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Microwave Assisted Synthesis and Antimicrobial Evaluation of Novel 4h-Pyrido [1, 2-A] Pyrimidine Derivatives.

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ABSTRACT

Design, synthesis, characterization and evaluation of novel pyrido [1, 2-a] pyrimidine derivatives as possible antimicrobial agents. The target novel pyrido pyrimidine molecule (E), was prepared by deprotonation of 2-(hydroxymethyl)-4H-pyrido[1,2-a] pyrimidine-4-one using sodium hydride followed by methylation of 2-(methoxymethyl)-4H-pyrido [1,2-a] pyrimidine-4-one then oxidation of 2-(methoxymethyl)-7-methyl-4H-pyrido [1,2-a] pyrimidine-4-one and finally followed by reduction reaction of 2-(methoxymethyl)-4-oxo-4H-pyrido [1,2-a] pyrimidine-7-carboxylic acid. A series of eight derivatives (E1-E8) of E were also synthesized. The synthesized compounds were characterized by spectroscopic techniques and were tested for antimicrobial activities against bacterial and fungal strains. On the analysis of these results, the compounds E1, E4, E5, E6, E7, and E8 showed promising activity at 10 µg/mL In particular, compounds E5-E8 exhibited remarkable activity due to the presence of amine group. However, the compound E4 having a chlorine group as substituent showed more activity towards gram negative bacteria than gram positive bacteria.E2 & E3 showed less activity towards all microorganisms owing to the presence of hydroxyl and aldehyde groups respectively.

Keywords: Novel pyrido-pyrimidine derivatives, characterization, antimicrobial activities.

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INTRODUCTION

Heterocyclic compounds are widely considered as the building blocks in the novel drug discovery as there is an abundant scope to develop various fused systems which can enhance the therapeutic activity of the molecule. Additionally, the bicyclic nitrogen-containing heterocyclic compounds, i.e. purines [1], quinazolines [2], pyridopyrimidines [3], pyrazoline derivatives [4] are well-known pharmacophore in drug discovery. The pyrimidine based heterocyclic systems are very interesting because of their physicochemical properties [5, 6] with relevance to the design of new drugs. The pyrimidine compounds play a prominent role in natural processes as three basic bases cytosine (C), thymine (T) and uracil (U) found in DNA & RNA. According to the literature survey, pyrimidines were also reported to possess various pharmacological activities as their presence in well established in various marketed drugs as antineoplastic (Uramustine, Teague, Floxuridine), antibacterial (Trimethoprim, Meteoric, Piromidicacid), antifungal (Flu cytosine), antiviral (Broxuridine, Idoxuridine) [7] etc. From the past few years, research on pyridopyrimidines has taken new dimensions. Owing to its high potential in therapeutic areas [8-9], we have planned to design and synthesize a pyrido pyrimidine molecule ethyl 2-(methoxymethyl)-4H-pyrido [1, 2-a] pyrimidine-7-carboxylate and its derivatives with a hope to develop new, potent, less toxic antimicrobial agents. In continuation of our research we studied the antimicrobial action of the resultant molecules against gram negative bacteria Escherichia coli (EC), Pseudomonas Aeruginosa (PA) and gram positive bacteria Staphylococcus Aureus (SA), Bacillus subtitles (BS) and along with a fungus Candida albicans (CA).

MATERIALS AND METHODS

Reagents such as methyl iodide, sodium hydride, aluminum chloride, sulphuric acid, potassium permanganate, diethyl form amide were purchased from Across Ltd and used as it is. All the solvents were of analytical grade and were distilled before use. Melting points are uncorrected. The solid IR spectra were recorded in KBr on Perkin Elmer FTIR spectrophotometer at GITAM, Visakhapatnam; however 1H NMR spectra were taken on Bruker 400 MHz NMR in DMSO-d6 using TMS as internal reference at Suven labs, Hyderabad. All synthesized and characterized compounds (E1-E8) were evaluated for their antibacterial activity against gram positive bacteria and gram negative bacteria together with a fungus Candida albicans using well diffusion method and compared with well-known antibacterial/antifungal drug, Cefixime/ ketaconazole. All these microwave reactions were performed by using a Flexi wave-Milestone Microwave Synthesis Platform instrument (model No.VA1601178FLEX49050).

