International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2013): 6.14 | Impact Factor (2015): 6.391

Evaluation and Anti-bacterial Activity of phenyl-2-acetyl- pentafluorobenzoate as Chromones Derivatives

Rohit Bhor

Department of Pharmaceutical Chemistry, PRES's College of Pharmacy, Chincholi, Tal-Sinner Dist-Nasik 422103, Maharashtra, India

Abstract: ***Chromones like 2-(pentafluorophenyl)-4H-chromone-4-one and Azoles like 2-[5-(pentafluorophenyl)-1H-pyrazol-3-yl] phenol have been reported to play an important role as antibacterial, antifungal and anti-inflammatory activity. Chromones derivatives and Azoles derivatives were synthesized and screened for antibacterial activity. The antibacterial activities of chromones derivatives, azoles derivatives were tested by the disc diffusion method by using nutrient agar medium against various microorganisms such as gram positive Staphylococcus aureus, gram negative Escherichia coli and P. aeruginosa.***

Keywords: Anti-bacterial activity; Azoles derivatives; Chromones derivatives; Gentamycin; Pentafluorobenzoic acid

1. Introduction

Chromones and pyrazol and its derivatives are important heterocyclic in organic and biochemistry. There are extensive studies on the synthesis and reactivity of Chromones and pyrazol derivatives. Many Pyrazol and Chromones derivatives have shown interesting biological properties such as antibacterial, anti-inflammatory, antioxidant, antitumor, antifungal and immune suppressant activities. Pyrazol and Chromones derivatives are prepared by using 1-(2-hydroxyphenyl) ethanone and pentafluorobenzoic acid reagent. These pyrrole derivatives and Chromones are screened for antibacterial activity. It reveals that chromones and pyrazol posses broad spectrum activity such as antimicrobial [1-4], anti-inflammatory [5], analgesic [6], antitumorial [7], antihypertensive [8], anticonvulsant and antiviral [9]. Since the past few decades, the literature has been enriched with progressive findings about the synthesis and pharmacological activities of various substituted chromones and pyrazol derivatives [10]. There are antifungal and antibacterial agent having different structure and used in the treatment of fungal and bacterial infection [11].

2. Literature Survey

Chromones and pyrazol and its derivatives are important heterocyclic in organic and biochemistry and have been found in many chromones containing natural products such as Khellin, sodium cromoglycate, diosmin, flavones, and flavonoids [12]. There are extensive studies on the synthesis and reactivity of Chromones and pyrazol derivatives. Many Chromones and pyrazol derivatives have shown interesting biological properties such as antibacterial, anti-inflammatory, antioxidant, antitumor, antifungal and immune suppressant activities [13].

