageous with considerable change in reaction rate with better yield, after overall observation it is found that pyrimidine derivatives possess cytotoxic and antioxidant activity. Synthesis of amino pyrimidine derivatives was carried out by microwave synthesis. This Microwave-assisted heating is an eco-friendly method.

Keywords:-Antioxidant activity, Cytotoxic activity, Microwave irradiation , pyrimidines etc

I. INTRODUCTION:

Nitrogen containing heterocyclic compound has received considerable attention due to their wide range of pharmacological activity.The increasing importance of pyrimidines and it's derivatives as intermediate for the Synthesis of biologically active compound has led to continued development of new simple procedure for their synthesis. Pyrimidine is the parent substance of large group of heterocyclic compound and play a vital role in many biological processes,as found in nucleic acid, several vitamin,co enzymes and purines, etc.pyrimidines are considered to be an important precursor because they are integral part of the genetic material like DNA and RNA as nucelotides and nucleosides but they also important numerous biological activities such as bacterisidesfungicide,vermicides and insecticides. They also found application in agricultural and industrial chemicals.The chemistry of pyrimidines(1) and it'sderivatives has been studied since past century due to their close Pharmacological association with diverse pharmacological properties. Though pyrimidine itself doesn't exist in nature but substituted pyrimidines are found as part of more complex system and are widely distributed.

These pyrimidines derivatives have been reported to be possess a variety of biological activities (2-6), notable among which are the antibacterial (7), anti-cancer (8), anti-inflammatory (9),antitubercular (10)and analgesic (11) activities. Pyrimidine derivative like Thienopyrimidinemoiety is a versatile lead molecule in the pharmaceutical development and has a wide range of biological activitiesantiviral (12), antimicrobial(13) ,analgesic anti-inflammatory(14) , anticonvulsant (15),reductase inhibitors (16)and antimalarial(17).
The synthesized compound were purified by using recrystallization (ethanol)or by chromatographic (ethyl acetate) method. The compounds were characterized by 1H NMR,13c NMR and IR analysis. The physical properties of the compounds were also included.

II. EXPERIMENTAL:

Instrumentation

Melting point of the synthesized derivatives was determined by digital melting point apparatus (SMP)10.The NMR spectra were recorded on a BRUKER DRX 400 spectrometer at 400MHz.IR spectra were recorded using BRUKER ALPHA FT-IR spectrometer.High resolution mass

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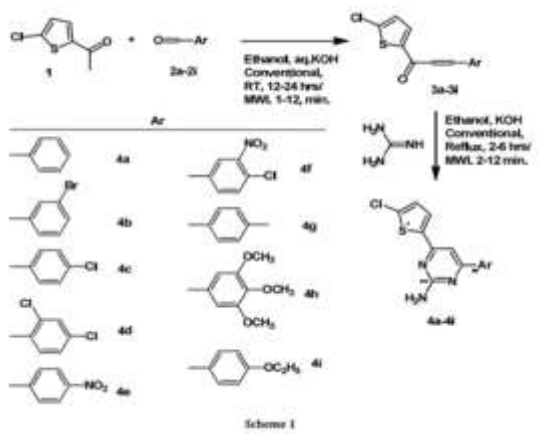
spectra were obtained on Agilent 6100 series single Quadrupole LC/MS

General procedure for the Synthesis of pyrimidines



Scheme 1

- **Conventional method**

The condensation of the chalcone (0.001)mol with guanidine hydrochloride (0.001mol) in alkaline medium in potassium hydroxide (0.003 mol) in the presense of ethanol (10ml) at reflux temperature 2to 6hour results the formation of corresponding pyrimidines (18-22) derivatives (scheme 1). Completion of the reaction was identified by observing on precoated thin layer chromatography plates, using ethyl acetate and hexane mixture as mobile phase.The pyrimidine derivative on purification obtained as fine wine red powder.