EXPERIMENTAL

Synthesis of ethyl 2-(methoxymethyl)-4H-pyrido [1, 2-a] pyrimidine-7-carboxylate (E):

Synthesis of above parent molecule involves four steps as mentioned in scheme-1

Preparation of 2-(methoxymethyl)-4H-pyrido [1, 2-a] pyrimidine-4-one (B) from 2-(hydroxymethyl)-4H-pyrido [1, 2-a] pyrimidine-4-one (A):

The compound a (1.1 mmol) and 10 ml of diethyl form amide was mixed in a flask with continuous stirring. To this reaction mixture sodium hydride (0.25 mmol) was added under nitrogen atmosphere followed by methyl iodide. The above reaction content was stirred for 8 hours at room temperature in conventional method while 20 minutes in microwave (MW). The resultant solution was quenched in water.15 ml of ethyl acetate was added to above aqueous layer. Stirred for 10 mins, organic layer was separated and further washed with water and saturated sodium chloride solution. The ethyl acetate layer was concentrated to get the crude product, which was recrystallized to get pure product (B).

Preparation of 2-(methoxymethyl)-7-methyl-4H-pyrido[1,2-a]pyrimidine-4-one (C)from 2-(methoxymethyl)-4H-pyrido [1,2-a] pyrimidine-4-one (B) :

An ethanolic solution of B (2.6 mmol) was taken into a flask and cooled to 25 ^{0}C .To this aluminum chloride ($AlCl_3$) (1.0 mmol) was added slowly in lot wise. The reaction mixture was stirred for 1 hour at same temperature in conventional method while 5 minutes in microwave (MW).The above reaction mass quenched in water. To the above aqueous layer diethyl ether was added, separated and washed with sodium

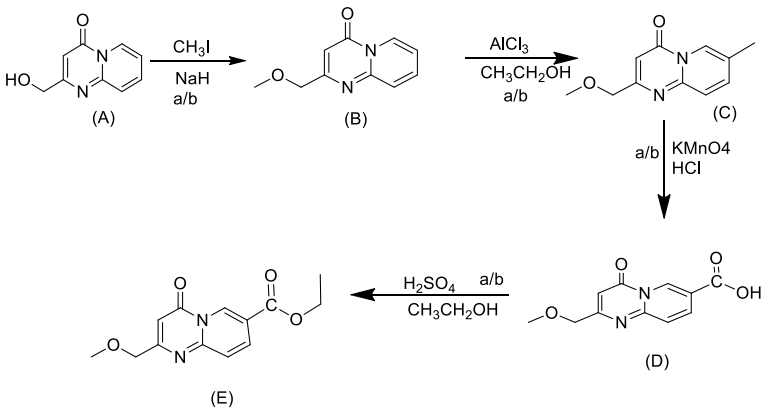
bicarbonate, followed by saturated sodium chloride solution. The organic layer obtained was concentrated and isolated in hexane to get desired product(C).

Preparation of 2-(methoxymethyl)-4-oxo-4H-pyrido [1, 2-a] pyrimidine-7-carboxylic acid (D) from 2-(methoxymethyl)-7-methyl-4H-pyrido [1, 2-a] pyrimidine-4-one (C):

Potassium permanganate was dissolved in 15 ml of water in a flask. To this a mixture of potassium hydroxide (0.24 mmol) and C (2.6 mmol) was added. The reaction mixture was refluxed for 4 hrs in conventional method while 10 minutes in microwave (MW) and cooled to room temperature, residue was filtered off. Aqueous layer was cooled to 5 °C and acidified with HCl. The resultant product (D) was filtered and washed with diethyl ether.

