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Pyrazoline derivatives as an anticancer activity

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Abstract*:* cancer is one of the leading hazards and the prominent cause of death in the world. Pyrazoline has a wide range of biological functions and is a powerful medicinal scaffold. Pyrazolines are known and important nitrogen containing five membered heterocyclic compounds. piperazine substituted dihydropyrazole derivatives exhibited superior anticancer activity. compound 1a,1b,1c,1d,2,3showed potent antitumor activity. Antitumor due to induce G_2/M arrest in HCC1806 cell and P21 accumulation significantly.

Keywords: pyrazoline, anticancer activity, cancer cell line.

1. Introduction:

Despite significant progress made in molecular and cell biology in recent decades, cancer still remains an enigma[1]. There were 17 million new cases of cancer and an estimated 9.6 million deaths in 2018 worldwide. It is forecasted that, there will be 27.5 million new cancer cases each year by 2040 in the world[2][3]. The lung, breast, bowel and prostate are the most common cancers occurring worldwide accounting for more than four in ten of all cancer diagnosed worldwide[4]. Cancer is not a single illness but rather a broad class of illnesses characterize by unchecked, fast, and pathological cell proliferation that has undergone aberrant transformations[5]. Despite recent advancements in cancer therapy, cardiovascular diseases continue to be the second major cause of mortality globally[6]. One of the biggest challenges in the fight against cancer is still resistance to chemotherapeutic drugs. malignancies continue to be a serious public health issue and the number one death worldwide[7]. Because of population increase and age, malignancies are causing an increasing amount of suffering in both developed and developing nations[8]. Chemotherapy remains the most popular way to extend patients' lives, despite the efficacy of new therapies including immunotherapy, photodynamic therapy, and hyperthermia. In the clinic, chemotherapeutic medicines like paclitaxel and vinblastine are mostly covered by tubulin targeting medications[9][10][11]. . Despite the fact that the causes of cancer are not completely understood, a number of factors, many of which are changeable (such as cigarette use and excess body weight), are

known to raise the likelihood of the disease (e.g., inherited genetic mutations and immune conditions). These risk factors may start a malignancy or encourage its growth by acting sequentially or concurrently[4]. It has been suggested that cancer growth is correlated with free radical damage to macromolecules. Increased antioxidant levels have been demonstrated to stop such macromolecule damage[12].

Cell lines in the *in vitro* screen

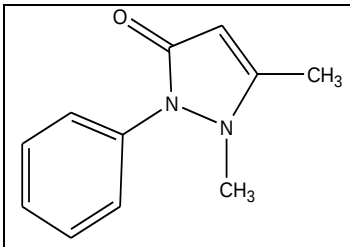
Table No. 1- human cancer cell lines

Cell line **Name** **Time** **Density**	**Panel name**	**Doubling**	**Inoculation**
CCRF-CEM	Leukemia	26.7	40000
HL-60(TB)	Leukemia	28.6	40000
K-562	Leukemia	19.6	5000
MOLT-4	Leukemia	27.9	30000
RPMI-8226	Leukemia	33.5	20000
SR	Leukemia	28.7	20000
A549/ATCC cell lung	Non-small	22.9	7500
EKVX Cell lung	Non-small	43.6	20000
NCI-H322M Cell lung	Non-small	35.3	20000
HOP-62 Cell lung	non-small	39	10000
HOP-92 Cell lung	non-small	79.5	20000
NCI-H226 Cell lung	Non-small	61	20000
NCI-H23 Cell lung	Non-small	33.4	20000
NCI-H460 Cell lung	Non-small	17.8	7500

NCI-H522 Cell lung	Non-small	38.2	20000
COLO 205	Colon	23.8	15000
HCC-2998	Colon	31.5	15000
HCT-15	Colon	17.4	5000
HT29	Colon	19.5	5000
HCT-15	Colon	20.6	10000
KM12	Colon	23.7	15000
SW-620	Colon	20.4	10000
SF-268	CNS	33.1	15000
SF-295	CNS	29.5	10000
SF-539	CNS	35.4	15000
SNB-19	CNS	34.6	15000
SNB-75	CNS	62.8	20000
U251	CNS	23.8	7500
LOX IMVI	Melanoma	20.5	7500
MALME-3M	Melanoma	46.2	20000
M14	Melanoma	26.3	15000
MDA-MB-435	Melanoma	25.8	15000
SK-MEL-2	Melanoma	45.5	20000
SK-MEL-28	Melanoma	35.1	10000
SK-MEL-5	Melanoma	25.2	10000
UACC-62	Melanoma	31.3	10000
UACC-257	Melanoma	38.5	20000
IGR-OV1	Ovarian	31	10000
OVCAR-3	Ovarian	34.7	10000
OVCAR-4	Ovarian	41.4	15000
OVCAR-5	Ovarian	48.8	20000
OVCAR-8	Ovarian	26.1	10000
NCI/ADR-RES	Ovarian	34	15000
SK-OV-3	Ovarian	48.7	20000
786-0	Renal	22.4	10000
A498	Renal	66.8	25000
ACHN	Renal	27.5	10000
CAKI-1	Renal	39	10000
RXF393	Renal	62.9	15000
SN12C	Renal	29.5	15000
TK-10	Renal	51.3	15000
UO-31	Renal	41.7	15000
PC-3	Prostate	27.1	7500
DU-145	Prostate	32.3	10000
MCF7	Breast	25.4	10000
MDA-MB-231/ ATCC	Breast	41.9	20000
MDA-MB-468	Breast	62	2000
HS578T	Breast	53.8	20000
T-549	Breast	45.5	20000
BT-549	Breast	53.9	20000

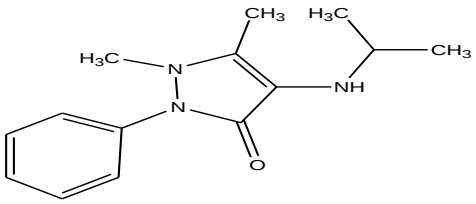
Pyrazole containing compound sulphenazole. It is a long acting leprosy therapy with sulfonamide antibiotic[13]. Pyrazole marketed product is sulphenazole. It is a long acting sulfonamide antibiotic used in the treatment of leprosy[13].

Currently, a number of therapeutic compounds with pyrazole and pyrazoline rings with various actions are marketed, including antipyrine, ramifenazone, morazone, celecoxib, fezolamine, and tepoxalin[14].