- **Microwave irradiation method**

The condensation of the chalcone (0.001)mol with guanidine hydrochloride (0.001)mol in alkaline medium in potassium hydroxide (0.003)mol in the presense of ethanol (10)ml ,the entire reaction was microwave irradiated at 180 watts for about 2-16min,then kept aside for 2-3hours resulted the formation of pyrimidines derivatives which is shown in (scheme 1). Reaction completion was identified by TLC precoatedplates.Ethyl acetate and hexane mixture was used as mobile phase. The pyrimidine derivatives on purification obtained as fine wine red powder.

Cytotoxic activity:

- **Brine shrimp lethality test (BSLT)**

BSLT have been used as bioassay (23-28) for a variety of toxic substances.Thismethodhas also been applied to compound in order to facilitate the isolation of biologically active compound. A general bioassay that appears of capable of detecting a broad spectrum of bioactivity, present in crude extract and in synthetic compound is the BSLT bioassay, to study the cytotoxic activity of 2,4,6 trisubstituted pyrimidines derivatives. It was carried out to investigate the cytotoxicityof the synthesized compound.

- **Antioxidant activity**

Free radicals are formed constantly in human system either as accidental product during metabolism or deliberately during the process of phagocytosis,or due to environmental pollutants ionizing radiation , ozone heavy metal poisoning. Free radicals being highly reactive can oxidize biomolecules leading to tissue injury and cell death.

- **Antimicrobial activity**

The synthesized compound in this work were screened in vitro for their antimicrobial activity against some strain of bacteria and fungi with different concentrations as follows. The antifungal activity of tested compound were evaluated by the reported method (29,30) using dimethyl sulfoxide (DMSO) as a solvent.The inhibition zone was compared with Amphotericin B as a reference. Antimicrobial activity also tested for the compound and were evaluated by reported method using DMSO as a solvent.The inhibition zone was compared with Ampicillin for gram(+)and Gentamycin for gram(-)as reference.

We choose some of the synthesized compound to study the various biological activities consisting of antiviral, analgesic and anti inflammatory,anticonvulsant,dihydrofolate reductase, anti-cancer etc.

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Table 1. Comparative reaction time and percentage yield of pyrimidine derivative by conventional and microwave irradiation method.(scheme 1)

Compound No	Reaction time		Yield (%)	
	Conventional (hr)	MWI (min)	Conventional	MWI
4a	4.5	5.5	35	48
4b	4.5	4.5	32	47
4c	5.5	5.0	42	56
4d	5.0	4.5	49	56
4e	5.5	6.0	34	43
4f	5.0	4.5	41	44
4g	5.0	5.0	39	52
4h	5.0	6.0	34	45
4i	6.0	6.5	39	51

Table 2.Melting point and elemental analysis of pyrimidines derivatives

Compound No	R_f value	M.p., °C	Elemental analysis, %	
			Calculated	Found
4a	0.62	120 ± 2	C: 58.39 H: 3.47 N: 14.59	C: 58.42 H: 3.45 N: 14.57
4b	0.59	138 ± 2	C: 45.82 H: 2.45 N: 11.45	C: 45.85 H: 2.47 N: 11.47
4c	0.64	130 ± 2	C: 52.14 H: 2.79 N: 13.03	C: 52.11 H: 2.82 N :13.00
4d	0.60	145 ± 2	C: 47.11 H: 2.24 N: 11.77	C: 47.09 H: 2.12 N: 11.79
4e	0.54	142 ± 2	C: 50.49 H: 2.70 N: 16.83	C: 50.52 H: 2.68 N: 16.85
4f	0.56	160 ± 2	C: 47.75 H: 2.17 N: 15.25	C: 45.77 H: 2.14 N: 16.85
4g	0.63	136 ± 2	C: 59.66 H: 3.77 N: 13.92	C: 59.69 H: 3.99 N: 13.90
4h	0.51	98 ± 2	C: 53.99 H: 4.23 N: 11.11	C: 53.97 H: 4.27 N: 11.14
4i	0.57	127 ± 2	C: 57.86 H: 4.21 N: 12.65	C: 57.89 H: 4.23 N: 12.62