Preparation of ethyl 2-(methoxymethyl)-4-oxo-4H-pyrido [1, 2-a] pyrimidine-7-carboxylate (E) from 2-(methoxymethyl)-4-oxo-4H-pyrido [1, 2-a] pyrimidine-7-carboxylic acid (D):

In the ethanolic solution of D (0.85 mmol), 5 ml of sulphuric acid was added with continuous stirring. The reaction mixture was refluxed for 2 hours in conventional method while 5 minutes in microwave (MW). On cooling to room temperature, it was quenched with sodium bicarbonate solution.15 ml of dichloromethane was added to above aqueous layer, organic layer separated and washed with sodium chloride solution. The obtained organic layer was concentrated to half of its volume, the remaining volume again taken into flask, cooled to 2-8°C and stirred for 1 hour. The desired product (E) was filtered off and washed with diethyl ether.



a. Conventional synthesis / b.Microwave synthesis

Scheme 1: Synthesis of Ethyl 2-(methoxymethyl)-4-oxo-4H-pyrido [1, 2-a] pyrimidine-7-carboxylate (E)

Synthesis of Ethyl 2-(methoxymethyl)-4-oxo-4H-pyrido [1, 2-a] pyrimidine-7-carboxylate (E1-E8) analogs.
2-(methoxymethyl)-4-oxo-4H-pyrido [1, 2-a] pyrimidine-7-carboxamide (E1):

The above synthesized and characterized product E was taken into a flask and liquid ammonia was added drop wise at 25°C.The reaction content was refluxed for 5hrs and 15 mins in conventional and MW means respectively. After completion of the reaction, the product (E1) was isolated and characterized.

($C_{11}H_{11}N_3O_3$): IR(νmax cm^{-1}): 3465,3369 (NH2), 1800 (C=O); 1240,1035 (C-O);3110(Ar-H), 1631, 1525 (C=N); 1HNMR (δppm) :3.4-3.7 (s, 3H, O-CH_3), 4.1-4.3(s, 2H, O-CH_2), 6.2-6.4(s, 1H, pyrimidine H), 5.8-6.7(d, 1H, pyridine H), 7.2-7.5(d, 1H, pyridine H), 7.8(NH proton), 8.1-8.3 (s, 1H, pyridine H) 13CNMR(δppm):57-59 (O-CH_3), 80-82 (O-CH_2), 118.4,123.2,126.4,136.4 (Pyridine carbons),147.8,155.1,158.6 (pyrimidine carbons); 172.4 (C-NH_2)

7-(hydroxymethyl)-2-(methoxymethyl)-4-oxo-4H-pyrido [1, 2-a] pyrimidine-4-one (E2):

The Methanolic solution of E was taken into hydrogenation flask with palladium catalyst; the reaction content was heated under reflux and MW for 10 min and 6 hrs conv. After completion of reaction it was

filtered. The methanol layer was concentrated and diethyl ether added. Stirred for 1 hr and filtered to obtain the desired product.

($C_{11}H_{12}N_2O_3$): IR(Vmax cm^{-1}): 3469 (OH), 1346 (C-N), 1795 (C=O); 1245,1032 (C-O);3115(Ar-H), 1640, 1528 (C=N); 1HNMR (δppm) :3.4-3.7 (s, 3H, O-CH_3), 4.1-4.3(s, 2H, O-CH_2), 3.5,3.7 (s, 1H, OH), 4.2-4.5(s, 2H, CH_2 –OH), 6.2-6.4(s, 1H, pyrimidine H), 6.0-6.8(s, 1H, pyridine H), 7.2-7.5(d, 1H, pyridine H), 7.5-7.8 (d, 1H, pyridine H) 13CNMR(δppm):57-59 (O-CH_3), 65-67 (CH_2 –OH) 80-82 (O-CH_2), 120.4, 124.2,128.6, 140.8 (pyridine carbons), 156.1, 160.8 (pyrimidine carbons);

2-(methoxymethyl)-4-oxo-4H-pyrido [1, 2-a] pyrimidine-7-carbaldehyde (E3):

In the flask containing E2, pyridinium chlorochromate and methylene dichloride was added. The reaction mixture was heated under reflux and MW for 5 min and 3 hrs for conv. After completion of the reaction, diethyl ether was added to isolate the desired product.

