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1,3,4-Oxadiazole as an Anticancer Agent

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Abstract

The modern era's fastest-growing disease is cancer, it poses a serious threat to people's lives. For the treatment of various cancers, the FDA has approved a number of medications. However, because of the rise in drug toxicity incidents, there is a continual need for the discovery of novel anti-cancer drugs. Five-membered heterocyclic ring with multifaceted biological action is the 1,3,4-oxadiazole. Their anti-proliferative actions are linked to a number of processes, including the inhibition of kinases, enzymes, and growth factors. Numerous 1,3,4-oxadiazoles have been found to be effective anticancer agents for a variety of cancer cell types. Oxadiazoles may target the NF-kB signaling system to exert their anti-cancer effects, according to certain reports. This study examines the importance of the 1,3,4-oxadiazole ring structure and how it can function as a model for a new anticancer drug. This in-depth analysis focuses on the research on 1,3,4-oxadiazole as a cancer preventative.

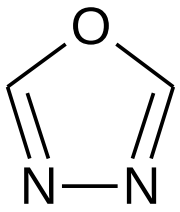
Introduction

Cancer is an unchecked cell proliferation caused by damaged DNA expression. Cancerous cells divide repeatedly, displacing healthy tissue. Cancer or neoplasms can be malignant or benign. The most dangerous side effects of any malignant cell treatment are secondary growths or metastatic disease. We learn about cancer from toxicology on two different fronts. First, toxicological studies shed light on the origin and propensity for the development of cancer. Additionally, numerous cancer therapies have detrimental toxicological side effects. Oftentimes, cancer treatment must strike a balance between the need to protect healthy cells and the need to eradicate dangerous cells.

Oxadiazoles are five-membered heterocyclic compounds with at least one other non-carbon atom and a nitrogen atom inside the ring. It has the chemical formula CH2N2O and is an azole. There are four different isomers of oxadiazole. Pharmaceutical companies use the three isomers, 1,2,4-oxadiazole, 1,2,5-oxadiazole, and 1,3,4-oxadiazole, in a number of products, including butalamine, raltegravir, oxolamine, fasiplon, and pleconaril.

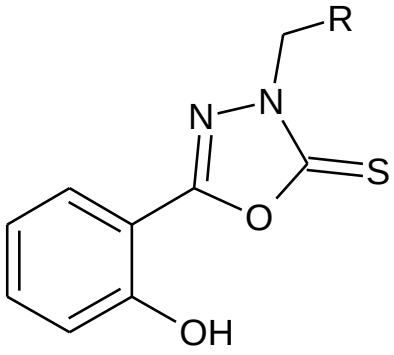
1,3,4-oxadiazole

According to reports, 1,3,4-oxadiazoles have strong anticancer potential against a variety of cancer cell types.



1,3,4-oxadizole

1. Hamdy M. Abdel Rehman et al. (2005) have reported [(5-(2-hydroxyphenyl)-3- substituted-2,3-dihydro-1,3,4-oxadiazole-2-thione], 1 derivatives were synthesized and 13 of them were selected by National Centre Institute (NCI) and evaluated for their in- vitro Anticancer activity. Seven of the investigated compounds **1i, 1j, 1k, 10, 1p, 1q, 1r** displayed high anticancer activity. (1)

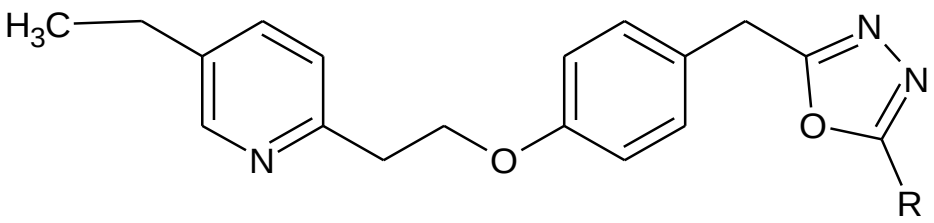


1

Where; R =

1i= -NH-C_6H_4(2Cl); **1j** = -NH-C_6H_4(3-Cl);
1K = -NH-C_6H_4(4-CI); **1o**= -NH-C_6H_4(2-COOH);
1p= -NH-C_6H_4(4-COOH); **1q**= -NH-C_6H_4(4COCH);
1r= -NH-C_6H_3(2-OH-4-COOH);

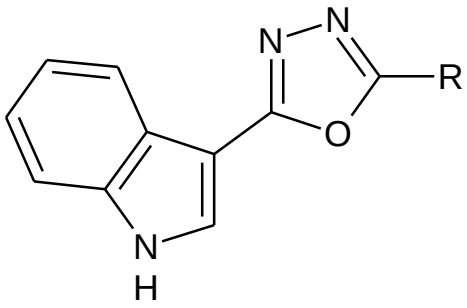
2. Akhilesh Kumar et al. (2008) reported that the substituted oxadiazole derivatives exerting antiproliferative action and growth inhibition on MCF-7 cells through apoptosis induction and that it may have anticancer properties valuable for application in drugs products. The compound **2a-c** exhibited an antiproliferative effect by induction by apoptosis that is associated with caspase 3 activation and dysregulation of Bcl-2 and Bay in MCF-7 cells. The results confirmed that the compounds **2a-c** resulted as agent f chemotherapeutic and cytostatic activity in human breast cancer cells. (2)



2

R = 2a-Phenyl, **2b** = Toluene; **2c** = Pyridyl

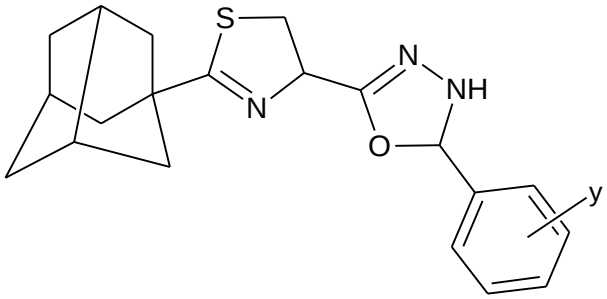
3. Dalip Kumar et al. (2009) have reported novel **3** 5-(3-indolyl)-2-(substituted)-1,3,4- oxadiazoles (**3a, 3b and 3c**) exhibited potent cytotoxicity (IC-1µM) and selectively against human cancer cell lines. Author concluded that compounds **3a, 3b and 3c** exhibited higher specificity and cytotoxicity activity against different cancer cell lines. (3)



3

R= 3a= 4-Pyridyl; **3b** = 3-Pyridil; **3c** = 4-BnO-3-$CH_3OC_6H_3$

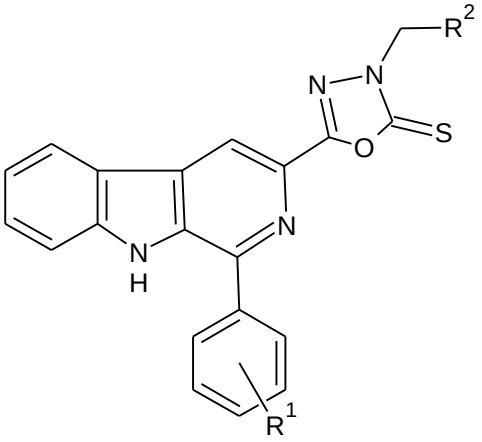
4. Shahid Hameed et al. (2009) have reported new admantylthiazolyl-1,3,4-oxadiazoles (4) derivatives, and the compounds were evaluated for in vitro antiproliferative activity against a large panel of human tumor-derived cell lines. Compounds **4** exhibited activity against human splenic b-lymphoblastoid (WIL-2NS) and human acute B-lymphoblastic leukemia (CRF-SB) cell lines. (4)



4

Y= 4a= 3-Cl

5. Suman Bala et al. (2010) examined the antitumoral activity of various 1,3,4-oxadiazole derivatives and reported heterocyclic 1,3,4-oxadiazole compounds with a variety of biological activities. The author came to the conclusion that a novel series of 3-alkyl-amino (methyl)-2-thioro-1,3,4-oxadiazole-5-yl] The most promising B-carboline compounds showed a wide range of anticancer effectiveness at GI_5o and TGI levels, and 5 of them were discovered to be effective antitumor agents. A new series of 1,3,4-oxadiazole and adamantanyl-1,3-thiozole derivatives, including 2-(2-admantyl-1,3,-thiozole-4-yl)5-(3-substituted phenyl)-1,3,4-oxadiazole-6 bearing various aryl groups, has been created and tested for in-vitro antiproliferative activity against a wide range of human tumor derived cell. (5)



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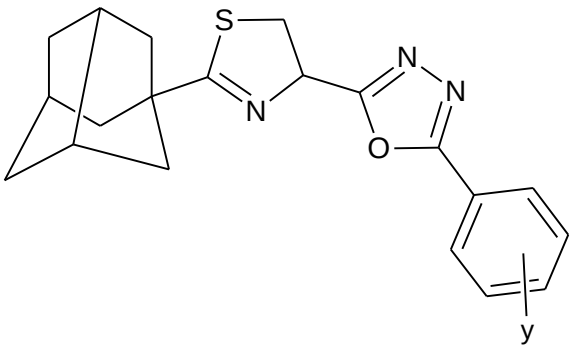
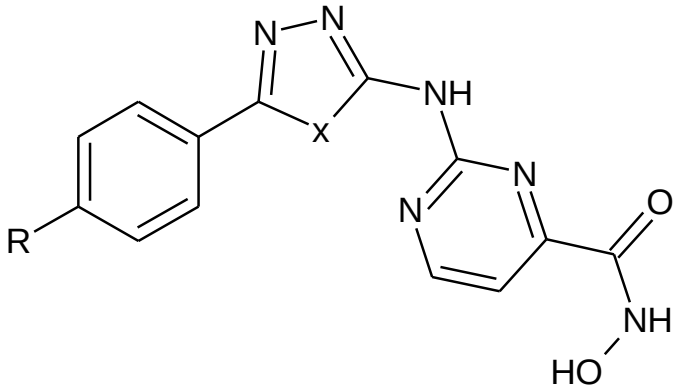


6

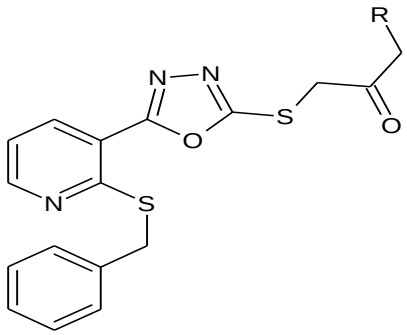
6. Harish Rajak et al. (2011) have reported that the antiproliferative potential of the compounds using in vitro histone deacetylase inhibitory assay and MIT assay, against Ehrlich ascites carcinoma cell in swiss albino mice. The results of the present studying indicates 2,5-disubstituted 1,3,4-oxadiazole thiadiazole (7) as promising surface recognition moiety for development of newer hydroxamic acid based histone deacetylase inhibitor. The result of in vitro studies showed that in oxadiazole series compounds **7a** and **7b** displayed maximum activity. (6)



7

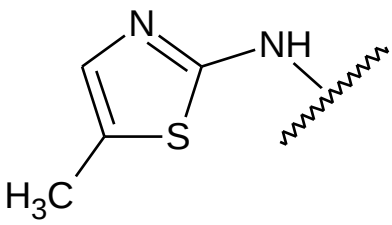
R= 7a= 4-OH; **7b**= 4-OH;
X= 7a= O; **7b**=S;

7. Navin B. Patel et al. (2012) have reported the compound **8a, 8b, 8c, 8d, 8e** and **8f** to be evaluated for their in vitro anticancer activity. Anticancer activity results showed that only compounds **8a** and **8b** have a growth inhibitory (GI)>50%. (7)

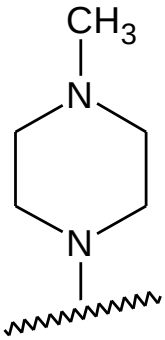


8

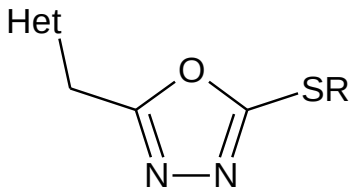
8a=



8b=



8. Momdouh. A. Z. Abu-Zaied et al. (2012) have reported the synthesis of novel 9 1,3,4- oxadiazole-2-thioglycoside derivatives. The synthesized compounds were screened against four human cancer cell lines namely MCF-7 (Breast), HEPG2 (Liver), HCT116 (Colone) and HEP2 (Larynx). Compound **9a** and **9b** appeared as the most active compound displaying potency and specificity higher than standard tamoxifen/5- flurouracil with IC50 less than standard. (8)



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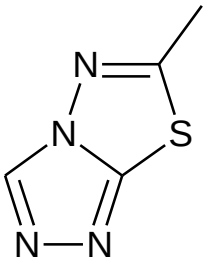
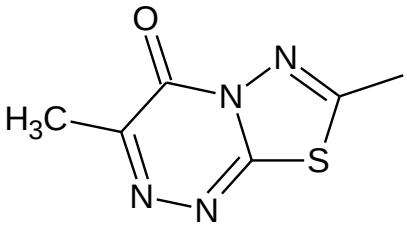
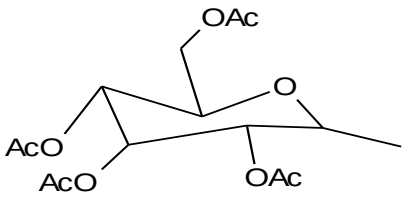


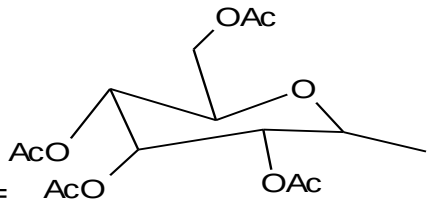
9a; Het=



9b= Het=

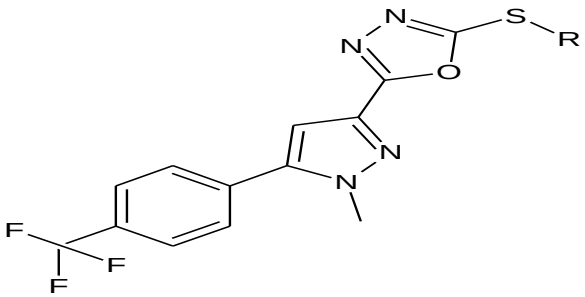


9a; R=



9b; R=

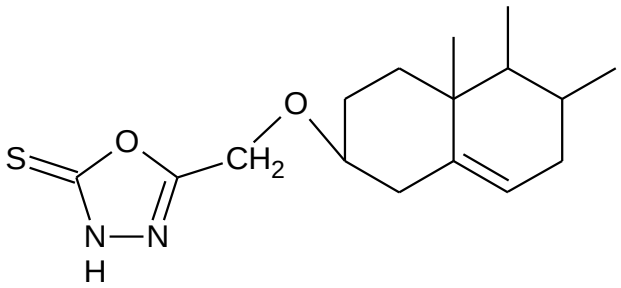
9. Pushpan Puthiyapurayil et al. (2012) have reported a novel 1,3,4-oxadiazole series with a cytotoxic N-methyl-4-(trifluoromethyl) phenyl pyrazole moiety. Amongst tested compound the **10a** was most promising anticancer agent with JC_{50} value of 15.54 µm in MCF-7 cells. The results revealed that **10a** exposure to drug concentration compound **10a** even results in reductions of 1.75 & 2.96 times in IC_{50} values at 45h & 72h. Therefore, conclusive in showing 1,3,4-oxadiazole bearing N-methyl-4(trifluoromethyl) phenyl pyrazole moiety make them certain head molecules for further optimization in the development of novel anticancer agents. (9)



