JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Chemotherapeutic properties of 1,3,4-Thiadiazoles: A Review

Mazhar Mehdi, Tazeem*, Aga Mansoor, S. Jamal Haider Zaidi
Department of Chemistry, Shia P. G. College, Lucknow (U.P.)
*Corresponding author's Email id: tazeem.chem09@gmail.com

Abstract: Thiadiazole derivatives are known since long time for its chemotherapeutic properties. From last few decades, this five-member thiadiazole moiety has become the center of interest for designing of new antibacterial, anticancer, anti fungal anti-inflammatory, analgesic, antimycobacterial, anticonvulsant, anti-diabetic, antiviral agents. The present study highlights the importance of 1,3,4-thiadiazole moiety as Chemotherapeutic agents.

Key word: Chemotherapeutic agents, antibacterial, anticancer, anti-inflammatory activity.

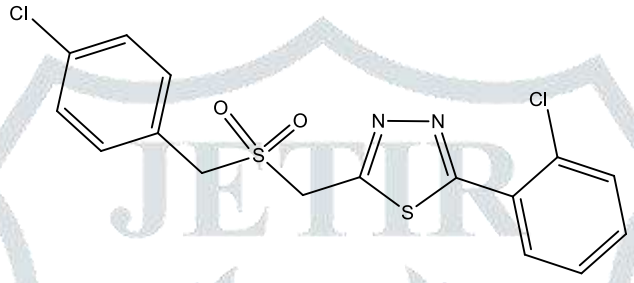
Introduction:

In the history there are number of evidence has been documented in the literature that showed the importance of substituted 1,3,4-thiadiazoles derivatives in antibacterial, antifungal and HIV activities [1,2]. The discovery of sulfur based drugs speedup the progress of development of sulfur containing heterocycles. There are numbers of thiadiazole based anti-cyclooxygenase/5-lipooxygenase agents are reported [3–7]. So far there are several Triazole based thiadiazole derivatives have been reported that show CNS depressant, antibacterial, antifungal, antitumour, anti-inflammatory, herbicidal, pesticidal and insecticidal properties [8-11]. Recently, 2-Amino-1,3,4-thiadiazole (ATDA), show promising anti tumor activity against renal,[12] colon,[13] ovarian,[14] and others cancer.[15] antiparasitic properties of 5-(5-nitrofuran-2-yl)-1,3,4-thiadiazoles is well documented in the literature and their biological properties get modulated by changing the substituents present on it.

In this review we focus on the recent development of thiadiazoles derivatives and their biological activity.

Antimicrobial activity:

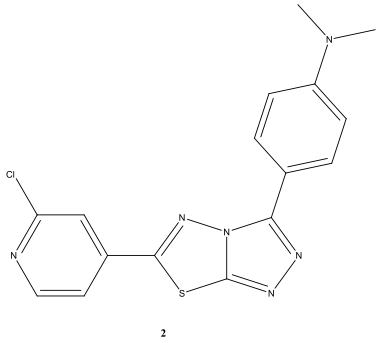
V. Padmavathi et al reported the synthesis of series of 2-(arylsulfonylmethyl)-5-aryl-1,3,4-thiadiazoles and all the compounds were tested against the Gram-positive bacteria *Staphylococcus aureus* (NCIM No. 5021), *Bacillus subtilis* (NCIM No. 2063), the Gram negative bacteria *Klebsiella pneumoniae* (NCIM No. 2957), *Proteus vulgaris* (NCIM No. 2027) and fungi *Fusarium solani* (NCIM No. 1330), *Curvularia lunata* (NCIM No. 716) and *Aspergillus niger* (NCIM No. 596). Compound **1** showed pronounced antimicrobial activity. Further, compound **1** exhibited maximum cytotoxicity. [16]



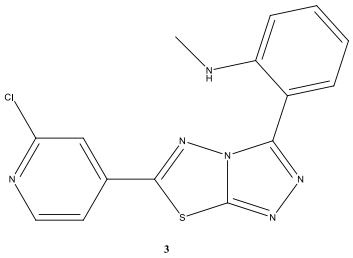
2-(((4-chlorobenzyl)sulfonyl)methyl)-5-(2-chlorophenyl)-1,3,4-thiadiazole