($C_{11}H_{10}N_2O_3$): IR(Vmax cm^{-1}): 1730 (CHO), 1240,1035 (C-O);3110(Ar-H), 1631, 1525 (C=N); 1HNMR (δppm) :3.4-3.7 (s, 3H, O-CH_3), 4.1-4.3(s, 2H, O-CH_2), 5.6-5.8(d, 1H, pyridine H) 6.2-6.4(s, 1H, pyrimidine H), 7.3-7.6(d, 1H, pyridine H), 8.0-8.2 (s, 1H, pyridine H), 9.5-10.4(CHO proton) 13CNMR(δppm):57-60 (O-CH_3), 81-83 (O-CH_2), 118.2, 122.7,130.5, 134.9 (pyridine carbons), 147.1,155.2, 163.6 (pyrimidine carbons); 183.4 (CHO)

7-(chloromethyl)-2-(methoxymethyl)-4H-pyrido [1, 2-a] pyrimidine-4-one (E4):

In the toluene solution of E2, thinly chloride was added and refluxed for 2hrs by conventional means and MW for 15min. After completion of the reaction, diethyl amine was added. Salts were filtered off, organic layer was concentrated and product was isolated in n-hexane.

($C_{11}H_{11}ClN_3O_2$): IR(Vmax cm^{-1}): 720 (C-Cl);1365 (C-N), 1785 (C=O); 1240,1032 (C-O);3109(Ar-H), 1645, 1532 (C=N); 1HNMR (δppm) :3.4-3.7 (s, 3H, O-CH_3), 4.1-4.3(s, 2H, O-CH_2), 4.4-4.8 (s, 2H, CH_2-Cl) , 6.2-6.4(s, 1H, pyrimidine H), 7.1-7.3(s, 1H, pyridine H), 7.3-7.5 (d, 1H, pyridine H), 7.5-7.8(d, 1H, pyridine H) ;13CNMR(δppm):45-48 (CH_2-Cl), 55-58 (O-CH_3), 80-82 (O-CH_2), 118.5, 125.2,130.3, 137.5 (pyridine carbons), 144.4,153.9, 156.7 (pyrimidine carbons); m/e: 238; Analysis: Calcd C, 55.36; H, 4.65; N, 11.74;O,13.41; Found: C, 55.34; H, 4.62; N, 11.71;O,13.38.

7-amino-2-(methoxymethyl)-4H- pyrido [1, 2-a] pyrimidine-4-one (E5):

The E1 was taken into a flask and bromine was added. Aqueous sodium hydroxide was added to the reaction mixture. After completion of reaction, reaction mass filtered, methylene dichloride was added and stirred for 30 minutes. The separated organic layer was concentrated and isolated in n-hexane.

($C_{10}H_{11}N_3O_2$): IR(Vmax cm^{-1}): 3470,3373 (NH2), 1365 (C-N), 1785 (C=O); 1240,1032 (C-O);3109(Ar-H), 1645, 1532 (C=N); 1HNMR (δppm) :3.2-3.5 (s, 3H, O-CH_3), 4.0-4.2(s, 2H, O-CH_2), 6.0-6.2(s, 1H, pyridine H), 6.2-6.5(s, 1H, pyrimidine H), 7.3-7.5 (d, 1H, pyridine H),8.2-8.6 (NH_2 proton), 9.1-9.3 (d, 1H, pyridine proton);13CNMR(δppm): 54-58 (O-CH_3), 80-82 (O-CH_2), 96.5,122.5, 129.2,132.6, (pyridine carbons), 147.4,156.9, 158.7 (pyrimidine carbons);m/e: 205; Analysis: Calcd C, 58.53; H, 5.40; N, 20.48;O,15.59; Found: C, 58.51; H, 5.42; N, 20.45;O,15.62.