10

10a= R= 4-CF_2-C_6H_4-CH_2

10. Shamusuzzaman et al. (2012) have reported new steroidal oxadiazole, pyrrole and pyrazole derivatives and evaluated for anticancer activity against human leukemia cell line (HL-60) by MTT assay. Compound **11** displayed the promising behavior by showing better anticancer activity. Compounds **12** and **13** also showed moderate to good anticancer activity. (10)



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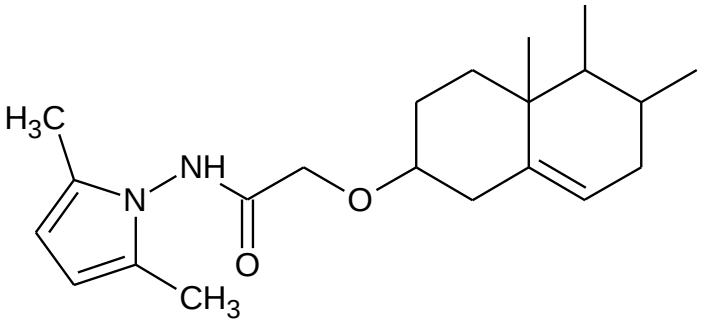

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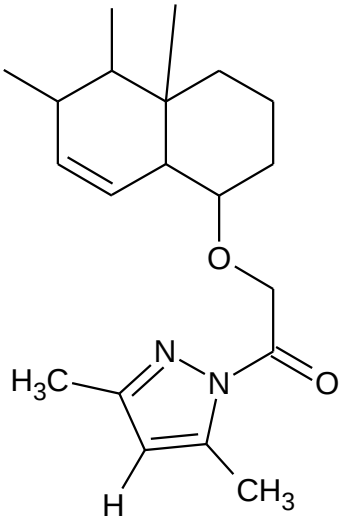
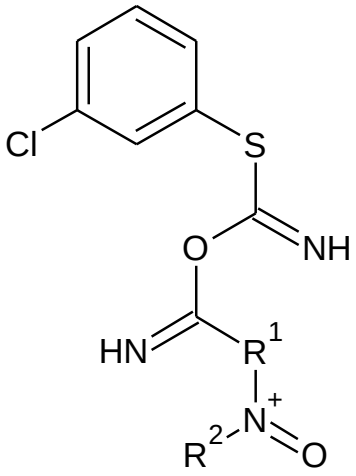


13

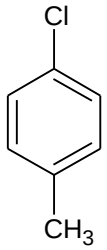
11. Gouging Tu et al. (2013) have reported that the seven compounds displayed inhibitory activities against k562 with the inhibition rate more than 50%. Compound **14a** exhibited the most potent activity against k562 with 85% inhibition ratio & could be used as lead compound to as an antiproliferative drug, look for new 1,3,4-oxadiazole compounds. 5f -$CH_2CH(CH_3)_2$. **14a** exhibited the best inhibitory activity & could be new 1,3,4-oxadiazole derivatives as antiproliferative agents. (11)



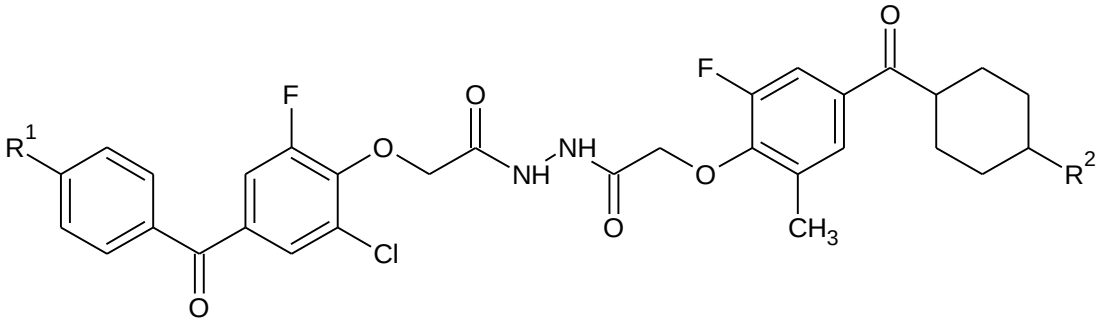
14

R^1= 14a= $CH_2CH(CH_3)_2$;

R^2=14a=



12. H.D. Gurupadaswamy et al. (2013) have reported 2,5-di(4-aryloylarylaryloxymethyl)-1,3,4-oxadiazoles **15a-j** were synthesized & evaluated for antiproliferative activity against human leukemia cell line. Author concluded that **15a** & **15b** with chloro group play dominant role in inhibiting the leukemia cell proliferative. (12)

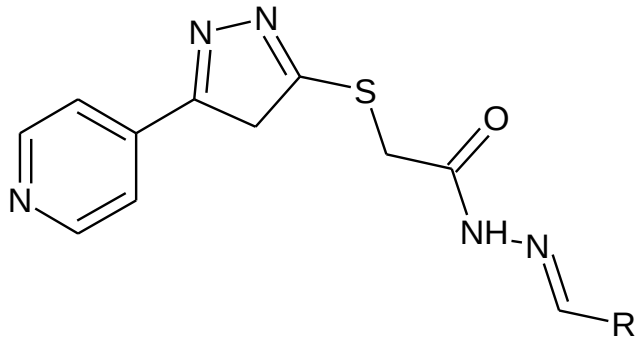


15

15a: R^1 = F; **R^2**=Cl; **15b: R^2**= Cl; **R^2** =Br

13. Fei Zhang et al. (2013) have reported N-benzylidene2-((5-(pyridin04-yl)-1,3,4- oxadiazol-2-yl)thio) acerohydrazide derivatives and evaluated for broad spectrum anticancer activity of compounds, **16d 16a, 16b, 16c** and **16e** against the four cancer cell lines (HEPG2, MCF7, SW1116 and BCG823). Compounds 16s showed the highest anticancer activity against the tested cancer cell lines and most

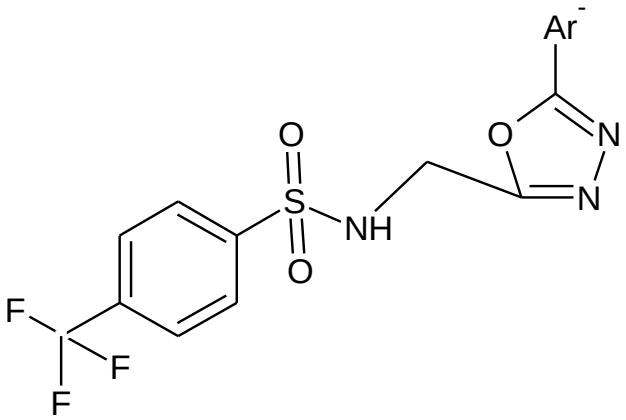
potent telomerase inhibitory activity. 1,3,4-oxadiazole derivatives **16a-16x** were evaluated for their antiproliferative activity against the HEGPG2, MCF7, SW1116 and BCG823. Author concluded that compounds **16a** exhibited the most potent activity against four different original cancer cells (HEPG2, MCF7, SW1116and BCG823) and it has more potent to inhibit telomerase activity. (13)



16

16a=R= 3,4-2HO-C_6H_3

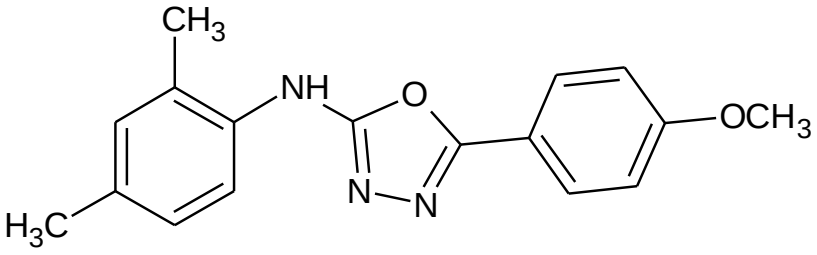
14. Basavapatna n. Prasanna Kumar et al. (2014) have reported 2,5-disubstituted-1,3,4-oxadiazole containing trifluromethyl benzenesulfonamide moiety **17(a-j)** and evaluated for their in vitro antiproliferative effect against four human cancer cell lines (K562, Colo-205, MDA-MB231, IMR-32). Compounds **17a** and **17b** showed good activity on all cell lines, the other compounds in the sequence, however, exhibited moderate activity. Compound **17a** containing Fluro group and **17b** with chloro groups seems to be the most active against all the four cell lines. (14)



17

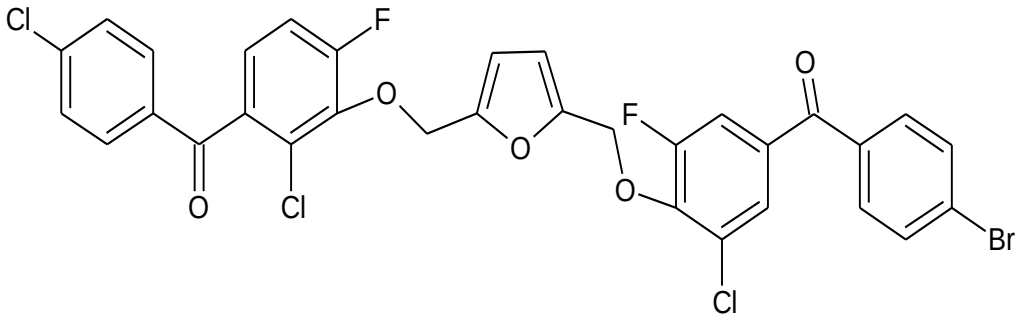
Ar =17a= 4-Flurophenyl; **17b**= 3,4-Dichlorophenyl

15. Mohamed Jawed Ahsan et al. (2014) have reported synthesis and anticancer activity of N-Aryl-5-substituted-1,3,4-oxadiazol-2-amine analogue. In that sixteen compounds were evaluated for their anticancer activity in one dose assay and showed moderate activity on various cell lines. N-(2,4-Dimethylphenyl)-5-(4-methoxyphenyl)-1,3,4- oxadiazol-2-amine **18** showed maximum activity with mean growth percent (GP) of 62.61 and was found to be most sensitive on MDA-MB-435 (melanoma), T-47D (breast cancer)), k-562 (leukemia), HCT-15 (colon cancer) cell lines. (15)



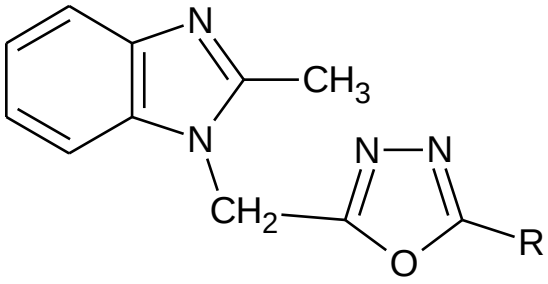
18

16. B.T. Prabhakar et.al (2014) have reported that 2,5-di-(4-aryloylaryloxymethyl)-1,3,4- oxzdiazole (DAO-9) **19** possessed anti-cancer property, it exhibits p53 induced apoptogenesis through caspase-3 mediated endonuclease activity in murine carcinoma. The results concluded that tumor inhibiting activity of DAO-9 is due to activation of the apoptotic signaling cascade, it could result in a specific anti-cancer treatment. (16)

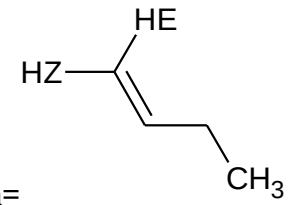


19

17. Mohammad Owais et al. (2014) have reported multistep synthesis of 1-[((5-alkenyl/hydroxyalkenylsubstituted)-1,3,4-oxzdiazol-2-yl]-2-methyl-1H- benzimidazole series and in vitro anti-cancer screening. A novel series of hydroxy and non-hydroxy long chain substituted 1,3,4-oxadiazole moiety bearing 2-methyl-1H- benzimedizole **20(a-d)** have been synthesized from cyclization reaction of 2-(2-1H- benzimedizole-1-yl) acetohydrazide (13) with different unsatured hydroxy and non- hydroxy fatty esters in the presence of phosphorous oxychloride and product obtained in appreciable yield Among the compounds **20(a-d),** compound **20a, 20b and 20c,** showed excellent anticancer activity. (17)

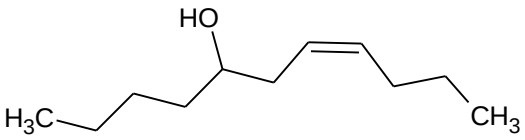


20

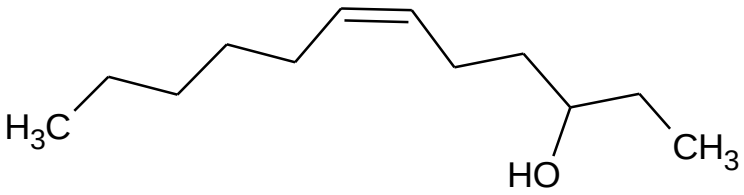


20a=

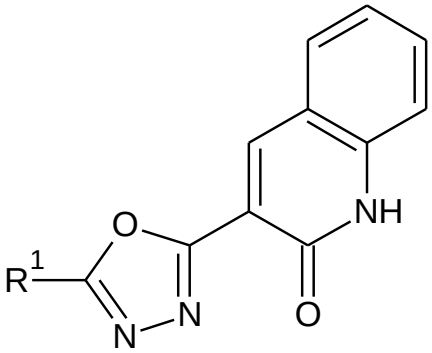
20b=



20c=

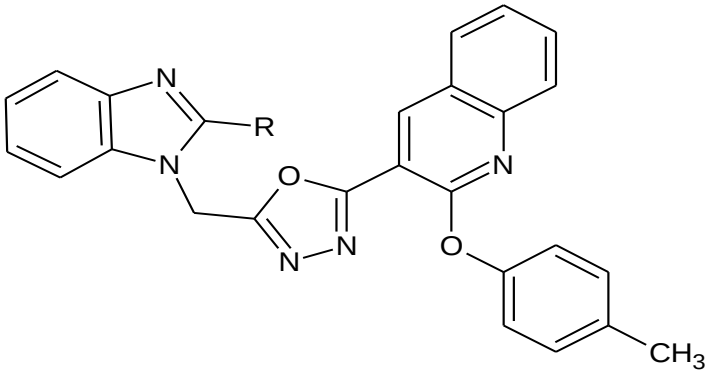


18. A novel 2,5-disubstituted 1,3,4-oxadiazole analogue's synthesis, characterisation, and in vitro anticancer evaluation were reported by Salahuddin et al. in 2014. 11 of the 24 compounds were chosen for evaluation using a single high dosage (10-5M). From those two substances, five doses were tested. The chemical 3-(5-benzyl-1,3,4-oxadiazol-2-yl)quinolin-21(1H)-one and 3-(1-5-(2-phenoxymethyl-benzoimidazol-1-ylmethyl)-3-[1,3,4]oxadiazol-2-yl]-2-p-tolyloxy-quinoline Results were good for 22 (NSC- 776971). The best results were obtained by the colon cancer cell line, with values ranging from 1.41 to 15.8 µM, according to Compound 21's GI50 value ranges. Compound 22 has GI50 values between 0.40 and 14.9 in, with the kidney cancer cell line recording the highest performance with values between 0.40 and 3.91µM. (18)