1

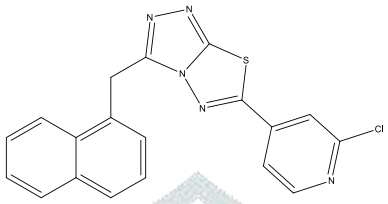
V. Mathew et al developed a series of 3,6-disubstituted-1,2,4-triazolo[3,4-b]-1,3,4 thiadizoles derivatives were prepared by the condensation of 4-amino-3-aryl/aralkyl substituted-5-mercapto-1,2,4-triazoles with various substituted aromatic/hetero aromatic acids through a single step reaction. The structure of the newly synthesized compounds was characterized by elemental analysis, IR, 1H NMR and mass spectral. Synthesized triazolo thiadiazoles investigated for their antibacterial, antifungal against *Staphylococcus aureus*, *Bacillus subtilis* (gram-positive bacteria), *Pseudomonas aeruginosa*, *Escherichia coli* (gram-negative bacteria) and two fungi *Aspergillus niger* and *Candida albicans*. None of the synthesized compounds have important antimicrobial activities. The tested compounds **2, 3** & **4** showed moderate antimicrobial activity against various tested bacterial and fungal strains.[17]



2



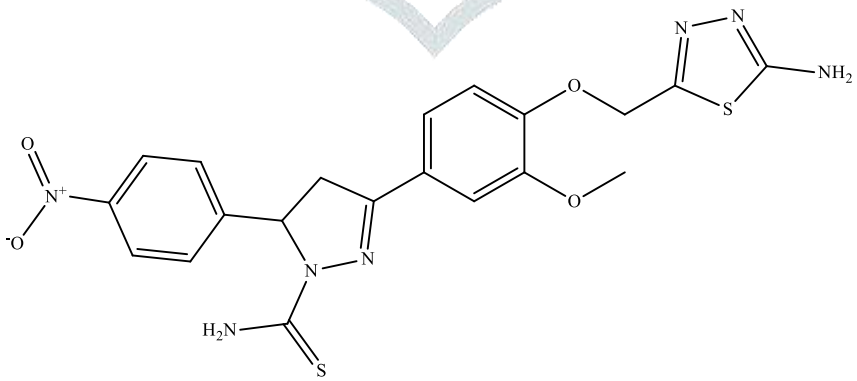
3



4

M. N. Noolvi et al. synthesized a series of 1,3,4-thiadiazole derivatives of 2-(4-formyl-2-methoxyphenoxy) acetic acid by cyclization of carboxylic acid group of 2-(2-methoxy-4-(3-oxo-3-substituted phenylprop-1-enyl)phenoxy) acetic acid with thiosemicarbazide in the presence of POCl3 or PPA. All the compounds have been tested for their in vitro antimicrobial activities against different bacterial cultures *S. aureus, Salmonella enterica, Vibrio cholera, Bacillus subtilis, Proteus mirabili, Escherichia coli* V517, *Mycobacterium smegmatics, Pseudomonas aeruginosa* and show significant activity. Among all the compounds, 1,3,4-thiadiazole derivative **5** showed activity most prominent activity against all the strains. It showed maximum activity (97%) against S. enterica (95%), against V. cholera and (87.9%) inhibition of E. coli V517 as compared with standard drug ampicillin.[18]

.