7-((dimethylamino) methyl)-2-(methoxymethyl)-4H-pyrido [1, 2-a] pyrimidine-4-one (E6):

In the Methanolic solution E3, hydrazine was added slowly. The reaction mixture was heated under MW /Conventional means. After completion of the reaction, it was allowed to cool till 25°C.Slowly water is added; product was isolated and recrystallized from hot ethanol.

($C_{13}H_{17}N_3O_2$): IR(Vmax cm^{-1}): 1342 (C-N), 1790 (C=O); 1242,1028 (C-O);3106(Ar-H), 1640, 1528 (C=N); 1HNMR (δppm) :3.2-3.5 (s, 3H, O-CH_3), 4.0-4.2(s, 2H, O-CH_2), 5.6-5.9(d, 1H, pyridine H), 6.2-6.5(s, 1H, pyrimidine H), 7.0-7.2 (NH_2 proton), 7.3-7.5 (d, 1H, pyridine H), 8.0-8.2 (s, 1H, pyridine proton);13CNMR(δppm): 54-58 (O-CH_3), 80-82 (O-CH_2), 116.7,117.5,122.5,133.6, (pyridine carbons), 152-154

(HC=N),147.4,156.7, 158.2 (pyrimidine carbons);m/e: 247; Analysis: Calcd C, 63.14; H, 6.93; N, 16.99;O,12.94; Found: C, 63.12; H, 6.91; N, 16.97;O,12.92.

(Z)-7-(hydrozonomethyl)-2-(methoxymethyl) - 4H-pyrido [1, 2-a] pyrimidine-4-one (E7):

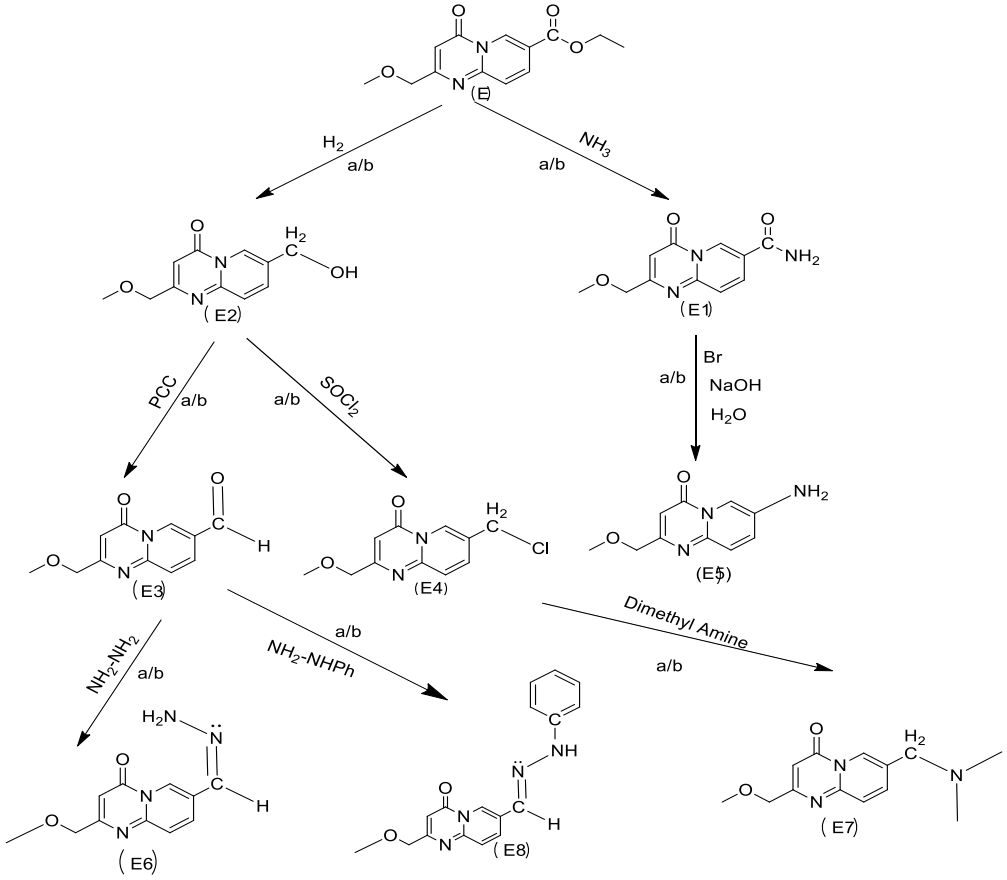
To methylene dichloride solution of E4, dimethyaniline was added. The reaction content was Microwave for 10min/ heated for 5 hrs by Conventional means. After completion of the reaction, salts were filtered, organic layer concentrated and isolated in diethyl ether to get the desired product.

