https://doi.org/ 10.33472/AFJBS.6.5.2024. 6756-6772

African Journal of Biological Sciences

Synthesis and Pharmacological Assessment of Novel Pyrido [2,3-D] Pyrimidines

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Article History
Volume 6, Issue 5, 2024
Received: 15 May 2024
Accepted: 22 May 2024
doi: ***10.33472/AFJBS.6.5.2024. 6756-6772***

Abstract

2-amino-3-cyanopyridines were prepared by using 4-hydroxy acetophenone as starting material which is treated with malononitrile and various types of benzaldehydes consists of electron withdrawing groups on it. Solvent used in this reaction condition is toluene, which gives more yield when compared with using of other solvent, the synthesized 2-amino-3-cyanopyridines were characterized by physical properties and spectral studies (IR, ^{1}H NMR). 5-substituted-7-(4-hydroxyphenyl)-pyrido [2,3-d] pyrimidines were synthesized by taking 2-amino-3-cyanopyridines as starting materials, which were treated with PhNCS/Urea/Thiourea. The synthesized 5-substituted 7-(4-hydroxyphenyl)-pyrido [2,3-d] pyrimidines were screened for antibacterial and antimitotic activity. Among all the synthesized compounds Compound 5C showed significant activity against *Bacillus subtilis*. From the results of antimitotic activity, all the title compounds (5a-7c) showed dose dependent inhibitory effect on seed germination, radical length, and mean weight of seedlings. Among all these 6b, 6c and 7b shows significant results on decrease percentage germination and radical length gained, mean weight at 2.5 mg/mL and 5.0 mg/mL as par with aspirin 2.5 mg/ml.

Keywords: 2-amino-3-cyanopyridines, Malononitrile, Benzaldehydes, Toluene, Pyrido [2,3-d] pyrimidines

1. Introduction:

Pyridines, pyrimidines, pyridopyrimidines and their fused heterocyclic ring systems are of current interest by virtue of their exceptional and versatile biological activities as calcium antagonists, arteriolar vasodilators, herbicide antidotes, anti bacterial agents, antitumor agents and hypotensive agents. Among all, pyridopyrimidine moiety was considered as the best known tyrosin kinase inhibitor for the treatment of chronic myelogenous leukemia and drug resistance emerges by amplification of the development of a mutation. Also pyridopyrimidines have antimicrobial activity against a number of bacteria and fungi (Chen *et al.,* 2015, Aminabee *et al.,* 2015).

The mortality and morbidity of cancer patients is the second highest among all diseases in the world, after heart disease. The demand for new compounds in the therapeutic area is higher than ever before. It has encouraged scientists to search for anti-tumor agents with novel chemical eternity & new model of action (El-Bendary *et al.,* 2019, Aminabee *et al.,* 2019).

Pyrido [2,3-d] pyrimidines forms the important class of compounds with a variety of pharmacological activities. Recently various derivatives of pyrido [2,3-d] pyrimidines were synthesized have been shown to exhibit promising biological and pharmacological activities. With these observations, an attempt is made to synthesize the compounds bearing pyrido [2,3-d] pyrimidine ring and studied the effect of various substituents on possible biological activities (Jangid *et al.,* 2020, Aminabee *et al.,* 2020).

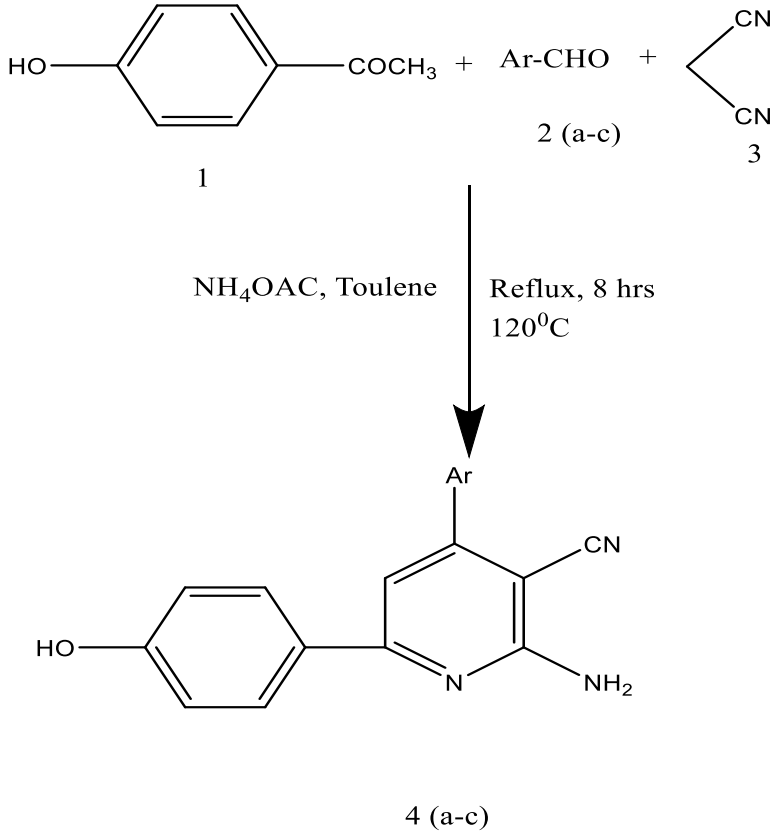
The common synthetic method used for pyrido [2,3-d] pyrimidines is based on the condensation followed by cyclization reaction of 2-amino-3-cyano-4,6-disubstituted pyridines with PhNCS/urea/thiourea etc.