21

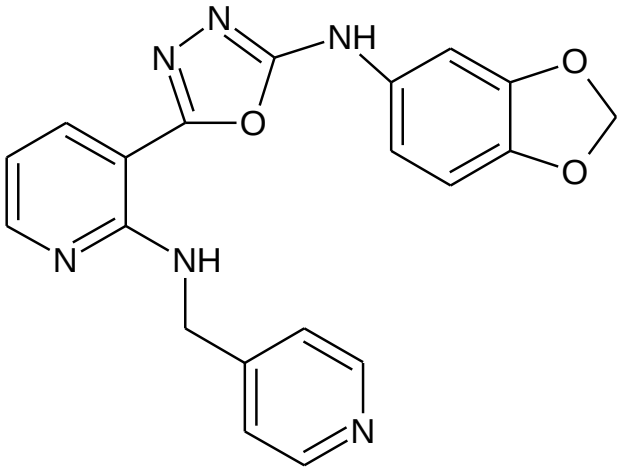
21R = $C_{10}H_7OCH_2$-$C_6H_5CH_2$-, 4-$NO_2C_6H_4$



22

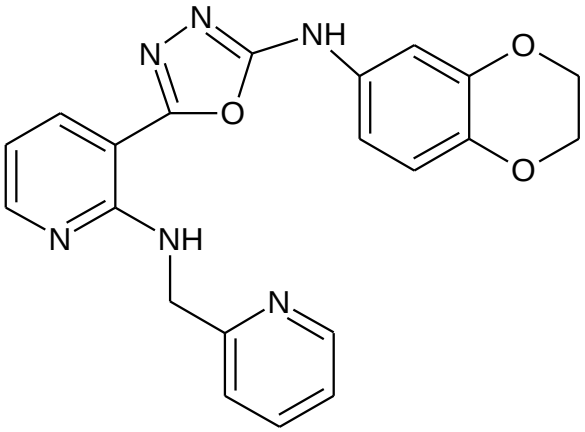
22R= $C_6H_5OCH_2$-, $C_{10}H_7OCH_2$-

19. Ouyangy et al. (2014) synthesized derivatives of oxadiazoles and evaluated for their ability to inhibit tubulin polymerization and arrest mitotic division of tumor cells compound **23** showed potent activity. (19)



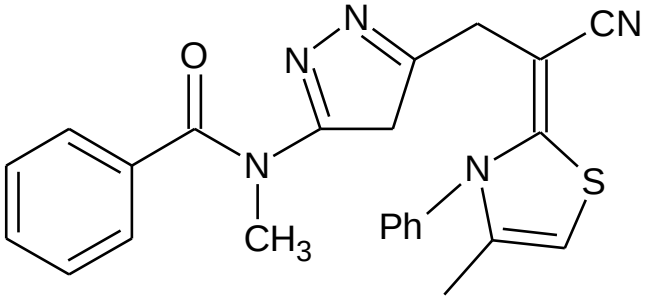
23

20. Tuma et al. (2010) synthesized and evaluated various 1,3,4,- oxadiazoles derivatives as to their ability to inhibit tubulin polymerization and block the mitotic division of tumour cells compound **24** exhibited potent activity. (20)



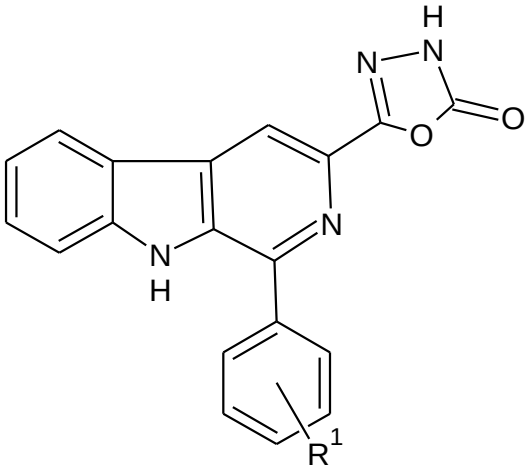
24

21. Samir Bondock et al. (2012) synthesized a new series of 1,3,4-oxadiazoles based hetero cycles **25** the antitumor activity of new compound have been screened. (21)

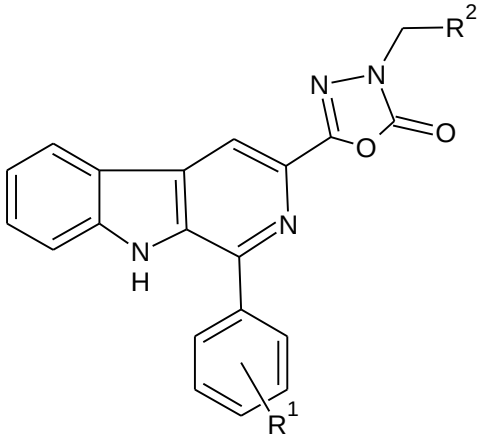


25

22. Maria Helana sarragiotto et al. (2014) reported synthesis an antitumour activity of novel 1-subsitutued pheny13-(2-oxo-1,3,4-oxadiazole-5-yl) B-carboline and their mannich bases. Compound of **26a-e** series with exception of **26a** showed a broad spectrum of antitumor activity with GI 50 values lower than 15 m for five cell line. The derivative **26a** having the N,N-dinie thylamino Phenyl group at c-1 displayed the highest activity with GI50 in the range of 0.67 to 3.20 m. A high selectivity and potent activity were observed for some mannich bases particularly towards resistant ovarian (NCI ADR RES) cell line **27a, 27b, 27c, 27d, 27e**, and ovarian (OVCAR-03) cell line. The assay results for **27a-e** Showed that the introduction of a alkylaminomethyl substituent at N3- position of 2 oxo 1,3,4,-oxadiazolyl group of **26a - c** was detrimental antitumor activity of the most of compound. (22)



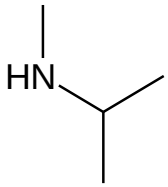
26



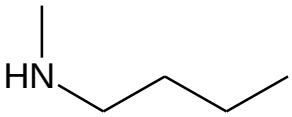
27

R^1= a) H; **b)**p-$N(CH_3)_2$; **c)** o-Cl; **d)** m-NO_2; **e)** p-OH

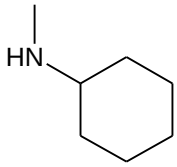
R^2 = 27a=

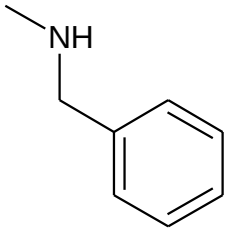


27b=



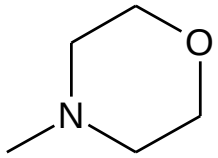
27c=



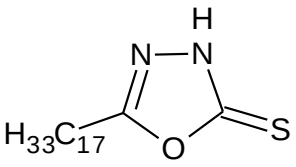


27d=

27e=

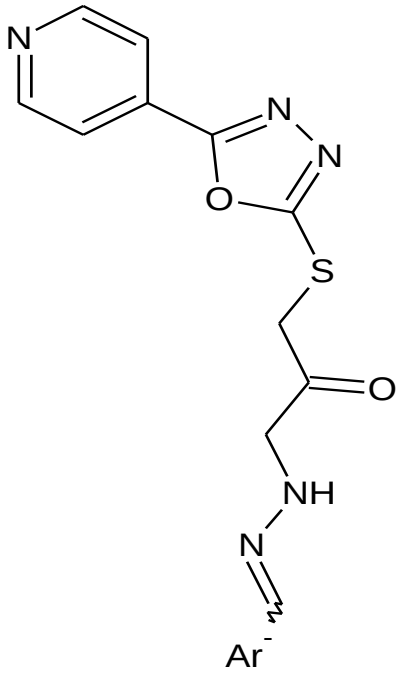


23. Fatma Salah El-Din Mohamed et al. (2014) have reported synthesis evaluation and molecular docking studies of 1,3,4 oxadiazole-2-thiol incorporating fatty acid moiety as antitumor agent. The most potent compound is **28** (E) -5-(heptadec-8-enyl)-1,3,4-oxadiazole-2-thiol **28a** with IC_{50} (2.82 g/ml) and (3.87 g/ml) against breast cell line MCF-7 and liver cell line HepG2 respectively. The present study demonstrate, the significant antitumor and antimicrobial activities of the 5-substituted -1,3,4-oxadiazole -2-thiol (thione) derivatives. (23)



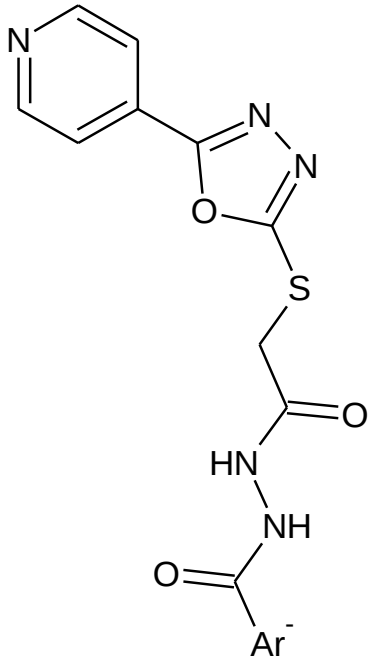
28

24. Aliaa Moh Kamal et al. (2015) had design, synthesized an antitumor activity of novel 5-Pyridyl-1,3,4-oxadiazole against the breast cancer cell line, derivatives MCF-7. On the basis of structure of the highly active reported oxadiazole analogue, various novel compounds were designed. All tested compounds exhibited significant anticancer activity against breast carcinoma cell line MCF-7. Compounds **29** and **30** were more active than the reference drug with IC_{50} values of 0.010µM and 0.012µM respectively. From the study it was concluded that these biologically active compounds with future further investigation could form a potential lead compound for enriching the anticancer libraries since they interacted smoothly with EGRR at the ATP binding site. (24)



29

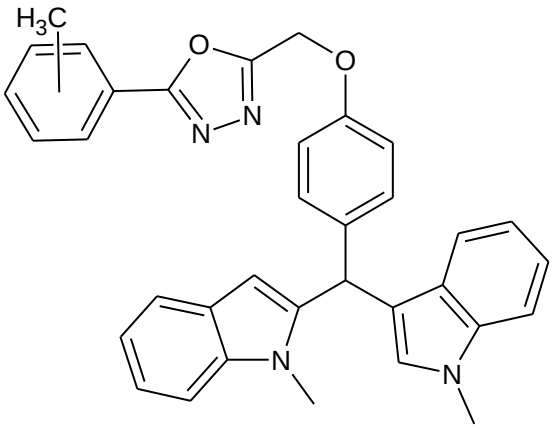
29Ar = 3-indolyl



30

30Ar= 4-ethylphenyl

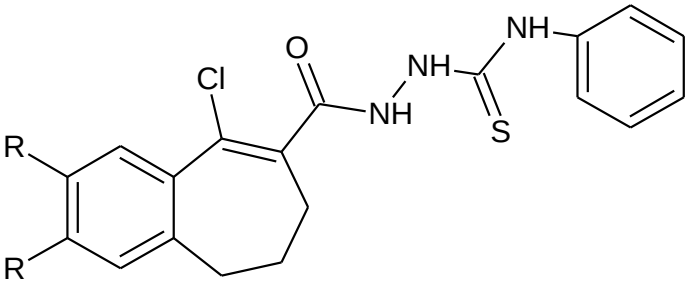
25. Mohamed Jawed Ahsan et al. (2015) have reported 1,3,4-oxadiazole linked bisindole derivatives **31a-j** and evaluated for anticancer activity against four human cancer cell lines (Mcf-7 KB, colo-205, and A-549). Author concluded that most at these new compounds exhibited significant anticancer activity as Compared to the standard drug etoposide. Among them, the Compounds **31a, 31b, 31c, 31d, 31e,** showed a higher activity than etoposide. (25)



31

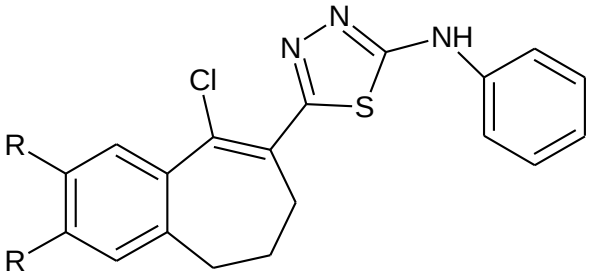
31a) R= H**; 31b) R=** 3,4,5-trimethoxy; **31c) R=** 4-methoxy;
31d) R= 3-methoxy; **31e) R=** 4-nitro

26. Lingaiah Nagarapu et al. (2015) have reported synthesis and evaluation of benzosuberone embedded with 1,3,4-oxadiazole**(32),** 1,3,4-thiadiazole**(33**) and 1,2,4- triazole **(34)** were synthesized and characterized by HNMR, 13CNMR, ESI/LC-MC, HRMS and evaluated for their in vitro anti proliferative activity against four human cancer cell lines(alveolar, pancreatic, breast, and cervical). Among the synthesized compounds **32a, 32b, 33a, 34d,** showed potent anti-proliferative activity with G150 values range of 0.079-0.957uM against four human cancer cell lines. From the study it was revealed that compounds **34d** have shown very close GI50 value 0.079uM as compared with positive control of colchicine against cervical cancer cell. (26)



