*Heterocyclic Letters*
*Vol. 12| No.3|571-576|May-July|2022*
*ISSN : (print) 2231–3087 / (online) 2230-9632*
*CODEN: HLEEAI*
*http://heteroletters.org*

# SYNTHESIS AND ANTIBACTERIAL SCREENING OF THIAZOLYL PYRAZOLE CONTAINING CHROMONES AND AURONES

**Nirmala R. Darekar[a], Bhausaheb K. Karale[a], Jaidip B. Wable[b], Hemantkumar N. Akolkar[c,*]**

*[a]Department of Chemistry, Radhabai Kale Mahila Mahavidyalaya, Ahmednagar, 414 001, Maharashtra, India.*
*[b]Department of Chemistry, K.J.S.S.C. College, Vidyavihar, Mumbai, Maharashtra, India.*
*[c]Department of Chemistry, Abasaheb Marathe Arts and New Commerce, Science College, Rajapur, Dist- Ratnagiri, 416 702, Maharashtra, India.*
*E-Mail: hemantakolkar@gmail.com (Corresponding Author)*

## ABSTRACT
Thiazolyl pyrazole anchored chalcones were converted into chromones and aurones. Formation of the target compounds was confirmed by spectral techniques like IR, $^1$H NMR and mass spectrometry. The newly synthesized compounds were screened for their antibacterial activities.

**KEYWORDS:** Thiazole, pyrazole, chromones, aurones.

## INTRODUCTION
1,3-Thiazole is well known sulphur and nitrogen containing five membered heterocyclic compound found in many clinically used drugs like Nizatidine, Meloxicam, Ritonavir, Tiazofurin, Bleomycin, Nitazoxanide, etc. Molecules containing thiazole nucleus are attractive targets for medicinal chemistry because of their wide spectrum of biological activities such as anti-inflammatory[i, ii], antibacterial[ii], antiproliferative[iii] and adenosine receptor antagonists[iv]. Pyrazole and its derivatives are known to possess antibacterial[v], fungistatic[vi], and anti-inflammatory[vii] activities. Chromone is an important class of oxygen-containing heterocyclic compounds and part of the flavonoid family. Chromone derivatives exhibit wide range of pharmacological activities such as antiallergic[viii], antitumor[ix], antimicrobial[x], antioxidant[xi], anti-inflammatory[xii], antiproliferative[xiii], *etc.* Aurones are found in some flowers, bark, seedlings, leaves and nectar of plant species. Recently aurones are known to have various biological activities such as anti-cancer[xiv], antioxidant[xv], anti-inflammatory[xvi] and antimicrobial[xvi].

Various biological activities associated with thiazole, pyrazole, chromones and aurones prompted us to synthesize thiazolyl pyrazole anchored fluorinated chromones and aurones.

