ejpmr, 2016,3(1), 233-238

SJIF Impact Factor 2.026

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article
ISSN 3294-3211
EJPMR

ALUM [KAl(SO$_4$)$_2$.12 H$_2$OCATALYZED ONE-POT MULTICOMPONENT SYNTHESIS OF BENZYLPYRAZOLYL HYDROXY COUMARIN AND HYDROXYQUINOLINONE DERIVATIVES

Santosh A. Jadhav[1], Mahesh G. Shioorkar[1], Omprakash S. Chavan[2] and Rajendra K. Pardeshi [3]*

[1]Department of Chemistry, Vivekanand College, Aurangabad (India)-431001.
[2]Department of Chemistry, Barwale College, Jalna (India)-431203.
[3]Department of Chemistry, Sant Ramdas College, Ghansawangi, Jalna (India)-431203.

***Correspondence for Author: Dr. Rajendra K. Pardeshi**
Department of Chemistry, Sant Ramdas College, Ghansawangi, Jalna, India-431203.

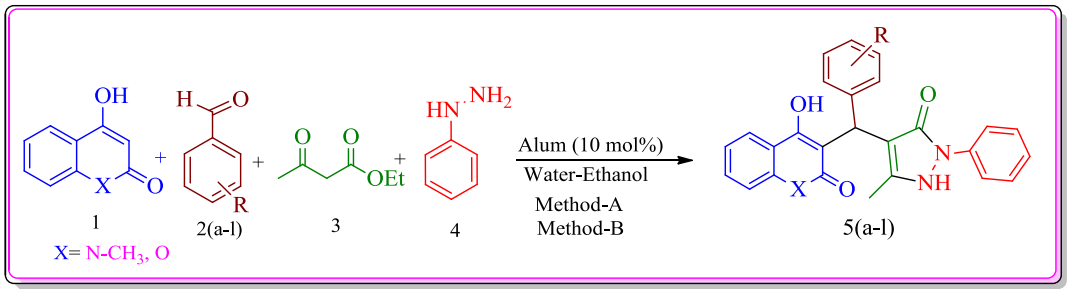
Article Received on 03/11/2015 **Article Revised on 25/11/2015** **Article Accepted on 17/12/2015**

ABSTRACT
An efficient and green approach has been developed for the synthesis of substituted aromatic benzyl pyrazolyl hydroxy quinolinone, hydroxy coumarin derivatives by Knoevenagel, Michael addition reaction, formation of hydroxy quinolinone or hydroxy coumarin with aromatic aldehydes, ethyl acetoacetateand phenyl hydrazine using Alum [KAl(SO4)$_2$.12H$_2$O] under aqueous ethanol conditions. Environmental acceptability, operational simplicity, low cost, excellent functional group compatibility and high yields are the important features of this protocol.

KEYWORDS: Benzylpyrazolylhydroxycoumarin, Hydroxy Quinolinone; Alum catalyzed, Multicomponent reaction.

INTRODUCTION
Multicomponent reactions (MCR) are accepted worldwide as an important method for the synthesis of natural and medicinally important productsin recent years.[1] These reactions avoid cost and time consuming processes for the purification of various precursors and isolation of intermediates.[2]

Now a day, many organic transformations have been carried out in water.[3-5] It is a unique readily available, inexpensive, nontoxic, safer and environmentally benign solvent. The water mediated conditions lead to enhanced reaction rates, higher yields of pure products and easier workup. Consequently, this protocol should be welcome in these environmentally mindful days.Alum (KAl(SO$_4$)$_2$·12H$_2$O), which is used for prominent organic transformations, such as the Biginelli[6] and Pechmann,[7] reactions and also used for the synthesis of 1,8-dioxo-octahydroxanthenes,[8] Isoquinolonic acids,[9] trisubstituteddimidazoles,[10] 1*H*-spiro[isoindoline-1,2'-quinazoline]-3,4'(3*H*)-diones,[11] 1,3,4-oxadiazoles,[12] and 1,5-benzodiazepines,[13] In this work, we wish to report straightforward an efficient multicomponent synthesis of benzylpyrazolyl hydroxy quinolinone and hydroxy coumarin derivatives in water-ethanolsolvent combination under microwave irradiation and conventional method (Scheme **1**).