- 2-amino-3-cyano-4,6-disubstituted pyridines described in chapter-1 were taken for the condensation with PhNCS/urea/thiourea to furnish novel pyrido [2,3-d] pyrimidines.
- To characterize the compounds using spectral methods (IR, ^{1}H NMR) methods and elemental analyses. The data related to structural characterization is given individually.
- To screen the synthesized pyrido [2,3-d] pyrimidines for their toxicity and possible biological activities like anti cancer and/or anti mitotic and anti microbial activities.
- To identify the active compounds for further development.

2. Materials and Methods:

Aromatic aldehydes (0.001 mol) + 4- hydroxyacetophenone (0.001 mol) + Malononitrile (0.001 mol) + Anhy. Ammonium acetate (0.008 mol), add 30 ml of toluene and heated to reflux for 8h.

Completion of the reaction was monitored by TLC, reaction\mixture was allowed to cool. The solvent was removed under reduced pressure and absolute ethanol was added to the residue. The precipitate was collected by filtration and purified by recrystallization by using ethanol to give the desired product (Patil *et al.*, 2018, Aminabee *et al.*, 2023).



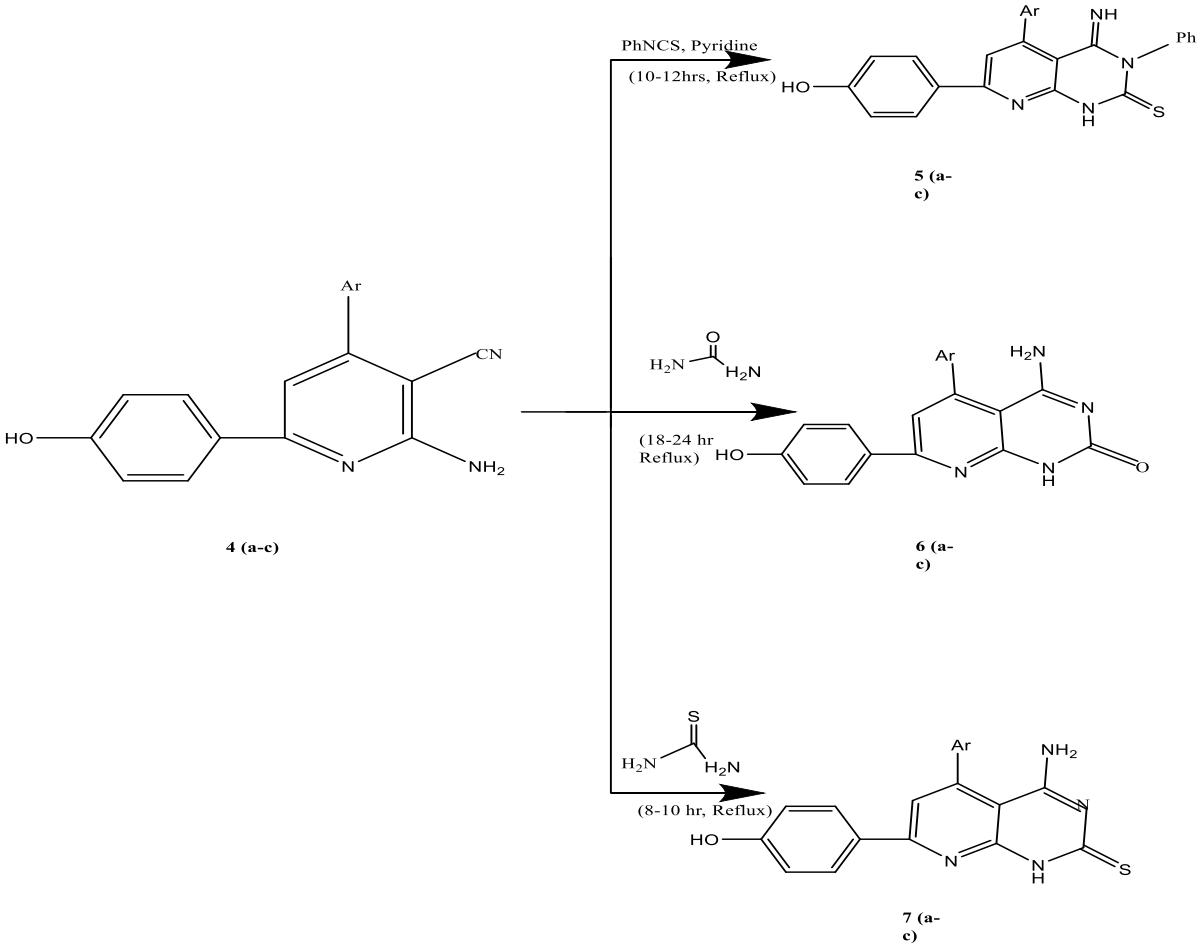
4 (a-c)