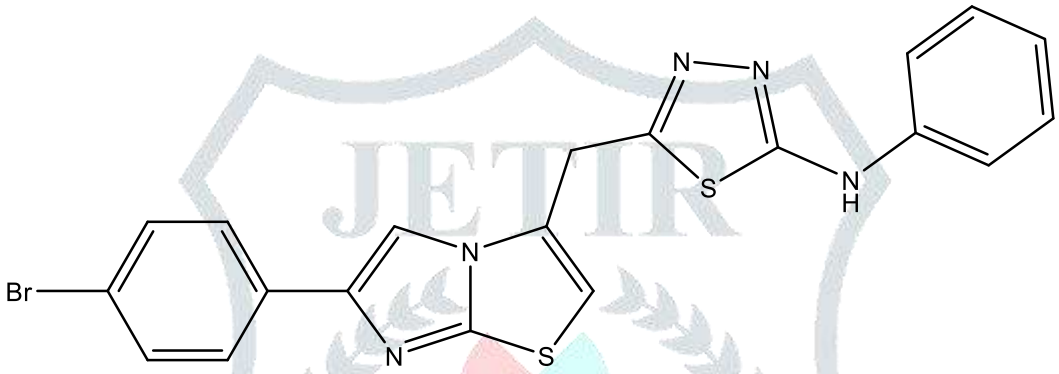


z-(4-((5-Amino-1,3,4-thiadiazol-2-yl)methoxy)-3-methoxyphenyl)-5-(4-nitrophenyl)-4,5-dihydro-1H-pyrazole-1-carbothioamide

5

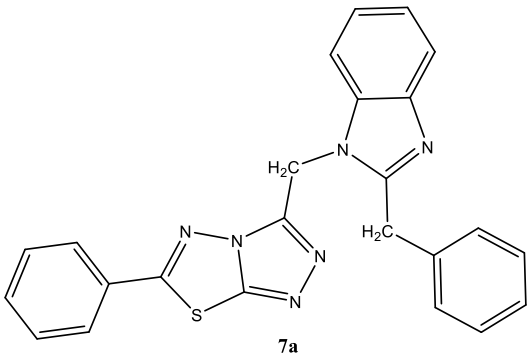
N. U. G. zeldemirci et al. reported the synthesis of imidazo[2,1-b]thiazole based thiazole derivatives and evaluated for their antibacterial and antifungal activities. The antimicrobial activities of the compounds were

assessed by the microbroth dilution technique against *Staphylococcus aureus* ATCC 29213, *Pseudomonas aeruginosa* ATCC 27853 and Escherichia *coli* ATCC 25922 as well as for antifungal activity against *Candida albicans* ATCC 10231, *Candida parapsilosis* ATCC 22019, *Candida krusei* ATCC 6258, *Trichophyton mentagrophytes var. erinacei* NCPF 375, *Microsporum gypseum* NCPF 580 and *Trichophyton tonsurans* NCPF 245. The preliminary results revealed that most of the compounds showed moderate to significant active. However, the most active compound was compound **6** had phenylamino group at the 2-position of the thiadiazole ring showed 16% inhibition. [19]

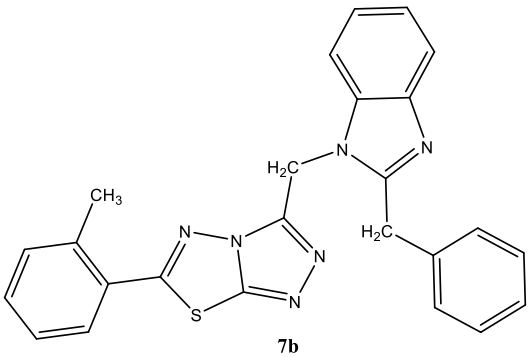


6

Y. J. Li et al. synthesized a novel series of 3,6-disubstituted 1,2,4-triazolo[3,4-b]-1,3,4-thiadiazoles by the condensation of 4-amino-5-[2-(4-chlorophenoxymethylbenzimidazole)-1-methylene]-3-mercapto-1,2,4-triazole with various (un)substituted aromatic acids in the presence of phosphorous oxychloride. All the newly synthesized compounds were investigated for their inhibitory activity to *E. coli* methionine aminopeptidase (EcMetAP1). Preliminary bioassay results showed that the compounds 7a and 7b exhibited higher inhibitory activity.[20]