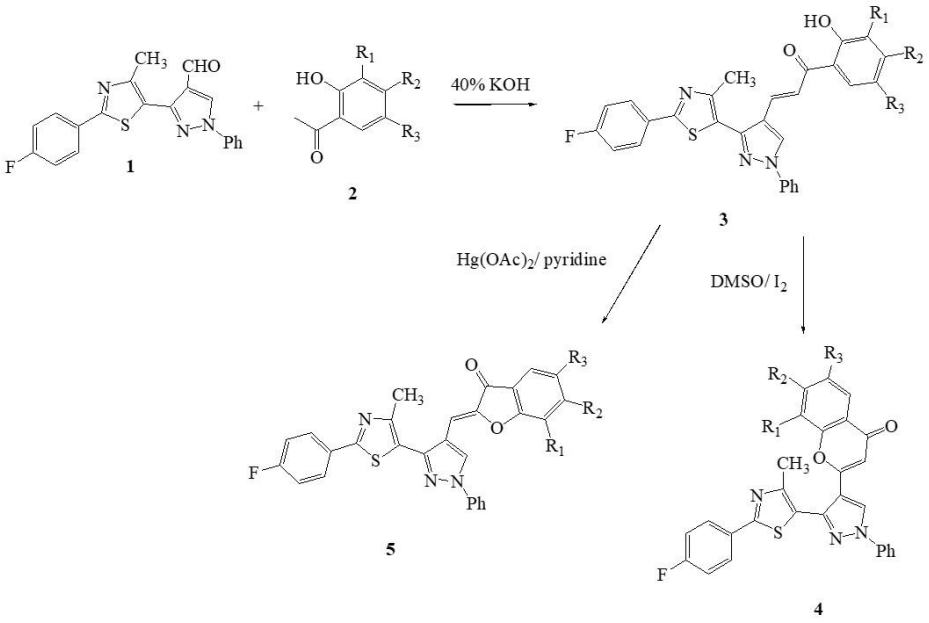
## EXPERIMENTAL

Physical constants of all synthesized compounds were determined in open capillary tubes in liquid paraffin bath and are uncorrected. The IR spectra were recorded on Shimadzu IR Affinity-1S FTIR spectrophotometer. The NMR spectra were recorded on Varian NMR 400 MHz spectrometer (Varian Inc., Switzerland) and chemical shifts are given in δ ppm relative to TMS using deuterated DMSO and deuterated chloroform as solvents. Mass spectra were recorded on Water's Acquity Ultra Performance TQ Detector Mass Spectrometer.

## RESULT AND DISCUSSION

Synthesis of (*E*)-3-(3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1*H*-pyrazol-4-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one **3** was carried out by known method [x, xvii]. Compound **3** on reaction with DMSO/$I_2$ gave 2-(3-(2-(4-Fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1*H*-pyrazol-4-yl)-4*H*-chromen-4-ones **4**. Also compound **3** on reaction with mercuric acetate in pyridine gave (*Z*)-2-((3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)benzofuran-3(2*H*)-ones **5**. All the synthesized compounds were characterized with the help of spectral techniques and screened for their antibacterial activities.

**Scheme-1:**




### General procedure for the synthesis of 2-(3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1*H*-pyrazol-4-yl)-4*H*-chromen-4-one 4

Chalcone **3** (0.001 mol) was dissolved in 15 mL of DMSO containing catalytic amount of iodine. The contents were heated at 130°C for 2.5 hr and left overnight undisturbed. The reaction mixture was poured over crushed ice and separated solid product **4** was filtered, washed with cold water followed by 10% sodium thiosulphate solution and again with cold water. Product was recrystallized from ethanol.

**2-(3-(2-(4-Fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)-6-methyl-4H-chromen-4-one (4a):** IR: 3145 (=C-H), 1647 (C=O), 1597 (C=N), 1562 (C=C), 1246 (C-O-C), 1170 (Ar-F) $cm^{-1}$; $^1$H NMR: δ 2.28 (s, 3H, Ar-$CH_3$), 2.36 (s, 3H, Thiazolyl-$CH_3$), 6.68 (s, 1H, Ar-H), 7.33 (t, 2H, *J*= 8Hz, Ar-H), 7.44 (t, 1H, Ar-H), 7.59 (t, 2H, *J*= 8Hz, Ar-H), 7.81 (s, 1H, Ar-H), 7.93-8.04 (m, 6H, Ar-H), 9.29 (s, 1H, pyrazolyl-H); Mass: *m/z* 494 $[M+H]^+$.

**6-Fluoro-2-(3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)-4H-**

**chromen-4-one (4b):** IR: 3146 (=C-H), 1645 (C=O), 1597 (C=N), 1562 (C=C), 1240 (C-O-C), 1170 (Ar-F) $cm^{-1}$; $^1$H NMR: δ 2.53 (s, 3H, Thiazolyl-$CH_3$), 6.67 (s, 1H, Ar-H), 7.23 (t, 2H, *J*= 8Hz, Ar-H), 7.28-8.08 (m, 10H, Ar-H), 9.54 (s, 1H, pyrazolyl-H); Mass: *m/z* 498 $[M+H]^+$.

**6-Chloro-2-(3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)-4H-chromen-4-one (4c):** IR: 3150 (=C-H), 1646 (C=O), 1595 (C=N), 1559 (C=C), 1243 (C-O-C), 1169 (Ar-F) $cm^{-1}$; $^1$H NMR: δ 2.54 (s, 3H, Thiazolyl-$CH_3$), 6.68 (s, 1H, Ar-H), 7.21 (t, 2H, *J*= 8Hz, Ar-H), 7.26-8.11 (m, 10H, Ar-H), 9.53 (s, 1H, pyrazolyl-H); Mass: *m/z* 514 $[M+H]^+$.