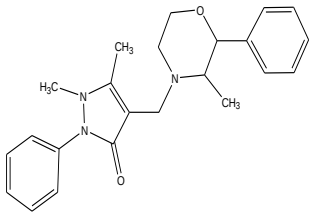
Antipyrine

(antibiotic, analgesic)



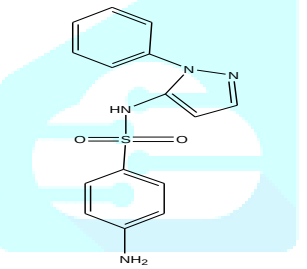
ramifenazone

(anti-inflammatory)



Morazone

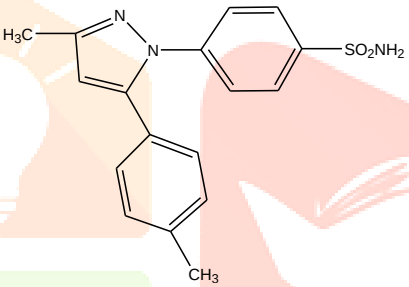
(analgesic)



4-Amino-*N*-(2-phenyl-2*H*-pyrazol-3-yl)-benzenesulfonamide

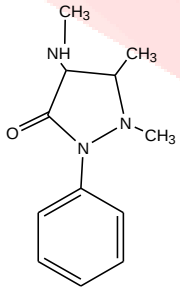
Sulphenazole

(antibacterial, leprosy)



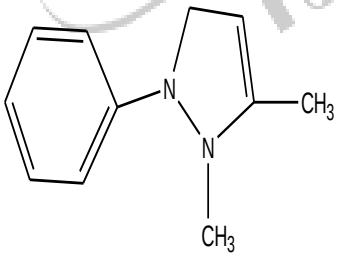
celecoxib

(anticancer ,anti-inflammatory)



1,5-Dimethyl-4-methylamino-2-phenyl-pyrazolidin-3-one

Analgin



1,5-Dimethyl-2-phenyl-2,3-dihydro-1*H*-pyrazole

phenazole

Fig.1 Marketed products containing pyrazoline

Pyrazolines are five membered heterocyclic compounds containing two nitrogen atoms[10][15]. It has only one endocyclic double bond and is basic in nature[16][17]. Pyrazolines is a dihydro derivative of pyrazole. 1-pyrazoline, 2-pyrazoline and 3-pyrazoline are the chemical forms of pyrazoline[6][18][19].

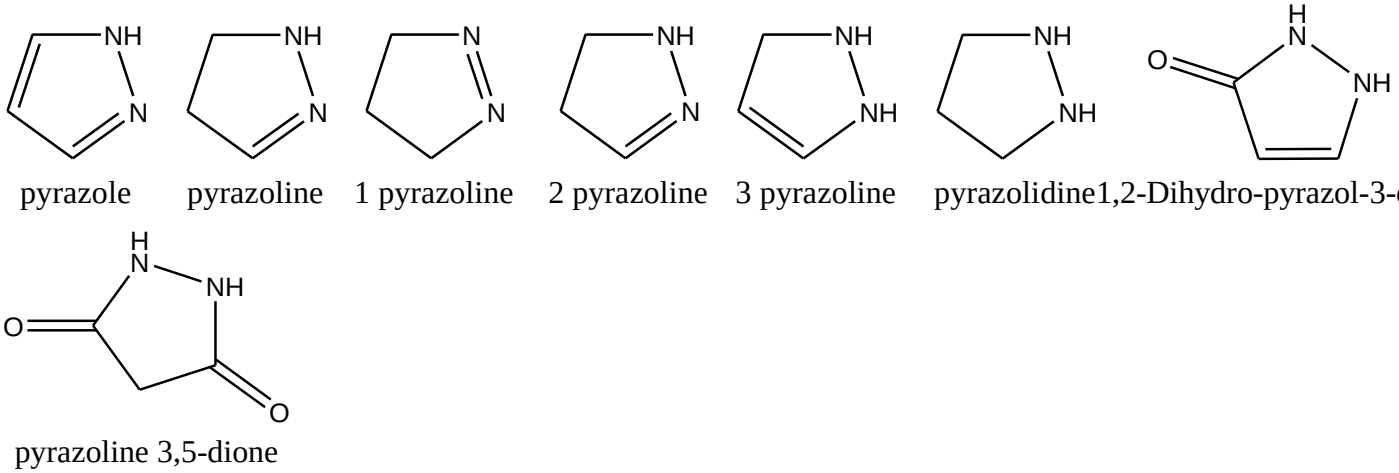


Fig.2 pyrazole derivatives

Pyrazolines exhibit a comprehensive of biological activity anticancer[20]. Many pyrazolines drugs are clinically allowed and used for various condition. Pyrazoline ring compounds such as Ibrutinib, which contains a fused pyrazoline, also have anticancer properties[21]. Pyrazoline derivatives have been found in the form of vitamins, alkaloids and pigments[22].

1.1 -1-pyrazolines:

The isomers of 1-pyrazolines that have a double bond between nitrogen and nitrogen. A diazoalkane and a cyclic or acyclic alkene are typically combined in a cycloaddition procedure to create them[6]. As they are transformed into cyclopropanes or other structures by photolysis or thermolysis they are useful intermediates even for the synthesis of complicated natural compounds. This pyrazoline form has a limited number of known biological applications. The sole natural substance with inhibitory efficacy against lettuce seedling hypocotyls is citreopyrone which has a 1-pyrazoline ring[23].

the utilization of polyoxometalate complexes of purinimide-pyrazoline compounds as a photodynamic therapy uses a photosensitizer. A number of chromanone-spiro-1-pyrazoline hybrids have recently been biologically evaluated with respect to the human leukemia cell line (HL-60), B cell precursor leukemia (NALM-6), and women melanoma (WM-115) cell lines, it was discovered that compound 2 had the highest cytotoxicity (IC_{50} = 3.0–6.8 μM). Since the non-substituted molecule displayed more than 330-fold reduced cytotoxicity against HL-60, the presence of a para-methoxyphenyl group proved crucial[6][24].

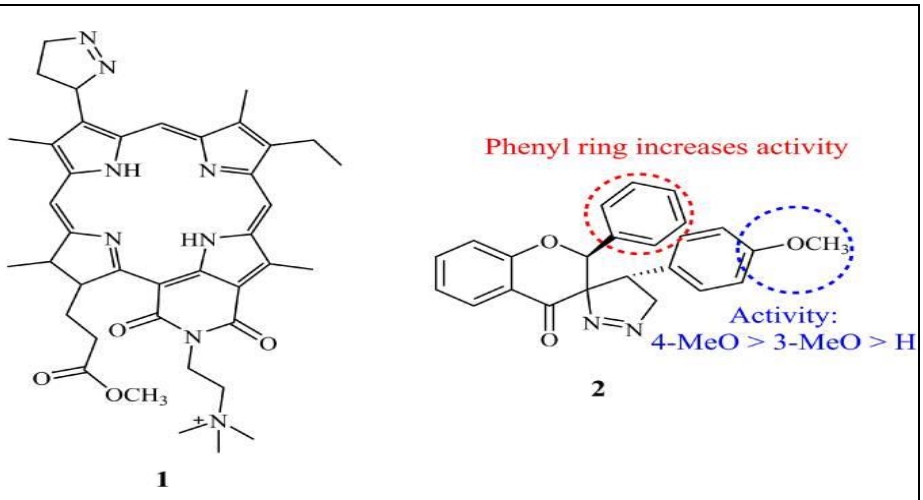


Fig.3 Marketed product containing 1- pyrazoline derivatives

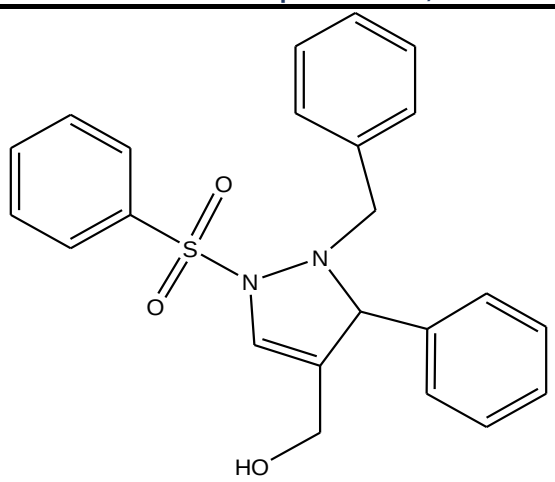
1.2- 2-pyrazolines*:*

the three pyrazoline isomers in plenty , 2-pyrazolines is a physiologically active chemical that is most frequently referred in literature with a variety of application with anti-inflammatory, anti-microbial, antiviral, antimalarial, trypanocidal, insecticidal, and anticancer properties[25][26]. The doubly bonded endocyclic between the N-2 and the C-3 of this pyrazoline is present[7][6]**.**