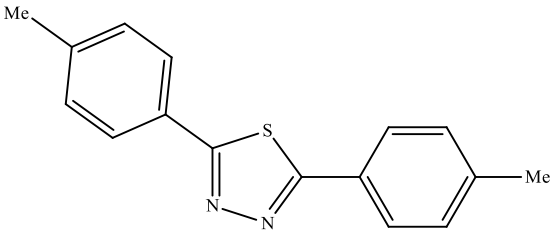


7a



7b

K. Gowda et al. reported the synthesis of a series of 2,5-disubstituted 1,3,4-thiadiazole and evaluated for their antioxidant and molecular docking studies. These molecules were developed by using substituted aldehydes and substituted dithioesters in presence of NCS (NChorosuccinimide). All the compounds showed good antibacterial and antioxidant activity among which, **8** possess excellent antibacterial and antioxidant activity.[21]

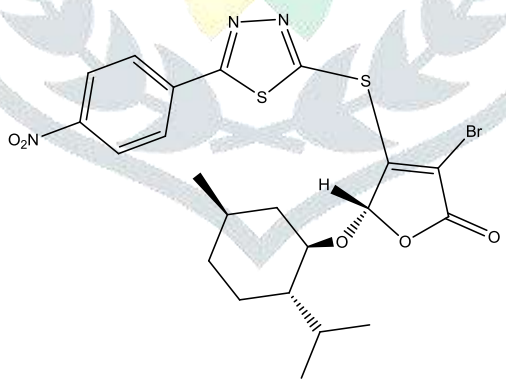


2,5-di-*p*-tolyl-1,3,4-thiadiazole

8

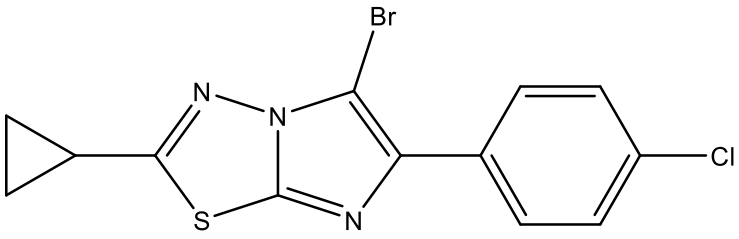
Anti cancer activity

Meng-Xue Wei et al reported a synthesis of new series of hybrid 1,3,4-thiadiazoles derivatives possessing γ-substituted butenolide moiety (Fig. 1) to evaluate their in vitro anticancer properties. All the compounds showed good anticancer activities against Hela cell lines. Of all the studied compounds, compound **9** exhibited the best inhibitory activity with an IC^{50} of 0.9 mM. After being treated with 0.1 mg/mL compound **9** for 24 h, the growth inhibition rate of Hela cell lines was 59.2%.[22]



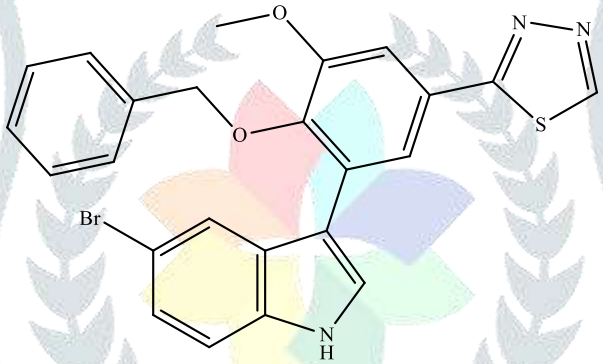
9

Malleshappa N. Noolvi et al. reported the synthesis of 2,5,6-trisubstituted imidazo[2,1-b][1,3,4]-thiadiazole derivatives and screened for their antitumor activity. All compounds were characterized by IR, 1HNMR,13CNMR and Mass spectroscopy. Among the tested compounds, 5-bromo-6-(4-chlorophenyl)-2-cyclopropylimidazo[2,1-b][1,3,4]thiadiazole **10** (NSC D-96022/1) was found to be the most active compounds against Leukemic cancer cell line. [23]