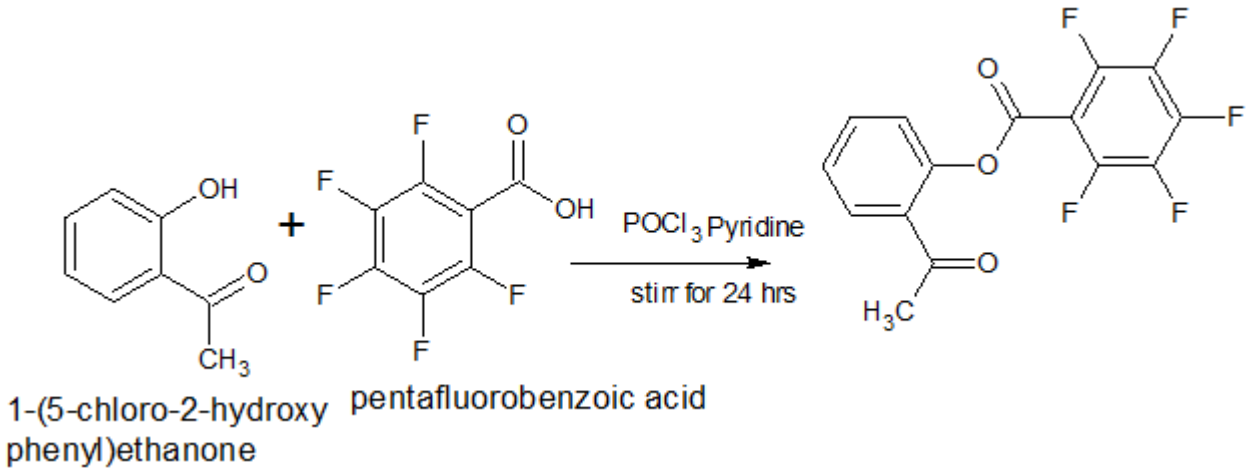
3. Methods

1-(2-hydroxyphenyl) ethanone, Pentafluorobenzoic acid, Pyridine, Hydrazine Hydrate, Guanidine Hydrochloride, Ethanol, Con.Hydrochloric acid phosphorus oxychloride i.e. $POCl_3$ etc. All reagents were purchased from Atmaja chemicals, Aurangabad. All chemicals were of analytical grade. All chromones and Pyrazole derivatives were synthesized by conventional method. All Chromones and Pyrazole derivatives were synthesized by conventional method. Melting points were determined by open tube capillary method. The purity of the compounds was checked on thin layer chromatography (TLC) plates (silica gel G) in chloroform: acetone (7:3) and chloroform: methanol (7:3) solvent systems, the spots were located under iodine vapors and UV light. The synthetic route for the title compounds is shown in Scheme 1. Perkin Elmer Spectrum1 FT-IR instrument consists of globar and mercury vapor lamp as sources. ^{1}H-NMR spectra were recorded by a Bruker AVANCE III 500 MHz (AV 500) spectrometer using TMS as internal standard in DMSO-d_6/$CDCl_3$ and mass spectra was obtained on JEOL GCMATE II GC-MS are presented as m/z.

Synthesis of phenyl- 2-acetyl pentafluorobenzoate (AA)

A mixture of 1-(2-hydroxyphenyl) ethanone (0.5g) and Pentafluorobenzoic acid (0.5g) react with each other in the presence of $POCl_3$ (5 ml) and Pyridine (15 ml) and then stir on magnetic stirrer for 24 h, and then it gives solid product after addition of ice cold water and it gives phenyl- 2-acetyl pentafluorobenzoate (AA).