Scheme1: **Alummediatedsynthesis of benzylpyrazolyl hydroxy quinolinone, hydroxycoumarines.**

3-substitutedhydroxyquinolinone and its arylidine analogues having excellent biological activity, such as hepatoprotative effects in human[14], On the basis of biological evaluation 4-hydroxyquinolinone and its analogues has wide spectrum of pharmacokinetic usability, it constituent an important area of research because of their use as anti-oxidant, anti-angiogenic, Brain anti-tumor in vivo, analgesic, dye-stuff, herbicides,

orally active antagonist and anti-inflammatory, anti-allergenic, anti-tubercles and cardiovascular agent, herbicidal [15-19] and competitive inhibitor.[20] 4-hydroxycoumarin and its 3-substitutedarylidine derivatives are of much importanceas they exist in many natural products and exhibit a wide range of biological activities such as antibacterial, anti-HIV,[21] antiviral,[22] anticoagulant,[23] antioxidant,[24] and anticancer activities.[25]

Nitrogen, containing five member heterocycles especially, azole plays an important role in medicinal field. The pyrazolones and substituted moieties such as phenazone, propyphenazone, ampyrone andmetamizole are useful antipyretic and analgesicdrugs,[26] myocardial ischemia.[27] In addition, pyrazolones possess kinase inhibitory properties, particularly of enzymeswhich catalyze the phosphorylation of serine and threonine inproteins, and is also used for treating diseases related to theseenzymes, such as rheumatoid arthritis, bone loss, cancer and other proliferative diseases like antimicrobial, antifungal,[28] antibacterial,[29] anti-inflammatory,[30] antitumor,[31] gastric secretion stimulatory,[32] antidepressant,[33] andanti-tubercularactivities.[34] The most commonly used synthetic methods for accessinbenzylpyrazolyl hydroxy coumarin, hydroxyl quinolinone derivativesinclude Perkin, Knoevenagel, Reformatsky, Pechmann and Wittig reactions. Recently, a number of classical methods for the synthesis of benzyl pyrazolyl hydroxy coumarin, hydroxyl quinolinone derivatives have been reported in the literature in the presence of various catalysts like sulfuric acid, phosphorus pentoxide, aluminum chloride, iodine, and trifluoroacetic acid, acetic acid etc.,[35-40] these synthetic approaches, however, suffer from disadvantages such as using hazardous solvent and or catalyst, low yield, lack of selectivity, and complicated workup in procedures, use of hazardous chemical compounds and are expensive. To convey these difficulties, it is essential to develop a simple and eco-friendly method for the synthesis of benzylpyrazolyl hydroxy coumarin, hydroxyl quinolinone derivatives, Present study is outcome of our continuous efforts which establish new green combination of alum and water-ethanol as catalyst and solvent (Scheme 1). They have become an increasingly attractive synthetic tool because of their green credentials such as convergence, atom-economy, energy and cost savings, with minimal waste. Present study is in continuation of our research work as searching of new and simple green synthetic protocols.[41-45] However, in this method used hazardous catalyst and or solvent and time there are some problems in using these liquid acid catalysts, e.g. massive waste liquors would be produced; process equipment would be eroded etc. In order to overcome these problems that the liquid acid catalyst brought into the reactions, study of eco-friendly and easy reusable heterogeneous polymeric acidic catalysts become meaningful.

This method describes synthesis using naturallyoccurringalum as catalystby conventional method and microwave irradiation technique.In our literature survey reveals that, there has been no any report synthesis of benzylpyrazolyl hydroxycoumarin, hydroxyl quinolinone derivatives, in presence ofalum as a catalyst, water-ethanol mediated underconventional or microwave irradiation method.