10

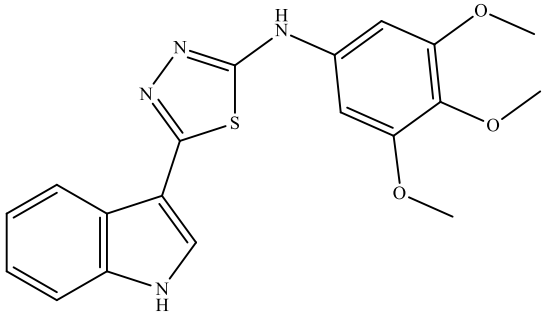
D. Kumar et al. synthesized a series of 5-(3-indolyl)-2-substituted-1,3,4-thiadiazoles and checked their cytotoxicity profile against prostate (PC3,DU145and LnCaP), breast (MCF7 and MDA-MB-231) and pancreatic (PaCa2) cancer cell lines. Among all the compounds Indolyl 1,3,4-thiadiazole **11** with 4-benzyloxy-3-methoxyphenyl and 5-bromo indolyl substituents found to be most active in suppressing the growth of cancer cells with IC_{50} 1.5 mM against pancreatic (PaCa2) cancer cell lines.[24]



2-(4-(Benzyloxy)-5-(5-bromo-3-indolyl)-3-methoxyphenyl)-1,3,4-thiadiazole

11

D. Kumar et al. prepared a series of 2-arylamino-5-(indolyl)-1,3,4-thiadiazoles and studied for their anticancer activity against selected human cancer cell lines. Most of the synthesized compounds showed significant cytotoxicity against the human breast cancer cell line (MDA-MB-231). Among these synthesized 2-arylamino-5-(indolyl)-1,3,4-thiadiazoles, compound **12** is the most potent cytotoxicity against the cancer cell lines (IC_{50} = 0.15-1.18 μM).[25]

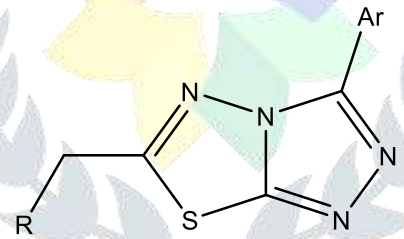


5-(1H-Indol-3-yl)-N-(3,4,5-trimethoxyphenyl)-1,3,4-thiadiazol-2-amine

12

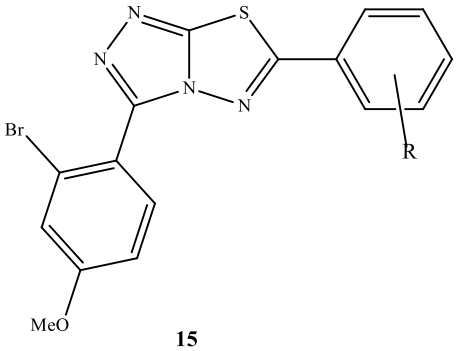
Analgesic & anti-inflammatory activity:

Mohd. Amir et al. reported the synthesis of several 3,6-disubstituted-1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazoles derivatives **11** by condensation of 4-amino-5-substituted-3-mercapto-(4H)-1,2,4-triazoles with various substituted aromatic acids and aryl/alkyl isothiocyanates. All the newly synthesized compounds were screened for their anti-inflammatory, analgesic, ulcerogenic, lipid peroxidation, antibacterial and antifungal activities. Few compounds showed potent anti-inflammatory activity along with minimal ulcerogenic effect and lipid peroxidation, compared to those of ibuprofen and flurbiprofen.[26]

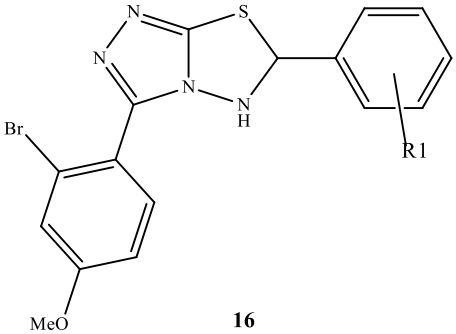


11

N. Chidananda et al. reported the synthesis of 3,6-disubstituted-1,2,4-triazolo[3,4-b][1,3,4]thiadizoles derivatives (**15** & **16**). All compounds were structurally confirmed by spectral analysis and were evaluated for their anti-inflammatory, analgesic, anti-oxidant and antimicrobial activities. Some of the tested compounds showed significant pharmacological activities.[27]