**6-Bromo-2-(3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)-4H-chromen-4-one (4d):** IR: 3144 (=C-H), 1648 (C=O), 1596 (C=N), 1567 (C=C), 1241 (C-O-C), 1171 (Ar-F) $cm^{-1}$; $^1$H NMR: δ 2.53 (s, 3H, Thiazolyl-$CH_3$), 6.67 (s, 1H, Ar-H), 7.23 (t, 2H, *J*= 8.4Hz, Ar-H), 7.27-8.16 (m, 10H, Ar-H), 9.53 (s, 1H, pyrazolyl-H); Mass: *m/z* 558 $[M+H]^+$.

**6,8-Dichloro-2-(3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)-4H-chromen-4-one (4e):** IR: 3146 (=C-H), 1651 (C=O), 1597 (C=N), 1561 (C=C), 1243 (C-O-C), 1170 (Ar-F) $cm^{-1}$; $^1$H NMR: δ 2.52 (s, 3H, Thiazolyl-$CH_3$), 6.66 (s, 1H, Ar-H), 7.21 (t, 2H, *J*= 8.4Hz, Ar-H), 7.26-8.18 (m, 9H, Ar-H), 9.54 (s, 1H, pyrazolyl-H); Mass: *m/z* 548 $[M+H]^+$.

**6-Chloro-2-(3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)-7-methyl-4H-chromen-4-one (4f):** IR: 3147 (=C-H), 1650 (C=O), 1595 (C=N), 1562 (C=C), 1242 (C-O-C), 1170 (Ar-F) $cm^{-1}$; $^1$H NMR: δ 2.32 (s, 3H, Ar-$CH_3$), 2.53 (s, 3H, Thiazolyl-$CH_3$), 6.67 (s, 1H, Ar-H), 7.22 (t, 2H, *J*= 8Hz, Ar-H), 7.27-8.16 (m, 9H, Ar-H), 9.51 (s, 1H, pyrazolyl-H); Mass: *m/z* 528 $[M+H]^+$.

**General procedure for the synthesis of (*Z*)-2-((3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)benzofuran-3(2*H*)-one 5**

A mixture of chalcone **3** (0.015 mol) and mercuric acetate (0.015 mol) was dissolved in 15 mL dry pyridine. The reaction mixture was refluxed for 5-6 h. After completion of reaction (checked by TLC) contents were cooled to room temperature and poured over crushed ice and neutralized with conc. HCl. The solid product **5** was filtered and recrystallized from glacial acetic acid.

**(Z)-2-((3-(2-(4-Fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)methylene)-5-methylbenzofuran-3(2H)-one (5a):** IR: 3086 (=C-H), 1712 (C=O), 1647 (C=N), 1597 (C=C), 1222 (C-O-C), 1172 (Ar-F) $cm^{-1}$; $^1$H NMR: δ 2.37 (s, 3H, Ar-$CH_3$), 2.52 (s, 3H, Thiazolyl-$CH_3$), 6.70 (s, 1H, Ar-H), 7.38 (t, 2H, *J*= 8Hz, Ar-H), 7.43-7.52 (m, 2H, Ar-H), 7.58-7.66 (m, 4H, Ar-H), 8.02-8.06 (m, 4H, Ar-H), 9.216 (s, 1H, pyrazolyl-H); Mass: *m/z* 494 $[M+H]^+$.

**(Z)-5-Fluoro-2-((3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)methylene)benzofuran-3(2H)-one (5b):** IR: 3086 (=C-H), 1710 (C=O), 1645 (C=N), 1598 (C=C), 1223 (C-O-C), 1171 (Ar-F) $cm^{-1}$; $^1$HNMR: δ 2.53 (s, 3H, Thiazolyl-$CH_3$), 6.71 (s, 1H, Ar-H), 7.34 (t, 2H, *J*= 9 Hz, Ar-H), 7.41-8.05 (m, 10H, Ar-H), 9.14 (s, 1H, pyrazolyl-H); Mass: *m/z* 498 $[M+H]^+$.

**(Z)-5-Chloro-2-((3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)methylene)benzofuran-3(2H)-one (5c):** IR: 3085 (=C-H), 1711 (C=O), 1646 (C=N), 1597 (C=C), 1221 (C-O-C), 1172 (Ar-F) $cm^{-1}$; $^1$HNMR: δ 2.51 (s, 3H, Thiazolyl-$CH_3$), 6.70 (s, 1H, Ar-H), 7.33 (t, 2H, *J*= 9 Hz, Ar-H), 7.43-8.10 (m, 10H, Ar-H), 9.13 (s, 1H, pyrazolyl-H); Mass: *m/z* 514 $[M+H]^+$.

