S. N. Lakhekar, 2025, 13:2
ISSN (Online): 2348-4098
ISSN (Print): 2395-4752

International Journal of Science, Engineering and Technology

An Open Access Journal

Synthesis, Characterization and Antibacterial Evaluation of New 2-Methoxynicotinonitrile Analogues

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Abstract- The new series of 2-methoxynicotinonitrile derivatives (solid) were prepared from mixture of Chalcones (solid) (0.001 mol) (1a-i), malononitrile (liquid) (0.078 ml) (0.001 mol) and 0.040 mg (0.001 mol) of sodium hydroxide in methanol (15ml) as a solvent by reflux technique for 7-8 hours at 80oC. all the newly synthesized compounds were evaluated for their antibacterial action in vitro against gram +ve bacteria S. aureus, B. subtilis and gram -ve bacteria P. aeruginosa, E. coli by agar well diffusion method. The tested compounds (2a) presented excellent and good antibacterial activity against P. aeruginosa and E. coli respectively. (2b) presented excellent and good antibacterial activity against B. subtilis and S. aureus, P. aeruginosa respectively. (2d) showed excellent activity against S. aureus. (2e) showed good antibacterial activity against B. subtilis w.r.t penicillin as a std. drug. The chemical structures of the compounds were proved by IR, 1H NMR, Mass, C13 NMR spectrometric data.

Keywords- 2-methoxynicotinonitrile, chalcone, malononitrile, antibacterial activity, agar well diffusion method, spectroscopic data.

I. INTRODUCTION

Pyridine is a six-membered basic heterocyclic organic compound. It has a bad fishy smell and is a colorless, flammable, water-soluble liquid. The electronegative nitrogen in the pyridine ring causes the molecule to be electron deficient.

In the field of medicinal chemistry, cyanopyridine serves as a common framework for compounds that contain nitrile groups. Numerous compounds that incorporate the cyanopyridine structure have demonstrated effectiveness in treating a variety of diseases, such as cancer, inflammation, diabetes, gout, heart failure, and infections caused by the human immunodeficiency virus1. As of now, one of the largest risks to human survival and growth is antimicrobial resistance. The introduction of innovative prescription medicines, preferably acting in new and interesting ways, is essential in addition

to enhancing the use of the antimicrobial medications currently on the market, preventing infections, and spreading awareness. The world is dealing with a downturn of availability to antibacterial agents. In the face of growing resistance, there is a insufficient ways for research and development, and further steps are urgently needed to assure fair access to both new and current and vaccines, lab tests, and prescription drugs.

The pyridine, class of heterocyclic compounds is extremely important due to their multipurpose biological and pharmacological activities. Pyridine derivative are found to exhibit good anticancer2-6, antioxidant7, antimicrobial (antibacterial, antifungal)8-15, analgesic, anti-inflammatory & pyretics16-18, anticonvulsant19, Herbicidal20, anti-HIV21, antitubercular22, antidibetics23 and various biological24activities.

In view of these literature survey and with a view to further increase the pharmacological activities of this class of compounds; the present study includes synthesis of new substituted 2-methoxy cyanopyridines and further studies expected to provide new antibacterial leads along with the understanding of the mechanism of their action.

II. PRESENT WORK AND METHOD

We thought it would be useful to synthesize a new series of 2-methoxynicotinonitrile derivatives and examine their antibacterial activities because of the significant role played by basic moiety as antibacterial agents. In the present investigation, these derivatives were synthesized using a conventional method by reacting, chalcones (solid)(1a-i) with malononitrile (liquid) and methanol in sodium hydroxide (solid) as a reaction solvent. (Scheme 1.1)

The structures of synthesized compounds were confirmed by spectral analysis (IR, 1HNMR, MS and 13CNMR).1H NMR spectra were measured in deuterochloroform (CDCl3) on NMR spectrophotometer AVANCE 300 using TMS as an internal standard. IR spectra were recorded on Shimadzu FT-IR Spectrometer using KBr pellets. The MASS were recorded on EI-SHIMADZU-GC-MS spectrometer and Pexciex API 2000 mass spectrometer. 13C NMR spectra were recorded on brucker AVANCE instrument at 300/400 MHz mass spectrometers in deuterochloroform (CDCl3) solvent.

Experimental

General procedure for synthesis of substituted methoxynicotinonitrile (Scheme 1.1).