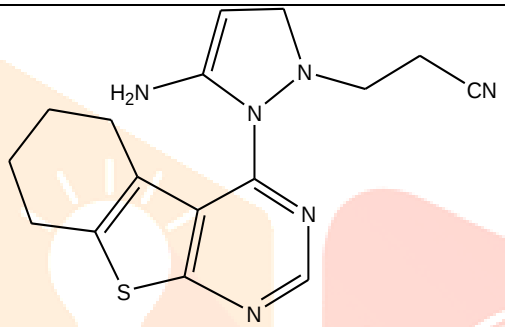
1.3- 3-pyrazolines*:*

3-pyrazoline isomers, they are underrepresented in this review[27]. They are created through iodo cyclization or cycloaddition processes, which are frequently aided by metal catalysts. The 3-pyrazoline hybride 3 was discovered to be one of the busiest thieno [2,3-d] pyrimidine derivatives in the library. It demonstrated selective cytotoxicity against HepG2 and MCF-7 (IC_{50} = 3.96-4.38μM)[28]. No inferences on the SAR can be made because pyrazoline 3 was the only one present in that paper. The intermediate counterpart of acyclic hydrazine, however, was inert at the studied concentration levels (IC_{50} values > 100μM)[29]. By inhibiting or decreasing Topoisomerase II, 3 has been shown to be capable of arresting the cell cycle, inducing apoptosis, and acting as a

cytostatic agent[7][6].



(1-Benzenesulfonyl-2-benzyl-3-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)-methanol



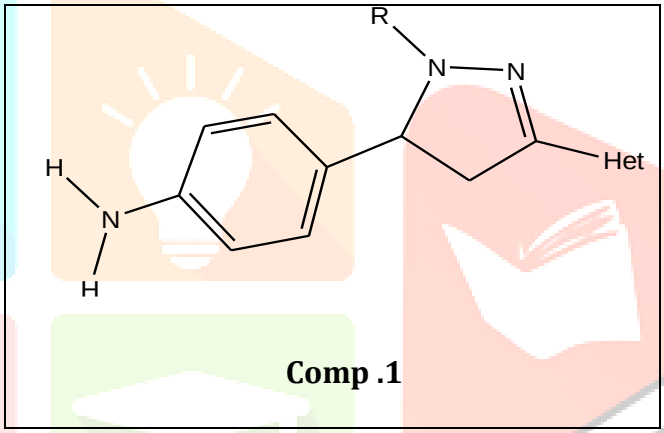
3-[3-Amino-2-(5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-yl)-2,5-dihydro-pyrazol-1-yl]-propionitrile

1.4-Physical and chemical characteristics:

Due to its lipophilic nature, 2-pyrazoline is soluble in propylene glycol but insoluble in water. The compounds containing the 2-pyrazoline group without a replacement at position of a substituent at the 1-position of the heterocyclic ring have been shown to react with benzaldehyde to produce 4-benzylidine derivatives at high temperatures (200 °C). They have a general inclination to transport. In the ring's conjugated portion (-N1-N2-C3-) a carbon atom and a nitrogen atom in the first position[30][31].

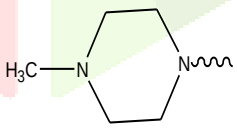
2. **Anticancer activity*:*** Cancer is a spectrum of diseases rather than a single illness distinguished by the uncontrolled proliferation of abnormal cells[34]. Due to a variety of causes, including stress, an improper diet, smoking, and other variables, cancer is one of the most difficult diseases in the world. Numerous clinical disorders are directly caused by the unchecked and fast multiplication of malignant cells[6][11]. Even though significant resources have been devoted to the therapeutic treatment of cancer, it continues to be a leading cause of death[8]. Due to toxicity, unforeseen resistance, and lack of selectivity, current medicines' clinical success is sporadic. As a result, more advanced anti-cancer drugs are always being created and evaluated to see how well they work against tumour cells. synthesized a series of pyrazoline derivatives. Particularly, some pyrazoline-containing substances have the ability to prevent the development of certain cancers, such as lung,

breast, brain, bone, mouth, stomach, liver, bladder, pancreas, cervix, colon, and prostate cancers, in addition to having cytotoxic effects[7]. Some chalcones, both synthetic and natural, have been shown to have antioxidant properties and to be effective against tumor cells by preventing the creation of superoxide and lipid peroxidation[30]. A licochacone Another anticancer chalcone that was derived from Glycyrrhiza inflate showed toxicity toward L1210 leukemia as well as B16 melanoma cells[35]. A novel class of chalcones that have been proposed as anti-mitotic drugs improving the lifespan of mice given dosages of 2.65–5.0 mg/kg of L1210 leukemia. Another natural chalcone, the ability to inhibit a variety of human malignancies, including breast cancer Hepatic stellate cells, osteosarcoma, and colon cancer in vitro[36]. Estrone, a powerful 17b-HSD1 inhibitor, had its molecular makeup changed, and this allowed researchers to find substances with strong antiproliferative effects but no hormonal effects. Cancer is considered to be one of the most intractable diseases because of the innate characteristics of cancer cells to proliferate uncontrollably, avoid apoptosis, invade and metastasize[37].