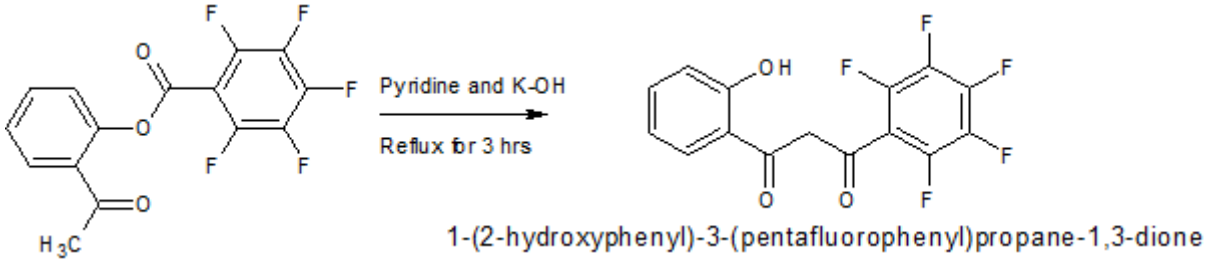
Scheme: 1



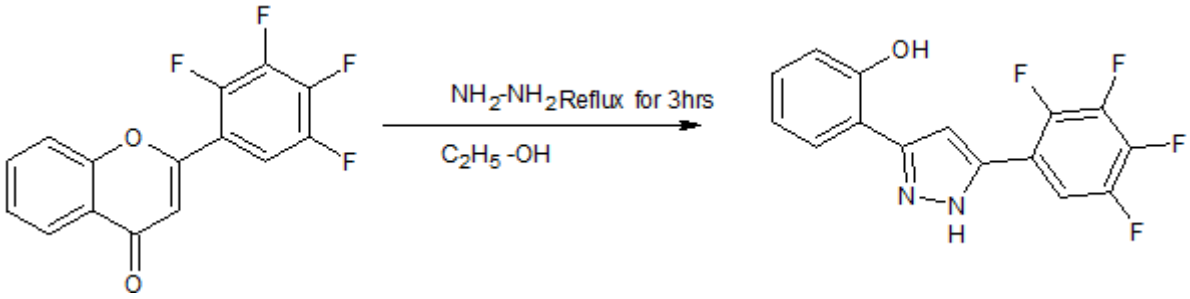
Synthesis of 1-(2-hydroxyphenyl)-3-(pentafluorophenyl) propane-1, 3-dione (AB)

A solution of phenyl- 2-acetyl pentafluorobenzoate (AA) react with potassium hydroxide (0.5g) and pyridine (5 ml) and reflux for 3 h and then Completion of the reaction was confirmed by TLC. The mixture was cooled by addition of ice. The precipitate the precipitate formed was washed with water and recrystalized from ethanol and then it gives 1-(2-hydroxyphenyl)-3-(pentafluorophenyl) propane-1, 3-dione (AB).

Scheme: 2



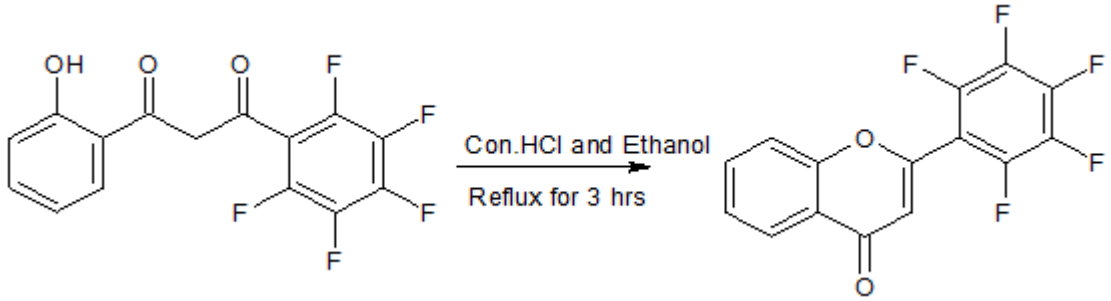
Scheme: 4



Synthesis of 2-(pentafluorophenyl)-4H-chromone-4-one (AC)

A solution of 1-(2-hydroxyphenyl)-3-(pentafluorophenyl) propane-1,3-dione (AB) react with con. Hydrochloric acid (5 ml) and ethanol (5 ml) and reflux for 2 h and then Completion of the reaction were confirmed by TLC. The mixture was cooled by addition of ice. The precipitate formed was washed with water and recrystalized from ethanol and then it gives 2-(pentafluorophenyl)-4H-chromone-4-one (AC).

Scheme: 3



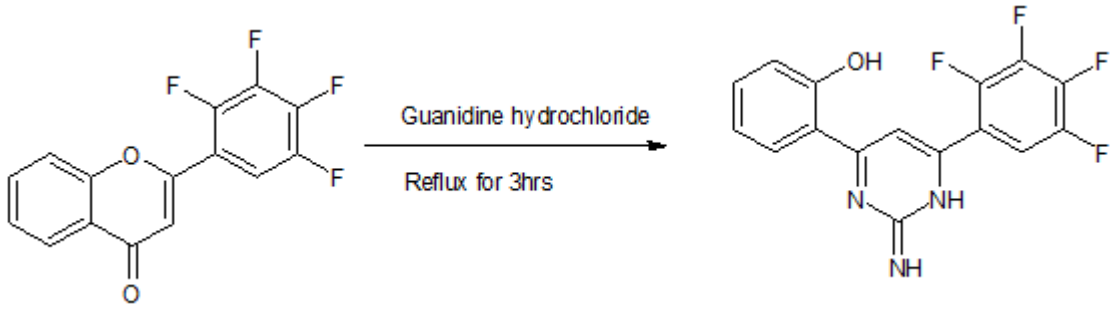
Synthesis of 2-[5-(pentafluorophenyl)-1*H*-pyrazol-3-yl] phenol (AD)