($C_{11}H_{12}N_4O_2$): IR(Vmax cm^{-1}): 1342 (C-N), 1790 (C=O); 1242,1028 (C-O);3106(Ar-H), 1640, 1528 (C=N); 3400 (N-H); 1HNMR (δppm) :2.5-2.7 (s, 6H, N-$(CH_3)_2$), 3.2-3.5 (s, 3H, O-CH_3), 4.0-4.2(s, 2H, N-CH_2), 4.1-4.4(s, 2H, O-CH_2), 7.0-7.3(d, 1H, pyridine H), 6.2-6.5(s, 1H,pyrimidine H),7.3-7.5(d, 1H, pyridine H),6.8-7.1 (s, 1H, pyridine proton);13CNMR(δppm):47-49 (N-$(CH_3)_2$), 54-58 (O-CH_3),64-68(N-CH_2) 80-82 (O-CH_2), 122.1,124.2,125.2,138.6 (pyridine carbons),147.6,156.5, 158.2 (pyrimidine carbons); m/e: 232; Analysis: Calcd C, 56.89; H, 5.21; N, 24.12;O,13.78; Found: C, 56.87; H, 5.23; N, 24.14;O,13.74.

(Z)-2-(methoxymethyl)-7-((2-phenylhydrozono) methyl)-4H-pyrido [1, 2-a] pyrimidine-4-one (E8):

To methylene dichloride solution of E3 phenyhydrazine was added. The reaction content was MW for 15min/ heated for 5 hrs by Conventional means. After completion of the reaction, salts were filtered, organic layer concentrated and isolated in diethyl ether to get the desired product.

($C_{17}H_{16}N_4O_2$): IR(Vmax cm^{-1}): 1348 (C-N), 1795 (C=O); 1246,1040 (C-O);3115(Ar-H), 1645, 1532 (C=N); 3400 (N-H); 1HNMR (δppm) :3.2-3.5 (s, 3H, O-CH_3), 4.0-4.2(s, 2H, O-CH_2), 5.6-5.9(d, 1H, pyridine H), 6.2-6.5(s, 1H, pyrimidine H), 7.0-7.2 (NH_2 proton),6.6-6.8(m, 1H, benzene proton),7.4-7.8 (m, 4H, benzene protons),7.3-7.5 (d, 1H, pyridine H), 8.0-8.2 (s, 1H, pyridine proton);13CNMR(δppm): 54-58 (O-CH_3), 80-82(O-CH_2), 116.3,117.4,122.1,133.9, (pyridine carbons),114.5,118.2,130.5,138.6(benzene carbons) 152-154 (HC=N),147.8,156.9,158.5(pyri a. Conventional synthesis / b. Microwave synthesis



Scheme 2: Synthesis of Ethyl 2-(methoxymethyl)-4-oxo-4H-pyrido [1, 2-a] pyrimidine-7-carboxylate (E1-E8) analogs

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Table 1: Comparison of reaction kinetics of conventional (CV) and microwave irradiation (MW) methods for synthesis of compounds B-E8.