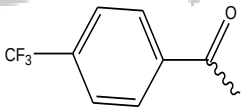


Comp .1

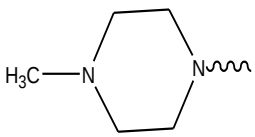
1a: Het



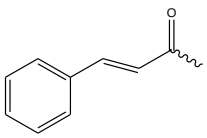
1a: R



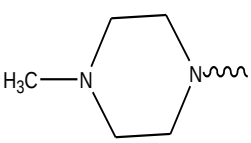
1b: het



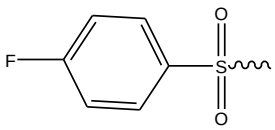
1b: R



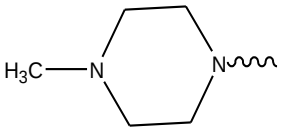
1c: het



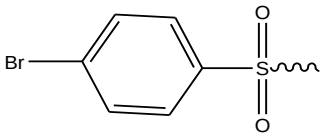
1c: R

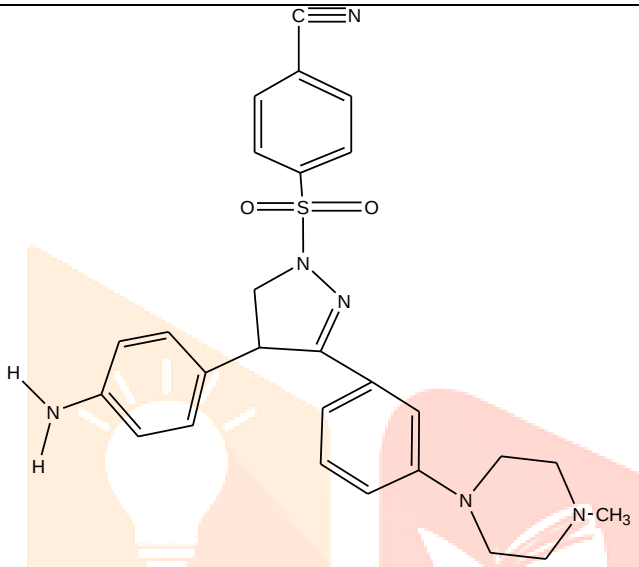


1d: het



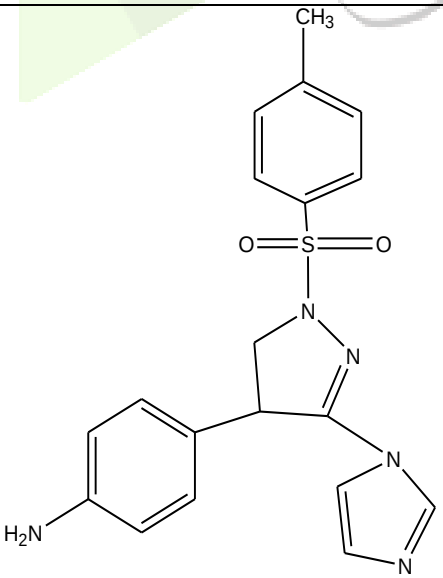
1d: R





4-{4-(4-Amino-phenyl)-3-[3-(4-methyl-piperazin-1-yl)-phenyl]-4,5-dihydro-pyrazole-1-sulfonyl}-benzonitrile

Comp. 2



4-[3-Imidazol-1-yl-1-(toluene-4-sulfonyl)-4,5-dihydro-1*H*-pyrazol-4-yl]-phenylamine

Comp.3

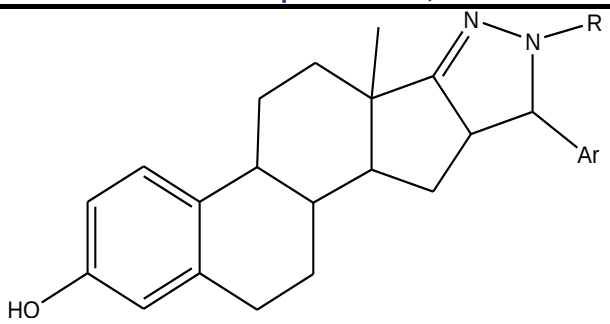
Anticancer due to relevance of inducing G_2/M arrest in HCC1806 cell and p21 accumulation (anticancer against HCC1806 call line) IC_{50}<3μM.

HCC- human cancer cell line.

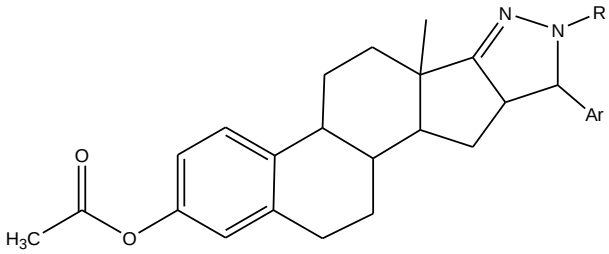
1a,2,3 showed good antitumor activity against MDA-MB-231

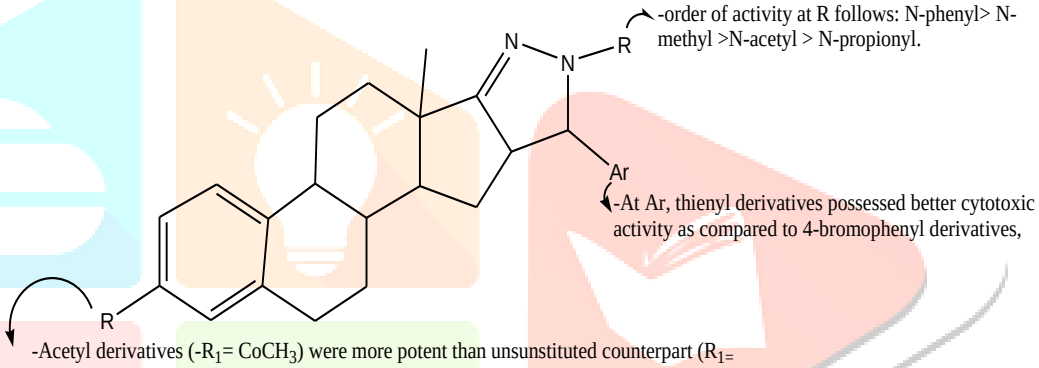
(Human breast cancer cell line)
(Inhibition rate >50%)
1a,1b,1c,1d,2,3showed the better cytotoxic activity, especially 6o displayed show best potent antitumor activity.
NCI-H1975(human lung cancer cell line)
(Inhibition rate>50%)
1a (inhibition rate was 93.2%. against NCI-H1975
1c (inhibition rate was 90% against human cancer cell line (HCC1806) and human lungs cancer cell line (NCI-H1975)
2 (inhibition rate was 100% against NCI-H1975, HCC1806, MDA-MB
The anticancer effect of potent compound 1a,2,3 selective inhibition against IC_{50}<10μM against HCC1806, Hela, A545, HCT176 against all four-cell line.
the best potent antitumor activity (IC_{50} < 3 μM). the structure–activity relationship (SAR) towards potent anticancer activity of heterocyclic substituted dihydropyrazoles against three cancer cell lines, various groups including EWG and EDG on the phenyl ring as well as aliphatic of the derivatization functionality were introduced.
We observed that compounds containing electron withdrawing substituents and halogen contributed to potential antitumor activity, such as CF_3, CN, F and Br. However, EDG led to poor cytotoxic activity.
the cytotoxic activity against human colorectal cancer cell line (HCT116), cervical carcinoma cell line (HeLa) and lung cancer cell line[32][33].

Compound **4** derived and produced a series of novel pyrazolinyl-estran-17-one derivatives based on these facts, and they then tested them for their ability to inhibit breast cancer *in vitro* and *in vivo*. The MCF-7 cell line was used as the test subject for an *in vitro* cytotoxicity assay, and the results revealed that all of the tested derivatives exhibited strong cytotoxicity at the nanomolar level. The most potent contender was compound **4**, with an IC_{50} of 43 0.58 μm, whereas compounds 4 if and 4c showed the most cytotoxic potential against MCF-7 cells with IC_{50} values ranging from 43 to 56 μm. Results of the xenograft study breast cancer showed that the derivatives had a significant impact on how much of the tumour grew. After 12 days of treatment with the most powerful chemical, the growth of the tumour volume was reduced by roughly 87.0%[38].



Comp .4a

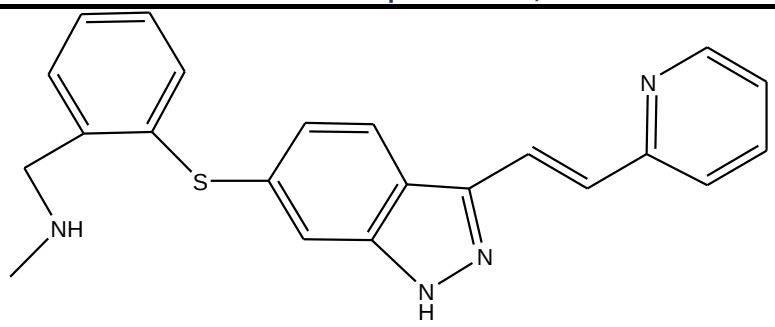




4b

4c (novel pyrazolinyl-estran-17-one)

Axitinib pazopanib, which include pyrazolines, are VEGFR inhibitors that have been utilised in clinical treatments. Several pyrazoline derivatives have also been found exhibit anti-angiogenesis activity[38]. The *in vitro* half-maximal inhibitor concentration(IC_{50}) of axitinib against VEGFR 1to3 were 0.1-0.3mmol/L[39].