A mixture of Chalcone (1a-i), malononitrile and methanol in NaOH was refluxed for 7-8 hours monitored by TLC using silicagel aluminium plate in eluent system of pet ether and ethyl acetate (7:3). The spots were visualized in an ultraviolet light chamber at λ=254-266nm. After completion of the reaction, the reaction mixture was cooled at room temperature and poured in crushed ice or cold water (100 ml). The separated solid product was filtered, washed with ice cold water, dried and then recrystallized from ethanol. (2a-i)

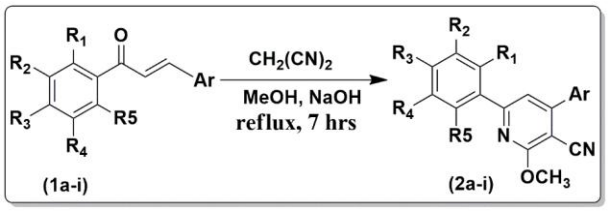
2.1.2: Procedure for synthesis of 4-(4-chlorophenyl)-6-(3,5-dibromo-2- hydroxyphenyl)-2-methoxynicotinonitrile. (2a)

Mixture of (E)-3-(4-Chlorophenyl)-1-(3,5-dibromo-2-hydroxypheny) pro-2-en-1-one or chalcones (1a) (Solid-0.416 mg) (0.001mol) and malononitrile (liquid)(0.078 ml) (0.001mol) in methanol (solvent) (15ml) containing sodium hydroxide (solid) (0.040 mg)(0.001 mol), was refluxed for 7-8 hrs at 800c. The Reaction was monitored by thin layer chromatography (TLC) plate every one hour. After completion of reaction, the reaction mixture was cooled at room temperature and transferred in ice cold water (100 ml). Filter to separate the solid product (2a i.e 4-(4-chlorophenyl)-6-(3,5-dibromo-2-hydroxyphenyl)-2-methoxynicotinonitrile) washed by ice cold water and after drying recrystallized from minimum amount of ethanol.

Similarly, remaining compounds of this series (2b-i) were also prepared by same procedure. The substitution pattern and physical data of synthesized 2-methoxy nicotinonitrile compounds are tabulated as in the

Scheme1.1: Synthesis of substituted methoxynicotinonitriles

Scheme1.1: Synthesis of substituted methoxynicotinonitriles



2.1.3. Spectral data of Selected compounds

Compound No. 2e :

4-(4-bromophenyl)-6-(3,5-dibromo-4-hydroxyphenyl)-2-methoxynicotinonitrile

IR (KBr)cm-1 :3404 (-OH str.), 3085 (Arom. C-H str.), 2920 (methoxy C-H str.), 2214 (-CN str.), 1593 (-C=N str.), 1407, 1492, 1546 (Ar-C=C str.), 1296 (C-O-C str.), 636-736 (C-Br str.)

1H NMR :12.50 (s, 1H, OH, D2O exch.), 8.0 (s, 2H, ArH), 7.9 (s, 1H, (CDCl3) (δ ppm) CH of Pyridine), 7.4-7.7 (m, 4H, Ar-H), 4.20 (s, 3H, OCH3),

M.S. (m/z) :539 (M+).13C NMR (CDCl3) (ppm): The total no. of carbon atoms in compound 2e are nineteen but carbon no. [7,11],[8, 10],[13,17] and [14, 16] of aromatic ring are equivalent in nature, hence it shows fifteen peaks in its 13C NMR spectrum. The peak at 152 ppm (C9) shows the presence of C-OH carbon of aromatic ring. The peak at 120 ppm (C18) due to cyanide group of carbon atom (-CN). The peak appeared at 160 ppm (C5) and 166 ppm (C1) are due to imine carbon (C=N) atom and (C-OCH3) group of carbon of pyridine ring respectively. The peak at 54 ppm (C19) shows the presence of OCH3 Carbon of pyridine ring. The values appeared at 158 (C3), 139 (C12), 135 (C6), 134 (C7 & C11), 132 (C14), 128 (C13 & C17), 124 (C15), 118 (C8 & C10),109 and 91 ppm (C2) due to aromatic carbons.

Compound No. 2g :

4-(4-chlorophenyl)-6-(3,5-dibromo-2,4-dihydroxyphenyl)-2-methoxynicotino- nitrile.