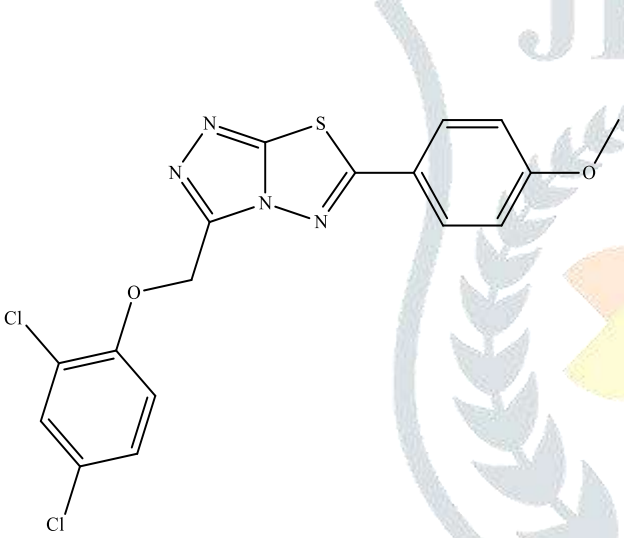


15

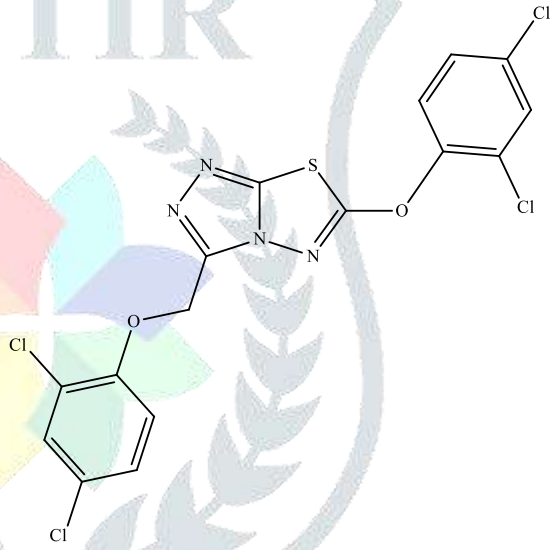


16

M.F. El Shehry et al. synthesized a series of 3-((2,4-dichlorophenoxy)methyl)-1,2,4-triazolo thiadiazoles derivates. All the newly synthesized compounds were tested for their anti-inflammatory and molluscicidal activities. The compounds **17** & **18** showed remarkable anti-inflammatory activities in dose dependent manner while compounds 4b exhibited promising molluscicidal activities.[28]



17



18

References:

[1] B.S. Holla, R. Gonsalves, S. Shenoy, Eur. J. Med. Chem. 35 (2000) 267–271.

[2] B. Tinperciuc, A. Parvu, M. Palage, O. Oniga, D. Ghiran, Farmacia (Bucharest) 47 (1999) 77–84.

[3] D.H. Boschelli, D.T. Connor, D.A. Bornemeier, R.D. Dyer, J.A. Kennedy, P.J. Kuipers, G.C. Okonkwo, D.J. Schrier, C.D. Wright, J. Med. Chem. 36 (1993) 1802–1810.

[4] P.C. Unangst, G.P. Shrum, D.T. Conner, R.D. Dyer, D.J. Schrier, J. Med. Chem. 35 (1992) 3691–3698.

[5] M.D. Mullican, M.W. Wilson, D.T. Conner, C.R. Kostlan, D.J. Shrier, R.D. Dyer, J. Med. Chem. 36 (1993) 1090–1099.

[6] I.P. Singh, A.K. Saxena,K. Shankar, Eur. J.Med.Chem.Chim. Ther. 21 (1986) 267–269.