Table 3. Characterization data of the pyrimidine derivative given below

Compound No	IR (cm^{-1}), ^1H NMR, ^{13}C NMR, Mass
4a	IR (ν_{max}, cm^{-1}): 3432 (NH_2), 1627 (C=N), 1408 (C=C), 771 (C-S). ^1H NMR ($CDCl_3$, 400 MHz, δ, ppm): 5.78 (2H, d, C-2-NH_2), 6.24 (1H, d, *J* = 4 Hz, C-4'-H), 6.31 (1H, d, *J* = 4.2 Hz, C-3'-H), 6.79 (1H, t, *J* = 3.2 Hz, C- 4''-H), 7.12 (2H, d, *J* = 8 Hz, C-3'' and 5''-H), 7.69 (1H, s, C-5-H), 7.83 (2H, d, *J* = 8.8 Hz, C-2'' and 6''-H).
4b	IR (ν_{max}, cm^{-1}): 3394 (NH_2), 1673 (C=N), 1621 (C=C), 775 (C-S), 858 (C-Br). ^1H NMR ($CDCl_3$, 400 MHz, δ, ppm): 6.87 (2H, s, C-2-NH_2), 7.28 (1H, d, *J* = 4 Hz, C-4'-H), 7.51 (1H, t, *J* = 7.6 Hz, C- 5''-H), 7.71 (1H, d, *J* = 4.6 Hz, C-3'-H), 7.77 (1H, s, C-5-H), 8.06 (1H, d, *J* = 3.6 Hz, C-4''-H), 8.21 (1H, d, *J* = 8 Hz, C-6''-H), 8.41 (1H, s, C-2''-H).
4c	IR (ν_{max}, cm^{-1}): 3421 (NH_2), 1628 (C=N), 1567 (C=C), 812 (C-Cl), 772 (C-S). ^1H NMR ($CDCl_3$, 400 MHz, δ, ppm): 6.83 (2H, s, C-2-NH_2), 7.27 (1H, d, *J* = 4 Hz, C-4'-H), 7.61 (2H, d, *J* = 7.4 Hz, C-3'' and 5''-H), 7.74 (1H, s, C-5-H), 8.03 (2H, d, *J* = 4 Hz, C-2'' and 6''-H), 8.23 (1H, d, *J* = 8.2 Hz, C-3'-H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 101.28 (C-5), 126.16 (C-3'), 127.36 (C-5'), 128.36 (C-2'' and 6''), 128.97 (C-3'' and 5''), 134.50 (C-4'), 135.81 (C-4''), 136.80 (C-2'), 141.51 (C-4), 159.99 (C-6), 163.25 (C-1''), 164.86 (C-2).
4d	IR (ν_{max}, cm^{-1}): 3406 (NH_2), 1627 (C=N), 1567 (C=C), 816 (C-Cl), 760 (C-S). ^1H NMR ($CDCl_3$, 400 MHz, δ, ppm): 6.93 (2H, s, C-2-NH_2), 7.11 (1H, d, *J* = 4 Hz, C-4'-H), 7.23 (1H, d, *J* = 4 Hz, C- 6''-H), 7.31 (1H, s, C-5-H), 7.57 (1H, d, *J* = 3 Hz, C-4''-H), 7.77 (1H, d, *J* = 4 Hz, C- 3'-H), 7.86 (1H, d, *J* = 8 Hz, C-3''-H).