A solution of 2-(pentafluorophenyl)-4H-chromone-4-one (AC) react with hydrazine hydrate (5 ml) and ethanol (10 ml) and reflux for 3 h and then Completion of the reaction were confirmed by TLC. The mixture was cooled by addition of ice. The precipitate formed was washed with water and recrystalized from ethanol and then it gives 2-[5-(pentafluorophenyl)-1*H*-pyrazol-3-yl] phenol (AD)

Synthesis of 2-[2-imino-6-(pentafluorophenyl)-1,2-dihydropyrimidin-4-yl]phenol (AE)

A solution of 2-(pentafluorophenyl)-4*H*-chromen-4-one (AC) react with guanidine hydrochloride (5 ml) and it was reflux for 3 h and then Completion of the reaction were confirmed by TLC. The mixture was cooled by addition of ice. The precipitate formed was washed with water and recrystalized from ethanol then it gives 2-[2-imino-6-(pentafluorophenyl)-1,2-dihydro pyrimidin-4-yl]phenol (AE)

Scheme: 5



Data Analysis:

Table 1: Physical Data for 2-acetyl-4-chlorophenyl pentafluorobenzoate derivatives

Sr. No.	*Compounds*	*Molecular Formula*	*Melting Point ^0C*	*% yields*	*Molecular Weight*
1	AA	$C_{15}H_7O_3F_5$	286-288°C	60.84%,	333
2	AB	$C_{15}H_7O_3F_5$	312-314°C	96.07%,	330
3	AC	$C_{15}H_5O_2F_5$	338-340°C	87.23%,	312
4	AD	$C_{15}H_7N_2OF_5$	320-322°C	86.20%,	326
5	AE	$C_{15}H_8N_3OF_5$	398-400°C	92.59%,	341

2-acetylphenyl pentafluorobenzoate (AA):

% Yield : 60.84%; Colorless solid; Melting point (^{0}C) : 286-288°C; R_f 0.9, Chloroform: Methanol (7:3); FTIR (KBr) ν cm^{-1} : 3010 (Ar C-H str), 1638 (Ar C=C str), 797 (Ar C-H def), 1158 (Ar C-F str), 1758 (Ester C=O str), 1367 C-O str); ^{1}H NMR (500 MHz CDCl3 δ ppm) : 2.34 (s, 3H, CH_3), 7.29-7.86 (m, 4H, aromatic protons); JEOL GCMATE II GC-MS (m/z) : 332(M^+), 333 (M^++1). Mol. Wt.:333.

1-(2-hydroxyphenyl)-3-(pentafluorophenyl) propane-1, 3-dione (AB):

% Yield : 96.07%; Colorless solid; Melting point (^{0}C) : 312-314°C; R_f 0.92, Chloroform: Methanol (7:3); FTIR (KBr) ν cm^{-1} : 3036 (Ar C-H str), 1540 (Ar C=C str), 842 (Ar C-H def), 1161(Ar C-F str), 1668 (Aryl Ketone C=O str), 1297(C-O str), 3680(Ar OH str); ^{1}H NMR (500 MHz CDCl3 δ ppm) : 3.81(s, 2H, CH_2), 5.35(s, 1H, OH), 6.82-7.60 (m, 4H, aromatic protons); GCMATE II GC-MS (m/z) : 329(M^+), 330 (M^++1). Mol. Wt.:330.

2-(pentafluorophenyl)-4*H*-chromen-4-one (AC):

% Yield : 87.23%; Colorless solid; Melting point (^{0}C) : 338-340°C; R_f 0.92, Chloroform: Methanol (7:3); FTIR (KBr) ν cm^{-1} : 3028 (Ar C-H str), 1525 (Ar C=C str), 807 (Ar C-H def), 1027(Ar C-F str), 1661 (Aryl Ketone C=O str), 1380 (C-O str); ^{1}H NMR (500 MHz CDCl3 δ ppm) : 6.54 (s, 1H, C-H), 7.47-8.08 (m, 4H, aromatic protons); GCMATE II GC-MS (m/z) : 311(M^+), 312 (M^++1). Mol. Wt.:312.