Experimental Scheme

Procedure for Synthesis of [5a, 5b, 5c]: The condensation of 2- amino-3-cyanopyridine (0.001 mol) and phenylisothiocyanate (0.002 mol) in pyridine (5-10 mL) under reflux for 10-12 h obtained required pyrido [2,3-d] pyrimidine. Completion of the reaction was monitored by TLC using Silica gel 60 F254 precoated plates. After completion of the reaction, it was allowed to cool (Rajasekaran *et al.*, 2017, Aminabee *et al.*, 2011). Then the reaction mixture was poured in to crushed ice, the solid separated was filtered and washed with water. It was dried and recrystallized from ethanol.

Procedure for synthesis of [6a, 6b, 6c]: The condensation of 2-amino- 3-cyanopyridine (0.001 mol) and urea (0.002 mol) in glacial acetic acid and conc. HCl (3:1) was heated under reflux for 18-24 h. Completion of the reaction was monitored by TLC using Silica gel 60 F254 precoated plates. After completion of the reaction, it was allowed to cool and poured into ice cold water

(Yao *et al.*, 2017, Aminabee *et al.*, 2016). The precipitate obtained was filtered, washed with ice cold water and then dried. Recrystallize it from methanol.



Procedure for synthesis of 5(a-c), 6(a-c) and 7(a-c)

Procedure for synthesis of [7a, 7b, 7c]: The condensation of 2-amino-3- cyanopyridine (0.001 mol) and thiourea (0.002 mol) was refluxed on an oil bath at 120-130^{0}C for 2 h with constant stirring. The temperature was raised gradually to 180^{0}C and finally mixture was heated at 210-220^{0}C for 2 h. Completion of the reaction was monitored by TLC using Silica gel 60 F254 precoated plates. After completion of the reaction, it was allowed to cool and poured into ice cold water (Vijayan *et al.,* 2019, Leelavati *et al.,* 2023). The precipitate obtained was filtered, washed with ice cold water and then dried. Recrystallize it from DMF- ethanol (1:2).

Infrared (IR) spectrum was recorded on Perkin-Elmer FTIR spectrophotometer; ^{1}H NMR spectra were recorded on Bruker 400 MHz instrument using DMSO-d6 as a solvent.

Anti Mitotic Activity: Cytotoxic properties of plant extracts and drugs being developed for cancer treatment are usually evaluated by variety of in vivo and in vitro tests carried out in animal or plant based models. In the present study we have evaluated the possibility of using the germinating mung beans (*Vigna radiata*), for rapid and inexpensive screening of drugs exhibiting cytotoxic properties (Bhandare *et al.,* 2017, Prasanth *et al.,* 2020).

Testing procedure: Mung beans (weighing 47.82 ± 1.50 mg) used in this study were obtained from the local market. They were soaked in tap water in the control group or in a drug solution in the test group for 6 h. The water or the drug solution was drained and the seedlings were kept moist (either with tap water or the drug solutions in covered petridish) until the radicles in the control group had grown to 1.0-1.5 cm (time 0, T0). At T0, the weight of seedlings, % germination, length of radical were recorded both in the control and test group. The seedlings were maintained at room temperature under moist conditions for an additional period of 48 h (T48). All the parameters recorded at T0 were again measured at T48. The change in weight and gain in radicle length between T0 and T48 were calculated. The seeds that did not germinate were simply weighted and no other parameters could be measured on these seeds (Kamble *et al.,* 2017, Shaik *et al.,* 2023). ***Drug solutions:*** Working dilutions of all drugs were made in tap water. Drug solutions of different concentrations were prepared by using DMSO and water.

Standard: Anti-inflammatory drug Aspirin was used at 0.5 mg/ml, 2.0 mg/ml concentration. Dilutions were made by using methanol and water (Khan *et al.,* 2020, Aminabee *et al.,* 2011).

Anti bacterial activity: MICs are defined as the lowest concentration of antimicrobial that will inhibit the visible growth of microorganism after overnight incubation. A current definition of the MIC is the lowest concentration which resulted in maintenance or reduction of inoculums

viability. Determination of the minimum inhibitory concentration (MIC) of the compounds was measured by two-fold serial dilution method (Saryan *et al.*, 2020, Aminabee *et al*., 2015).

3. Results and Discussion

2-amino-3-cyanopyridines were synthesized which were taken as starting materials for synthesis of pyrido [2,3-d] pyrimidines. A series of pyrido [2,3-d] 0pyrimidines has been synthesized using the appropriate synthetic procedures and various reagents. All the compounds were characterized by IR, ^{1}H NMR (Table 1).