**(Z)-5-Bromo-2-((3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)methylene)benzofuran-3(2H)-one (5d):** IR: 3087 (=C-H), 1710 (C=O), 1648 (C=N), 1596 (C=C), 1221 (C-O-C), 1170 (Ar-F) $cm^{-1}$; $^1$HNMR: δ 2.53 (s, 3H, Thiazolyl-$CH_3$), 6.71 (s, 1H), 7.35 (t, 2H, *J*= 9 Hz), 7.47-8.11 (m, 10H), 9.15 (s, 1H, pyrazolyl-H); Mass: *m/z* 558 $[M+H]^+$.

**(Z)-5,7-Dichloro-2-((3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-**

**yl)methylene)benzofuran-3(2H)-one (5e):** IR: 3084 (=C-H), 1712 (C=O), 1647 (C=N), 1594 (C=C), 1223 (C-O-C), 1173 (Ar-F) $cm^{-1}$; $^1$HNMR: δ 2.54 (s, 3H, Thiazolyl-$CH_3$), 6.72 (s, 1H, Ar-H), 7.33 (t, 2H, *J*= 9 Hz, Ar-H), 7.42-8.07 (m, 9H, Ar-H), 9.12 (s, 1H, pyrazolyl-H); Mass: *m/z* 548 $[M+H]^+$.

**(Z)-5-Chloro-2-((3-(2-(4-fluorophenyl)-4-methylthiazol-5-yl)-1-phenyl-1H-pyrazol-4-yl)methylene)-6-methylbenzofuran-3(2H)-one (5f):** IR: 3085 (=C-H), 1710 (C=O), 1649 (C=N), 1596 (C=C), 1222 (C-O-C), 1170 (Ar-F) $cm^{-1}$; $^1$HNMR: δ 2.31 (s, 3H, Ar-$CH_3$), 2.53 (s, 3H, Thiazolyl-$CH_3$), 6.71 (s, 1H, Ar-H), 7.33 (t, 2H, *J*= 9 Hz, Ar-H), 7.44-8.09 (m, 9H, Ar-H), 9.13 (s, 1H, pyrazolyl-H); Mass: *m/z* 528 $[M+H]^+$.

**Table-1: Physical data of the synthesized compounds**

| Compd | $R_1$ | $R_2$ | $R_3$ | M. P. (°C) | Yield (%) |
|---|---|---|---|---|---|
| 4a | H | H | Me | 155 | 64 |
| 4b | H | H | F | 164 | 62 |
| 4c | H | H | Cl | 157 | 68 |
| 4d | H | H | Br | 120 | 64 |
| 4e | Cl | H | Cl | 180 | 72 |
| 4f | H | Me | Cl | 174 | 67 |
| 5a | H | H | Me | 187 | 61 |
| 5b | H | H | F | 182 | 59 |
| 5c | H | H | Cl | 177 | 63 |
| 5d | H | H | Br | 191 | 66 |
| 5e | Cl | H | Cl | 196 | 69 |
| 5f | H | Me | Cl | 170 | 62 |

## BIOLOGICAL SCREENING

The antibacterial activity of synthesized compounds was against the standard Gram-negative bacteria, *Pseudomonas fluorescens* (NCIM 2059), *Escherichia coli* (NCIM 2576) and Gram-positive bacteria, *Bacillus subtilis* (NCIM 2162), *Staphylococcus aureus* (NCIM 2602). Ampicillin served as positive control for antibacterial activity. The *in vitro* preliminary screening values (% inhibition) against microorganisms tested are summarized in **Table 2.** All bacterial cultures were first grown in Luria Burtony media at $37^0$C at 180 rpm. Once the culture reaches 1 O.D., it is used for anti-bacterial assay. Bacterial strains *Pseudomonas fluorescens* (NCIM 2059), *Escherichia coli* (NCIM 2576) as Gram-negative and *Bacillus subtilis* (NCIM 2162), *Staphylococcus aureus* (NCIM 2602) as Gram-positive were obtained from NCIM (NCL, Pune) and were grown in Luria Burtony medium from Hi Media, India. The assay was performed in 96 well plates after 8 Hrs. and 12 Hrs. for Gram negative and Gram positive bacteria respectively[14]. 0.1 % of 1 O.D. culture at 620 nm was used for screening inoculated culture was added into each well of 96 well plate containing the compounds to be tested. Optical density for each plate was measured at 620nm after 8 hrs for Gram-negative bacteria and after 12 Hrs. for Gram- positive bacteria.