S.No.	Compound	Reaction Time(% Yield)		S.No.	Compound	Reaction Time(% Yield)	
		MW (min)	CV(h)			MW(min)	CV(h)
1	B	20 (91)	8(78)	7	E3	5 (91)	3(79)
2	C	5 (87)	1(81)	8	E4	15 (84)	2(69)
3	D	10 (84)	4(78)	9	E5	15 (86)	3(71)
4	E	5 (88)	2(72)	10	E6	20 (92)	4(85)
5	E1	15 (77)	5(66)	11	E7	10 (90)	5(76)
6	E2	10 (82)	6(72)	12	E8	15 (86)	5(71)

All synthesized novel molecules were characterized by ^{1}H NMR, Mass spectroscopic methods. These derivatives were further evaluated for their antimicrobial activity.

Antimicrobial assay

The synthesized compounds (E1–E8) were assessed for antimicrobial assay against gram negative bacteria EC-Escherichia coli , PA-Pseudomonas Aeruginosa and gram positive bacteria BS-Bacillus subtitles ,SA-Staphylococcus Aureus , along with a fungus CA-Candida albicans using the well diffusion method. The compounds were dissolved in DMSO and activity was determined using serial dilution method. The whole procedure was carried out as reported [10-16]. Cefixime and ketaconazole were used as antibacterial and antifungal reference drugs, respectively. The zone of inhibition (mm) was determined at 10 µg/ml concentration for each compound in triplicate experiments; the values were averaged and are presented in Table 2.

RESULTS AND DISCUSSION

Synthesis of novel pyrido pyrimidine molecule:

Synthesis of novel pyrido pyrimidine molecule was achieved by following the procedure as depicted in the Scheme 1 and 2. TLC was run throughout the reaction to optimize the reaction for purity and completion. The isolated products from both the methods showed same melting point and spectral pattern. Designed series of molecules (B-E and E1- E8) was characterized by spectral techniques before evaluating for antimicrobial studies.

The pyrido pyrimidine analogs, (Scheme-2), have been synthesized from Ethyl 2-(methoxymethyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-7-carboxylate as a starting compound.E1 was synthesized by reaction with ammonia to afford 2-(methoxymethyl)-4-oxo-4H-pyrido [1,2-a] pyrimidine-7-carboxamide which is characterized by an IR band of NH_2 stretching of amide displayed at 3465 cm^{-1}.

E2 was synthesized by hydrogenation reaction of E to afford 7-(hydroxymethyl)-2-(methoxymethyl)-4-oxo-4H-pyrido [1,2-a] pyrimidine-4-one which is characterized by an IR band of OH stretching displayed at 3469 cm^{-1} and at 154.9,153.1 in 13C-NMR.A couple of compounds were successfully prepared from E2 by oxidation with pyridimium chlorochromate and chlorination with thinly chloride to afford 2-(methoxymethyl)-4-oxo-4H-pyrido [1,2-a] pyrimidine-7-carbaldehyde (E3) and 7-(chloromethyl)-2-(methoxymethyl)-4H-pyrido[1,2-a]pyrimidine-4-one (E4) respectively. Both these compounds were confirmed by characteristic IR bands of CHO stretching of aldehyde at 1730 cm-1 and C-Cl stretching at 720 cm^{-1}.E7 was synthesized from chlorinated product E4 by lamination reaction with dim ethylamine. An IR band of C-N stretching observed at 1342 cm^{-1} and at 154.2, 153.1 in 13C-NMR.Two strong absorption bands appeared in the range between 3340 and 3200 cm^{-1} in the IR spectra of compounds (E5- E6) was attributed to NH_2 group of substituted pyrido pyrimidine, however peaks at 1604 to 1623 cm-1 were due to C=N absorptions (pyrimidine ring). The other major peaks observed in the IR of these compounds were 3130–3050; 1550-1520 cm^{-1} could be assigned to aromatic hydrogen and C=C of the ring. Major proton NMR spectral peaks appeared at δ 3.2-3.9 and 6.7- 7.8 ppm in the compounds (E5-E6) was assigned to NH_2 and aromatic protons. In the 13C NMR spectra, the signals

in the range δ 110-135 ppm were due to aromatic carbons and signals in the region δ 150-170 ppm were due to pyrimidine carbons. Other proton and carbon peaks were found to be well consistent with the expected structures. All the compounds showed a single peak in their mass spectra suggesting their purity.