2-[5-(pentafluorophenyl)-1*H*-pyrazol-3-yl] phenol (AD):

% Yield : 86.20%; Colorless solid; Melting point (^{0}C) : 320-322°C; R_f 0.88 ,Chloroform: Methanol (7:3); FTIR (KBr) ν cm^{-1} : 3035 (Ar C-H str), 1631 (Ar C=C str), 747 (Ar C-H def), 1273 (Ar C-F str), 3540 (Ar OH str), 1320 (C-O str) 3385 (N-H str); ^{1}H NMR (500 MHz CDCl3 δ ppm) : 7.01-8.26 (m, 4H, aromatic protons) 5.35(s, 1H, O-H), 6.81 (s, 1H, C-H),12.62(s, 1H,N-H); GCMATE II GC-MS (m/z) : 325(M^+), 326 (M^++1). Mol. Wt.:326.

2-[2-imino-6-(pentafluorophenyl)-1,2-dihydropyrimidin-4-yl] phenol (AE):

% Yield : 92.59%; Colorless solid; Melting point (^{0}C) : 398-400°C; R_f 0.80, Chloroform: Methanol (7:3); FTIR (KBr) ν cm^{-1} : 3061 (Ar C-H str), 1618 (Ar C=C str), 754 (Ar C-H def), 1027 (Ar C-F str), 3573 (Ar OH str), 1343(C-O str) 3390 (N-H str); ^{1}H NMR (500 MHz CDCl3 δ ppm) : 7.02-7.66 (m, 4H, aromatic protons) 5.35(s, 1H, O-H), 6.31 (s, 1H, C-H),13.89(s, 1H,N-H) 13.76 (s, 1H,N-H); GCMATE II GC-MS (m/z) : 340(M^+), 341 (M^++1). Mol. Wt.:341.

Pharmacological Studies [12]

In vitro Antibacterial activity by disc diffusion method:

Antibacterial Activity

The compounds like CA to CE were evaluated for their *in vitro* antibacterial activity against various microorganisms such as gram positive *Staphylococcus aureus*, gram negative

Escherichia coli and Pseudomonas aeruginosa by in vitro method like disc diffusion method was performed using Mueller Hinton Agar (M173) medium. Each compound was tested at concentration 100 µg/mL in DMSO. The zone of inhibition was measured after 24 h incubation at 37ºC. Standard: Gentamycin (100 µg/mL of DMSO).

Table 2: Antibacterial activity screening result of synthesized compound measuring the zone of inhibition in millimeter

Comp. No.	Diameter of zone of inhibition (mm)		
	Escherichia coli	Staphylococcus aureus	Pseudomonas aeruginosa
	ATCC 25922	ATCC 25923	ATCC 27853
AA	12	17	18
AB	12	18	12
AC	13	26	21
AD	16	27	20
AE	17	25	24
Gentamycin	20	36	28

4. Discussion

The syntheses of compounds AA to AE were undertaken as per the scheme 1 to 5. The required phenyl-2-acetyl pentafluorobenzoate (AA) was prepared by mixture of 1-(2-hydroxyphenyl) ethanone (0.5g) and Pentafluorobenzoic acid (0.5g) react with each other in the presence of $POCl_3$ (5 ml) and Pyridine (15 ml) and then stir on magnetic stirrer for 24 hrs, and then it gives solid product after addition of ice cold water and it gives phenyl-2-acetyl pentafluorobenzoate (AA). IR spectra were obtained on a Perkin Elmer Spectrum1 FT-IR instrument (KBr pellets). Perkin Elmer Spectrum1 FT-IR instrument consists of globar and mercury vapor lamp as sources. ^{1}H-NMR spectra were recorded by a Bruker AVANCE III 500 MHz (AV 500) spectrometer using TMS as internal standard in DMSO-d_6/$CDCl_3$ and mass spectra was obtained on JEOL GCMATE II GC-MS are presented as m/z.