RESULT AND DISCUSSION

We first, focus on green approach for the selection of multicomponent reaction. Initially,optimized reaction condition and performed series of reactions with various proportional mixtures set of solvent and catalyst with different time of reaction, for the better compatibility and found that 10 mole % of alum in water-ethanol was best catalyst-solvent combination resulting in excellent yield(Table **1**, entry**16**). On increasing amount of catalyst by 10 mole %, no significant increase in yield of product was observed (Table **1**, entry **17**).While decreasing amount of catalyst less than 10 mole % yield was fall down (Table **1,** entry **15**). A corresponding good yield was observed in Acetic acid and Montmorillonite with combination of water-ethanol as solvent (Table **1,** entry **7, 11**). As model reaction, phenyl hydrazine (1.0 mmol), ethyl acetoacetate (1.0 mmol), benzaldehyde (1.0 mmol) and 4-hydroxycoumarin or 4-hydroxyquinolinone (1.0 mmol) was stirred or microwave irradiated in the presence of alum catalyst in water-ethanol as solvent gave excellent yield in a very short reaction time (Table **1**, entry**16**).

Table 1.**Optimization of reaction condition for the synthesis of 5a.**

Entry	Catalyst (mol %)	Solvent	Conventional	MWI
			Time (min.)/Yield(%)[a]	Time (min.)/Yield(%)[a]
1	No catalyst	Neat	60/00	6/00
3	Acetic acid (05)	H_2O	60/58	6/60
4	Acetic acid (10)	H_2O	60/76	6/80
5	Acetic acid(15)	H_2O	60/77	6/80
6	Acetic acid(10)	EtOH	60/70	6/74
7	Acetic acid (10)	EtOH-H_2O	60/83	6/89
8	Montmorillonite(05)	H_2O	60/50	6/55
9	Montmorillonite(10)	H_2O	60/68	6/71
10	Montmorillonite(10)	EtOH	60/59	6/69
11	Montmorillonite(10)	EtOH-H_2O	60/68	6/73

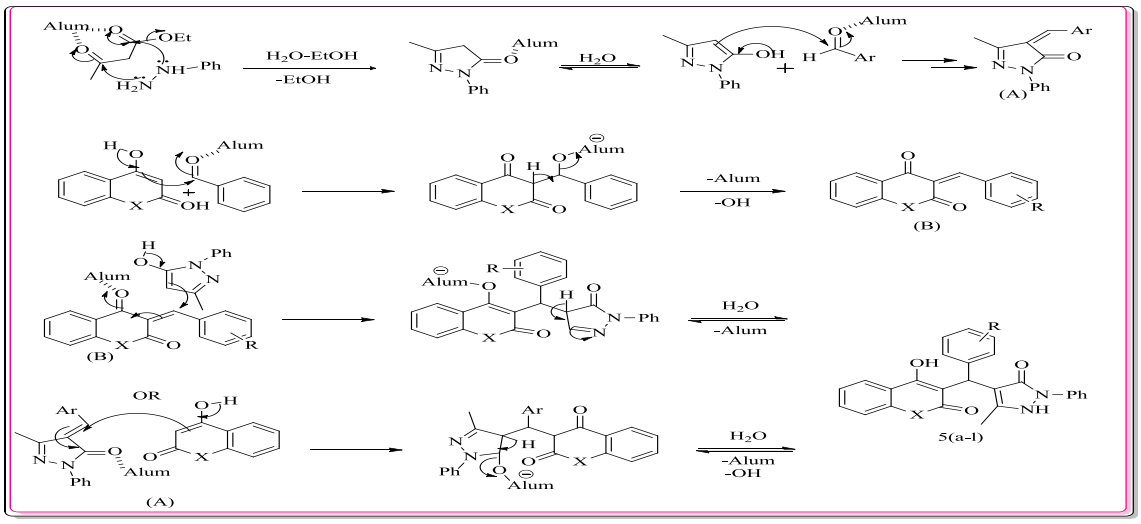
12	Alum(05)	H_2O	40/59	4/63
13	Alum (10)	H_2O	40/73	4/79
14	Alum (15)	H_2O	60/72	6/78
15	Alum(10)	EtOH	30/68	3/73
16	Alum(10)	EtOH-H_2O	30/94	3/98
17	Alum (15)	EtOH-H_2O	30/94	3/98
Reaction condition: Benzaldehyde (1mmol), ethyl acetoacetate (1mmol), phenyl hydrazine(1mmol), hydroxy coumarin or 1-methyl 4-hydroxy quinolinone (1mmol) and alum (10 mol %), water-ethanol (2:1). [a]Isolated yield.				