IR (KBr)cm-1 : 3405 (-OH str.), 2206 (-CN str.), str.), 1442, 1492, 1542 (-C=C str.), 1577 (-C=N str.), 1245 (C-O-C str.) 725 (C-Cl str.), 540-690 (C-Br str.)

1H NMR :14.00 (s, 1H, OH, D2O exch.), 13.40 (s, 1H, OH, D2O exch.),(CDCl3) (δ ppm)8.1 (s,1H,Ar-H),7.9 (s, 1H, CH of Pyridine), 7.4-7.8 (m, 4H, 4.2 (s, 3H, OCH3),

M.S. (m/z) : 510 (M+)

Antibacterial Activity of synthesized 2-methoxynicotinonitriles

In the present investigations, the antibacterial activity of newly synthesized above said derivatives were evaluated against gram-positive bacteria like Staphylococcus aureus, Bacillus subtilis and gram negative bacteria like, Escherichia coli, Pseudomonas aeruginosa25-28by using agar well diffusion method.29-30

In present work Agar well diffusion assay29-30 was used for In Vitro Antibacterial activity of the synthesized Pyridine Compounds. In vitro antibacterial activity was performed by using Mueller Hinton Agar (MHA) received from Himedia (Mumbai). The MHA plates were arranged by pouring 15 ml of molten media into sterile Petri plates. The plates were allowed to solidify for 5 min and 0.1 % inoculums suspension was swabbed uniformly and the Inoculums were allowed to dry for 5 min. The concentration of compounds were set at (10 µg/disc) were loaded on 5 mm sterile individual discs. The loaded discs were placed on the surface of medium and the compound was allowed to diffuse for 5 min and the plates were kept for incubation at 37°C for 24 h. The dimethyl sulfoxide (DMSO) solvent and Penicillin (Antibiotic drug) at 50 µg/mL concentration was used as standard or positive control for antibacterial activity of pyridine (2a-i) compounds. At the end of incubation, inhibition zones formed around the disc were measured with transparent ruler in millimeter. The results were recorded in table 1.1c

III. RESULT & DISCUSSION

1. Antibacterial Activity

The compound 2a (solid), presented excellent and good antibacterial activity against bacterial strains P. aeruginosa and E. coli respectively. The compound 2b (solid), showed excellent and good antibacterial activity against bacterial strains B.

subtilis and S. aureus, P. aeruginosa respectively. The compound 2d (solid) showed excellent antibacterial activity against S. aureus. The compound 2e showed good antibacterial activity against B. subtilis. It was found that among (2a-i) compounds, some of the compounds showed excellent, good, moderate and weak activity against various pathogens.

2. Spectral Analysis

IR Spectra

The IR spectra of synthesized substituted2-methoxynicotinonitrilescompounds (2e, 2g) showed the absorption bands in the region of 1593-1547 cm-1 due to –C=N str. The absorption band between 3444-3404 cm-1is due to OH stretching and 2214-2206 cm-1 is due to –CN stretching. The absorption band between 3085-2908 cm-1is due to Aromatic C-H stretching. The aromatic C=C str. observed in the region 1542-1396 cm-1. Beside these band between 546-736 cm-1 due to strong C-Br stretching. Band in the region of 725-759 cm-1due to strong -C-Cl stretching. The IR spectrum of the compounds (2e,2g) showed the absorption bands in the region of 2920-2882 cm-1 due to methoxy C-H str.The absorption band due to ether(C-O-C) stretching at 1296-1245 cm-1.

1H NMR Spectra:

1H NMR spectra of synthesized substituted 2-methoxynicotinonitriles (2e, 2g) revealed that a singlet signal in the range of δ 4.20 ppm corresponds to –OCH3 proton. Aromatic C-H Proton appeared as singlet signal for 2H and 1H proton at δ8.0 and δ8.1 ppm respectively. In the compounds 2e and 2gAromatic C-H proton appeared as multiplet signal for 4H proton at δ 7.4-7.8 ppm. Aromatic C-H proton in pyridine ring appeared as singlet at δ 7.9 ppm. Phenolic (-OH) proton appeared as a singlet in between δ 12.50-14.00 ppm

Mass Spectra

The mass spectra of synthesized substituted methoxy cyanopyridine (2e, 2g) products demonstrated that molecular ion peak which associate with their molecular weight of the compounds.