The synthesis of compounds AA-AE was undertaken as per the scheme 1 to 5. The required phenyl-2-acetyl pentafluorobenzoate (AA) was prepared by the action of 1-(5-chloro-2-hydroxy-4-methylphenyl) ethanone, Pentafluorobenzoic acid. The results revealed that majority of the synthesized compounds showed varying degrees of inhibition against the tested microorganisms. In general, the inhibitory activity against the tested gram-positive bacteria was higher than that of the gram-negative bacteria. The results indicated that the Nitrogen and oxygen containing compounds, having more antimicrobial activity. Moreover, the compounds AC, AD and AE, having the side chain showed higher activity than AA and AB, against *E.coli, S. aureus, Pseudomonas aeruginosa*. The replacement of oxygen to nitrogen resulted in a slightly increased antimicrobial activity. Our study revealed that all the compounds had stronger antibacterial activity against Gram positive bacteria when compared to Gram negative bacteria. The antimicrobial activity revealed that newly synthesized compound AC, AD and AE, showed good significant activity. The results of the preliminary antimicrobial testing of the prepared compounds, the typical broad spectrum antibacterial drug like Gentamycin was shown in Table 2 and Fig.1.

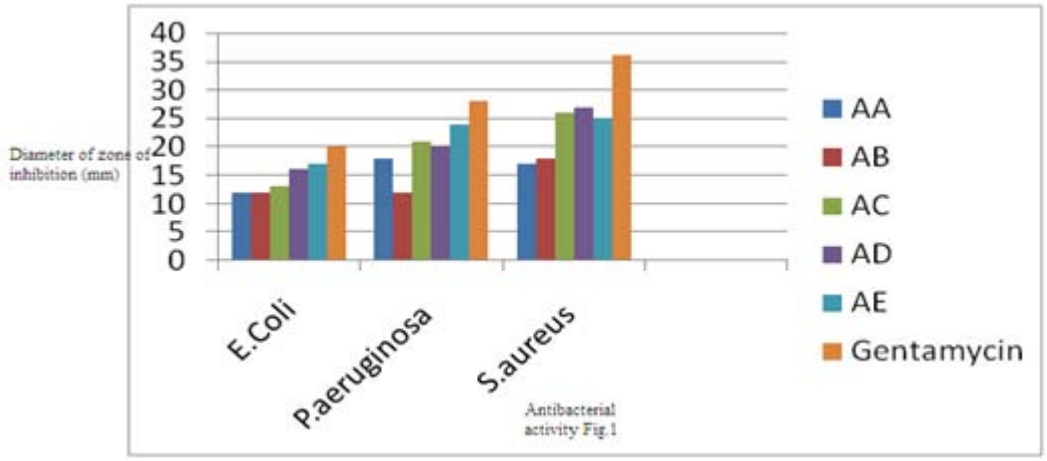


Table 1: Antibacterial activity screening result of synthesized compound measuring the zone of inhibition in millimeter

5. Conclusions

Various phenyl-2-acetyl pentafluorobenzoate derivatives (AA) were synthesized from a mixture of 1-(2-hydroxyphenyl) ethanone (0.5g) and Pentafluorobenzoic acid (0.5g). The structure antibacterial activity relationship of the synthesized compounds was based on the structure of antibacterial properties of the synthesized derivatives showed a significant activity as compared with standard drugs like Gentamycin.

6. Future Scope

The results revealed that majority of the synthesized compounds showed varying degrees of inhibition against the tested microorganisms. In general, the inhibitory activity against the tested gram-positive bacteria was higher than that of the gram-negative bacteria. The results indicated that the Nitrogen and oxygen containing compounds, having more antimicrobial activity like antibacterial and antifungal activity.

7. Acknowledgment

The authors are thankful to Dr. V.D.Wagh, College of Pharmacy, Chincholi, Mr. Vikas Kunde and BAC-Test Laboratory in Nashik for providing necessary facilities and to carry out this work and in-vitro antibacterial activity.