Thus we decided reaction carried out in alum as green catalyst, and water-ethanol as green solvent, all example were tested reasonably good to excellent yields could be achieved in less time of reaction (Table **2**). An electronic effect was observed, electron withdrawing groups to aryl aldehydes were well tolerate and gave better yield (Table **2**, entry 2-3) and simple hydrazine hydrate with benzaldehyde gave good yield (Table **2**, entry 12), while six membered heterocyclic compound gave corresponding yield (Table **2**, entry 13).

Finally, the product was confirmed by spectral data (IR, ^{1}HNMR and MS), presence of N-H form this is due to range 3150-3165 cm^{-1}shows IR band, ^{1}HNMR shows at δ 2.1 and mechanistic path (Scheme **2**) and compared with reported method.[39-40]

Table 2. **Synthesis of benzyl pyrazolyl hydroxy quinolinone, hydroxy coumarin derivatives catalyzed by alum in water in different reaction condition**

Entry	Product	Aldehyde	Hydrazine	Yield (%)[b] / Time (min.)	
				Conventional	MWI
1	5a	Benzaldehyde	Phenyl hydrazine	89/50	91/4
2	5b	4-Nitro benzaldehyde	Phenyl hydrazine	94/30	98/3
3	5c	3-Nitro benzaldehyde	Phenyl hydrazine	91/60	94/5
4	5d	4-Fluoro benzaldehyde	Phenyl hydrazine	86/60	88/7
5	5e	4-Chloro benzaldehyde	Phenyl hydrazine	88/60	89/7
6	5f	4-Methyl benzaldehyde	Phenyl hydrazine	84/60	87/6
7	5g	4-Methoxy benzaldehyde	Phenyl hydrazine	86/60	88/6
8	5h	4-Hydroxybenzaldehyde	Phenyl hydrazine	73/60	77/5
9	5i	Benzaldehyde	4-Nitro phenyl hydrazine	83/60	85/6
10	5j	3-Nitro benzaldehyde	4-Nitro phenyl hydrazine	89/50	91/5
11	5k	4-Methoxy benzaldehyde	4-Nitro phenyl hydrazine	82/60	84/7
12	5l	Benzaldehyde	Hydrazine hydrate	89/40	90/6
13	5m	5- methyl, pyridyl-3-carbaldyhyde	Phenyl hydrazine	73/50	78/6
Reaction condition: substituted aryl aldehydes (1.0 mmol), ethyl acetoacetate (1.0 mmol), phenyl hydrazide (1.0 mmol), hydroxy coumarin or 1-methyl 4-hydroxy quinolinone (1.0 mmol) and alum (10 mol %), water-ethanol (2:1). [b]Isolated yield.					



Scheme 2: Possible reaction mechanism.