All the synthesized compounds were found to be inactive against gram negative bacterial strains of *P. fluorescens* and *E. coli.* All the synthesized compounds were found to be inactive against gram positive bacterial strains of *S. aureus*. Compounds **4d**, **4f** and **5d** showed good activity against gram positive bacterial strain of *B. subtilis* compared to the standard drug Ampicillin at a concentration of 100 μg/mL also compound **5d** showed good activity at a concentration of 30 μg/mL compared to the standard.

**Table-2: Antibacterial screening of some synthesized compounds (% inhibition)**

| Comp | Gram Negative | | | | | | Gram Positive | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *P. fluorescens* | | | *E. coli* | | | *S. aureus* | | | *B. subtilis* | | |
| | **100** | **30** | **10** | **100** | **30** | **10** | **100** | **30** | **10** | **100** | **30** | **10** |
| **4a** | - | - | - | - | - | - | - | - | - | - | - | - |
| **4b** | 2.2 | - | - | 14.2 | - | - | - | - | - | 55.4 | 22.3 | 7.8 |
| **4c** | - | - | - | - | - | - | - | - | - | - | - | - |
| **4d** | 7.4 | 1.0 | - | 43.1 | 8.7 | - | - | - | - | **72.6** | 49.8 | 45.6 |
| **4e** | - | - | - | - | - | - | - | - | - | - | - | - |
| **4f** | 7.5 | 6.4 | 0.8 | 19.8 | 17.7 | 7.6 | - | - | - | **83.4** | 63.7 | 40.9 |
| **5a** | - | - | - | - | - | - | - | - | - | - | - | - |
| **5b** | - | - | - | - | - | - | - | - | - | - | - | - |
| **5c** | - | - | - | - | - | - | - | - | - | - | - | - |
| **5d** | 8.4 | - | - | 27.4 | 20.7 | 13.1 | - | - | - | **87.1** | **71.8** | 55.5 |
| **5e** | 4.4 | - | - | 13.1 | - | - | 13.7 | - | - | 55.6 | 54.7 | 19.6 |
| **5f** | 8.3 | 3.9 | - | - | - | - | 17.5 | 17.5 | 12.9 | 66.4 | 49.2 | 28.8 |
| **AMP** | **97.0** | **95.2** | **92.2** | **96.6** | **92.0** | **92.1** | **95.0** | **93.8** | **91.1** | **98.5** | **95.0** | **90.5** |

AMP-Ampicillin; Concentrations in μg/mL.

## CONCLUSION

The main objective of this research work was to synthesize thiazole anchored chromones and aurones followed by their antibacterial activities. The newly synthesized compounds were characterized with the help of spectral techniques. Some of the compounds showed good to moderate activity towards bacterial species when compared to standard Ampicillin.

## ACKNOWLEDGEMENT

Authors are thankful to Dr. Dhiman Sarkar, National Chemical Laboratory, Pune and his team for providing biological screening.

## REFERENCES

i. Helal, M. H. M.; Salem, M. A.; El-Gaby, M. S. A. & Aljahdali, M.; Synthesis and biological evaluation of some novel thiazole compounds as potential anti-inflammatory agents; *Eur J Med Chem* 2013, **65**, 517-526.

ii. Aggarwal, R.; Kumar, S.; Kaushik, P.; Kaushik, D. & Gupta, G. K.; Synthesis and

iii. pharmacological evaluation of some novel 2-(5-hydroxy-5-trifluoromethyl-4,5-dihydropyrazol-1-yl)-4-(coumarin-3-yl)thiazoles; *Eur J Med Chem* 2013, **62**, 508-514.

iv. Grozav, A.; Gaina, L. I.; Pileczki, V.; Crisan, O.; Silaghi-Dumitrescu, L.; Therrien, B.; Zaharia, V. & Berindan-Neagoe, I.; The Synthesis and Antiproliferative Activities of New Arylidene-Hydrazinyl-Thiazole Derivatives; *Int J Mol Sci* 2014, **15**, 22059-22072.

v. Muijlwijk-Koezen, J. E.; Timmerman, H.; Vollinga, R. C.; Drabbe Kunzel, J. F.; de Groote, M.; Visser, S. & Jzerman, A. P., Thiazole and thiadiazole analogues as a novel class of adenosine receptor antagonists; *J Med Chem* 2001, **44**, 749-762.