4e	IR (ν_{max}, cm^{-1}): 3404 (NH_2), 1606 (C=N), 1568 (C=C), 1519 (Ar-NO_2), 771 (C-S). ^1H NMR ($CDCl_3$, 400 MHz, δ, ppm): 6.51 (2H, s, C-2-NH_2), 6.95 (1H, d, *J* = 4 Hz, C-4'-H), 7.12 (1H, d, *J* = 8.2 Hz, C-2''-H), 7.45 (1H, s, C-5-H), 7.73 (1H, d, *J* = 7.8 Hz, C-6''-H), 7.81 (1H, d, *J* = 4 Hz, C-3'-H), 8.12 (1H, d, *J* = 8 Hz, C-5''-H), 8.44 (1H, d, *J* = 7.4 Hz, C-3''-H).
4f	IR (ν_{max}, cm^{-1}): 3393 (NH_2), 1632 (C=N), 1571 (C=C), 1533 (Ar-NO_2), 768 (C-S). ^1H NMR ($CDCl_3$, 400 MHz, δ, ppm): 6.97 (2H, s, C-2-NH_2), 7.28 (1H, d, *J* = 4 Hz, C-4'-H), 7.87 (1H, s, C-5-H), 7.97 (1H, d, *J* = 8 Hz, C-5''-H), 8.04 (1H, d, *J* = 3.8 Hz, C-3'-H), 8.51 (1H, d, *J* = 8.4 Hz, C-6''-H), 8.83 (1H, s, C-2''-H).
4g	IR (ν_{max}, cm^{-1}): 3400 (NH_2), 1619 (C=N), 1568 (C=C), 801 (C-Cl), 756 (C-S). ^1H NMR ($CDCl_3$, 400 MHz, δ, ppm): 1.58 (3H, s, C-4''-CH_3), 6.95 (1H, d, *J* = 4.2 Hz, C-4'-H) , 7.05 (1H, d, *J* = 4.5 Hz, C-3'-H), 7.22 (1H, s, C-5-H), 7.29 (2H, d, NH_2), 7.72 (2H, m, C-3''and 5''-H), 8.03 (2H, m, C-2'' and 6''-H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 21.38 (C-4''-CH_3), 101.33 (C-5), 125.9 (C-4), 126.97 (C-2'' and 6'') 127.29 (C-3'), 129.47 (C-3'' and 5''), 134.13 (C-5'), 134.60 (C-6), 140.94 (C-4'), 141.82, (C-4''), 159.63 (C-1''), 163.26 (C-2'), 166.15 (C-2). MS (*m/z*, %): 302.3 [M+H, 100]⁺.
4h	IR (ν_{max}, cm^{-1}): 3384 (NH_2), 3004 (C-H-CH_3), 1590 (C=N), 1572 (C=C), 1226 (C-O-C), 770 (C-S). ^1H NMR ($CDCl_3$, 400 MHz, δ, ppm): 3.71 (3H, d, C-4''-OCH_3), 3.92 (6H, d, C-3'' and 5''- OCH_3), 6.76 (2H, s, C-2-NH_2), 7.21 (1H, d, *J* = 4 Hz, C-4'-H), 7.48 (2H, s, C-2'' and 6''-H), 7.67 (1H, s, C-5-H), 8.02 (1H, d, *J* = 4.2 Hz, C-3'-H).
4i	IR (ν_{max}, cm^{-1}): 3395 (NH_2), 1636 (C=N), 1602 (C=C), 1227 (C-O-C), 771 (C-S). ^1H NMR ($CDCl_3$, 400 MHz, δ, ppm): 1.38 (3H, t, C-4''-CH_3), 4.12 (2H, d, C- 4''- OCH_2), 6.69 (2H, s, C-2-NH_2), 7.05 (2H, d, *J* = 8.2 Hz, C-3'' and 5'-H), 7.25 (1H, d, *J* = 4 Hz, C-4'-H), 7.64 (1H, s, C-5-H), 7.99 (1H, d, *J* = 4.2 Hz, C-3'-H), 8.16 (2H, d, *J* = 8.6 Hz, C-2'' and 6''-H).

(DMSO) as solvent.