N-Methyl-2-[3-(2-pyridin-2-yl-vinyl)-1*H*-indazol-6-ylsulfanyl]-benzamide

Comp.5 (Axitinib)

Tyrosine kinases are the enzymes that stimulate cells to grow abnormally, which leads to cancer. Tyrosine kinase inhibitors (TKIs) include the medicine crizotinib. Pfizer's Xalkori brand of crizotinib is used to treat advanced lung cancer. It is sold as capsules and should be taken twice day with a glass of water. It works by blocking the anaplastic lymphoma kinase (ALK) enzyme, which is hyperactive and prevents cell growth. Comp **6** Crizotinib is a potent inhibitor of c-Met and ALK with IC_{50} of 11µm and 24 µm in cell based assays[40].

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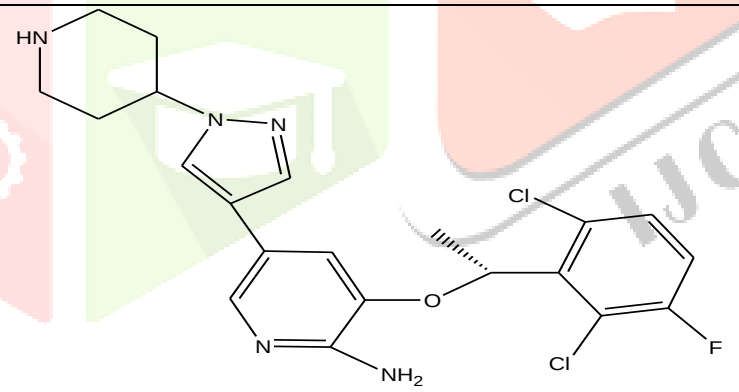
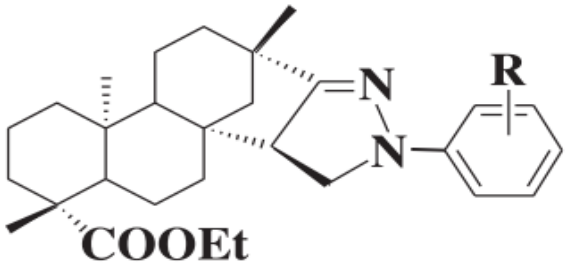


3-[1-(2,6-Dichloro-3-fluoro-phenyl)-ethoxy]-5-(1-piperidin-4-yl-1*H*-pyrazol-4-yl)-pyridin-2-ylamine

Comp .6 (Crizotinib)



1,4a,7,7,8a-Pentamethyl-tetradecahydro-phenanthrene-1-carboxylic acid ethyl ester; compound with 1-isopropenyl-4,5-dihydro-1*H*-pyrazole

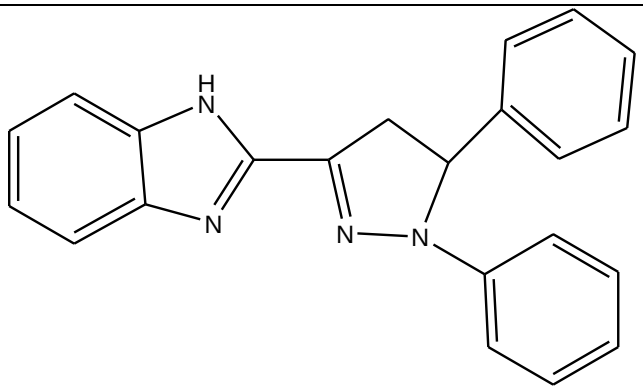
Comp.7 (Fused based pyrazoline isosteviol)

Compound **7** shows various cell line like human gastric cancer cell line (SGC 7901), lung carcinoma epithelial cells (A549), and (Hela cell lines) immortal cell line, the majority of pyrazoline derivatives 7a7ad shown stronger inhibitory effects against Raji cell. It's interesting to note that a few pyrazole compounds outperformed cisplatin in terms of Raji cell inhibition. The chemical 12 with the p-CH3 substitution showed superior cytotoxic effects among the mono-substituted pyrazoline derivatives with IC_{50} values of 29.39, 13.67, 3.91, and 29.14 µM against SGC 7901, A549 Raji and Hela cells in lines[41].

7a: R = H (76%); 7b: R = o-F (58%); 7c: R = m-F (51%); 7d:3,5-Me_2(81%)

Table No. 2

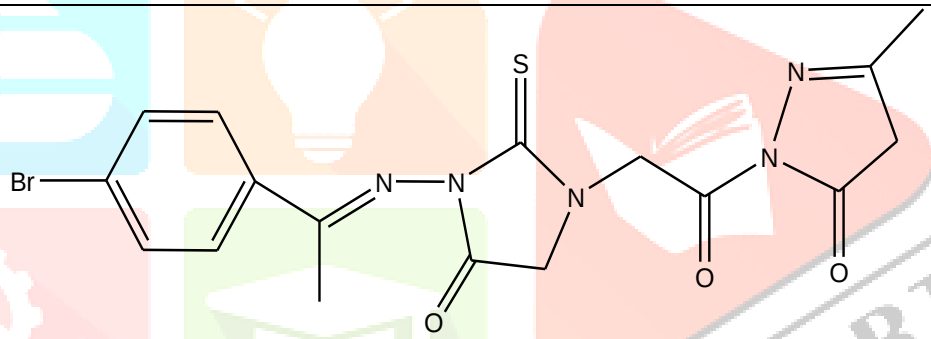
Compound	R	Cytotoxic activities (IC_{50} µM)			
		SGC7901	A549	Raji	Hela
7a	H	>50	>50	>50	>50
7b	o-F	>50	28.33	23.95	>50
7c	m-F	34.67	32.63	27.23	>50
7d	3,5-Me_2	>50	>50	>50	>50



2-(1,5-Diphenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-1*H*-benzoimidazole

Comp .8

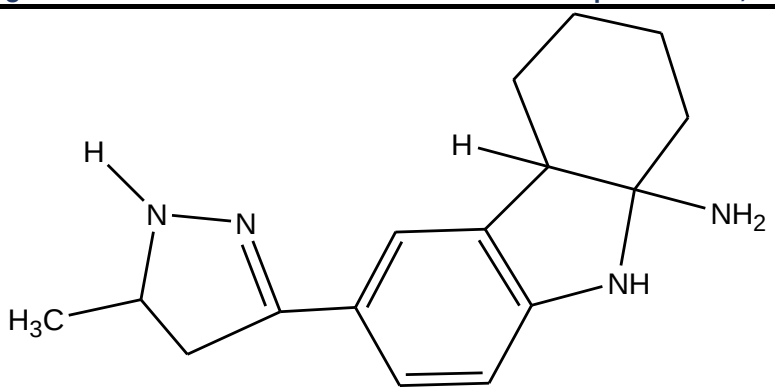
Compound **8** shows The biological activity and synthesis of chiral dihydro pyrazoles, such as 2-(1,5-diphenyl-4,5-dihydro-1H-pyrazol-3-yl)-1H-benzimidazole, demonstrate promising activity against the leukemia cell lines CCRF-CEM and RPMI-8226, with GI_{50} values of 2.23μM and 2.76 μM. [18].