References

[1] Potewar, T. M., Ingale, S. A., & Srinivasan, K. V. (2007). Efficient synthesis of 2, 4- disubstituted thiazoles using ionic liquid under ambient conditions: a practical approach towards the synthesis of Fanetizole. Tetrahedron, 63(45), 11066- 11069.

[2] Cho, M. K., & Kim, S. G. (1998). Differential Expression of XenobioticMatabolizing Enzymes by Benzylisothiazole in Association with Hepatotoxicity: Effects on Rat Hepatic Epoxide Hydrolase, Glutathione S-Transferases and Cytochrome P450s. Toxicological Research, 14(3), 293- 300.

[3] Chang, S., Zhang, Z., Zhuang, X., Luo, J., Cao, X., Li, H., & Ding, K. (2012). New thiazole carboxamides as potent inhibitors of Akt kinases. Bioorganic & Medicinal Chemistry Letters, 22(2), 1208-1212.

[4] Park, J. H., El-Gamal, M. I., Lee, Y. S., & Oh, C. H. (2011). New imidazo [2, 1-b] thiazole derivatives: synthesis, in vitro Synthesis Characterization and Pharmacological Evaluation of Some Novel Trisubstituted Thiazole Derivatives © Copyright reserved by IJPRS 437 anticancer evaluation, and in silico studies. European Journal of Medicinal Chemistry, 46(12), 5769-5777.

[5] Hoffer, M., & Grunberg, E. (1974). Synthesis and antiprotozoal activity of 1-(3- chloro-2-hydroxypropyl)-substituted nitroimidazoles. Journal of Medicinal Chemistry, 17(9), 1019-1020.

[6] Winter, C. A., Risley, E. A., Nuss, G. W. (1962). Carrageenan induced oedema in hind paw of the rat as an assay for antiinflammatory drugs. Experimental Biology Med, 111, 544-547.

[7] Reji, T. F. A. F., Devi, S. K. C., Thomas, K. K., Sreejalekshmi, K. G., Manju, S. L., & Rajasekharan, K. N. (2008). Synthesis and cytotoxicity studies of thiazole analogs of the anticancer marine alkaloid dendrodoine. Indian Journal of Chemistry (Section B), 47, 1145-1150.

[8] Molvi, K. I., Sudarsanam, V., Patel, M. M., & Haque, N. (2008). Design, synthesis and pharmacological evaluation of novel tetrasubstituted thiophene analogues as antiinflammatory agents. Journal of Enzyme Inhibition and Medicinal Chemistry, 23(6), 819-828.

[9] Molvi, K. I., Vasu, K. K., Yerande, S. G., Sudarsanam, V., & Haque, N. (2007). Syntheses of new tetrasubstituted thiophenes as novel anti-inflammatory agents. European Journal of Medicinal Chemistry, 42(8), 1049-1058.

[10] Mansuri, M., Ahmed, A., Shaikh, A., Haque, N., Sheth, A. K., & Molvi, K. I. (2012). Synthesis, antibacterial, anti-inflammatory and antiplatelet activities of some trisubstituted thiazoles. Inventi Rapid: Med Chem., 4, 1-6

[11] Bekhit, A. A., Hymete, A., Asfaw, H., & Bekhit, A. E. D. A. (2012). Synthesis and Biological Evaluation of Some Pyrazole Derivatives as Anti-Malarial Agents. Archiv der Pharmazie, 345(2), 147-154.

[12] Mhasalkar, M. Y., Shah, M. H., Nikam, S. T., Anantanarayanan, K. G., & Deliwala, C. V. (1970). 4-Alkyl-5-aryl-4H-1, 2, 4- triazole-3-thiols as hypoglycemic agents. Journal of medicinal chemistry, 13(4), 672-674.

Author Profile

Mr. Rohit J.Bhor [M.Pharm, Ph.D. appear in PIMS Deemed University] (Asst.Prof) in Pharmaceutical Chemistry at College of Pharmacy, Chincholi, Sinner, Nashik, Maharastra, India