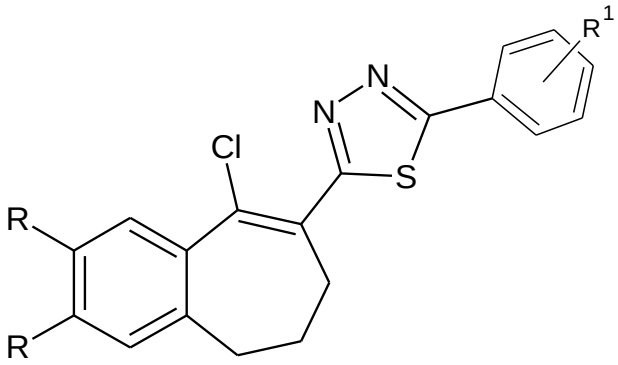
32

32a; R= H
32b; R= CH_3



33

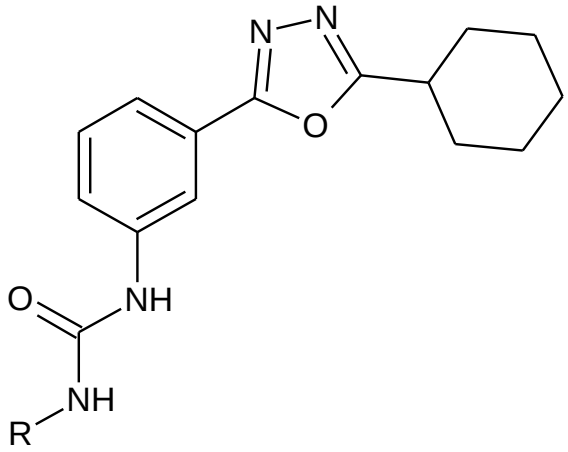
33a; R= H



34

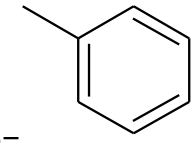
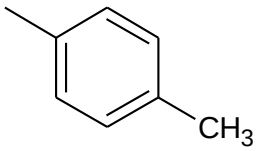
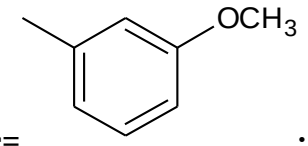
34d= CH_3

27. S. Kavitha et al. (2016) have reported synthesis and biological evaluation of novel 2,5 substitute 1,3,4-oxadiazole derivatives. The Compound **35a, 35b** and **35c** of 1,3,4-oxadiazole derivatives showed significant activity against MCF-7 and Hela cells. Result revealed that introduction of urea sulphonamide group in oxadiazole enhances activities. Considering the outcomes above, the current research is considered to synthesis 1,3,4-oxadiazole derivatives for their improves the biological activity. (27)

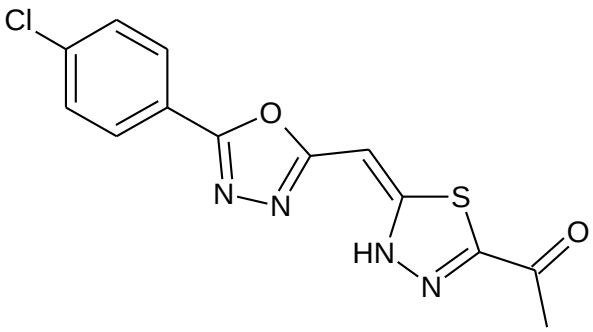


35

R=

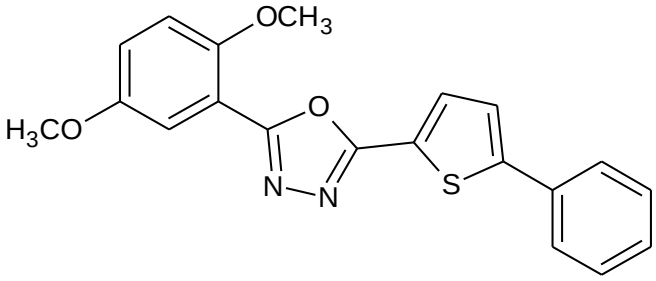
35a=  **;** **35b=**  **;** **35c=**  **;**

28. Wael A.EL-Sayed et al. (2017) have reported new 1-thia-4-azaspiro[4.5] decane and their derivatives thiozolopyrimidine and 1,3,4-thiadiazole thioglycosides and evaluated for anticancer activity against the cell culture of HepG-2, PC-3 (human prostate adino carcinoma) and HCT116 (colorectal carcinoma) cell lines. Author concluded that number of compound showed moderate to high anticancer activity and **36** compound showed highest anticancer activity. (28)

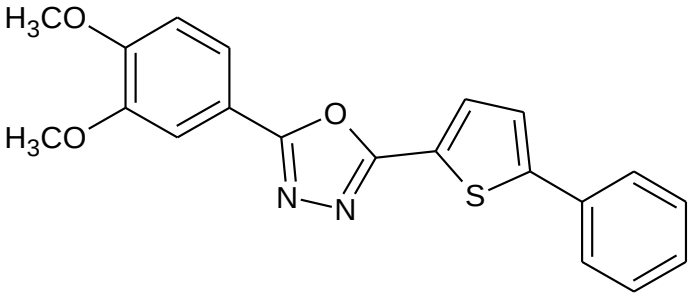


36

29. The creation of 2,5-Disubstituted 1,3,4-oxadiazole compounds and their assessment as anticancer agents have been described by Navin Polkam et al.. A series of regioisomeric (2,5-dimethoxybenzoic acid, geriatric acid) analogues were prepared by swapping the carboxylic moiety to its oxadiazole bioisostere and have been screened for in vitro anticancer studies by using MTT colorimetric assay. Among the screened compounds, **37**(2-(2,5-dimethoxyphenyl)-5-(5-phenylthiophen-2-yl)-1,3,4-oxadiazole) demonstrated superior activity against MDA231 cells. Product **37** displayed excellent activity against DU145, HCT15 and **38** (2-(2,5-dimethoxyphenyl)-5-(5-phenylthiophen-2-yl)-1,3,4-oxadiazole) against MDA231calls. Analogue **37** have come out to be the best anticancer agents. (29)

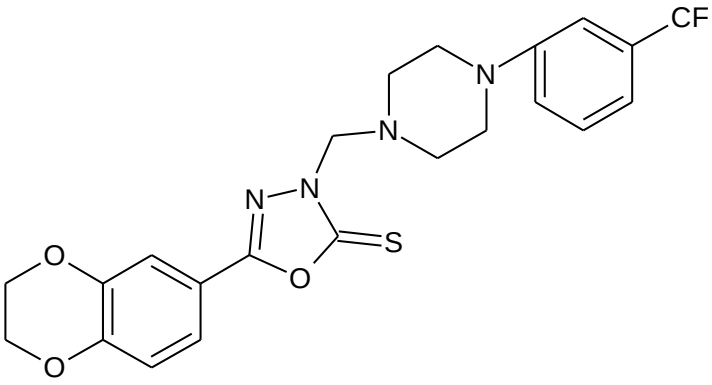


37



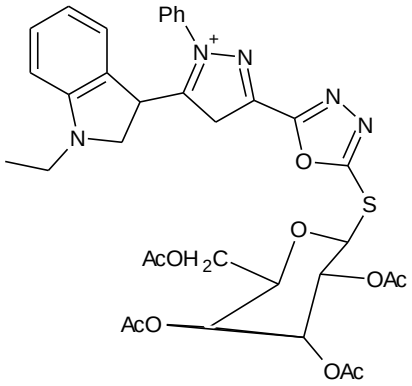
38

30. Juan Sun and Shen-Zhen Ren (2017) have reported the synthesis of series of novel 1,3,4-oxadiazole-2(3H)-thione derivatives containing piperazine skeleton were designed and biological activities of these compounds against four different cancer cells (HepG2, Hela, SW1116, BGC823). The result showed that compound **39** possessed excellent antitumor activity compared with the 5-Flurouracil widely used in cancer treatment, compound **39** exhibit the most potent FAK inhibitory activity with IC_{50} of 0.78μm. It could conclude that compound **39** might be a potential inhibitor of FAK. (30)

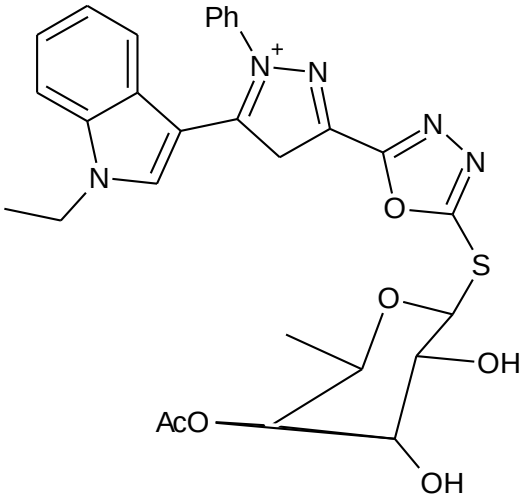


39

31. Wael A.E-Sayed et al (2017) reported novel [(Indolyl)pyrazolyl)]-1,3,4-oxadiazole thioglycosides and analogs of acyclic nucleosides: production and anticancer efficacy. The anticancer activity of newly synthesized compound was studied against colorectal carcinoma (HCT116), breast pounds was studied adenocaranoma (MCF) and prostate: cancer (PC3) human tumor cell lines and a number of compound showed moderate to high activities. The activity results of tested compound against breast Mcf-1 cancer cells revealed that compound **40** and **41** was the most active among this series. It is clear from result that compound **41** was selective on PC3. The anticancer and docking results indicates the importance of attachment of sugar moieties to oxadiazole ring system in number of most active compound. (31)

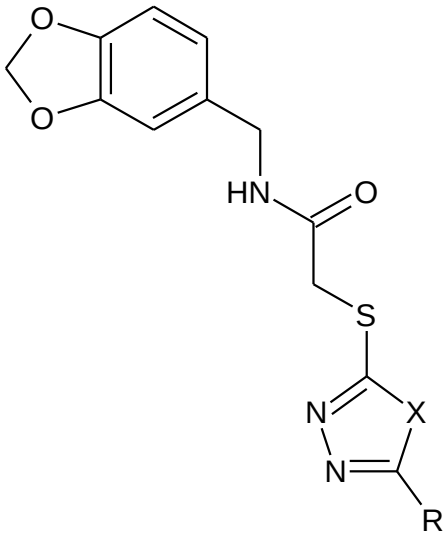


40



41

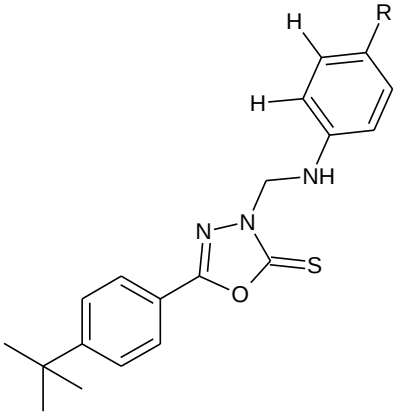
32. Ahmet Ozdemir et al. (2017) have reported the compound were evaluated for their the inhibitory effects on MMPs, N(1,3-Benzodioxol-5-ylmethyl)-2-([S-(((5,6,7,8- tetrahydronaphthalen-2-yl)oxy)methyl)-1,3,4-oxadiazol-2-yl]thio) acetamide **42** and N-(1,3-benzodioxol-5-ylmethyl)-2-[(5-phenyl-1,3,4-oxadiazol-2yl)thiojacetamide **42b** Compound **42a** and **42b** were also the most effective MMP-9 inhibitor in series. Author concluded that the compound **a** and **b** was found to be the most promising anticancer agent against A549 cell line. (32)



42

R=42 a= ((5,6,7,8-Tetrahydronaphthalen-2-yl)oxy)methyl;
43 b= Phenyl
X= 43a=O; **43b**=O

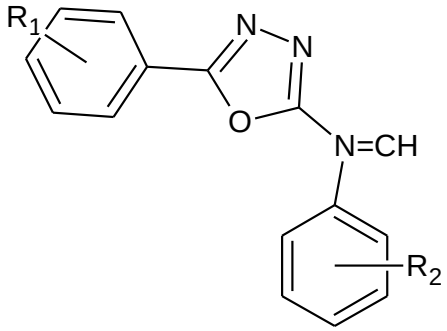
33. Nalini yadav et al.(2017) have reported that the compound **43a** and **48b** showed promising cytotoxicity against Hela cell line, **43a** and **43b** successfully inhibited cell cycle progression and displayed cell death in Hela cell. Author concluded that the two compounds **43a** and **43b** showed best apoptotic activity on Hela cervical cancer cell, promising compound **43a** and **43b** may be considered as a suitable lead for further development of anticancer drug in future. (33)



43

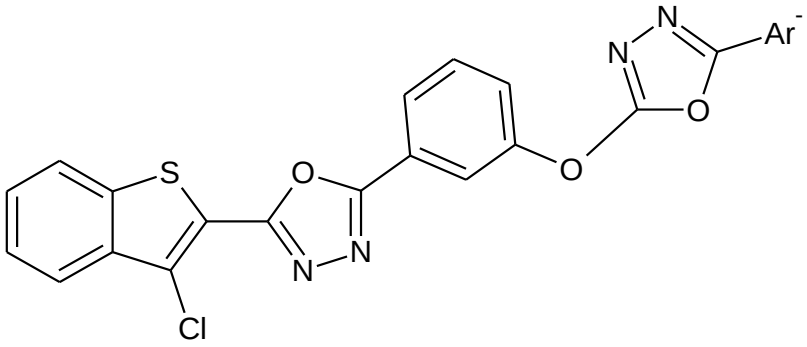
43a= R = NO_2
43b= R= F

34. Partha Pratim Roy et al (2017) have reported synthesis and evaluation of anticancer activity of 1,3,4-oxadiazole derivatives against Ehrlich Ascites Carcinoma bearing mice and their correlation with histopathology of liver. Compound **44** remarkably decrease the body weight tumour volume, viable cell count, increase in tumour weight (%) inhibition, lifespan, non-viable cell count of EAC tumour bearing mice when compared with the drug treated groups (III-X). Among all tested compound compound **44a** exhibit highest tumour weight inhibition 73.15% and tumour cell count inhibition 35 65.07% at the dose of 20mg/kg. (34)



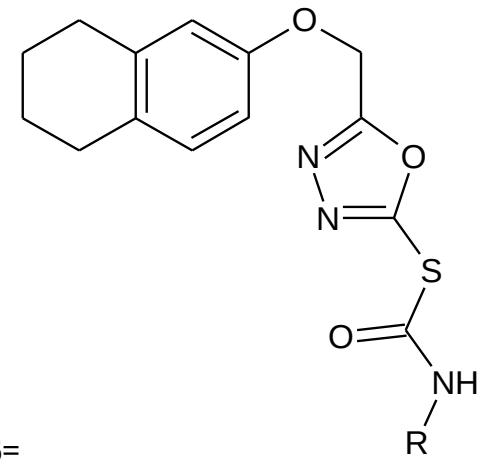
45

35. Chakrabhavi Dhananjaya Mohan, et al. (2018) have reported novel 1,3,4-oxadiazole **(45a)** induces anticancer activity by targeting NF-KB in Hepatocellular carcinoma cells. Several 1,3,4-oxadiazoles have been reported to possess good anticancer potential gainst various types of cancer cells. Some of the reports also suggested that oxadiazole possibly target NF-KB signalling pathway to induce their anticancer activity. Author concluded that compound analogs how cytotoxic effect against hepatocellular carcinoma (HCC) cells, and the lead compound (**45)** 2-(3-chorobenzo[b]thiophen-2-yl)-5-(3-methoxyphenyl) good antiproliferative efficacy. (35)