EXPERIMENTAL

All chemicals were purchased from Merck, Aldrich and Rankem and used without further purification. Melting pointswere obtained on Buchi Melting Point B540 and areuncorrected. ^{1}H NMR spectra were recorded in solvent $CDCl_3$, at 400 MHz using TMS as the internal standard on a Bruker AM-400 spectrometer. Analytical thin-layer chromatography ($CHCl_3$: MeOH) was carried out on precoated plates (silica gel 60 F254), and spots were visualized with ultraviolet (UV) light. All other solvents and reagents were used as obtained from commercial sources and used without further purification.

General Procedure for preparation of benzylpyrazolyl hydroxy quinolinone, hydroxy coumarin derivatives 5(a-l)

Conventional (Method A)

A mixture of phenyl hydrazine (1.0mmol), ethyl acetoacetate (1.0 mmol), aryl aldehyde (1.0 mmol), hydroxy coumarin or hydroxy quinolinone (1.0 mmol) and alum (10 mol%) in 2-4ml of water-ethanol (2:1) was stirred at 30-40 °Cuntil the reaction mixture solidified. After completion of the reactionwas monitored by TLC, reaction mass was added in water to precipitate a solid compound. The precipitated crude product was purified by recrystallization from hot ethanol.

Microwave irradiation (Method B)

A mixture of phenyl hydrazine (1.0 mmol), ethyl acetoacetate (1.0 mmol), aryl aldehyde (1.0 mmol), hydroxy coumarin or hydroxy quinolinone (1.0 mmol) and alum (10 mol%) in 2-4ml of water-ethanol (2:1) was subjected to microwave irradiation at 400 Wuntil the reaction mixture solidified. After completion of the reactionwas monitored by TLC, reaction mass was added in water to precipitate a solid compound. The precipitated crude product was purified by recrystallization from hot ethanol. Melting range (Observed: 232°C, reported 232-234°C[39-40]). All the isolated compounds were further characterized by FT-IR and ^{1}H NMR.

Spectral Characterization Data Of Sellected Compound

(5a): 4-((4-hydroxy-2-oxo-2*H*-chromen-3-yl)(phenyl)methyl)-5-methyl-2phenyl-1*H*-pyrazol-3(2H)-one:

White solid,m.p. 232^{0}C, IR (KBr cm^{-1}): 3155, 3060-3150, 3050, 2865, 1730-1775,1697,1460-1560.
^{1}HNMR (400 MHz, $CDCl_3$): δ2.21 (s, 1H, -NH), 2.25 (s, 3H, $-CH_3$); 6.02 (s, 1H, CH-Ar); 16.72 (s, 1H, -OH);7.40-7.80 (m, 4H, CH-Ar); 7.20-7.35 (m, 5H, -CH-Ar); 6.90-7.68 (m, 5H, CH-Ar).
LRMS: m/z for (Coumarins) $C_{26}H_{19}NO_4$ [M+H] $^+$Calcd 424.0
HRMS: m/z for (Coumarins) $C_{26}H_{20}NO_4$ [M+H] $^+$Calcd 424.1
Anal.Calcd (Coumarins): for $C_{26}H_{20}NO_4$ [M+H] $^+$ C,73.57; H,4.75; N,6.60; O,15.08; Found: C, 73.64; H,4.68; N, 6.52; O,15.1

(5a): 4-hydroxy-1-methyl-3-((5-methyl-3-oxo-2-phenyl-2,3-dihydro-1*H*pyrazol-4 yl)(phenyl)methyl)quinolin-2(1*H*)-one:

White solid,m.p. 232^{0}C, IR (KBr cm^{-1}): 3155, 3060-3150, 3050, 2865, 1697,1460-1560.
^{1}HNMR (400 MHz, $CDCl_3$): δ3.41 (s, 3H, $-CH_3$), 2.21 (s, 1H, -NH), 2.25 (s, 3H, $-CH_3$); 6.02 (s, 1H, CH-Ar); 16.72 (s, 1H, -OH);7.40-7.80 (m, 4H, CH-Ar); 7.20-7.35 (m, 5H, -CH-Ar); 6.90-7.68 (m, 5H, CH-Ar).
LRMS: m/z for (Quinolinone) $C_{27}H_{22}N_3O_3$ [M+H] $^+$Calcd 437.0
HRMS: m/z for (Quinolinone) $C_{27}H_{23}N_3O_3$ [M+H] $^+$Calcd 437.1
Anal.Calcd (Quinolinone): for $C_{27}H_{23}N_3O_3$ [M+H] $^+$ C, 74.12; H, 5.30; N, 9.60; O, 10.97; Found: C, 74.18; H, 5.26; N, 9.66; O, 11.3