Table 1: IR and H NMR chemical shift values of the compounds 4A-4C, 5A-5C, 6A-6C AND 7A-7C

Compound	**IR**	**^{1}H NMR**
(4a)	**IR [cm^{-1}, KBr]:** 3461, 3353 (NH_2), 3241 (OH), 2212 (CN), 1594 (C=N), 755 (C-Cl).	**^{1}H NMR (400 MHz, DMSO-d6) δ:** 6.864-6.842 (2H, d, *J*=8.8,C-3"&5"), 6.950 (1H, s, NH_2), 7.091 (1H, s, C-6H), 7.181-7.143 (1H, t, C-5"H), 7.230- 7.267 (1H, t, C-4"H), 7.501-7.482 (1H, d, *J*=7.6,C-3"H), 7.653-7.634 (1H, d, *J*=7.6, C-6"H), 7.996-7.9(2H, d, *J*=8.8 C-2" & C-6"), 9.925 (1H, s, OH).
(4b)	**IR [cm^{-1}, KBr]:** 3462 (OH,)3353, 3228 (NH2), 2207 (CN), 1599 (C=N), 772 (C-Cl).	**^{1}H NMR (400 MHz, DMSO-d6) δ:** 6.866-6.844 (2H, d, *J*=8.8 Hz,C3" & 5"), 6.911 (2H, brs, C4NH2), 7.170 (1H, s, C6H), 7 .6297.608 (2H, d, *J*=8.4Hz, C-2' & C- 6'H), 9.910 (1H, s, C-4"-OH),7.700-7.679 (2H, d, *J*=8.4Hz, C-3′& C- 5′-H), 7.993-8.014 (2H, d, *J*=8.4 Hz, C- 2" & 6"-H).
(4c)	**IR [cm^{-1}, KBr]:** 3403,3327 (NH_2), 3189 (OH), 2217 (CN), 1591 (C=N), 778 (C-Cl).	**^{1}H NMR (400 MHz, DMSO-d6) δ:** 6.79 (2H, brs, C-4-NH2), 6.893-6.871 (2H, d, *J*=8.8 Hz,C-2"& 6"H), 7.126 (1H, s, C-6H), 7.214-7.194 (1H, d, *J*=8.0 Hz, C-6'-H), 10.086 (1H, s, C-4"-OH), 7.364-7.344 (1H, d, J=8.0 C-5H), 7.483(1H, s, C-3-'H), 7.997-7.760 (2H, d, J=8.4 Hz, C-3" & 5"-H).

(5a)	**IR [Cm^{-1}, KBr]:** 3244 (NH), 3115 (OH) 1221 (C=S), 1465 (C=N), 757 (C-Cl).	**^{1}H NMR (400 MHz, DMSO-d6) δ:** 6.364 -6.342 (5H, m, Ar-H), 6.716-6.696 (1H, d, J=8.0 Hz, C-6''-H), 6.901 (1H, s, C-6-H), 7.148-7.111 (1H, t, C- 5''-H),7.354-7.314 (1H, t, C-4-H''), 7.501-7.482 (2H, d, J=7.6 Hz, C-3'''&5'''-H), 7.886-7.864 (1H, d, J=8.8 Hz, C- 3″-H), 8.087-8.071 (2H, d, J=6.4 Hz, C-2''' & 6'''-H), 8.951 (1H, s, C-4-NH), 9.771 (1H, s, C-4'''-OH), 11.314 (1H, s, NH).
(5b)	**IR [Cm^{-1}, KBr]:** 3243 (NH), 3116 (OH), 1221(C=S), 1460 (C=N), 779 (C-Cl).	**^{1}H NMR (400 MHz, DMSO-d6) δ:** 6.290-6.231 (5H, m, Ar-H), 7.059-7.035 (2H, d, J=8.8 Hz, C-3'''&5'''-H), 7.130-7.111 (2H, d, J=7.6Hz, 3'' & ''5- H), 7.148 (1H, s, C-6-H), 7.334-7.314 (2H, d, J=7.6 Hz, C-2''&6''-H), 7.500-7.478 (2H, d, J=8.8 Hz, C- 2''' & 6'''-H), 8.759 (1H, s, C-4-NH), 9.771 (1H, s, C-4'''OH), 11.210 (1H, s, NH).
(5c)	**IR [Cm-1, KBr]:** 3244, (NH), 3118 (OH), 1220 (C=S), 1461 (C=N), 781 (C-Cl).	**^{1}H NMR (400 MHz, DMSO -d6) δ:** 6.364 -6.330 (5H, m, Ar-H), 6.892-6.871 (2H, d, J=8.4 Hz, C-3'''&5'''-H) , 7.130 (1H, s, C-6-H), 7.216- 7.195 (1H, d, J=8.4 Hz, C- 5''-H), 7.363-7.35(1H, d, J=7.6 Hz, C- 6''-H) 7.482 (1H,s 3''-H), 7.997-7.975 (2H, d, J=8.8 Hz, C- 2'''&6'''-H) , 8.918 (1H, s, C-4-NH), 10.086 (1H, s, C- 4'''-OH), 11.021 (1H, s, NH).
(6a)	**IR [Cm-1, KBr]:** 3511 (OH), 3279,3238 (NH_2), 1684 (C=O), 1463 (C=N), 752 (C-Cl).	**1H NMR (400 MHz, DMSO-d6) δ:** 6.864-6.842 (2H, d, J=8.8 Hz, C-3''&5''-H), 6.950 (2H, (1H, t, C-4'-H), 7.267-7.230 (1H, t, C-5'-H), 7.501-7.480 (1H, d, J=8.4Hz, C-3'-H), 9.925 (1H, s, C-4''-OH) 7.653-7.633 (1H, d, J=8.0 Hz C- 6'-H), 8.313 (1H, s, NH), 7.996-7.974 (2H, d, J=8.8 Hz, C-2''&6''H).
(6b)	**IR [Cm-1, KBr]:** 3360, 3219 (NH_2) , 3107 (OH) , 1698 (C=O), 1456 (C=N), 756 (C-Cl).	**^{1}H NMR (400 MHz, DMSO-d6) δ:** 6.866-6.844 (2H, d, J=8.8 Hz, C-3''&5''-H), 6.911 (2H, brs,C-4-NH2), 9.910 (1H, s, NH) 7.700-7.679 (2H, d, J=8.4 Hz, C-2'&6'-H), 7.170 (1H, s, C-6-H), 7.629-7.608 (2H, d, J=8.4 Hz, C- 3'& C- 5'H), 8.014-7.993 (2H, d, J=8.4 Hz, C- 2''&6''-H) 9.393

