REVIEW ARTICLE

Pyrazoline Derivatives as Privileged Scaffolds in Medicinal Chemistry: A Comprehensive Review of their Anticancer Potentials

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ABSTRACT

Despite significant advances in diagnostic technologies and targeted therapies, cancer remains a formidable global health challenge due to its complex biology and adaptive resistance mechanisms. Heterocyclic complexes are contemporary in almost 90% of novel medications, and they cross the chemistry-biology boundary where a prodigious deal of innovative systematic understanding, research, and application is occurring. One of the significant regularities in the medicinal chemistry is fused heterocyclic complexes, due to their broad-spectrum therapeutic functions. Amongst these, nitrogens-containing derivatives, like pyrazoline, isoxazoline, quinazoline and pyrimidine derivative are essential due to their multiple therapeutic applications including anticancer, anti-microbial, anti-alzheimier, anti-viral, anti-inflammatory, antimalarial and antitubercular properties. Additionally, to being effective against a wide range of newly emerging infectious diseases, heterocyclic compounds with pyrazoline moiety may also result in the development of potent derivatives, which are necessary for cancer treatment. 2-Pyrazolines are commonly investigated and more stable than 1- or 3-isomers of pyrazoline analogues. These derivatives can be synthesized via both conventional and greener techniques, including refluxing, microwave assisted synthesis, ultrasonic sonication mediated and oil bath mediated synthesis. This review focusses on the biological significance and anticancer applications of the pyrazoline derivatives. As a result, this review will be helpful in the future when designing new medications to treat cancer and its biological effects.

Keywords: Pyrazoline, 2-Pyrazoline, Heterocyclic chemistry, Anticancer, Breast cancer, Biological applications

INTRODUCTION

Cancer is the one amongst main diseases that cause mortality and morbidity all over, which poses a severe danger to people's ability to live healthily. Every year, almost 10 million people are diagnosed with various forms of cancer. They have a high level of molecular heterogeneity, which results in medication resistance to make the treatment challenging still [1]. Clinical markers can used to determine the developing tumors, based on initial diagnoses, track the tumor progression and assess the needed therapies to minimize the death rates due to the cancer [2]. Chemotherapy has been widely used for effective cancer treatments compared to targeted therapy, radiotherapy and surgery [3]. The World Health Organization reports that among emerging nations, cancer positions as the second principal cause of death. Researchers are working hard to create a new anti-neoplastic drug that is efficient and causes fewer toxic effects in the human body [4]. Heterocyclic compounds play a vital role in a diverse range of physiological functions linked to this class of molecules which makes it significant. The study of chemistry and biology in heterocyclic compounds is a fascinating field for future purposes [5]. The biological reactions frequently exhibit preference specificities due to the existence of heteroatoms or groups. The development of anticancer drugs becoming more interesting in naturally occurring heterocyclic molecules. The purpose of these novel strategies of heterocyclic compounds with numerous promising anticancer properties includes the development of activities by focusing on the tumor and other cancers such as lung, breast, colon and so on [6]. The heterocyclic compounds of pyrazoline and isoxazoline derivatives which belong to the azole family constitute extensive potential biological properties such as antioxidant, COX-2 inhibitor,antimicrobial and anticancer activities [7]. Pyrazoline is a five-membered heterocyclic molecule with nitrogen which offers a new source for synthesizing different derivatives with potent biological activities. Various types of heterocycles made up of pyrazoline derivatives are not only used in medications but also act as fungicides, insecticides, dyes and rubber chemicals [8]. Pyrazoline is a heterocyclic compound having two adjacent nitrogens at 1-2 positions with one endocyclic double bond with a wide spectrum of activity [9]. Its structure consists of a pyrazole ring with a saturated bond between those two positions.

The broad range of research on the biological activity of pyrazolines relies on cell-based assays and lacks molecular target identification. Pyrazoline has numerous pharmacological characteristics including anticancer, anti-inflammatory, analgesic, anti-depressant and anti-microbial properties [10]. Focusing towards anticancer activities, pyrazoline and their derivatives exhibited activities against breast cancer [11], cervical cancer [12], liver cancer [13], lung cancer [14], prostate cancer [15], colon cancer [13] and ovarian cancer [16]. Pyrazolines are closely tied with pyrazoles which have one fewer binary bond in their structure. Three isomers of pyrazoline exist, 1-pyrazoline, 2-pyrazoline, and 3-pyrazoline, distinguished by the presence or absence of a double bond. The most prevalent one was 2-pyrazoline. Derivatives of pyrazoline have a single endocyclic bond [9]. Pyrazolines are basic substances that can react with acids to produce salts. They have a potent fluorescence in solution, which makes them effective fluorescent brighteners. Due to their biological activity, pyrazolines and substituted pyrazolines have received a lot of importance among researchers [17]. The formation of pyrazolines can be accomplished through various methods, including the reaction of α,β-unsaturated ketones or aldehydes with hydrazines and 1,3-dipolar cycloaddition of nitrile Schiff bases (imines) to alkenes. Many compounds like ibipinabant, ramiphenazone, oxyphenbutazone, phenylbutazone and antipyrine contain the 2-pyrazoline scaffold [18]. The biologically important FDA-approved anticancer drugs bearing pyrazoline moiety along with the mechanism are given in figure 1. In this review, the literature survey was steered from PubMed, ScienceDirect, Embase and Google Scholar databases during the period of 2011-2025. As a search strategy, the keywords include pyrazoline, 2-pyrazoline, pyrazoline derivatives, anticancer activity, anti-breast cancer activity, cervical, lung, liver, prostate, ovarian and colon cancer, medicinal properties of pyrazolines and heterocyclic compounds. The keywords were utilized individually and in combination for collecting the literature. Following that, the titles and abstracts of each article were reviewed to remove any irrelevant ones. So, in order to help with cancer care, this review is going to concentrate on pyrazoline and its derivatives' structures, mechanisms, and features.