2-(2-{3-[1-(4-Bromo-phenyl)-ethylideneamino]-4-oxo-2-thioxo-imidazolidin-1-yl}-acetyl)-5-methyl-2,4-dihydro-pyrazol-3-one

Comp.9

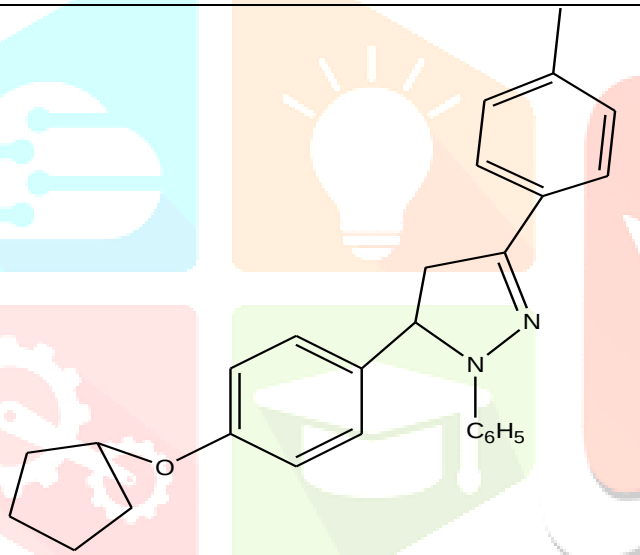
Comp **9** shows *in-vitro* cytotoxicity against breast carcinoma cell line and has the best activity against MCF-7 Cell line (IC_{50}=3.98μg/mL) [42].



3-(5-Methyl-4,5-dihydro-1*H*-pyrazol-3-yl)-4b,5,6,7,8,9-hexahydro-carbazol-8a-ylamine

Comp.10

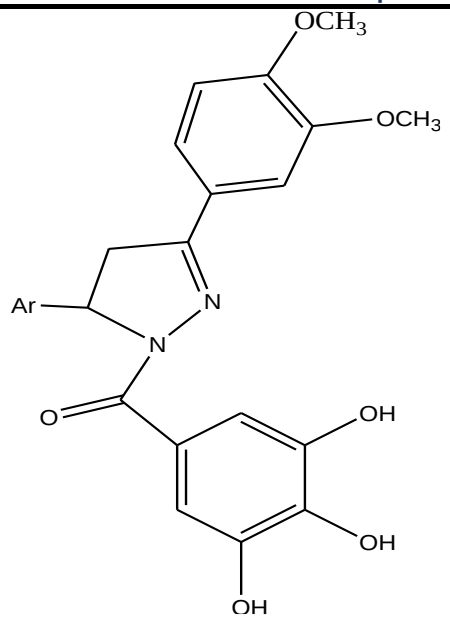
Comp **10** is active against human kidney cancer cell line A498 with LC_{50} and TGI (Total Growth Inhibition) values >70 and GI_{50} values, 74.5 and 55.2µM respectively[43].



5-(4-Cyclopentyloxy-phenyl)-1-phenyl-3-*p*-tolyl-4,5-dihydro-1*H*-pyrazole

Comp.11

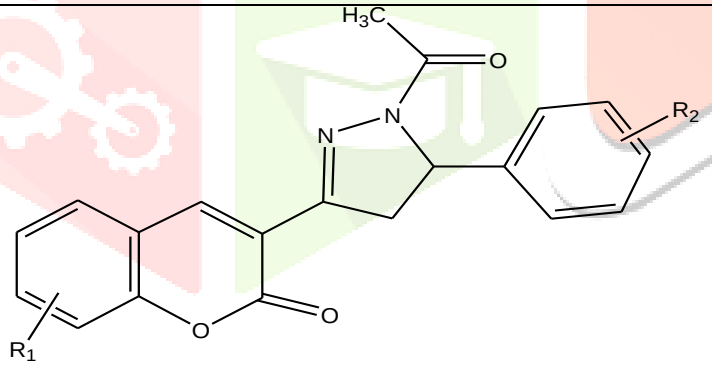
Comp **11** shows cytotoxicity against HepG2, MCF-7, HeLa, and PC 3cell lines were IC_{50} values 7.2, 5.6, 5.5, and 7.8 µM, respectively. And also showed good inhibitory activity against EGFR with IC_{50} value of 2.16 µM[44].



[3-(3,4-Dimethoxy-phenyl)-5-methyl-4,5-dihydro-pyrazol-1-yl]-(3,4,5-trihydroxy-phenyl)-methanone

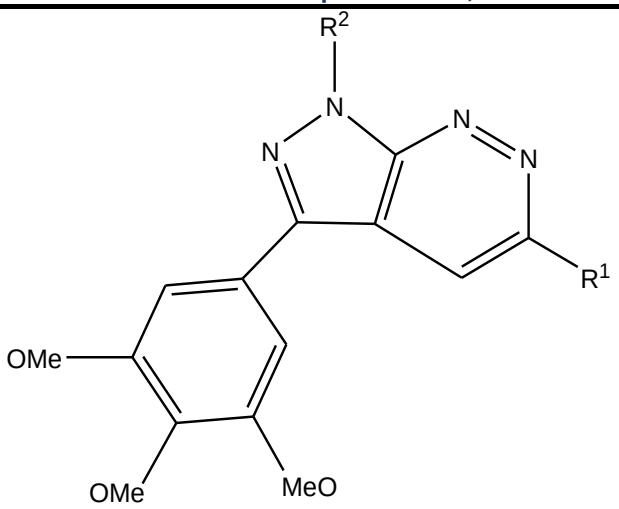
Comp. 12

Comp **12** shows cytotoxicity against hepatocellular carcinoma (Hep-G2) and colon carcinoma (HCT-116), an IC_{50} value of 660µg/mL against Hep-G2 cells and 915µg/mL against HCT-116 cells[45].



Comp.13 (Coumarin with pyrazoline moiety AT C-3).

Comp **13**[(R1 and R2=H, without substitution)] shows cytotoxic effectiveness for human prostate cancer prevention (PC3), human epidermoid carcinoma (A431), and human gastric cancer (SGC7901) cell lines and having IC_{50} = 2.69 µM, the most effective substance against SGC7901[46].



1,5-diaryl-3-(3,4,5 Synthesis of 1,5-diaryl-3-(3,4,5-trimethoxyphenyl) pyrazolo [4,3- - trimethoxy phenyl) pyrazolo [4,3-ee] [1,2,4] triazines.

Comp. 14

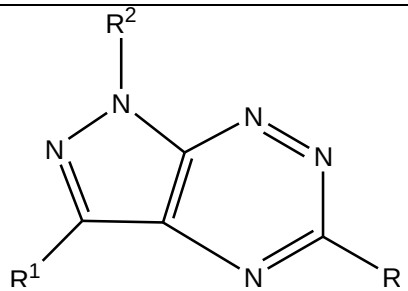
14a, 14b, 14c; R^1 = phenyl

14a: R^2= 2-methoxyphenyl
14b: R^2: 3-methoxyphenyl
14c: R^2:4-methoxyphenyl

Table No. 3

Comp	R_1	R_2	MTT Assay ($IC_{50}\mu M$)				
			CEM	CEM DNRBulk	K562	K562Tax	A549
14b	Ph	3-OCH_3-ph	109	118	182	94.3	5.41
14c	Ph	4-OCH_3-ph	8.41	99.3	117	159	0.61

Compound **14** These compounds showed a specific inhibitory effect on the A549 cell line and appear to be effective against leukaemia cell lines, including the typically exceedingly chemosensitivity CEM lymphoblasts.[47].