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III. MATERIALS AND METHODS

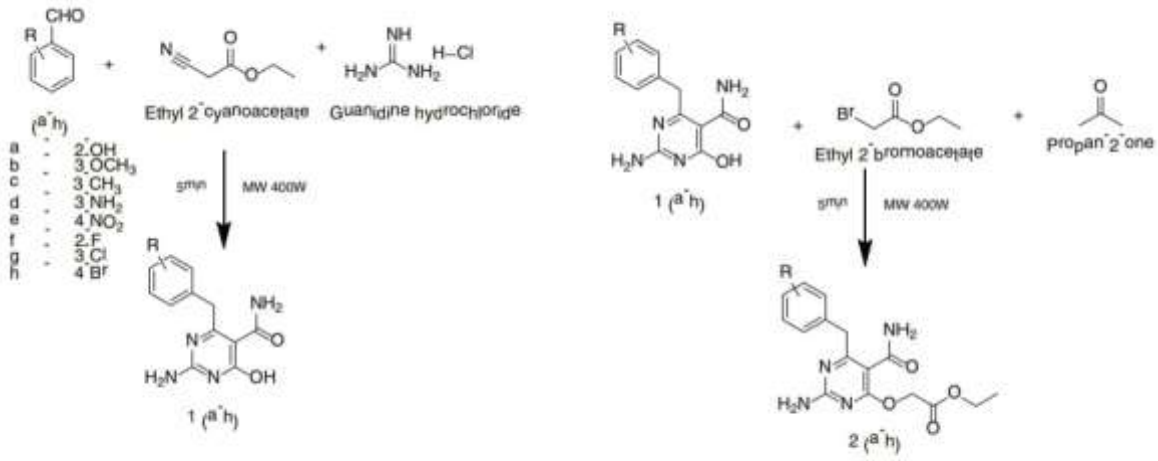
All the chemicals used to synthesize the title compounds were of synthetic reagent grade and purchased from Aldrich Chemical Co. and Merck Chemical Co. Melting points of all the compounds obtained by an open capillary tube method and uncorrected. The IR spectra of all molecules were recorded on Shimadzu IR Affinity instrument (HCP, Guntur, AP) with KBr. The proton NMR spectra are obtained from Punjab University, Chandigarh, by using Brukar NMR 400 Hz spectrophotometer with tetramethylsilane as internal standard. The MS data was recorded on Shimadzu GCMS QP5000 from Vijayawada, AP.A pre-coated SiO2 gel (HF254, 200#) aluminum TLC plates from E. Merck was used to analyze the purity of all compounds and detected under UV light. Further purification was achieved by performing Column
chromatography by using 100-200# silica gel and mobile phase as ethylacetate: n-hexane. The structure of molecules was confirmed based on the above spectral data. A series of2-amino-4-hydroxy-6-(substituted benzyl)pyrimidine-5-carboxamide(1a-h) and Ethyl2-((2amino-5-carbamoyl-6-(substituted benzyl) pyrimidin4-yl)oxy)acetate (2a-h) derivatives were synthesized according to reportedprocedure.8

1 | 2-amino-4-(2-[2-carbamothioylhydrazinyl]2-oxoethoxy)-6-(substituted benzyl) pyrimidine-5-carboxamide (3a-h)

Each compound of 2 (a-h), thiosemicarbzide (0.03 mol) and potassium hydroxide (2.5 g) in ethanol (100 mL) was kept for microwave irradiation for 3 minutes at 450 W and the precipitate was filtered, washed with water and recrystallized from ethanol to give title compounds 3 (a-h).

2 | 2-amino-4-(2-[2-carbamothioylhydrazinyl]2-oxoethoxy)-6-(1-[substitutedphenyl]prop1-en-1-yl)pyrimidine-5-carboxamide(4a-h)

Each compound of thiosemicarbazide derivatives (3ah), acetaldehyde (0.01 mol), and sodium hydroxide (1 g) in ethanol (100 mL) was irradiated for 5 minutes at 450 W in microwave and the precipitate was collected by filtration, washed with distilled water and purified by recrystallization with ethanol to give title compounds 2-amino-4-(2-[2-carbamothioylhydrazinyl]2-oxoethoxy)-6-(1-[4-substituted phenyl]prop-1-en-1-yl) pyrimidine-5-carboxamide (4a-h). The detailed scheme of synthesis is given in Scheme .