(5m): 4-((4-hydroxy-2-oxo-2*H*-chromen-3-yl)(5-methylpyridin-3-yl)methyl)-5-methyl-2-phenyl-1*H*-pyrazol-3(2H)-one:

IR (KBr) cm^{-1}: 3158, 3150-3050, 3060, 2865,1730-1775, 1697, 1460-1560.
^{1}HNMR (400 MHz; $CDCl_3$): δ 2.22 (s, 1H, $-CH_3$), 16.75(s, 1H, -OH), 2.28 (s, 3H, $-CH_3$), 2.1 (s, 1H, -NH), 7.60(s, 1H, CH-Ar), 8.35 (s, 2H, CH-Ar), 5.98 (s. 1H -CH), 7.40-7.85(m, 4H, CH-Ar), 6.80-7.40 (m, 4H, CH-Ar).
LRMS: m/z for (Coumarins) $C_{26}H_{20}N_3O_4$ [M+H] $^+$Calcd 439.0
HRMS: m/z for (Coumarins) $C_{26}H_{21}N_3O_4$ [M+H] $^+$Calcd 439.1
Anal.Calcd (Coumarins): for $C_{26}H_{21}N_3O_4$ [M+H] $^+$C, 71.6; H, 4.82; N, 9.56; O, 14.56; Found: C, 71.12; H, 4.74; N, 9.61; O,14.60

(5m): 4-hydroxy-1-methyl-3-((5-methyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)(5 methylpyridin-3-yl)methyl)quinolin-2(1*H*)-one:

IR (KBr) cm^{-1}: 3158, 3150-3050,3060, 2865,1697, 1460-1560.
^{1}HNMR (400 MHz; $CDCl_3$): δ 2.22 (s, 1H, $-CH_3$), 16.75(s, 1H, -OH), 2.28 (s, 3H, $-CH_3$), 2.1 (s, 1H, -NH), 7.60(s, 1H, CH-Ar), 8.35 (s, 2H, CH-Ar), 5.98 (s. 1H -CH), 7.40-7.85(m, 4H, CH-Ar), 6.80-7.40 (m, 4H, CH-Ar).
LRMS: m/z for (Quinolinone) $C_{27}H_{23}N_4O_3$ [M+H] $^+$Calcd 452.0
HRMS: m/z for (Quinolinone) $C_{27}H_{24}N_4O_3$ [M+H] $^+$Calcd 452.1
Anal.Calcd (Quinolinone): for $C_{27}H_{24}N_4O_3$ [M+H] $^+$C, 71.67; H, 5.35; N, 12.38; O, 10.61; Found: C, 71.69; H, 5.29; N, 12.44; O,10.66

CONCLUSIONS

In summary, we have reported a green synthesis of benzyl pyrazolyl hydroxy coumarin and quinolinone derivatives by using Alum as a novel, green catalyst under aqueous ethanol conditions. The advantages of this protocol over other procedures are higher yields, cleaner reaction profile, and simplemethodology, making it an attractive process for the synthesis of benzyl pyrazolyl hydroxy coumarin and quinolinone derivatives. We believe that the present methodology addresses the current drive towards green chemistry. An effort toward the synthesis of other important drug molecules with a coumarin and quinolinone moiety by microwave irradiation as well as conventional method is ongoing in our laboratory. Also work is in progress to obtain biological activity such as antibacterial, antifungal, and anticancer of these important compounds.