3.2.4. 13CNMR spectra:

In synthesized substituted 2-methoxynicotinonitrilescompound (2e), The peak at 152 ppm (C9) shows the presence of C-OH carbon of aromatic ring. The peak at 120 ppm (C18) due to cyanide group of carbon atom (-CN). The peak appeared at 160 ppm (C5) and 166 ppm (C1) are due to imine carbon (C=N) atom and (C-OCH3) group of carbon of pyridine ring respectively.

The peak at 54 ppm (C19) shows the presence of OCH3 Carbon of pyridine ring. The values appeared at 158 (C3), 139 (C12), 135 (C6), 134 (C7 & C11), 132 (C14), 128 (C13 & C17), 124 (C15), 118 (C8 & C10),109 and 91 ppm (C2) due to aromatic carbons.13C NMR spectrum of (2e) showed that the fifteen number of peaks in the spectrum typically corresponds to the nineteen number of various equivalent and nonequivalent carbon. The chemical shifts (δ) of carbon signals give some clues about the characteristics of each environment.

Table no. 1.1a: Substitution pattern of 2-methoxynicotinonitriles

Entry	Product	R_1	R_2	R_3	R_4	R_5	R_5
1	**2a**	OH	Br	H	Br	H	4-Chlorophenyl
2	**2b**	OH	Br	H	Br	H	4-Bromophenyl
3	**2c**	OH	Br	H	Br	H	-thiophenyl
4	**2d**	H	Br	OH	Br	H	4-Chlorophenyl
5	**2e**	H	Br	OH	Br	H	4-Bromophenyl
6	**2f**	H	Br	OH	Br	H	-thiophenyl
7	**2g**	OH	Br	OH	Br	H	4-Chlorophenyl
8	**2h**	OH	Br	OH	Br	H	4-Bromophenyl
9	**2i**	OH	Br	OH	Br	H	-thiophenyl

Table no. 1.1b: The physical data of synthesized 2-methoxynicotinonitriles 2-

Entry	Product	M/F & M/W	Yield %	M.P.(°C)	Color
1	**2a**	$C_{19}H_{11}Br_2ClN_2O_2$ (494)	72	210-212	White solid
2	**2b**	$C_{19}H_{11}Br_3N_2O_2$ (539)	68	198-200	White solid
3	**2c**	$C_{17}H_{10}Br_2N_2O_2S$ (466)	74	188-190	Pale yellow
4	**2d**	$C_{19}H_{11}Br_2N_2O_2Cl$ (494)	71	155-157	White solid
5	**2e**	$C_{19}H_{11}Br_3N_2O_2$ (539)	60	161-163	White solid
6	**2f**	$C_{17}H_{10}Br_2N_2O_2S$ (466)	74	144-146	White solid
7	**2g**	$C_{19}H_{11}Br_2N_2O_3Cl$ (510)	63	183-185	White solid
8	**2h**	$C_{19}H_{11}Br_3N_2O_3$ (555)	69	132-134	White solid
9	**2i**	$C_{17}H_{10}Br_2N_2O_3S$ (482)	70	153-155	Cream like solid

Table 1.1c. Antibacterial activity Result of 2-methoxynicotinonitriles

Sample	Diameter of zone of inhibition (mm)			
	Gram +ve Bacteria		Gram –ve Bacteria	
	B. subtilis	*S. aureus*	*E. coli*	*P. aeruginosa*
2a	11	15	25	29
2b	24	22	22	25
2c	17	ND	13	10
2d	20	23	19	ND
2e	23	19	ND	20
2f	14	ND	10	ND
2g	ND	11	16	11
2h	ND	17	18	11
2i	13	ND	09	16
Penicillin (Std. Drug)	28 mm	26 mm	30 mm	32 mm

N.D: Not Detected

IV. CONCLUSION

It has been found that 2-methoxy-3-cyanopyridine is a crucial biologically active framework with a wide range of physiological actions. All of these compounds were completed using conventional techniques, which resulted in significant time savings and good yields. The synthesized compounds were analyzed by IR, 1H NMR, Mass, C13 NMR spectrometric data. The tested compounds 2a, presented excellent and good antibacterial activity against P. aeruginosa and E. coli respectively.2b, presented excellent and good antibacterial activity against B. subtilis and S. aurous, P. aeruginosa respectively. 2d showed excellent activity against S. aureus. 2eshowed good antibacterial activity against B. subtilisw.r.t penicillin as a std. drug.