Mechanism 1

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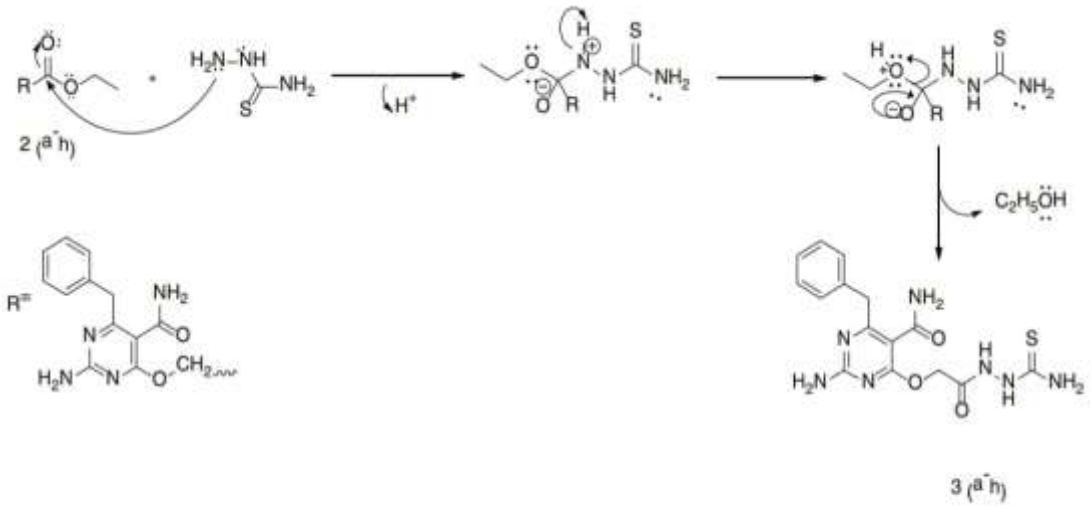
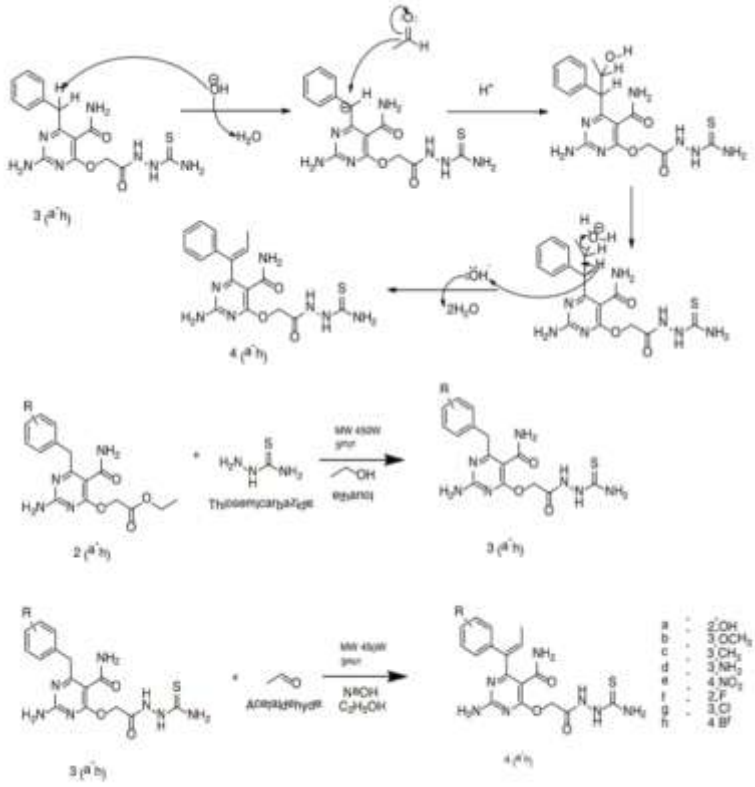