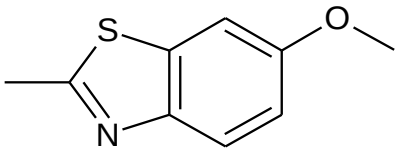


45

36. Mehlika dilek altintop et al. (2018) have reported thiazole/Benzothiazol-based 1,3,4-oxadiazole **46** derivatives where synthesized and evaluated for their cytotoxic effect on A549, C6 and NIH/3T3 cell lines. Compound **46a, 46b** and **46c** are evaluated for their effect on apoptosis caspase-3 activation Akt, FAK, MMP and ultra structural morphological changes. Compound **46b** was identified as most promising anticancer agent due to its significant anti-tumor effect on both cancer cell lines. (36)

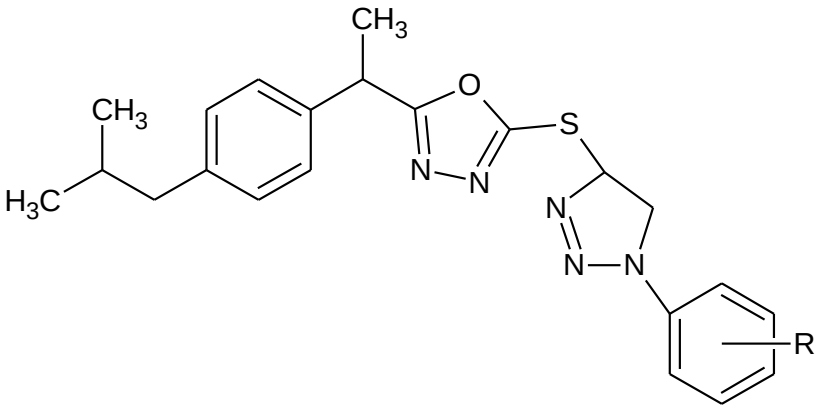


46=

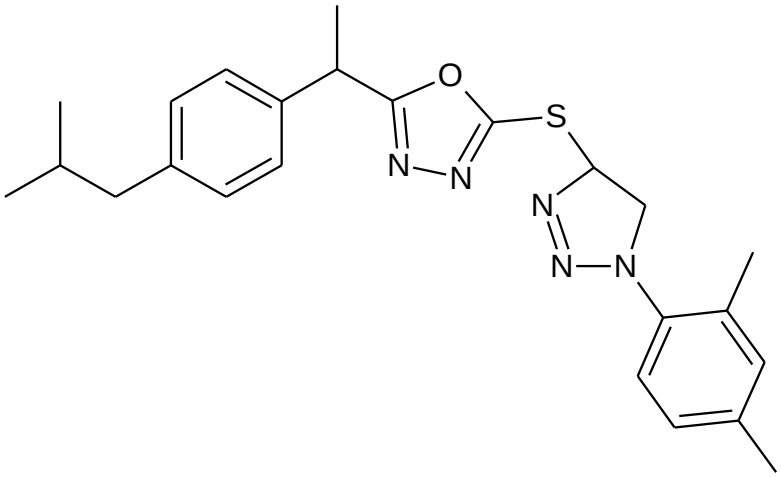


46b=

37. Jaya Shree Anireddy et al. (2018) have reported new Ibuprofen-1,3,4-oxadiazole-1,2,3- triazole Hybrids and evaluated for anticancer activity **(47)** 2-(((1-(2,4-dimethlphenyl)- 5-(1-(4isobutylphenyl)ethyl)-1,3,4-oxadiazole **(47a)** exhibited anticancer activity with IC_{50} at 27.50 and 31.03 µg/ml against Hela and MCF-7 cell lines, respectively. Author concluded that compound **47a** exhibited best anticancer activity against Hela and MCF- 7 cancer cell lines. (37)

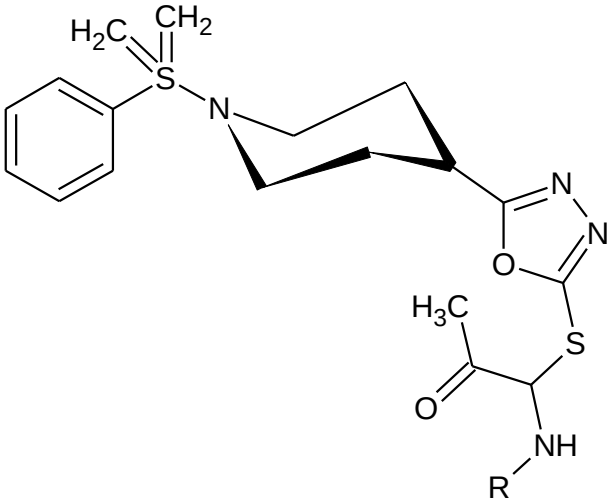


47

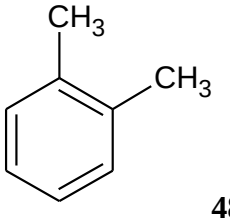


47a=

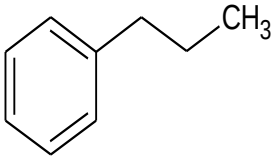
38. Aziz-ur-Rehman (2018) reported synthesis of some new propanamide derivatives bearing 4-piperidinyl-1,3,4-oxadiazole, and their evaluation for anticancer activity. Compound **48a-i** was confirmed by spectroscopic techniques like (H-NMR), (C-NMR) and (EL-MS). Compound **48a, 48b**, **48c** show best anticancer potential. All the compound were screened for their anticancer activity and were found to possess moderate to high anticancer potential. Compound **48a, 48b, 48c** having high anticancer potential. The ascending order of anticancer activity of compound **48a**, **48b, 48c** was due to different substituted alkyl group at aromatic ring of propanamides. Compound **48a** with impressive good inhibition requires further studies for possible development of addition to existing anticancer agent in pharmaceutical industry. (38)



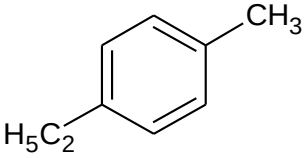
48



48a=R=

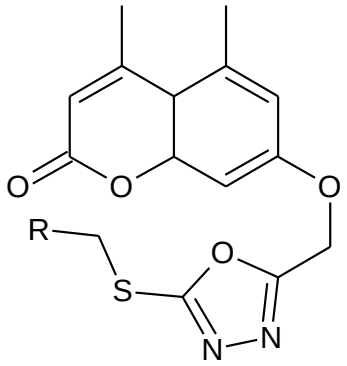


48b=R=



48c=R=

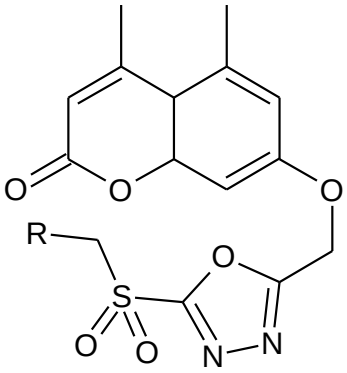
39. Sanjeev Dhawan et al. (2018) reported synthesis, computational studies and antiproliferative activities of coumarin-tagged 1,3,4-oxadiazole **(49)** conjugates against MDa-MB231 and MCF-7 human breast cancer cell. The evaluation studies revealed that compound **49** was the most potent molecule with an IC_{50} value of <5µm against the MCF-7 cell. The cytotoxicity efficacy of all synthesized compound were tested on two different BC cell lines. Compound **50** containing di-substituted electron with drawing chorine group at 2-4 position of benzyl ring was found to 1.4 times more active against MCF-7 cell line compared to tamoxifen. To prevent recurrence of disease tamoxifen is the gold standard therapy administered to breast cancer cell patient.



49

49= R: 2,4-Di-Cl-Ph$(CH_2)_1$

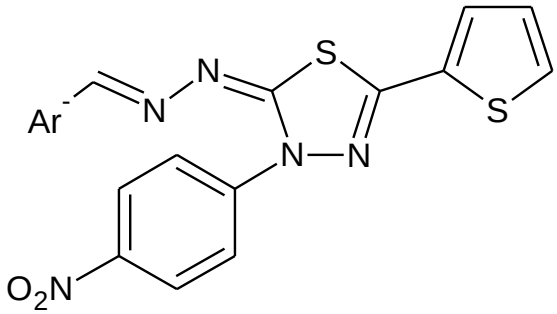
Interestingly compound **50a** and **50b** showed a similar trend with lower inhibitory concentration IC_{50} in estrogen negative (ER-) cell than estrogen positive (ER+) cell. (39)



50

50a R= $CH_3(CH_2)_1$; **50b-R**= $ph(CH_2)_1$

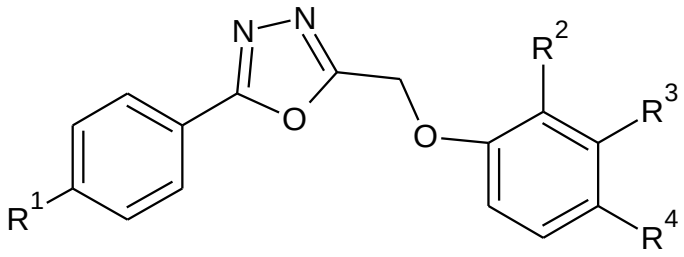
40. Sobhi M Gomha et al. (2018) have reported 5-(thiophen-2-yl)-1,3,4-thiadiazole derivaties and evaluated for compound **51a** has promising activities against HepG-2 and A-549 cell lines. Compound **51a** was investigated against 2 carcinoma cell lines. cisplantin, a standard anticancer medication, was compared to human hepatocellular carcinoma and lung cancer cell lines using colorimetric MTT assay. Author concluded that new series of 1,3,4,-thiadiazole derivatives show in vitro antitumor activity against human lung cancer cell lines and human hepatocellular carcinoma cell lines. (40)



51

51a=Ar = 4-MeOCH

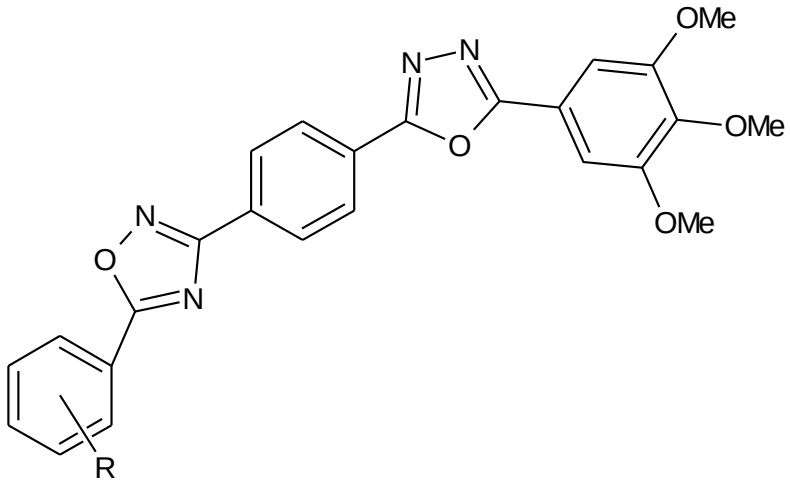
41. K. Lakshmithendral et al. (2019) have reported a series of 2-(phenoxymethyl)-5-phenyl-1,3,4-oxadiazole. **52 (a-o)** were synthesize and demonstrated significant anti- breast cancer activities. In particular, the compound **52a** and **52b** were shown as the most anticipating among the series against MCF-7 and MDA-MB-453 cell lines. (41)



52

	R^1	R^2	R^3	R^4		R^1	R^2	R^3	R^4
52a=	H	OCH_3	H	H	**52b=**	OCH_3	OCH_3	H	H

42. Ravikumar Polothi et al. (2019) have reported 1,2,4-oxadiazole linked 1,2,3-oxadiazole derivatives **53 (a-j)** evaluated for their in vitro anticancer activity against three human cancer cell line (lung, breast). The IC_{50} values for compounds **53a, 53b, 53c,** and **53d** against three human cancer cell lines ranged from 0.34 ± 0.025 to 2.45 ± 0.23 µm, indicating strong anticancer activity. The majority of the substances significantly reduced the growth of three distinct human cancer cell lines, MCF-7, A459, and MDA-MB231. Compounds **53a, 53b, 53c and 53d** were showed potent anticancer activity. (42)

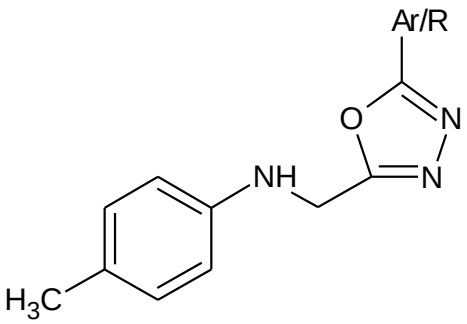


53

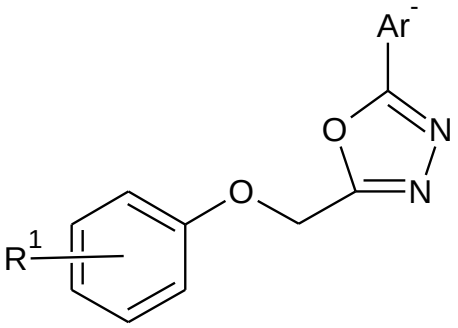
53a: R=3,4,5-trimethoxy;
53b: R= 4-nitro;
53c: R= 3-nitro;
53d: R= 4-cyano;

43. Mohamed Jawed Ahsan et al. (2018) have reported 1,3,4-oxadiazole analogues. They were reported as potent cytotoxic agents and tubulin inhibitors compounds for 2- (5- ([4-chloro, phenyl) amino] methyl) -1,3,4-oxadiazol-2-yl) phenol **54** and 2-[(2,4- dichlorophenony) methyl] -5-(3,4-

dimethoxyphenyl)-1,3,4-oxadiazole 56 showed maximum cytotoxicity with the mean percent growth inhibitions (GI_S). Author concluded that compound **55** showed superior activity than the Imatinib and Gefitinib over 42 and 28 cell lines. Compound **55** showed higher selectivity towards the renal cancer cell lines. (43)