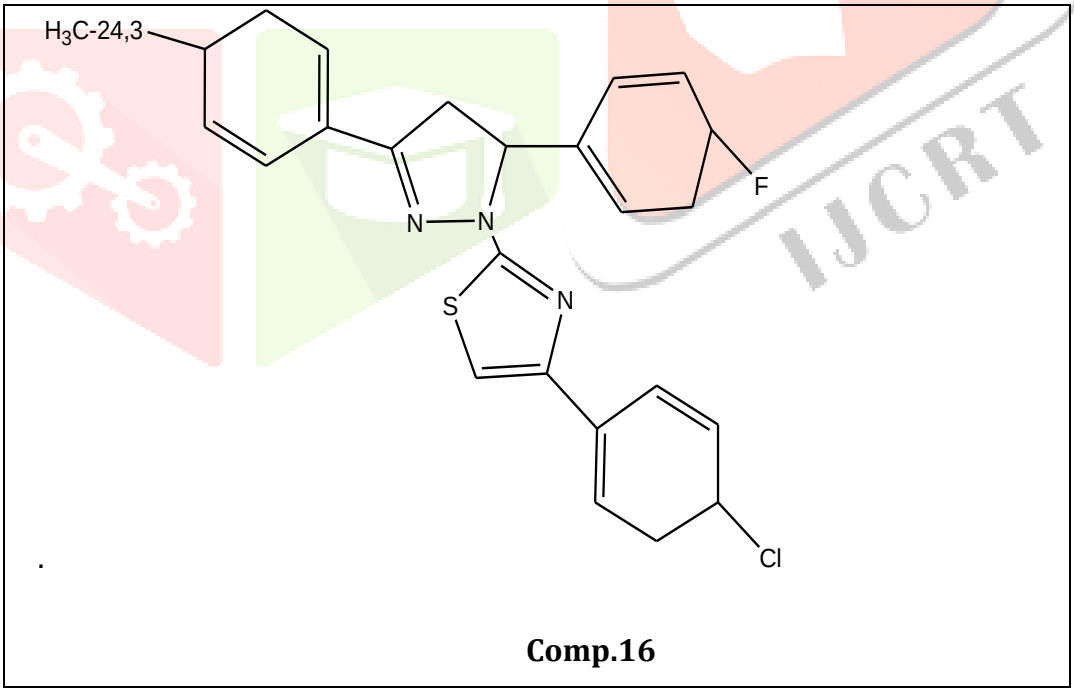
pyrazolo[4,3-e][1,2,4]triazines

Comp.15

Com **15** synthesised pyrazolo[4,3-e][1,2,4]triazines [8,9,15,16,19-21] demonstrated modest efficacy against several human tumour cell lines, including prostate cancer (PC-3), breast cancer (MCF-7), non-small-cell lung cancer (H460), and colorectal adenocarcinoma (Colo205). Table 2 lists their cellular toxicity and structural details. In Colo205 cells, the 3-methyl-1-phenyl-5-phenylaminopyrazolo[4,3-e][1,2,4]triazine derivative demonstrated the greatest reduction in cell viability with an IC_{50} value of 4 µM. [47].

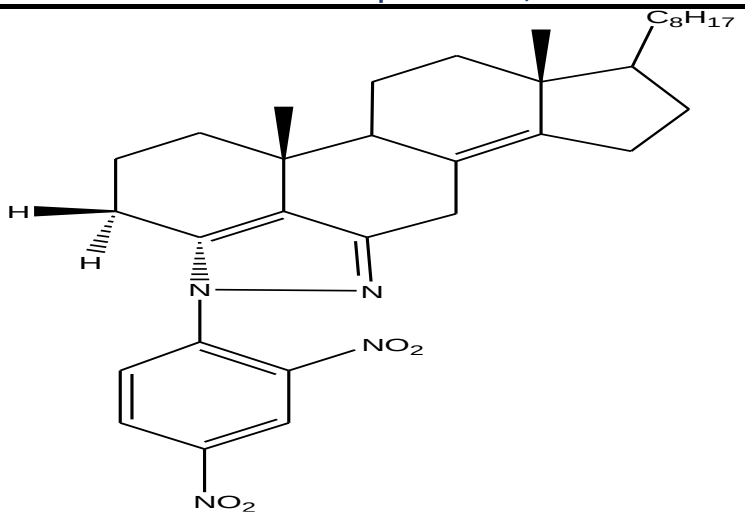
Table No. 4

			MTT Assay, IC_{50} (µM)			
R	R^1	R^2	PC-3	MCF-7	H460	Colo205
SCH_3	C_2H_5	4-NO_2-ph	98	78	36	75
Ph	CH_3	Ph	98	NA[1]	NA[1]	NA[1]
SO_2CH_3	CH_3	Ph	25	50	25	25
NH-Ph	CH_3	Ph	81	90	86	4



Comp.16

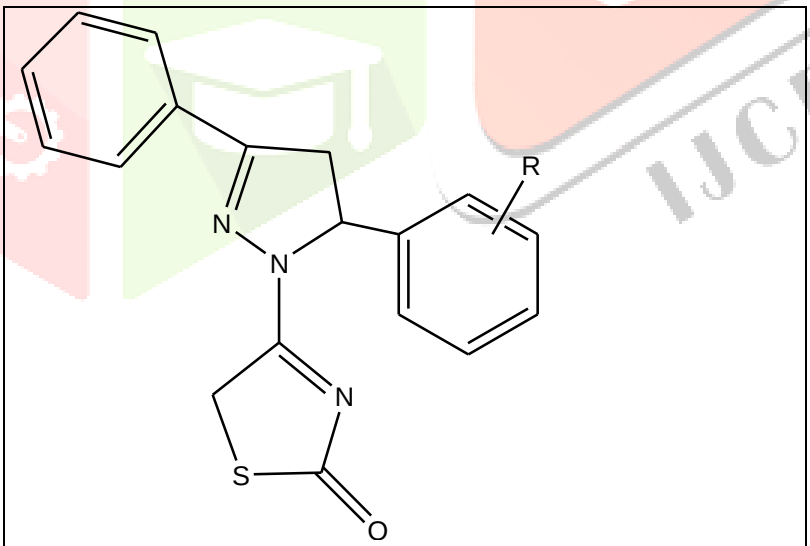
Compound **16** significantly inhibited MCF-7 cell proliferation with an IC_{50} of 0.07 µM, which was comparable to the erlotinib (a positive control) at 0.02 µM. Compound **16** would be a powerful anticancer drug as a result since it has a sizable amount of EGFR TK inhibiting action[48].