[7] L.V.G. Nargund, G.R.N. Reddy, V.J. Hariprasad, Pharm. Sci. 83 (1994) 246–248.

[8] D.H. Boschelli, D.T. Connor, C.R. Kostlan, J.B. Kramer, M.D. Mullican, J.C. Sircar, US 5,102,897, April 7, 1992.

[9] A.R. Farghaly, E.D. Clercq, H. El-Kashef, ARKIVOC 10 (2006) 137.

[10] Z.Y. Zhang, M. Li, L. Zhao, Z.M. Li, R.A. Liao, Chin. J. Org. Chem. 13 (1993) 397.

[11] R. Gupta, S. Sudan, V. Mengi, P.L. Kachroo, Indian J. Chem., Sect. B 35 (1996) 621.

[12]. Elson, P. J.; Kvols, L. K.; Vogl, S. E.; Glover, D. J.; Hahn, R. G.; Trump, D. L.; Carbone, P. P.; Earle, J. D.; Davis, T. E. Invest. New Drugs 6,(1988) 97–103.

[13]. Asbury, R. F.; Kramar, A.; Haller, D. G. Am. J. Clin. Oncol. 10, (1987) 380–382.

[14]. Asbury, R. F.; Wilson, J.; Blessing, J. A.; Buchsbaum, H. J.; DiSaia, P. J. Am. J. Clin. Oncol. 9 (1986), 334–336.

[15]. Asbury, R. F.; Blessing, J. A.; McGuire, W. P.; Hanjani, P.; Mortel, R. Am. J. Clin. Oncol. 13 (1990) 13, 39–41.

[16] V. Padmavathi, G. Sudhakar Reddy, A. Padmaja, P. Kondaiah, Ali-Shazia, European J.al of Med. Chem. 44 (2009) 2106–2112.

[17] V. Mathew, J. Keshavayya, V.P. Vaidya, Euro. J. Med. Chem. 41 (2006) 1048–1058.

[18] Malleshappa N. Noolvi, Harun M. Patel, Sarita Kamboj, Swaranjit Singh Cameotra, Arabian Journal of Chemistry 9, (2016) S1283–S1289.

[19] Nuray Ulusoy Gu¨ zeldemirci, Omer Kuçukbasmacı, Erou. J. Med. Chem. 45 (2010) 63–68.

[20] Ying Jun Li, Li Jun Liu, Kun Jin, Yong Ting Xu, Su Qin Sun, Chin. Chem. Let. 21 (2010) 293–296

[21] Kemparaje Gowda, Hassan A. Swarup, Sandhya C. Nagarakere, Shobith Rangappa, Rangappa S. Kanchugarkoppal & Mantelingu Kempegowda, Synthetic Com., 50 (2010) 1528-1544.

[22] Meng-Xue Wei, Lei Feng, Xue-Qiang Li, Xue-Zhang Zhou, Zhi-Hui Shao, Euro. J. Med. Chem. 44 (2009) 3340–3344.

[23] Malleshappa N. Noolvi, Harun M. Patel, Navjot Singh, Andanappa K. Gadad, Swaranjit Singh Cameotra c, Arvind Badiger, Euro. J. Med. Chem. 46 (2011) 4411-4418

[24] Dalip Kumar, N. Maruthi Kumar, Kuei-Hua Chang, Kavita Shah, Euro. J. Med. Chem. 45 (2010) 4664-4668.

[25] Dalip Kumar, N. Maruthi Kumar, Brett Noel, Kavita Shah, Euro. J.Med. Chem. 55 (2012) 432-438.

[26] Mohd. Amir, Harish Kumar, S.A. Javed, Euro. J.Med. Chem. 43 (2008) 2056-2066

[27] N. Chidananda, Boja Poojary, V. Sumangala, N. Suchetha Kumari, Prashanth Shetty, T. Arulmoli, . Euro. J.Med. Chem. 51 (2012) 124-136.

[28] M.F. El Shehry, A.A. Abu-Hashem, E.M. El-Telbani, Euro. J.Med. Chem. 45 (2010) 1906–1911.