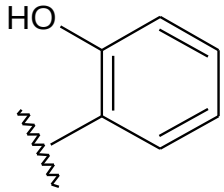


54

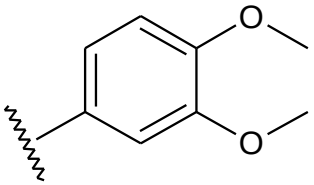


55

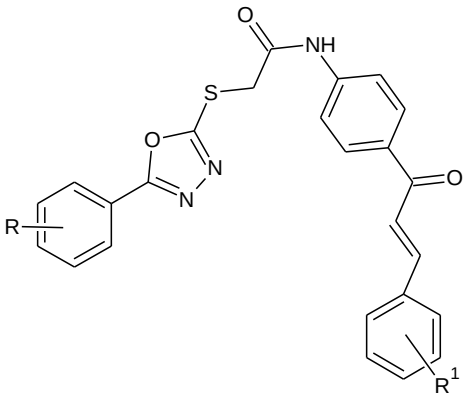
54; Ar=



55; R^1= 2,4,-Cl_2; Ar=



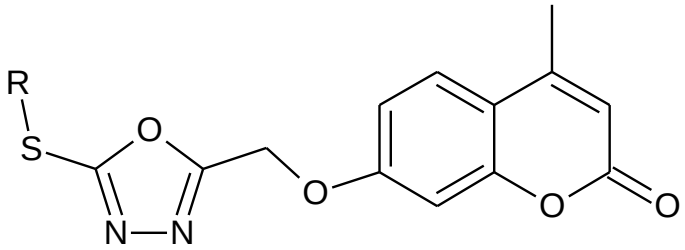
44. Mohamed Abdel Aziz et al. (2019) have reported a new series of **(56)** 1,3,4- oxadiazole/chalcone hybrids was designed, synthesized, identified with different spectroscope methods have been biologically tested as IL-6, SRC, and EGFR inhibitors.. The synthesized compounds showed promising anticancer activity, particularly against leukemia with 56c being the most potent. Compound **56c** showed the strongest cytotoxic activity with IC_{50} against k-562, Jurkat and KG-la leukemia cell lines. Author concluded that compounds **56a 56b** and **56c** showed the highest cytotoxicity activity against leukemia cell lines K-562. Compound **56c** exhibited the highest activities against human cancer cells. (44)



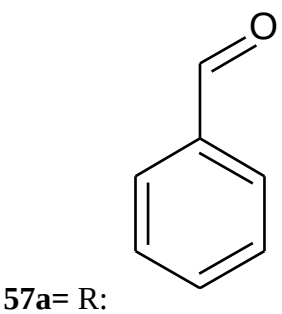
56

Compound	R	R^1
56a	H	H
56b	4-OCH_3	3,4,5-tri-OCH_3
56c	3,4,5-tri-OCH_3	4-OCH_3

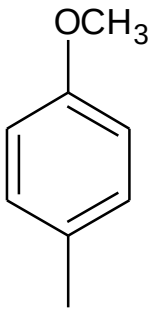
45. Nerella Sridhar Goud et al. (2019) have reported coumarin-1,3,4-Oxadiazole hybrids as selective carbonic anhydrase IX and XII inhibitors and evaluated for their inhibitory activity against the four physiologically relevant human carbonic anhydrase (hCA EC4.2.1.1) isoforms CAI, CAIL, CA IX and CA XII. According to the CA inhibition results, the coumarin 1,3,4-oxadiazole derivatives **57** selectively inhibited CA IX and CA XII, two isoforms that are linked to tumors, as opposed to CA I and II isoforms. Compounds **57a** and **57b** may therefore provide prospective leads for the creation of selective anticancer drugs because they display of hCA IX and XII. The author came to the conclusion that hybrids of coumarin 1,3,4-oxadiazole are intended to target the hCA IX and XII transmembrane a unique mode of action through the inhibition tumor-associated isoforms. Four hCA isoforms, including the cytosolic isoforms hCA I and II and the transmembrane tumor-associated isoforms hCA IX and XII, were the targets of the target compounds' screening. (45)



57

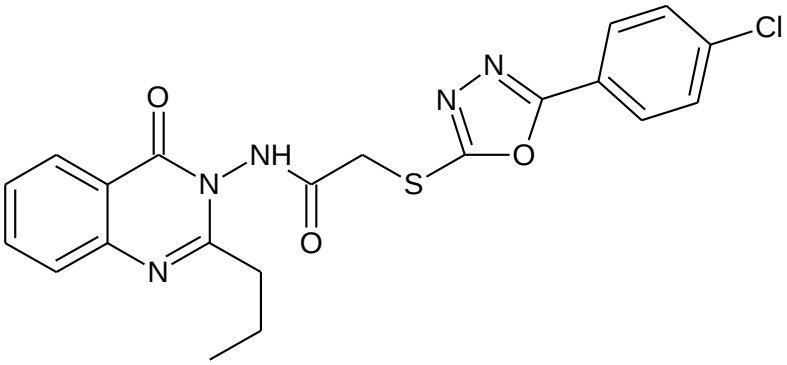


57a= R:



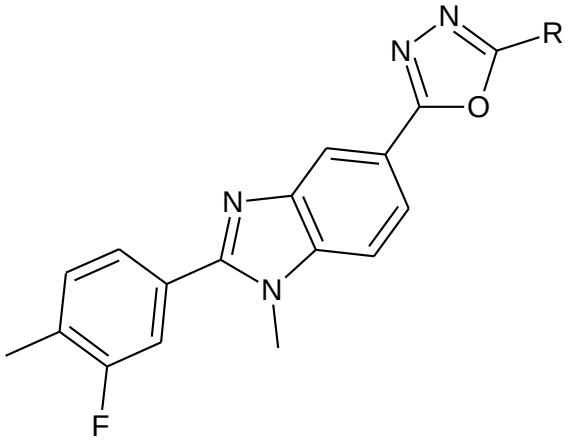
57b= R:

46. Elham Jafari et al. (2019) have reported compound 2-(5-(4-chloro-phenyl)-1,3,4-Oxadizol-2-ylthio) N-(4-oxo-2-propyl quinazolin) 3 (4H) acetamide **(58)** exhibited remarkable cytotoxic activity at 10 and 100 µm against HeLa cell line. Author concluded that compound **58** showed cytotoxicity against HeLa and MCF-7 cell lines and highest cytotoxic activities with the IC_{50} value of 7.52 um against HeLa cell line. Substitution of propyl group at 2 position of quinazolinone improved the cytotoxic activity against HeLa possibly due to electronic effect. (46)

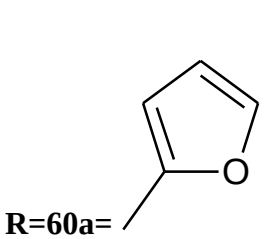


58

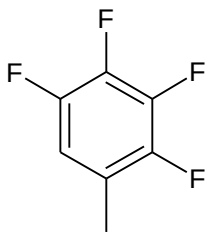
47. Swamy Sreenivasa et al. (2019) have reported a new series of (Benzo [d]imidazole-5-yl)-5-(substituted)-1,3,4-Oxadiazoles **(59).** The author revealed that the compounds **59a** and **59b** of the series emerged as potent anticancer agents against A375 melanoma cancer cell line with IC_{50} 47.06 µm. In silico studies also revealed that compounds **59a** and **59b** showed highest interaction with 20H, protein of VEGF12-2 Tyrosine Kinase. The author concluded that 1,3,4-oxadiazole linked tetrafluro substituted benzene rings have powerful anticancer properties. Compound **59a** and **59b** are found to be more selective towards melanoma cancer than the breast cancer cell lines. (47)



59

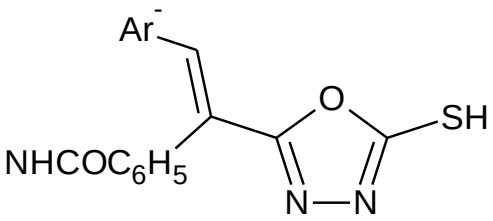


R=60a=



R=59b=

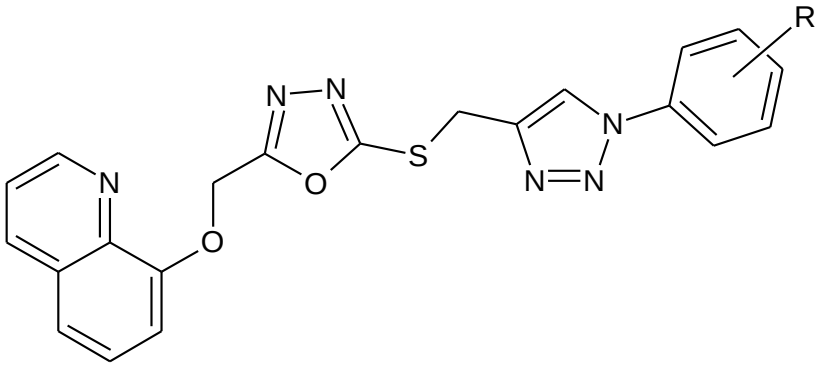
48. Shaheen Begum et al. (2019) have reported compound 60a and 60b showed cytotoxicity against MCF-7, HeLa, and A549 cell lines. Compound (3,4,5-trimethoxy phenyl analog) **(60a)** exhibited potent cytotoxicity. The cytotoxicity of 60a was discernible with IC_{50} of 17.12 µm, against MCF 7 cell lines which is almost comparable to the standard anticancer agent cisplastin (IC_{50} 12.6 µm). (48)



60

61a= Ar= 3,4,5-$(OCH_3)_3C_6H_2$

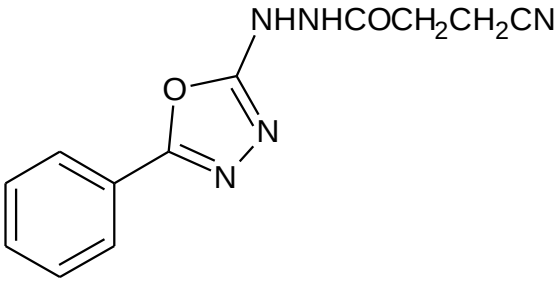
49. Quinoline-Based 1,3,4-Oxadiazole-1,2,3-triazole conjugates were described by Mohammad Abid et al. (2019). A normal Chinese hamster ovary (CHO) cell line was used to investigate the toxicity of compounds that showed moderate to good activity in cancer cells, i.e. 61(a-e). The author came to the conclusion that among a panel of human cancer cell lines, compound 61a was shown to be a lead with strong anticancer activity in A-549 cells. (49)



61

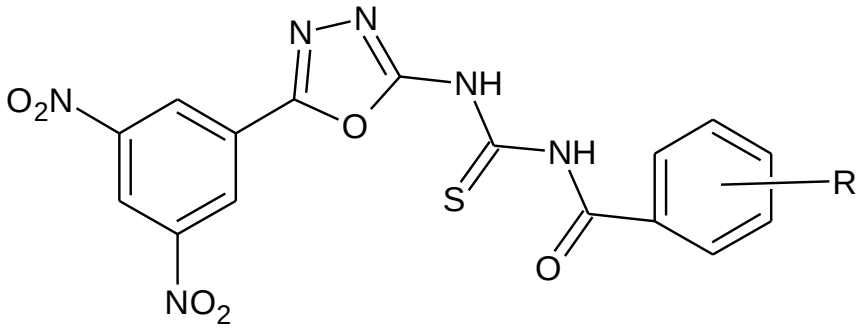
61a= R= O-Cl

50. Lmyaa A. Dahham et al. (2020) have reported synthesis, characterization & anticancer activity studies of new N-(5-phenyl-1,3,4, oxadiazole-2-yl) propane hydrazide (62) and its transition metal complexes. A new ligand of N(5-phenyl-1,3,4-oxadiazole) and it's Cu(II), Co(II) & Ni(II) complexes were synthesized. Cancer cell line of ovaries was exhibited for concentration ranging from (6.25,100 microgram/ml) to both the (L) and the complex [Ni (L) C12] for 24 hr & 37 degree Celsius the study showed that there is a significant effect of these compound when used on ovarian cancer cell called line SKO V-3 cells. The study show the effect of ligand (L) on growth cell of ovarian cancer, where the lowest rate of cell growth was found at the lowest concentration 6.25 µg/ml and the highest inhibition rate at concentration 100µg/ml. It also note that ligand has less toxic activity against cancer cell of ovarian cancer cell line (SKO V-3 cells) than the effectiveness of nickel complex(II). The results also showed that the type and concentration of the compound used are two important factors in determining the rate of cell inhibition, as it was found that the increase in the concentration of both the ligand and its complex of nickel (II) increases the rate of inhibition of cell growth of cancerous lines. (50)



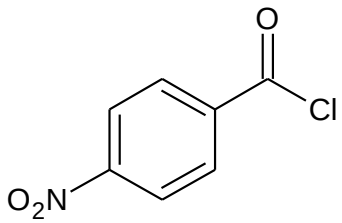
62

51. Akshay R. Yadav et al. (2020) have reported new series of novel N-substituted 1,3,4-oxadiazole**(63)** derivatives, and evaluated for anticancer activity on MCF7 cell line. Further the compounds **63(a-c)** has been moderate tested for its anticancer activity and out of these all, compound **63a** showed most notable anticancer activity against breast cancer cell line. Author concluded that series of novel 1,3,4-oxadiazole derivatives has anticancer activity highlighted that tested compound **63a** exhibited significant activity by tryphan blue exclusion method. (51)

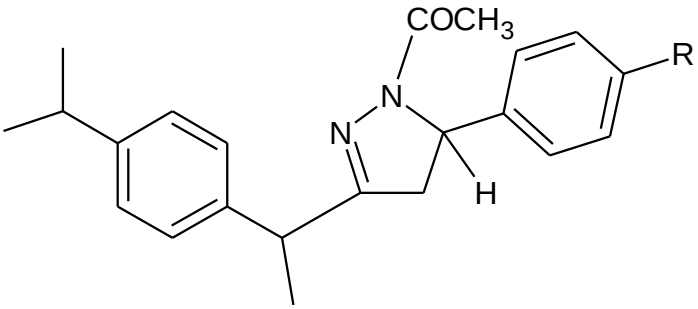


63

63a=



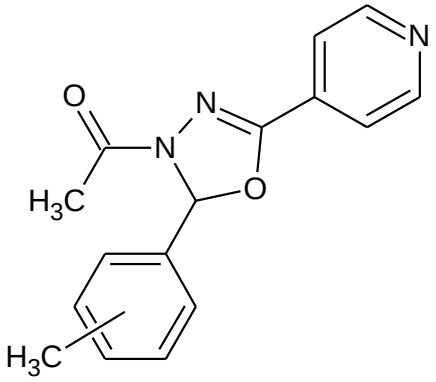
52. Leaqaa A Raheem Alrubaie et al. (2020) have reported Ibuprofen N-acyl-1,3,4-oxadiazole **(64)** exhibited preliminary anticancer activity against MCF-7 cell lines. Author concluded that compounds have very good antitumor activity against the MCF -7 cell lines of breast cancer at the tested concentration that related to many studies. The **64b** and **64c** derivatives with 4-NO and 4-fluoro substitution, respectively, both exhibit modest increase in anticancer efficacy compared to the unsubstituted **64a** compound's 84% inhibition. While there is some decrease in the antitumor activity by **64d** with 4- methoxy substitution. (52)