		(1H, s, C-4''-OH).
(6c)	**IR [Cm^{-1}, KBr]:** 3457 (OH), 3251,3119 (NH_2), 1723 (C=O), 1435 (C=N), 779 (C-Cl).	**^{1}H NMR (400 MHz, DMSO -d6) δ:** 6.79 (2H, brs, C-4-NH_2), 6.893-6.871 (2H, d, J=8.8 Hz, C-2''&6''-H), 7.126 (1H, s, C-6H), 7.214-7.194 (1H, d, J=8.0 Hz,C-6'-H), 7.364-7.344 (1H, d, J =8.0 Hz, C-5'-H), 7.483 (1H, s, C-3-'H), 7.997-7.76 (2H, d, J=8.4 Hz, C-3''&5''-H), 8.993 (1H, s, NH), 10.086 (1H, s, C-4''-OH).
(7a)	**IR [Cm^{-1}, KBr]:** 3233, 3100 (NH_2), 3006 (OH), 1224 (C=S), 1464 (C=N), 797 (C-Cl).	**^{1}H NMR (400 MHz, DMSO-d6) δ:** 6.886- 6.864 (1H, d, J=8.8 Hz, C-3'-H), 7.202-7.170 (1H, t, C-4'- H), 7.272-7.253 (1H, d, J=7.6 Hz,C-6'-H), 7.667 (2H, brs, C-4-NH2) 7.721-7.700 (2H, d, J=8.4 Hz, C-3'' & 5''-H), 7.767 (1H, s, C-6-H), 8.571-8.531 (1H, t, C-5'-H), 8.918-8.900 (2H, d, J=7.2 Hz, C-2'' & 6''-H), 10.010 (1H, s, C- 4''-OH), 10.886 (1H, s, NH).
(7b)	**IR [Cm^{-1}, KBr]:** 3459 (OH), 3258, 3108 (NH_2), 1216 (C=S), 1464 (C=N), 762 (C-Cl).	**^{1}H NMR (400 MHz, DMSO-d6) δ:** 6.841-6.862 (2H, d, J=8.4 Hz, C- 3'' & 5''- H), 6.918 (2H, brs, C-4-NH2),7.713 (1H, s, C-6-H), 9.308(1H, s, NH), 7.605-7.625 (2H, d, J=8.0 Hz,C-3'&5'-H), 7.750-7.771 (2H, d, J=8.4 Hz, C-2' & 6'-H), 7'997-8.O1 (2H, d, J=8.4 Hz, C-2'' & 6''-H), 9.925 (1H, s, C- 4''-OH), 9.308 (1H, s, NH).
(7c)	**IR [Cm^{-1}, KBr] :** 3397 (OH), 3102, 3081 (NH_2), 1217 (C=S), 1453 (C=N), 7658 (C-Cl).	**^{1}H NMR (400 MHz, DMSO -d6) δ:** 6.794-6.773 (2H, d, J=8.4 Hz, C-3''&5''-H), 6.81 (2H, brs, C-4-NH2), 6.889-6.868 (2H, d, J=8.4 Hz, C-2''&6''-H), 7.367-7.346 (1H, d, J=7.6 Hz, C-5'-H), 7.486 (1H, s, C-3'-H), 8.998 (1H, s, NH), 10.067 (1H, s, C-4''-OH).