ACKNOWLEDGEMENTS

We are grateful to Principal of Sant Ramdas College Ghansawangi, Dist. Jalna, affiliated to Dr Babasaheb Ambedkar Marathwada University, Aurangabad,INDIA, for providing laboratory facility.

SUPPLEMENTORY DATA

Supplementary data can be attached with manuscript as on www//http.ejpmr.in

REFERENCES

1. (a) Domling, A. Chem. Rev., 2006; 106: 17–89. (b) Ramon, D. J.; Yus, M. Angew. Chem., Int. Ed., 2005; 44: 1602–1634. (c) Domling, A.,Ugi, I. Angew. Chem., Int. Ed,. 2000; 39: 3168–3210.
2. (a) Damiano, Rocchi., J. Francisco González and J. Carlos Menéndez., Green Chem., 2013; 15: 511. (b) Tietze, L. F. Chem. Rev., 1996; 96: 115–136.
3. Pawar, S. S., Shingare, M. S.,Thore, S. N., Letters in Organic Chemistry., 2007; 4(7): 486-490.
4. Gong, K., Z.-W. He, Y. Xu., D. Fang, Z.-L.Liu.,Monatshefte fur Chemie., 2008; 139(8) 913–915.
5. Pinaka, A., Vougioukalakis, G. C.,Yannakopoulou, E., Papadopoulos, K., Chirality., 2013; 25(2): 119–125.
6. Azizian, J.,Mohammadi, A. A., Karimi, A. R., Mohammadizadeh, M. R., Appl. Catal., A., 2006; 85: 300.
7. Dabiri, M., Baghbanzadeh, M., Kiani, S., Vakilzadeh, Y.,Monatsh. Chem., 2007; 138: 997.
8. Madje, B. R., Ubale, M. B., Bharad, J. V.,Shingare, M. S.,S. Afr. J. Chem., 2009; 63: 36.
9. Azizian, J., Mohammadi, A. A., Karimi, A. R., Mohammadizadeh, M. R.,J. Org. Chem., 2006; 71: 350.
10. Mohammadi, A. A., Mivechi, M., Kefayati, H., Monatsh. Chem., 2008; 139: 935.
11. Mohammadi, A. A., Qaraat, H., Monatsh. Chem., 2009; 140: 401.
12. Dabiri, M., Salehi, P., Otokesh, S., Baghbanzadeh, M., Bahramnejad, M., Monatsh. Chem., 2007; 38: 253.
13. Mahajan, D., Naqvi, T., Sharma, R. L., Kapoor, K. K., Aust. J. Chem., 2008; 61: 59.
14. Bernard Refouvelet., C. Guyon., Y. Jacquot., C. Girund., F. Bevalot., European J. of Med. Chem., 2004; 229-235.
15. Arya K., Agrawal. M., Biorg. Med. Chem. Lett., 2007; 17: 86-93.
16. Oeveren. A. V., Marschke. K. B., Lopez F. J., Vilar., A. N. Zhi, L.,Biorg. Med. Chem. Lett., 2007; 17: 1527-1531.
17. Kumabe. R., Nishino.,Tetrahedron Lett., 2004; 45: 703-706.
18. Chimichi S., Boccalini, M., Hassan., M.M.M., Viola., G., Dall Acqua F., Curini., M. Tetrahedron,. 2006; 62: 90-96.
19. Josef Japilek., Robert M., Matus P., Katarina K. M.; J. C.Molecule., 2009; 14: 1145-1159.
20. Bunting, J. W., Luscher., Mark A. Redman., J. Biorg. Chem., 1987; 15(2): 125-140.
21. Hesse, S., Kirsch, G., Tetrahedron Lett., 2002; 43: 1213.
22. Lee, B. H., Clothier, M. F., Dutton, F. E., Conder, G. A., Johnson, S. S., Bioorg. Med. Chem. Lett., 1998; 8: 3317.
23. J.-C. Jung, Y.-J.Jung.,O.-S. Park, Synth. Commun., 2001; 31: 1195.
24. Melagraki, G., Afantitis, A., Igglessi-Markopoulou O., Detsi, A., Koufaki, M., Kontogiorgis C., Eur. J. Med. Chem., 2009; 44: 3020.
25. J.-C.Jung., J.-H. Lee., S. Oh, J.-G. Lee, O-S. Park, Bioorg.Med.Chem. Lett., 2004; 14: 5527.
26. Himly, M., Jahn-Schmid, B., Pittertschatscher, K., Bohle, B., Grubmayr, K.C., Ebner, J. Allergy Clin. Immunol., 2003; 111: 882–888.
27. T. W. Wu, L. H. Zeng, J. Wu and K. P. Fung., Life Sci., 2002; 71: 2249–2255.
28. Al-Haiza,M. A., El-Assiery, S. A., Sayed, G. H., Acta Pharm. (Zagreb Croatia), 2001; 51: 251–261.
29. Moreau, F. Desroy, N., Genevard, J. M., Oliveira, C., Floquet, S. A., Denis, S., Escaich, K., Wolf, Busemann, M., Aschenbsenner, A., Bioorg. Med. Chem. Lett., 2008; 18: 4022–4026.
30. Badawey, E. A., El-AshmaweyM. I. M., Eur. J. Med. Chem., 1998; 33: 349–362.
31. Pasha F. A., Muddassar, M., NeazM. M., Cho, S. J. J., Mol. Graphics Modell., 2009; 28: 5461.
32. RosiereC. E., Grossman, M. I., Science., 1951; 113: 651.
33. Bailey D. M., Hansen, P. E., Hlavac, A. G., Baizman,E. R., J. Pearl, A. F. Feigenson, M. E.,J. Med. Chem., 1985; 28: 256–260.
34. Gunasekaran, P., Perumal, S., Yogeeswari, P., Sriram, D.,Eur. J. Med. Chem., 2011; 46: 4530.
35. Brufola, G., Fringuelli, F., Piermatti, O., Pizzo,F., Heterocycles., 1996; 43: 1257.
36. Yadav J.S., Reddy, B.V.S., Basak, A. K., Visali, B., Nagaiah, K., Eur. J. Org. Chem., 2004; 546.