Mechanism 2



SCHEME 1 2-amino-4-(2-[2-carbamothioylhydrazinyl]-2-oxoethoxy)-6-(1-[4-substituted phenyl] prop-1-en-1-yl)pyrimidine-5-carboxamide (4a-h)

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SPECTRAL DATA OF SYNTHESIZED COMPOUNDS

1|2-amino-4-(2-[2-carbamothioylhydrazinyl]2-oxoethoxy)-6-(1-[2-hydroxyphenyl]prop1-en-1-yl)pyrimidine-5-carboxamide (4a)

Yellow crystals, %yield 82, m.p 188C-190C. FTIR (KBr in cm−1): 3545 (OH), 3356 & 3249 (NH), 3025 (Ar-CH), 2946 (CH3 CH), 1741 (C O), 1674 (C N), 1627 (C C), 1213 (C S), 1029 (C O C). 1H NMR (DMSO, δ ppm):2.19 (s, 2H, CSNH2), 2.77 (s, 1H, CS-NH), 3.64 (s, H, C CH linkage), 4.45 (s, 2H, OCH2 linkage), 5.10 (s, 1H, OH), 5.52 (s, 2H, NH2), 6.00 (s, 2H, CONH2), 7.29-7.87 (m, 4H, Ar-H), 8.87 (s, 1H, CO-NH). MS m/z: 391 [M+].

2|2-amino-4-(2-[2-carbamothioylhydrazinyl]2-oxoethoxy)-6-(1-[3-methoxyphenyl]prop1-en-1-yl)pyrimidine-5-carboxamide (4b)

Yellow crystals, %yield 69, m.p 193C-195C. FTIR (KBr in cm−1):3358 & 3242 (NH), 3024 (Ar-CH), 2946 (CH3 CH), 2836 (OCH3), 1740 (C O), 1647 (C N), 1601 (C C), 1213 (C S), 1029 (C-O-C). 1H NMR (DMSO, δ ppm): 2.36 (s, 2H, CSNH2), 2.69 (s, 1H, CS-NH), 3.41 (s, 3H, OCH3), 3.94 (s, H, C CH- linkage), 4.70 (s, 2H, OCH2 linkage), 5.43 (s, 2H, NH2), 6.11 (s, 2H, CONH2), 6.79-7.20 (m, 4H, Ar-H), 8.97 (s, 1H, CO-NH). MS m/z: 405 [M+].

3|2-amino-4-(2-[2-carbamothioylhydrazinyl]2-oxoethoxy)-6-(1-[3-methylphenyl]prop1-en-1-yl)pyrimidine-5-carboxamide (4c)

Yellow crystals, %yield 72, m.p 138C-140C. FTIR (KBr in cm−1):3357 & 3301 (NH), 3023 (Ar-CH), 2946 (CH3 CH), 1740 (C O), 1668 (C N), 1631 (C C), 1213 (C S), 1110 (C-O-C). 1H NMR (DMSO, δ ppm):2.12 (s, 2H, CSNH2), 2.51 (s, 1H, CS-NH), 2.88 (s, 3H, CH3), 3.90 (s, H, C CH linkage), 4.72 (s, 2H, OCH2 linkage), 5.25 (s, 2H, NH2), 5.91 (s, 2H, CONH2), 7.19-7.71 (m, 4H, Ar-H), 8.52 (s, 1H, CO-NH). MS m/z: 389 [M+].