Anti Mitotic Activity: The title compounds were screened for preliminary cytotoxic evaluation on germinating seeds of Vigna radiate (mung bean) for rapid and inexpensive screening of drugs exhibiting cytotoxic properties. Aspirin was used as a standard reference drug. Various

parameters measured at T0 and T48 are % germination, change in radical length, change in weight were reported for evaluating the cytotoxicity. The extent of water imbibitions and seedling growth is indicated by gain in weight. All the compounds had shown increase in weight except aspirin which showed decrease in weight. The increase in weight of seedlings when dissolved in sample solutions is mainly due to the water imbibitions (Saundane *et al.,* 2015, Aminabee *et al.,* 2015).

All the title compounds (5a-7c) showed dose dependent inhibitory effect on seed germination, radical length, and mean weight of seedlings. Among all these compounds 6b, 6c and 7bshows significant results on decrease percentage germination and radical length gained, mean weight at 2.5 mg/mL and 5.0 mg/mL as par with aspirin 2.5 mg/ml (Table 2 and 3, Figure 1 and 2).

Table 2: % Germination of Seeds at T0

Name of the drug	**% of germination**			
Concentration (mg/ml)	**0.5 (mg/ml)**	**1.0 (mg/ml)**	**2.5 (mg/ml)**	**5.0 (mg/ml)**
Aspirin	-	25	-	22
control	100			
5a	85.0	80.0	37.5	28.0
5b	92.5	89.0	30.4	34.7
5c	93.5	80.0	37.5	31.8
6a	96.8	84.6	29.1	20.0
6b	90.0	88.5	17.3	15.3
6c	86.7	85.7	16.6	12
7a	90.7	89.0	43.4	33.3
7b	87.6	87.5	24	23.9
7c	85.7	84.2	34.7	24