37. Narsaiah, A.V., Nagaiah,K., Synth. Commun., 2003; 21: 3825.
38. Mohammad Ali Zolfigol., Ahmad Reza Moosavi-Zare., Mahmoud Zarei; C. R. Chimie., 2014; 17: 1264–1267.
39. Ghosh, P. P., Pal, G., Paul, S., Das, A. R., Green Chemistry, 2012; 14: 2691.
40. Srinivasrao, Y., Abhishek, P., Ravikrishna, D., Tetrahedron Lettters, 2015; 56: 4770-4774.
41. Jadhav, S. A., Shioorkar, M. G., Chavan, O. S., Shinde, D. B., Pardeshi, R. K. Heterocyclic Lett., 2015; 5(3): 375-382.
42. Jadhav, S. A., Shioorkar, M. G., Chavan, O. S., Pardeshi, R. K., Der Pharma Chemica, 2015; 7(2): 127-131.
43. Omprakash S. Chavan., S. B. Chavan., S. A. Jadhav., M. G. Shioorkar., M. A. Baseer. Heterocyclic Lett., 2015; 5(3): 391-394.
44. Shioorkar, M. G.,Ubale, M. B., Jadhav, S. A., Pardeshi, R. K., Der Chemica Sinica. 2015; 6(4): 110-113.
45. Jadhav, S. A., Shioorkar, M. G., Chavan, O. S., Chavan, R., Aniket Sarkate, Devanand Shinde and Rajendra Pardeshi, European Journal of Chemistry, 2015; 6(4): 410-416.