64

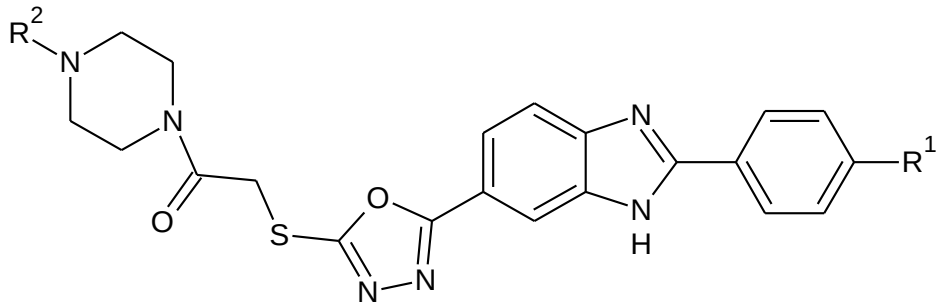
64a=R= H**;**
64b= R= NO_2**;**
64c=R= F**;**
64d= R= Cl**;**

53. Tawfeck A. Yahya et al. (2020) have reported to synthesize and evaluate the novel 2,3-dihydro-1,2,4-oxadiazole and 4,5-dihydro-1,2,4-triazole derivatives for cytotoxic activities. The Author concluded that a series of benzylidene isonicotinohydruzide derivatives (1), 1,3,4-oxadiazole-3(2H)-yl) ethanones and 1-(5-4-substituted phenyl)-3-(pyridin-4-yl)-4,5-dihydro-1,2,4-triazol-1-yl) Ethanones have been synthesized and evaluated for their antitumor activities. The biological activities of all the synthesize compounds were examined against breast cancer MCF7 cell lines. **65** 1-(2-substituted phenyl-5-(pyridin-4yl)-1,3,4-oxadiazole-3(2H)-yl)-ethanone, the result of the in vitro cytotoxic activity revealed that the compound **65** exhibited equipotent cytotoxic activity. (53)



65

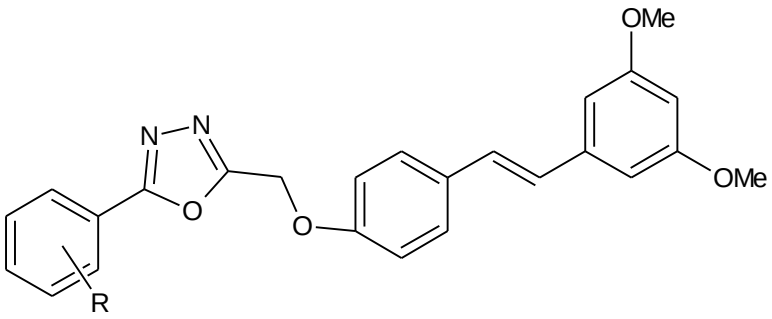
54. Ulviye Acar Cevik et al. (2020) have reported synthesis, anticancer testing, and molecular docking studies of new human topoisomerase type 1 poisons based on benzimidazole-1,3,4-oxadiazole derivatives. Five cancer cells, including Hela, MCF7, A549, HepG2, and C6, were used to assess the in vitro anticancer properties of benzimidazole oxadiazole derivatives. Their structures were elucidated by IR. H-NMR, C-NMR, 2D-NMR and HRMS spectroscopic methods. Among all screen compounds **66(a-h)** Exhibited potent selective cytotoxic activities against various tested cancer lines. Especially compounds **66a** and **66b** exhibited the most antiproliferative activity than Hoechst 33342 and doxorubicin against Hela cell line, with IC_{50} of 0.224 ± 0.011µm and 0.205 ± 0.010 µm respectively. Compound **66a** and **66b** displayed potent and selective anticancer activity against Hela cell lines compare to doxorubicin and Hoechst. (54)



66

Compound	**R^1**	**R^2**
67a	$-OC_2H_5$	$-C_2H_5$
67b	$-OC_2H_5$	

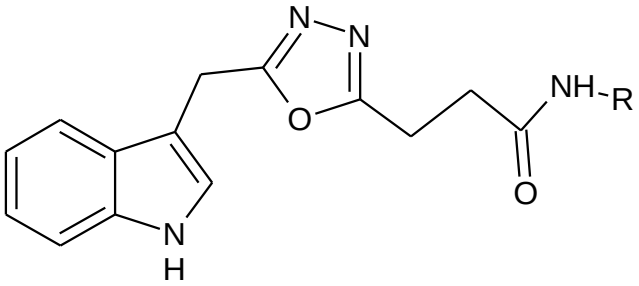
55. Bharathi Kumari Y et al. (2020) have reported synthesis, anticancer evaluation and molecular docking studies of **67** 1,2,3-oxadiazole linked resveratrol derivatives and compounds were evaluated against four different human cancer cells including MDA MB-231 (breast) and A549 (lung) cell lines, as well as MCF-7. Author concluded that all these derivatives were evaluated for their anticancer activity against human cancer cell lines (MCF-7, MDA MB-231 and A549). Among them, compounds **68a** and **68b** were exhibits more potent anticancer activity than adriamycin. (55)



67

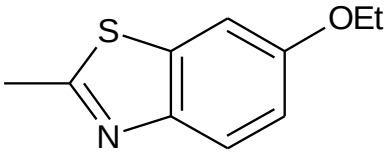
67a; R= 3,4,5-trimethoxy; **67b**; R= 4-Cyano;

56. Belgin sever et al. (2020) have reported that the compound **(68), 68a** is most significant anticancer activity using IC50 values against the HCT 116, A549, and A375 cell lines of 6.43 ± 0.72 µm, 9.62 ± 1.14 µm and 8.07 ± 1.36 µm. Author concluded that, compound **68a** exhibits anticancer effects preventing EGFR dependent activation. The compound **68a** high anticancer potency as a promising EGFR inhibitor for further anticancer studies. (56)

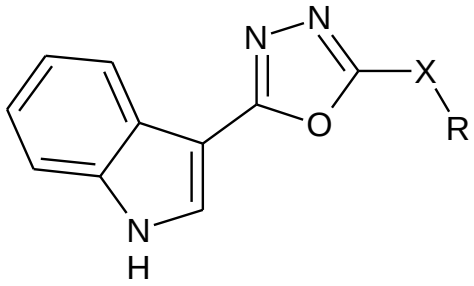


68

R=68a=



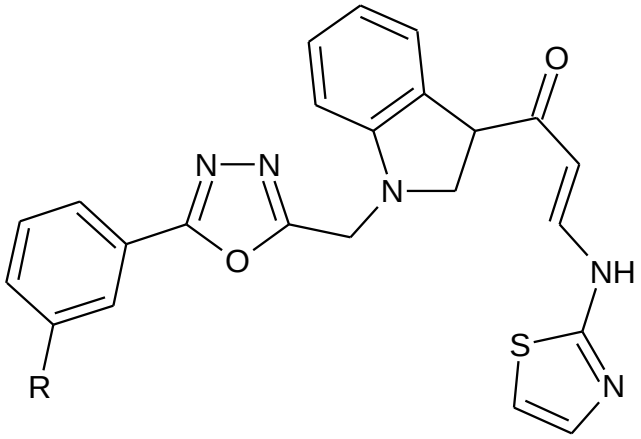
57. Rania Hamdy et al. (2020) have reported design, synthesis and evaluation of new bioactive oxadiazole derivatives as anticancer agents investigated as a selective Bcl-2 inhibitory anticancer agent. Author concluded that compound **69**, among the human cancer cell lines expressing Bcl-2, possessed the most potent anticancer action because it had a 4-trifluoromethyl-phenyl group linked directly to the Oxadiazole ring. (57)



69

Compound	**R**	**X**
70a	4-CF_3-C_6H_4	-

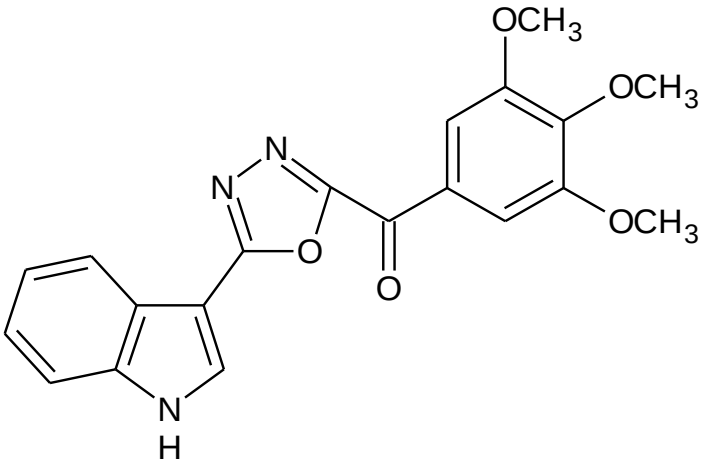
58. Prabhakar Kumar Werma et al. (2020) developed (E)-1-(1) (5-substituted -1,3,4, oxadiazol-2-yl) Methyl)-1H- indol-3-yl)-4-(thiazol-2-yl amine) but-2-ene-1-one **(70)** and evaluated for antitumor activity by MTT assay against four different cancer cell lines such as HT-29 for colon A375 for melanoma, MCF-7 for breast cancer, and A549 for lungs. Using combretastatin-A4 as reference standard. Among the different derivatives **70a. 70b, 70f, 70g, 70j** were exhibited more potent than the positive control. (58)



70

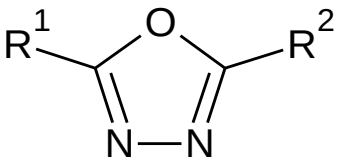
R=70a=H;
70b= 3,4,5-trimethoxy; **70f=** 4-fluro, **70g=** 4-nitro; **70j=** 4-trifluromethyl

59. Rachna sadana et al. (2021) have reported Indolyl-Alfa-keto-1,3,4-oxadiazoles**(71)** derivatives with in vitro anti cell proliferation activity against various cancer cells such as human lymphoblast (u937), leukemia (Jurkat and 5B) and human breast (BT474). Compound **71** exhibited significant antiproliferative activity against a panel of cell lines. Author concluded that compound **71** with 3,4,5-trimethoxyphenyl moiety showed strong antiproliferative activity against u937, Jurkat, B1474 and 5B cancer cells. (59)

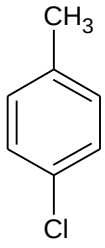
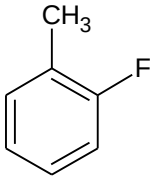
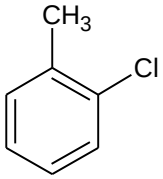
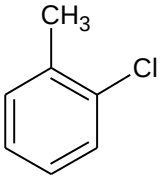
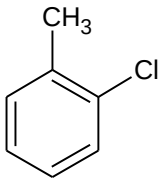
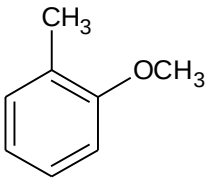


71

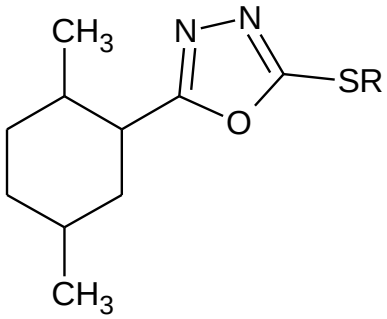
60. Mayur YC et al. (2021) reported that phosphyrylation of thymidine IP assigned identified that 1,3,4-oxidiazole molecule displayed anticancer partially by inhibition of phosphorylation of thymidine. The TP assay Identified **72a, 72b** and **72c** as potentialinhibitors with anticancer activity against both the cell lines. Compound **72a, 72b** and **72c** showed most potent anticancer activity against MCF with IC_{50} value of 1.85-0.28 -2.50 -0.36 and 4.50± 0.2 respectively. Compound **72a** and **72b** showed the best binding interaction with amino acid residue HISH6, GIY 145 and SER44 TYR199 of TP. (60)



72

	R^1	**R^2**
72a=		
72b=		
72c=		

61. N. Polkam et al. (2021) reported a series of new 1,3,4-oxadiazole derivatives screening for anticancer activity against an array of human cancer cells revealed the superior activity of **73** 2-(2,5-dimethoxyphenyl)-5-propylthio-1,3,4-oxadiazole. An anticipatedcompounds **73a** and **73b** with propylthio and butylthio group exhibited the highest activity against breast cancer cell lines. (61)

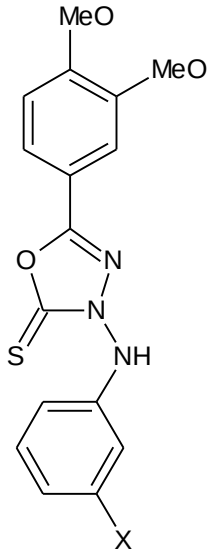


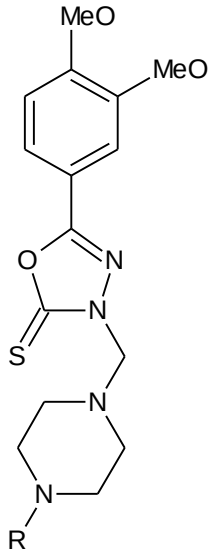
73

73a: R = Pr; **73b: R** = Bu^n

62. Ali A. El-Emam et al.(2021) have reported synthesis of 1,3,4-oxadiazole N-Mannich bases and antiproliferative activity of the compound was evaluated against cancer (pc3) human colorectal cancer (HCT-116) human hepatocellular carcinoma (HepG-2) human epithelioid carcinoma (Hela) and human breast cancer (MCF7) cell lines The optimum anti proliferative activity was attained by compound **74a, 75a, 75b, 75c**.