vi. Berghot, M. A. & Moawad, E. B.; Convergent synthesis and antibacterial activity of pyrazole and pyrazoline derivatives of diazepam; *Eur J Pharm Sci* 2003, **20**, 173-176.

vii. Sridhar, R.; Perumal, P. T.; Etti, S.; Shanmugam, G.; Ponnuswamy, M. N,; Prabavathy, V. R. & Mathivanan, N.; Design, synthesis and anti-microbial activity of

1H-pyrazole carboxylates; *Bioorg Med Chem Lett* 2004, **14**, 6035-6040.

viii. Mohammed, K. O. & Nissan, Y. M.; Synthesis, molecular docking, and biological evaluation of some novel hydrazones and pyrazole derivatives as anti-inflammatory agents; *Chem Biol Drug Des* 2014, **84**, 473-488.

ix. Oganesyan, E. T.; Saraf, A. S. & Ivchenko, A. V.; Synthesis and antiallergic activity of novel chromone derivatives; *Pharm Chem J* 1993, **27(1)**, 52-54.

x. Kimura, Y.; Sumiyoshi, M.; Taniguchi, M. & Baba, K.; Antitumor actions of a chromone glucoside cnidimoside A isolated from Cnidium japonicum; *J Nat Med* 2008, **62(3)**, 308-313.

xi. Hon, K. S.; Akolkar, H. N.; Karale B. K.; Synthesis and characterization of novel 2 (1-benzyl-3-[4-fluorophenyl]-1H-pyrazol-4-yl)-7-fluoro-4H-chromen-4-one derivatives; *J Heterocycl Chem* 2020, **57(4)**, 1692-1697.

xii. Pietta, P. J.; Flavonoids as antioxidants; *J Nat Prod* 2000, **63**, 1035-1042.

xiii. Kim**,** H**.** P**.;** Mani**,** I**.;** Iversen**,** L**.** & Ziboh**,** V**.** A**.;** Effects of naturally-occurring flavonoids and biflavonoids on epidermal cyclooxygenase and lipoxygenase from guinea-pigs**;** *Prostaglandins Leukot Essent Fatty Acids* 1998, **58**, 17-24.

xiv. Ferry, D. R.; Smith, A.; Malkhandi, J.; Fyfe, D. W.; deTakats, P. G.; Anderson, D.; Baker, J. & Kerr, D. J.; Phase I clinical trial of the flavonoid quercetin: pharmacokinetics and evidence for in vivo tyrosine kinase inhibition; *Clin Cancer Res* 1996, **2**, 659-668.

xv. Zheng, X.; Wang, H.; Liu, Y. M.; Yao, X.; Tong, M.; Wang, Y. H. & Liao, D. F.; Synthesis, Characterization, and Anticancer Effect of Trifluoromethylated Aurone Derivatives; *J Heterocycl Chem* 2015, **52**, 296-301.

xvi. Detsi, A.; Majdalani, M.; Kontogiorgis, C. A.; Hadjipavlou-Litina, D. & Kefalas, P.; Natural and synthetic 2'-hydroxy-chalcones and aurones: synthesis, characterization and evaluation of the antioxidant and soybean lipoxygenase inhibitory activity; *Bioorg Med Chem* 2009, **17**, 8073-8085.

xvii. Bandgar, B. P.; Patil, S. A.; Korbad, B. L.; Biradar, S. C.; Nile, S. N. & Khobragade, C. N.; Synthesis and biological evaluation of a novel series of 2,2-bisaminomethylated aurone analogues as anti-inflammatory and antimicrobial agents; *Eur J Med Chem* 2010, **45**, 3223-3227.

xviii. Akolkar, H.; Karale, B. and Darekar, N.; Synthesis and antibacterial screening of novel (*E*)-3-(3-(2-(4-fluorophenyl)-4- methylthiazol-5-yl)-1-phenyl-1*H*-pyrazol-4-yl)-1-(2-hydroxyphenyl)prop-2-en-1- ones; *Int. Res. J. Pharm*. 2019, **10(5)**, 196-199.

xix. Singh, R.; Nawale, L.; Arkile, M.; Shedbalkar, U.; Wadhwani, S.; Sarkar, D. & Chopade, B.; Chemical and biological metal nanoparticles as antimycobacterial agents: A comparative study; *Int J Antimicrob Agents* 2015, **46(2)**, 183-188.

Received on May 26, 2022.