I extend my sincere thanks to the principal for granting permission and providing laboratory facilities and IR spectral analysis to carry out the present research work. I am also thankful to the principal and microbiology department of Netaji Subhashchandra Bose Arts, Commerce, and Science College, Nanded, who helped me with the evaluation of antibacterial activity. I would like to say thanks to Director, IICT, Hyderabad for spectral analysis.

REFERENCES

1. Yingjie Chang, Xuben Hou, Hao Fang. (2023). Cyanopyridine as a privileged scaffold in drug discovery, Academic Press, 163-198.
2. Ahmed, M., Mona, M., Hassan, A., Ola, R., Omaima, S., Mohamed, E., Zaki, S., Hayam, A. (2016). New 3-cyano-2-substituted pyridines induce apoptosis in mcf 7 breast cancer cells. Molecules, 21(230), 1-25.
3. Mansour, S. Y., Sayed, G. H., Marzouk, M. I., & Shaban, S. S. (2021). Synthesis and anticancer assessment of some new 2-amino-3-cyanopyridine derivatives. Synthetic Communications, 51(8), 1160-1170.
4. Khaled, A., M., A.; Ghada, H., A.; Abeer, M., E. (2017). Eco-friendly synthesis of novel cyanopyridine derivatives and their anticancer and PIM-1 kinase inhibitory activities. European Journal of Medicinal Chemistry, 134,357-365.
5. Dev S, Dhaneshwar S, Mathew B. (2018). Virtual combinatorial library design, synthesis and in vitro anticancer assessment of-2-

amino-3-cyanopyridine derivatives. Comb Chem High Throughput Scree, 21, 138-48.

6. Basem Mansour, Yomna A. Salem, Khaled M. Attallah, O. A. El-kawy, Ismail T. Ibrahim, and Naglaa I. Abdel-Aziz.(2023). Cyanopyridinone- and cyanopyridine-based cancer cell pim-1 inhibitors: design, synthesis, radiolabeling, biodistribution, and molecular modeling simulation. ACS Omega, 8 (22), 19351-19366
7. Li, Q., Zhang, C., Tan, W., Gu, G., & Guo, Z. (2017). Novel amino-pyridine functionalized chitosan quaternary ammonium derivatives: design, synthesis, and antioxidant activity. Molecules, 22(1), 156.
8. Elsayed, M.A., Elsayed, A.M. &Sroor, F.M. (2024). Novel biologically active pyridine derivatives: Synthesis, structure characterization, in vitro antimicrobial evaluation and structure-activity relationship. Med Chem Res 33, 476-91.
9. Achagar, R., Elmakssoudi, A., Thoume, A., Dakir, M., Elamrani, A., Zouheir, Y., &Chehimi, M. M. (2022). Nanostructured Na2CaP2O7: A new and efficient catalyst for one-pot synthesis of 2-amino-3-cyanopyridine derivatives and evaluation of their antibacterial activity. Applied Sciences, 12(11), 5487.
10. Marinescu, M., & Popa, C. V. (2022). Pyridine compounds with antimicrobial and antiviral activities. International journal of molecular sciences, 23(10), 5659.
11. Dongre, R. P. (2023). Synthesis, characterization, and evaluation of the antimicrobial activity of some cyanopyridine derivatives. Journal of Advanced Scientific Research, 14(09), 18-22.
12. Patel, P. A., Bhadani, V. N., Purohit, H. D., Bhatt, P. V., & Purohit, D. M. (2015). Synthesis of Some new2-Amino/Methoxy-4-(3-methoxy-4-((3-methyl-4-(2, 2, 2-trifluoroethoxy) pyridin-2-yl) methoxy) phenyl)-6-arylnicotinonitrileDerivative and its biological activity. Chemistry & Biology Interface, 5(6).
13. Parikh, K. S., & Patel, R. P. (2009). Synthesis and characterization of some cyanopyridine compounds in therapeutic interest. Int J Chem Tech Res, 1, 581-86.
14. Mamedov, I., Mamedov, E., Gasimova, I., & Mamedova, Y. (2023). Synthesis of 2-Amino-3-cyanopyridine Derivatives and Investigation of Their Antibacterial and Antifungal Properties. Indonesian Journal of Chemical Research, 11(1), 23-28.
15. SurendraB. L., and Rajendra P. Y. (2020). Design, synthesis, and characterization of the some novel 2-amino-pyridine-3-carbonitrile and 2-amino-4h-pyran-3-carbonitrile derivatives against antimicrobial activity and antioxidant activity. Asian journal of pharmaceutical and clinical research ,13(12), Online - 2455-3891
16. Nigade, Ganesh & Chavan, Pradeep & Deodhar, Meenakshi. (2010). Synthesis and analgesic activity of new pyridine-based heterocyclic derivatives. Medicinal Chemistry Research. 21. 27-37.
17. Manna, F., Chimenti, F., Bolasco, A., Bizzarri, B., Filippelli, W., Filippelli, A., & Gagliardi, L. (1999). Anti-inflammatory, analgesic and antipyretic 4, 6-disubstituted 3-cyano-2-aminopyridines. European journal of medicinal chemistry, 34(3), 245-254.
18. Drabu, S., Archna, Singh, S., Munirajam, S., & Kumar, N. (2007). Synthesis and antiinflammatory activity of some 2-amino pyridines. Indian journal of heterocyclic chemistry, 16(4), 411-412.
19. Salam, O., Al-Omar, M., Khalifa, N., Amr, A. & Abdallah, M. (2013). Analgesic and Anticonvulsant Activities of Some Newly Synthesized Trisubstituted Pyridine Derivatives. Zeitschrift für Naturforschung C, 68 (7-8), 264-268.
20. Qingyun Ren, Wenyan Mo, Ling Gao, Hongwu He, Yucheng Gu, ChemInform Abstract: Facile Synthesis and Herbicidal Activity of Novel Multisubstituted Pyridine Derivatives., ChemInform, 41, 24, (2010).
21. Changunda, Charles & Rousseau, Amanda & Basson, Adriaan & Bode, Moira. (2021). Synthesis of novel pyridine and pyrimidine derivatives as potential inhibitors of HIV-1 reverse transcriptase using palladium-catalysed C-N cross-coupling and nucleophilic aromatic substitution reactions. Arkivoc.
22. Harun Patel, Kavita Chaudhari, Pritam Jain, Sanjay Surana. (2020). Synthesis and in vitro antitubercular activity of pyridine analouges