4|2-amino-4-(2-[2-carbamothioylhydrazinyl]2-oxoethoxy)-6-(1-[3-aminophenyl]prop1-en-1-yl)pyrimidine-5-carboxamide (4d)

Yellow crystals, %yield 73, m.p 201C-203C. FTIR (KBr in cm−1):3358 & 3302 (NH), 3023 (Ar-CH), 2947 (CH3 CH), 1740 (C O), 1667 (C N), 1629 (C C), 1213 (C S), 1111 (C O C). 1H NMR (DMSO, δ ppm):2.48 (s, 2H, CSNH2), 3.23 (s, 1H, CS-NH), 4.16 (s, H, C CHlinkage), 4.84 (s, 2H, OCH2 linkage), 5.30 (s, 2H, NH2), 5.71 (s, 2H, NH2), 6.22 (s, 2H, CONH2), 7.05-7.64 (m, 4H, Ar-H), 9.01 (s, 1H, CO-NH). MS m/z: 390 [M+].

5 | 2-amino-4-(2-[2-carbamothioylhydrazinyl]2-oxoethoxy)-6-(1-[4-nitrophenyl]prop1-en-1-yl)pyrimidine-5-carboxamide (4e)

Yellow crystals, %yield 79, m.p 168C-170C. FTIR (KBr in cm−1):3389 & 3280 (NH), 3014 (Ar-CH), 2950
(CH3 CH), 1734 (C O), 1670 (C N), 1614 (C C), 1558 & 1379 (NO2), 1206 (C S), 1013 (C O C). 1H NMR (DMSO, δ ppm):2.22 (s, 2H, CSNH2), 2.79 (s, 1H, CS-NH), 3.68 (s, H, -C CH- linkage), 4.39 (s, 2H, OCH2 linkage), 5.40 (s, 2H, NH2), 6.61 (s, 2H, CONH2), 7.21-7.99 (m, 4H, Ar-H), 9.36 (s, 1H, CO-NH). MS m/z: 420 [M+].

6 | 2-amino-4-(2-[2-carbamothioylhydrazinyl]2-oxoethoxy)-6-(1-[2-flurophenyl]prop-1-en1-yl)pyrimidine-5-carboxamide (4f)

Yellow crystals, %yield 63, m.p 192C-194C. FTIR (KBr in cm−1): 3389 & 3281 (NH), 3017 (Ar-CH), 2950 (CH3-CH), 1735 (C O), 1661 (C N), 1626 (C C), 1206 (C S), 1074 (C F), 1013 (C O C). 1H NMR (DMSO, δ ppm):2.32 (s, 2H, CSNH2), 2.80 (s, 1H, CSNH), 3.68 (s, H, C CH- linkage), 4.60 (s, 2H, OCH2 linkage), 5.11 (s, 2H, NH2), 6.61 (s, 2H, CONH2), 7.41-7.94 (m, 4H, Ar-H), 9.17 (s, 1H, CO-NH). MS m/z: 393 [M+].

7|2-amino-4-(2-[2-carbamothioylhydrazinyl]2-oxoethoxy)-6-(1-[3-chlorophenyl]prop1-en-1-yl)pyrimidine-5-carboxamide (4g)

Yellow crystals, %yield 78, m.p 176C-178C. FTIR (KBr in cm−1):3328 & 3211 (NH), 3075 (Ar-CH), 2919 (CH3 CH), 1735 (C O), 1645 (C N), 1608 (C C), 1242 (C S), 1026 (C O-C), 787 (C Cl). 1H NMR (DMSO, δ ppm):2.52 (s, 2H, CSNH2), 3.30 (s, 1H, CSNH), 4.07 (s, H, C CH linkage), 5.04 (s, 2H, OCH2 linkage), 5.81 (s, 2H, NH2), 6.60 (s, 2H, CONH2), 7.22-7.51 (m, 4H, Ar-H), 9.23 (s, 1H, CO-NH). MS m/z: 409 [M+].

IV. CONCLUSION:

New polycyclic fused bpyrimidine have been synthesizes using both microwave assisted and conventional method .the later method proved very efficient in reducing reaction time ,microwave is more superior than conventional method.All synthesized compound having all pharmacological activities.

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