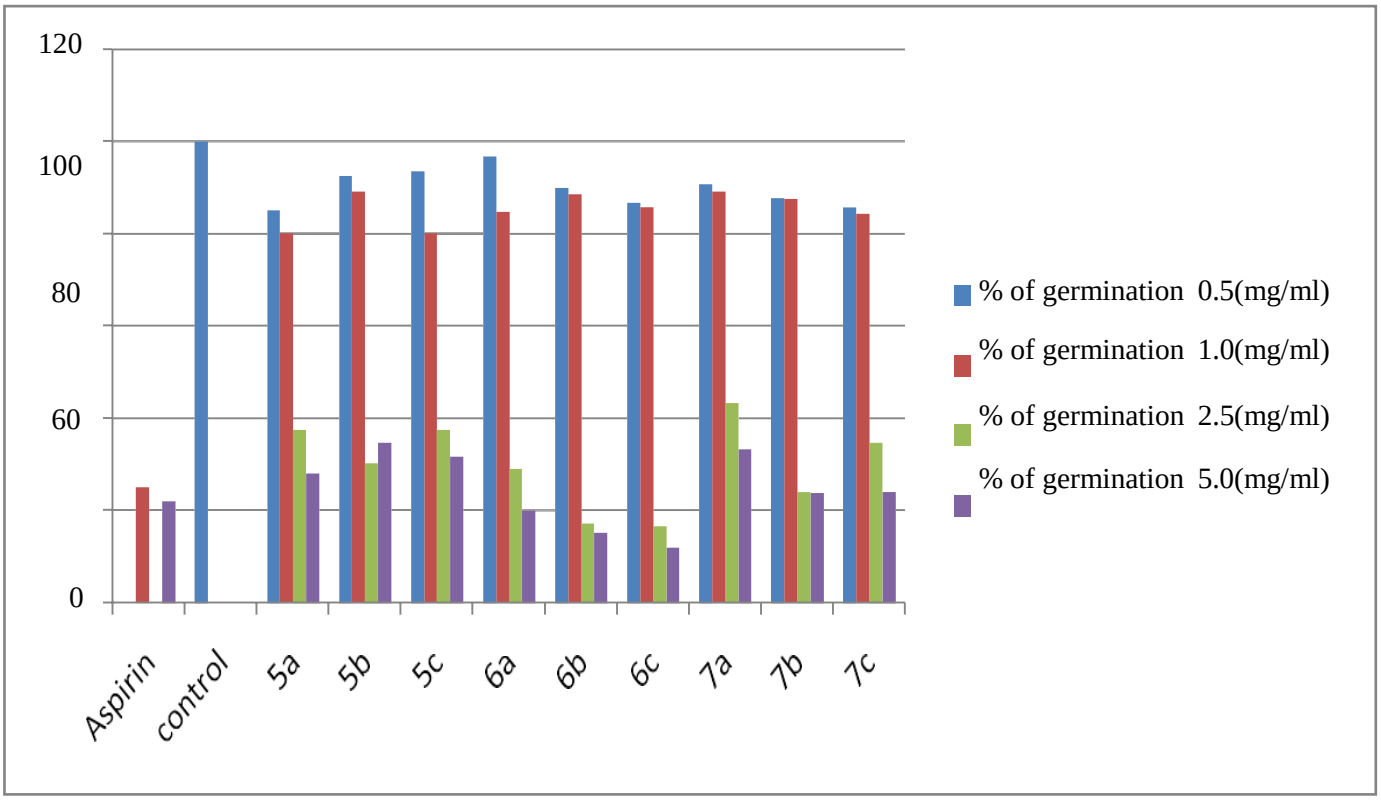


Figure 1: Grpahical representation of % Germination of seeds at T0

Table 3: % Length Gained At Different Concentrations

Compound Name	**Difference in MRL between T0 and T48**				**% Length gained**			
Conc. (mg/ml)	**0.5**	**1**	**2.5**	**5**	**0.5**	**1**	**2.5**	**5**
Aspirin	1.4	-	0.98	-	54.19	-	37.9	-
5a	1.91	1.76	1.24	1.17	74.03	68.2	48	45.3
5b	1.89	1.74	1.32	1.13	73.26	67.4	51.1	43.7
5c	2.13	1.65	1.22	1.24	82.56	63.9	47.2	48
6a	1.92	1.54	1.07	1.19	74.42	59.6	41.4	44.5
6b	2.01	1.67	1.43	1.11	77.91	64.7	55.4	43
6c	1.82	1.75	1.34	1.05	70.54	67.8	51.9	40.6
7a	1.99	1.85	1.43	1.15	77.13	71.7	55.4	44.5
7b	1.89	1.78	1.24	1.15	73.26	68.9	48	44.5
7c	2.12	2.01	1.43	1.25	82.17	77.98	55.4	48.4
Control	2.58				100			

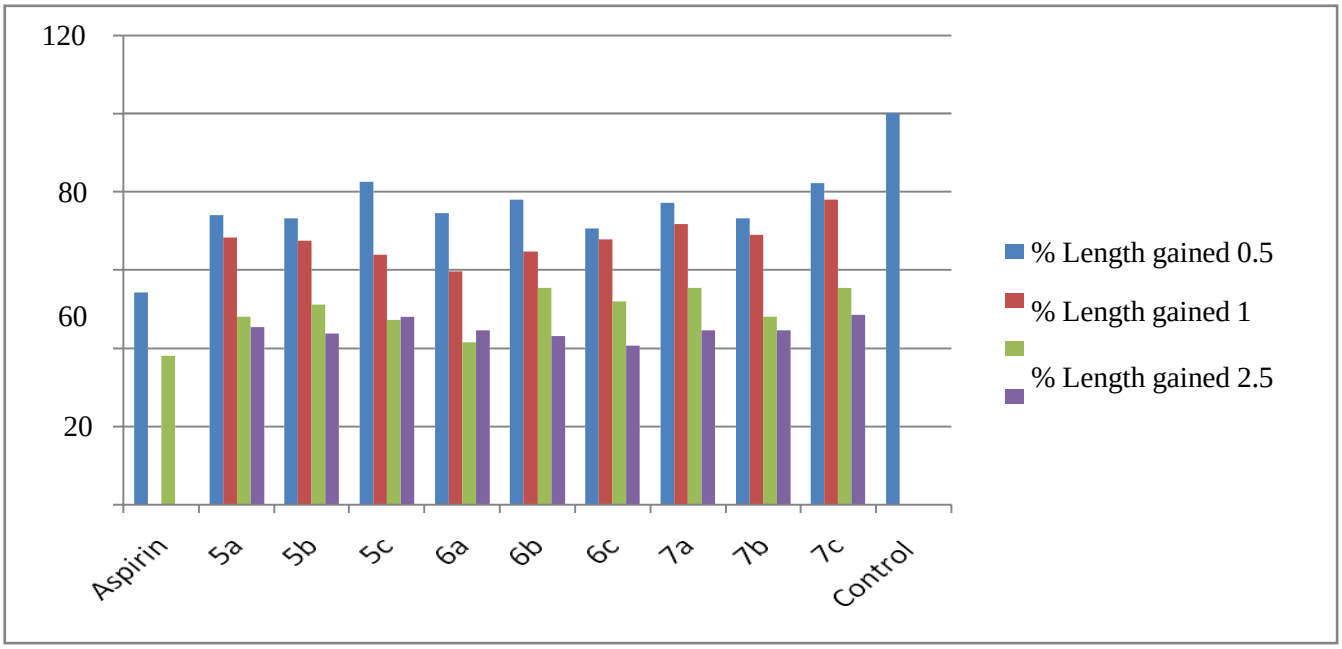


Figure 2: Graphical representation of % length gained at different concentrations