9-(2,4-Dinitro-phenyl)-3a,5b-dimethyl-3-octyl2,3,3a,4,5,5a,5b,6,7,8,9,11-dodecahydro-1H-9,10-diaza-cyclopenta[j]acephenanthrylene

Comp.17

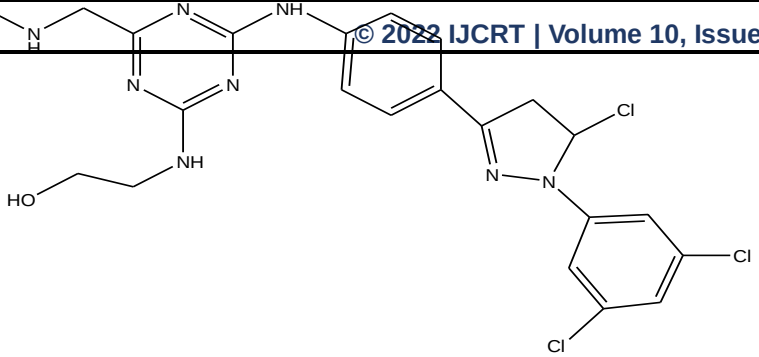
Comp **17** shows Different levels of anticancer inhibition were seen when a variety of B-ring-derived pyrazoline-substituted cholestane derivatives were tested in vitro against the human cancer cell lines SW480, HeLa, A549, HepG2 and HL-60. The 2,4-dinitrophenylhydrazine derivative had the highest efficacy of all the pyrazoline derivatives, with half maximal inhibitory concentrations (IC_{50}) of 15.39μM(HL60), 18.31μM (A549), and 23.52 μM. (HepG2)[49].



5-aryl-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl

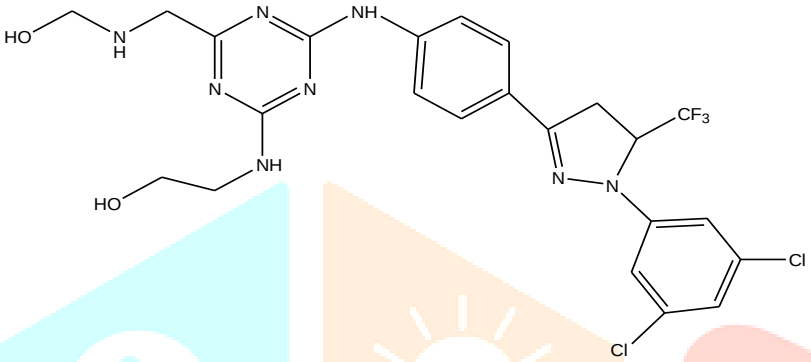
Comp.18

compound **18 (**new triazolones-based) with the 5-aryl-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl framework and their anticancer properties. The National Cancer Institute tested the *in vitro* anticancer activity of



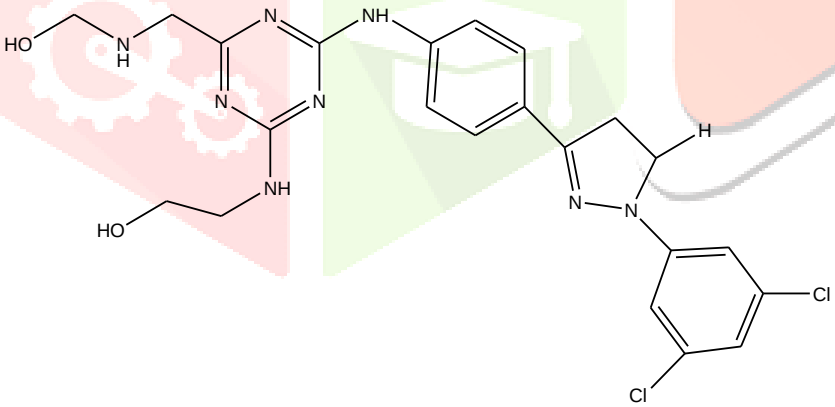
2-{4-{4-[5-Chloro-1-(3,5-dichloro-phenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-phenylamino}-6-[(hydroxymethyl-amino)-methyl]-[1,3,5]triazin-2-ylamino}-ethanol

Comp. 19a



2-{4-{4-[1-(3,5-Dichloro-phenyl)-5-trifluoromethyl-4,5-dihydro-1*H*-pyrazol-3-yl]-phenylamino}-6-[(hydroxymethyl-amino)-methyl]-[1,3,5]triazin-2-ylamino}-ethanol

Comp: 19b



2-{4-{4-[1-(3,5-Dichloro-phenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-phenylamino}-6-[(hydroxymethyl-amino)-methyl]-[1,3,5]triazin-2-ylamino}-ethanol

Comp. 19c

various substances, and found that the majority of them showed anticancer activity against leukaemia, melanoma, lung, colon, CNS, ovarian, renal, prostate, and breast cancer cell lines. The most effective anticancer substance was discovered to have a selective effect on colon cancer cell lines, particularly on HT 29 (log GI_{50} = -6.37)[50].

Table No.5

Compound (GI)	Mean growth	Most sensitive cell line	Growth inhibition of most sensitive cell line (%)
19a	9.09	LOX IMVI (Melanoma) SK-MEL-28 (Melanoma) RXF-393(Renal) SF-295(CNS)	-53.44 -55.82 -47.03 -68.27
19b	33.33	CCRF-CEM (Leukaemia) SF-295 (CNS) LOX IMVI (Melanoma) RXF-393	-6.50 -15.49 -48.52 -27.23
19c	45.23	LOX IMVI (Melanoma) HT29 (Colon)	-36.95 -47.03

The obtain compound (i.e.,19a, 19b,19c) the National Cancer Institute's (NCI-USA) division of drug development through the compare program. The 58-cell panel is derived from nine different cancer strains: leukaemia, lung, melanoma, colon, CNS, ovary, renal, breast, and prostate cancers.

Compound **19a** displayed GI_{50} values between 1.18 and 2.58 µM and LC50 values between 5.16 and >100 µM. According to Molecules 2018, 23, 1956, 6 of 20, both compounds (**19a and 19b)** were found to be particularly efficient against SF-539 (CNS), with GI50 values of 1.35 and 1.18 µM, respectively. In terms of cytotoxicity, compound 19b demonstrated the best results against SF-539 (CNS, LC50 = 5.15 µM), while compound **19a** demonstrated the best results against ACHN (renal, LC50 = 5.16µM)[51].

Conclusion:

Pyrazoline Are five membered heterocyclic compounds containing two nitrogen atoms. Pyrazolines is a dihydro derivative of pyrazole. 1-pyrazoline, 2-pyrazoline and 3-pyrazoline are the chemical forms of pyrazoline. Compound **1a,2,3,6,8,17,18**, shows moderate anticancer activity against HCC1806, Hela, A549, HCT176, HePG2, leukemia, melanoma, colon, CNS, ovarian, breast cancer cell line. among those compounds **7** against SGC 7901, A549 Raji and Hela cells IC_{50} values of 29.39, 13.67, 3.91, and 29.14 µM. Comp **11** against HePG2, MCF-7, HeLa, and PC3 cell line IC_{50} 7.2,5.6,5.5,7. 8µM.Comp **15** against prostate cancer (PC-3), breast cancer (MCF-7), non-small-cell lung cancer (H460), and colorectal adenocarcinoma (Colo205) IC_{50} 4 µM. Comp**16** significantly inhibited MCF-7 cell proliferation with an IC_{50} of 0.07 µM. it would be a powerful anticancer drug.

it has a stable amount of EGFR TK inhibiting action. Other molecules show poor anticancer activity,

Future scope:

This review article data very useful for research scholars to design and development or more potent anticancer molecules active against spectra cell lines based on repeated anticancer structural data of pyrazole derivative.

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