N-Mannich bases 3-arylaminomethyl-5-(3,4-dimthoxyphenyl)-1,3,4-oxadiazole- 2(3H)-thiones**(74).** 3-[(4-substitutedpiperazin-1-yl)methyl]-5(3,4-dimethoxyphenyl)-1,3,4-oxadiazole- 2(3H)-thiones**(75)**. (62)

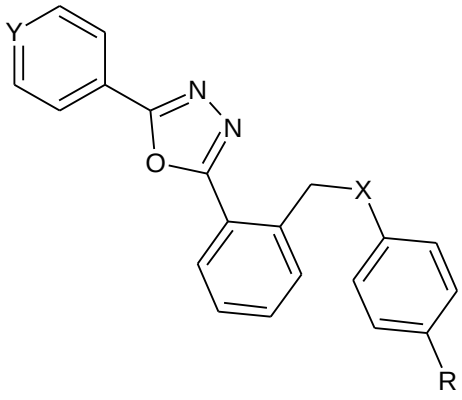




74 **75**

74a=2,4-Cl_2; **75a**= C_6H_5; **75b**= $C_6H_5CH_2$; **75c**= 2-$Cf_3C_6H_4CH_2$

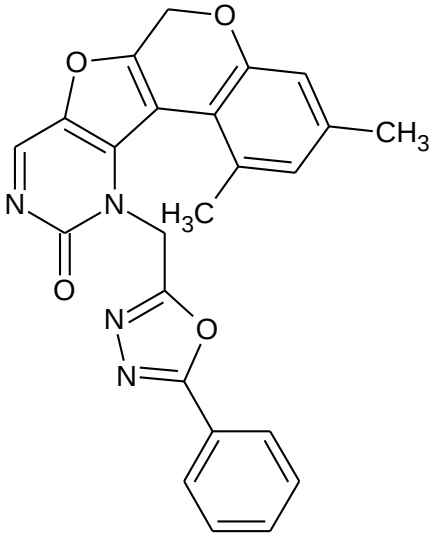
63. George Mihai Nitulescu et al (2021) have synthesis and anticancer evaluation of New 1,3,4-oxadiazole derivatives. In order to develop novel chemotherapeutic agents with potent anticancer activities a series of new 2,5-diaryl/hetroaryl 1,3,4-oxidiazole **(76)** were designed and synthesized. The compound were evaluated for their anticancer potential a two standard human cell lines H7-29 (colon adenocarcinoma) and MDA- MB231 (Breast adenocarcinoma). The promising effect of compound **76** especially on MDA-MB231 cell line motivates further studies to improve anticancer profile and to reduce the toxicological risk. (63)



76

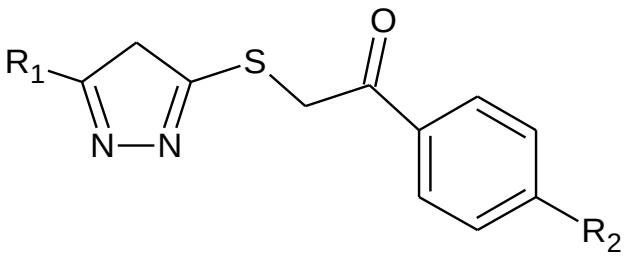
76a: x=s, y=N, R-H

64. Az-eddine EL Manouri et al. (2021) reported a new series of furo[2,3-d] pyrimidine-1,3,4-oxadiazole (78) hybrid derivatives were synthesized. All synthesized 1,3,4-oxadiazole hybrids were evaluated for their cytotoxic activity in four human cancer cell lines: fibroscarcoma (HT-1080), breast (MCF-7 and MDA-MB-231) and lung carcinoma (A549). Among the synthesized derivatives, **77** showed the best cytotoxic activity against four human cancer cell lines. The molecular docking study confirmed that the anticancer activity of the synthesized compounds is mediated by the activation of caspase 3. (64)



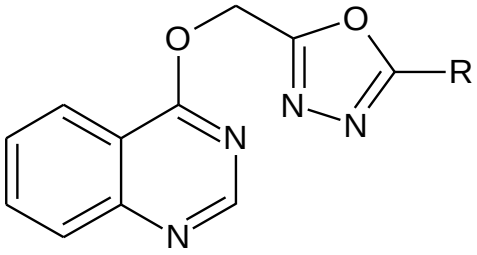
77

65. Ebraheem Abdu Musad et al (2021) have reported 1,3,4-oxadiazole containing hybrids as potential anticancer agents. Hybridization of 1,3,4-oxadiazole moiety with other heterocyclic pharmacophoresis a promising approach to overcome various disadvantages of current anticancer drug such as drug resistance, toxicity and other side effects. 1,3,4-oxadiazole-hetrocycle hybrids occupy a significant position in the discovery of anti-tumor drug. Among the reported oxadiazole-based hybrids reviewed here, compounds **78** and **79,** showed the highest anticancer activity with IC_{50} value in the nonomolar range. (65)



78

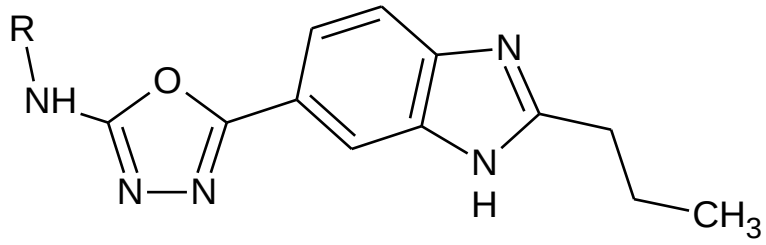
R_1= 2-NH_2-pyridine;
R_2= H



79

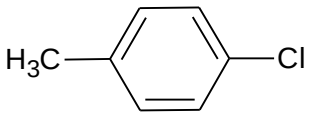
R= -CH_2-ph(3,4-diOCH_3)

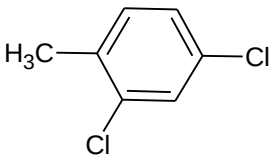
66. R katikiraeddy et al. (2021) reported synthesis anticancer activity and molecular docking studies of hybrid benzimidazole 1,3,4-oxadiazole 2-N alkyl / aryl amine. In present study the synthesis of benzimdazolyl-2-amino-1,3,4-oxadiazole (81) derivatives and their in vitro anticancer activity against Hela, MCF-7 and A549 cell line were reported. Compound **80a**, **80b, 80c** were found to have excellent anticancer activity. In vitro anticancer activity of compound was tested using M using colorimetries assay as per ATCC protocol. (66)



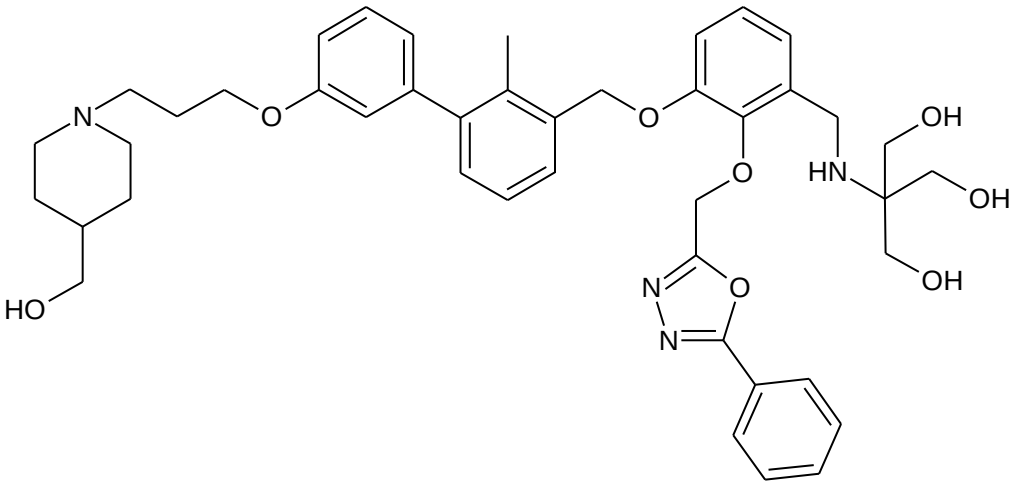
80

80a; R= -CH_2-CH_2-CI;

80b; R= 

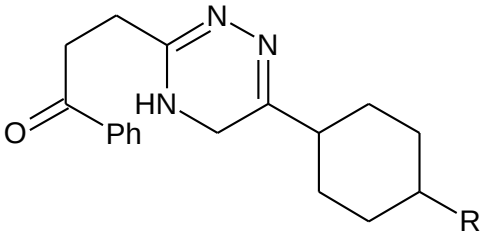
80c; R= 

67. Huibin zhang et al. (2021) have reported 1,3,4-oxidiazole derivatives as potential antitumor agents inhibiting the programmed cell dealth-1 (programmed cell death- ligand and 1 interaction. These novel small-molecules inhibitor exhibited remarkable inhibitory activity of the P0-1/PD- 1 blockage in the TR-Fret assay, among them, **81** was the most promising small molecule inhibitor with on IC_{50} value of 0.0380 m. IN addition compound **81** had no significant toxicity basing on the cell based experience. Importantly compound **81** with a TGI value of 35.74% and more potent efficacy in a mouse tumor model compared to that in the control group. Moreover, when compound **81** combined with 5-Fu, with a TGI value of 64.59% It can greatly increase the antitumor activity which shown potential antitumor synergistic effects. (67)



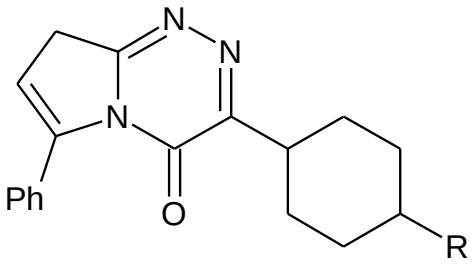
81

68. Abu-Hashem et al. (2021) Reported synthesis of new pyrazoles oxadiazoles triazoles pyrrolotriazepinones and pyrrolotriazepines as potential cytotoxic agents. The chemical structure of a newly prepared compound was determine though the spectrums data, including IR, NMR and MS. The prepared compound were tested for their in vitro antitumor activities compound **82, 83** and **84** displayed activity against several type of cancer cell lines. The target of recent study us to prepare and evaluate the cytotoxicity activity of new compound such pyrozoles 1,3,4-oxadiazoles. All the result demonstrated that pyrole triazeopinones **82**, 1,2,4-trizepinones **83** pyrrolo triazines 84 possess promising and wonderful in vitro antitumor activity verses carcinoma cell lines where compared to 5-flurouracil drug. (68)



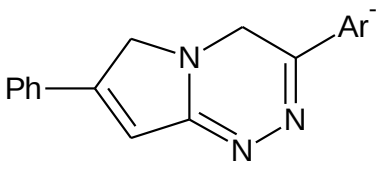
83

83a; R= H
83b; R= Cl
83c; R= OCH_3



82

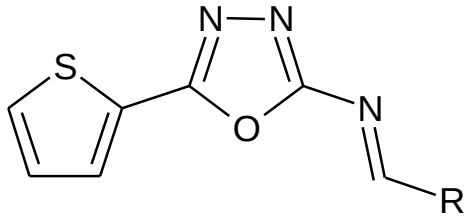
82a; R= H
82b; R= Cl
82c; R= OCH_3



84

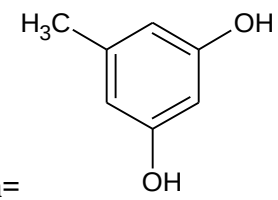
84a; R=C_6;
84b; R = C_6H_4Cl-P
84c; R = $C_6H_4OCH_5$-P

69. Bistuall chandtashekhoippa revanasiddappa et al. (2021) have reported Insilica design ADMFT screening MMGBBA binding free, energy of novel 1,3,4-oxidiazole **(85)** linked schiff bases as PARP-1 inhibited targeting breast cancer. The selected 1,3,4-oxadiazole schiff base conjugates seems to be one of the potential source for the further development of anticancer agents against PARP-1 enzyme The result reveled that some of the compound **85a, 85b, 85c, 85d, 85e, 85f** with good glide scares showed very significant activity against breast cancer. (69)

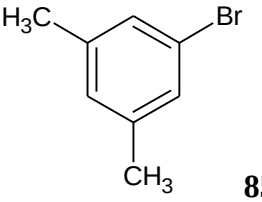


85

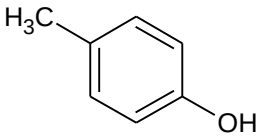
R=



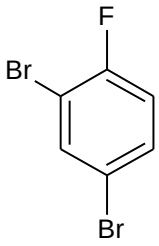
85a=



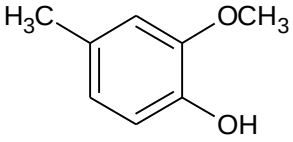
85b=



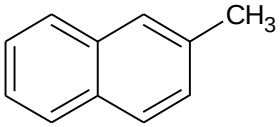
85c=



85d=

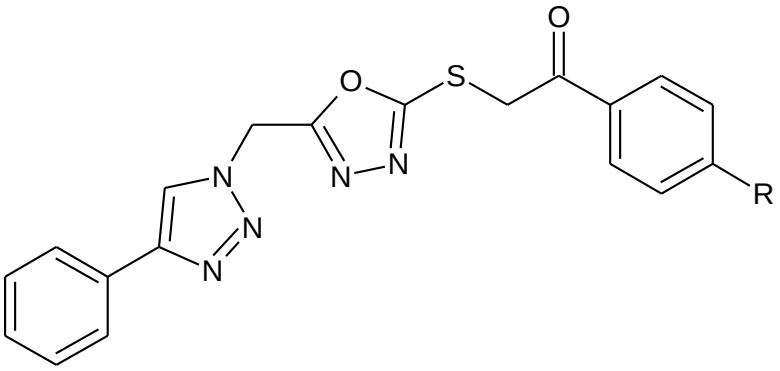


85e=



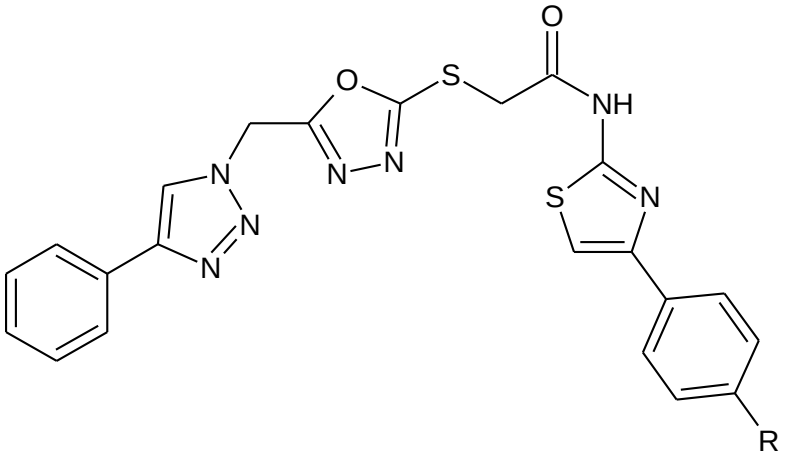
85f=

70. A series of 1,3,4-oxidiazole-1,2,3-triazole hybrids bearing various pharmacophoric societies has been developed and synthesized, according to Mohamed A. Mahmoud et al. (2022). They were tested against four human cancer cell lines for their antiproliferative effectiveness. The preliminary activity test showed that the most active compounds **(86), (86a), (86b),** and **(87(a-d))** significantly reduced the proliferation of cancer cells contrasted with erlotinib. Receptor for epidermal growth factor tyrosine kinase (EGFR-TK) was inhibited by this substance with an IC_{50} value of 0.11 to 0.73 M. The analysis's conclusion showed that the human cancer cell line's hybrid-induced expression of caspase-3, caspase-9, and cytochrome c was at Panc-1, the highest level. (70)



86

86a; R= Cl; **86b**; R= Br



87

87a: R=H; **87b:** R=CH_3; **87c:** R=OCH_3; **87d:** R= Cl

Conclusion:

Cancer records millions of death every year and affects around 20 million people all over the world. As cancer cases are still raising it is predicted that about 30 million people will be diagnosed with cancer by 2040 in high-developed countries. Finding new cancer drugs with effective treatment thus becomes or effective drugs are one of the utmost need. Biological evaluation of 1,3,4-oxadiazole revealed that some of their derivatives are potent anticancer agents. This comprehensive review represent the recent 1,3,4-oxadiazole and its derivatives, which in the years starting in 2015 are regarded as promising antibacterial agents. This review could aid medicinal chemists in creating novel leads with a 1,3,4-oxadiazole nucleus that are more effective and have fewer adverse effects.

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