Antimicrobial Activity

In this study, the well diffusion method was performed for preliminary screening the antimicrobial activity of new pyrido pyrimidine derivatives, against two gram positive bacteria Staphylococcus Aureus(SA), Bacillus subtitles(BS) and two gram negative bacteria Escherichia coli(EC), Pseudomonas Aeruginosa(PA) along with a fungus Candida albicans(CA) to determine their zone of inhibition in vitro. Results are listed in Table 2.

Cefixime and ketaconazole were used as antibacterial and antifungal reference drugs, respectively. The zone of inhibition (mm) was determined at 10 µg/ml concentration for each compound in triplicate experiments; the values were averaged and depicted in Table 2.From the results illustrated in Table 2, it is clear that all the synthesized pyrido pyrimidine derivatives have displayed antimicrobial activity against gram positive, gram negative and fungus. Antimicrobial evaluation results of novel compounds against bacteria and fungi are encouraging.

The observed values revealed that type of substituent directly attached to pyrido pyrimidine ring has a significant impact on the antibacterial/antifungal activities of these novel analogs. In particular, compound number E1 having an amine group showed promising activity towards gram negative bacteria whereas E7,compound having a tertiary amine group showed activity towards gram positive bacteria.

Compounds E5, E6 and E8 also showed promising activity due to the presence of an amine group confirming the presence of the amine group has an impact on antibacterial activity of a compound. E4 compound having a chlorine group as substituent showed more activity towards gram negative bacteria than gram positive bacteria.E2 & E3 showed less activity towards all microorganisms owing to the presence of hydroxyl and aldehyde groups respectively.

Table 2: The zone of inhibition values of the synthesized compounds for antibacterial and antifungal activity at 10 µg/ml concentration

		Bacteria				Fungus
S. No.	**Compound**	**EC**	**PA**	**BS**	**SA**	**CA**
1	E	12 ± 0.4	10 ± 0.7	10 ± 0.9	9 ± 0.4	7 ± 0.7
2	E1	17 ± 0.5	17 ± 0.5	10 ± 0.7	11 ± 0.2	16 ± 0.6
3	E2	10 ± 0.8	9 ± 0.6	--	8± 0.2	10 ± 0.3
4	E3	8 ± 0.7	11 ± 0.7	12 ± 0.8	10 ± 0.4	11 ± 0.3
5	E4	17 ± 0.5	15 ± 0.4	12 ± 0.8	10 ± 0.4	13 ± 0.7
6	E5	19 ± 0.4	17 ± 0.4	15 ± 0.5	16 ± 0.5	18 ± 0.2
7	E6	15 ± 0.4	18 ± 0.7	15 ± 0.6	16 ± 0.6	16 ± 0.6
8	E7	16 ± 0.3	12 ± 0.3	16 ± 0.5	15 ± 0.5	17 ± 0.7
9	E8	17 ± 0.5	14 ± 0.2	17 ± 0.7	16 ± 0.4	17 ± 0.7
9	Cefixime	22	17	18	16	-
10	Ketaconazole	-	-	-	-	23

-- No activity; values were expressed in Mean± SEM of three individual experiments.

Escherichia coli (EC), Pseudomonas Aeruginosa (PA), Staphylococcus Aureus (SA), Bacillus subtitles (BS), Candida albicans (CA).

CONCLUSION

The present work provides the conventional and green preparation of new pyrido pyrimidine molecule and its derivatives. MW method had emerged better alternative of conventional method in context of yield, easy workup and time saving. All the newly synthesized compounds have been screened for their antimicrobial activities. Most of the tested compounds exhibited activities against the strains used. Our

present work demonstrated that the presence of the amine group has a significant effect on the activity which was followed by a chloro group.

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CONFLICT OF INTERESTS: Declared none

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