Antibacterial Activity: All the synthesized pyrido [2,3-d] pyrimidines have been evaluated for their antibacterial activity (MIC) against gram positive (B. subtilis, S. aureus) and gram negative (*E. coli, P. vulgaris*) organisms using two fold serial dilution method. The results of this evaluation compared with ampicillin as reference standard. The antibacterial activity results (MICs µg/ mL) were reported. Compound 5c, 7a, 7b showed significant activity against B. subtilis with MIC value of 80 µg/ mL. Compound 5c, 6a, 6b and 7b showed significant activity against S. aureus with MIC value of 40 µg/ mL. Compounds 5c, 6a, 7a showed significant activity against both the gram negative organisms (*E. coli and P. vulgaris*) with the MIC value of 80 µg/ mL. The obtained data revealed that most of the compounds showed moderate activity against the bacterial strains. It is noticed that compounds 5c,7a exhibited potent activity against the four organisms (*S. aureus, B. subtili, E. coli and P. vulgaris*) used for the screening with the MIC values of 80, 80, 80, 80 µg/ mL respectively compared with standard [13]. Due to the presence of 2-Chloro, 2, 4-Di Chloro phenyl moieties at 5^{th} position of 7-(p-hydroxyphenyl) pyrido [2,3- d] pyrimidin-(2H)-one. The presence of strong electron releasing group i.e. Chlorine present at either 2^{nd} or 4^{th} or 2^{nd} & 4^{th} position on phenyl ring which is present on 5th position of 7-substituted aryl pyrido [2,3-d] pyrimidine ring system

containing compounds (5a, 6b, 6c, 7b) exhibited moderate activity with MIC value of 40 µg/ mL. Similarly compounds 5b, 6a and 7a which process the above mentioned structural frame work acts against *E. coli* with the MIC value of 80 µg/ mL (Table 4).

Table 4: Antibacterial Activity Detection by Two-Fold Serial Dilution Method

Compounds & Standard	**MIC of tested compounds (µg/mL) against**			
	Gram positive		**Gram negative**	
	B. subtilis **NCIM 2549**	***S. aureus*** **NCIM 2122**	***E. coli*** **NCIM 2803**	***P. vulgaris*** **NCIM 2027**
5a	80	160	160	320
5b	160	160	320	160
5c	80	80	80	80
6a	160	160	80	80
6b	320	160	160	320
6c	160	320	160	160
7a	80	80	80	80
7b	160	80	160	320
7c	320	160	320	160
Ampicillin	40	40	40	40

2-amino-3-cyanopyridines 4(a-c) were prepared by using 4-hydroxy acetophenone as starting material, which is treated with malononitrile and various types of benzaldehydes consists of electron releasing groups on it. Solvent used in this reaction condition is toluene, which gives more yield when compared with using of other solvent i.e. ethanol. The synthesized 2- amino-3-cyanopyridines were characterized by physical properties and spectral studies .5- substituted-7-(4-hydroxyphenyl)-pyrido [2,3- d] pyrimidines (5a-7c) were synthesized by taking 2-amino-3-cyanopyridines as starting materials, which were treated with PhNCS/Urea/Thiourea (Zhang *et al.,* 2016, Aminabee *et al.,* 2015).

The synthesized 5-substituted-7-(4- hydroxyphenyl)-pyrido [2,3-d] pyrimidines were screened for antibacterial and antimitotic activity. Among all the synthesized compounds, compound 5a, 5c, 7a showed significant activity against *B.subtilis* with MIC value of 80 µg/ mL. Compound

5c, 7a and 7b showed significant activity against S. aureus with MIC value of 80 µg/ mL. Compounds 5c, 6a, 7a showed significant activity against both the gram negative organisms (*E. coli and P. vulgaris*) with the MIC value of 80 µg/ mL. From the results of antimitotic activity, all the title compounds (5a-7c) showed dose dependent inhibitory effect on seed germination, radical length, and mean weight of seedlings (Kumar *et al.,* 2019, Shaik *et al.,* 2023, Leelavati et al., 2023). Among all these compounds 6b, 6c and 7b shows significant results on decrease percentage germination and radical length gained, mean weight at 2.5 mg/mL and 5.0 mg/mL as par with aspirin 2.5 mg/ml.

4. Conclusion:

The title compounds were screened for preliminary cytotoxic evaluation on germinating seeds of *Vigna radiate* (mung bean) for rapid and inexpensive screening of drugs exhibiting cytotoxic properties. Aspirin was used as a standard reference drug. Various parameters measured at T0 and T48 are % germination, change in radical length, change in weight were reported in tables 2, 3, 4 for evaluating the cytotoxicity. The extent of water imbibitions and seedling growth is indicated by gain in weight. All the compounds had shown increase in weight except aspirin which showed decrease in weight. The increase in weight of seedlings when dissolved in sample solutions is mainly due to the water imbibitions. All the title compounds (5a-7c) showed dose dependent inhibitory effect on seed germination, radical length and mean weight of seedlings. Among all these compounds 6b, 6c and 7b shows significant results on decrease percentage germination and radical length gained, mean weight at 2.5 mg/mL and 5.0 mg/mL as par with aspirin 2.5 mg/ml.

Acknowledgements:

The authors express their heartfelt gratitude to the management of V.V. Institute of Pharmaceutical Sciences, Gudlavalleru, Krishna District, Andhra Pradesh and KVSR Siddhartha College of Pharmaceutical Sciences, Vijayawada. Their unwavering support and provision of research facilities played a pivotal role in the successful completion of the present study.

Conflict of Interest:

No conflicts of interest among authors associated in publishing this article.

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