against the resistant Mycobacterium tuberculosis, Bioorganic Chemistry, 102, 104099
23. Athulya Chandran, E., M., V., Mathew Valooran, N., & Kumar R., A. (2023). A Recent Update on Pyridine Derivatives as a Potential Lead for Diabetes Mellitus. Journal of Chemical Reviews, 5(2), 159-182.
24. A. Kistan., V. Kanchana., C. Esther Jeyanthi and K. Uma. (2023). Antimicrobial, antifungal, larvicidal, and antioxidant activity of freshly prepared cyanopyridine derivatives. rasayan journal of chemistry, 16(4), 2171-2180.
25. Ducki, S., Forrest, R., Hadfield, J. A., Kendall, A., Lawrence, N. J., McGown, A. T., & Rennison, D. (1998). Potent antimitotic and cell growth inhibitory properties of substituted chalcones. Bioorganic & medicinalchemistry letters, 8(9), 1051-1056.
26. Z. N. Siddiqui, T. N. M. Musthafa, A. Ahmad, A.U. Khan., Bioorg. Med. Chem. Lett., 21, 2860-65, 2011.
27. Aktar, B. S. K., Oruç-Emre, E. E., Demirtaş, İ., Yağlioğlu, A. Ş., İyidoğan, A. K., Güler, Ç., & Adem, Ş. (2018). Synthesis and biological evaluation of novel chalcones bearing morpholine moiety as antiproliferative agents. Turkish Journal of Chemistry, 42(2), 482-492.
28. Sato, M., Tsuchiya, H., Akagiri, M., Fujiwara, S., Fujii, T., Takagi, N.,&Iinuma, M. (1994). Growth inhibitory properties of chalcones Candida. Letters in applied microbiology, 18(1), 53-55.
29. Rozmer, Z., &Perjési, P. (2016). Naturally occurring chalcones and their biological activities. Phytochemistry reviews, 15, 87-120.
30. Nelson, G., Alam, M. A., Atkinson, T., Gurrapu, S., Sravan Kumar, J., Bicknese, C., .& Williams, M. (2013). Synthesis and evaluation of p-N, N-dialkyl substituted chalcones as anti-cancer agents. Medicinal Chemistry Research, 22, 4610-4614.1). Mapping and situation analysis of basic WASH. PLOS ONE, 11(16), 1-12.