Pyrazoline Derivatives Against Cervical Cancer

Alam *et al*., 2017(12) tested a sequence of 1-(5-(3-(aryl)-1-phenyl-1H-pyrazol-4-yl)-3-(pyridin-3-yl)-4,5-dihydro-pyrazol-1-yl) ethanone derivatives (1-3) for their cytotoxicity via the 3-(4,5-dimethyl-thiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay against HeLa (cervical cancer) cell line. These compounds possessed potent anti-cervical cancer activity. Also, they exhibited superior IC_{50} values against the tested cancer cell line [12]. A series of hetero-aromatic scaffolds on curcumin containing pyrazoline substituted analogs were evaluated to determine the anti-proliferative activity against the HeLa cell line using MTT assay. (5-(5-Methoxy-1-methyl-1H-indol-3-yl)-3-(3-methoxyphenyl)-4,5-dihydro-1H pyrazol-1-yl)(6-methylpyridin-3-yl)methanone (4) has exhibited potent activity with better interactions and three-H-bond interactions higher than the parent molecule, determined by the molecular docking studies [19]. The pyrazoline derivatives associated N-methyl indole moiety were tested to assess the antineoplastic action towards the HeLa cancerous cell line by employing the MTT and colchicine assay. (5-(5-Methoxy-1-methyl-1H-indol-3-yl)-3-(3-methoxy phenyl)-4,5-dihydro-1H pyrazol-1-yl) (6-methyl pyridin-3-yl) methanone (5) showed better anti-cancer activity, lacking noxiousness to non-cancerous cells. The colchicine competition experiment proved that they have a potential tumor therapy by binding to tubulin's colchicine and blocking tubulin assembly. Analysis of the compound's molecular docking and interaction patterns revealed that it inhibits tubulin polymerization. The tested compound has also arrested the G2/M phase and induced cell apoptosis subsequently [20]. 1-Isobutyl-N-(4-(5-(4-methoxy phenyl)-4,5-dihydro-1H-pyrazol-3-yl) phenyl)-1H-imidazo [4,5-c] quinoline-4-amine (6) was investigated for its potential against cervical cancer. It was assessed using the Trypan blue exclusion assay and found to be possessing good anti-tumor activity against the HeLa cancer cell line [21]. The acetylated pyrazoline was synthesized by cyclization reaction and subjected to antiproliferative screening. Among the tested compounds, 1-acetyl-5-(2,4,5-trimethoxyphenyl)-3-(2-naphthyl)-4,5-dihydro-1H-pyrazole (7) has potent anti-tumor activity against the HeLa cancer cell line with a better IC_{50} value, assessed by the MTT assay [22]. 1,1′-(5,5′-(1,4-phenylene) bis (3- (naphthalen-1-yl) - 4,5-dihydro-1H-pyrazole-5,1-diyl)) diethanone (8) was produced and was tested against the HeLa cancer cell line. The synthesized derivatives were evaluated by Enzyme-linked Immunosorbent Assay (ELISA). Among the series of derivatives, it has a promising anti-cancer activity [23]. A novel series of D-condensed 2-pyrazoline was synthesized and evaluated by the ELISA.(3S,16R,17S)-3′-Methyl-1′-methyl-2′-pyrazolino[4′,5′:17,16]androst-5-en-3-ol (9) has a promising cell cycle disturbance and was examined by *in vitro* studies against the Human cervical cancer cell line HeLa, which has shown potent anti-neoplastic activity [24].

Patel *et al*., 2021[25] prepared a series of pyrazoline scaffolds by the process of cyclization that were screened using the MTT assay against a HeLa cancer cell line. The tested compounds exhibited better cytotoxicity and were found to have higher efficacy with better binding potential to the CDK2 protein, determined according to molecular docking studies. Among the tested compounds, 5-(9-Ethyl-9H-carbazol-3-yl)-3-(2-oxo-2H-chromen-3 yl)-4,5-dihydro-1H-pyrazole-1-carboxamide (10) and 3-(1-(3-Chlorophenyl)-5-(9-ethyl-9H-carbazol-3-yl) 4,5-dihydro-1H-pyrazol-3-yl)-8-methoxy-2H-chromen-2-one (11) were found to be most active and exhibits a potential to arrest cell cycle progression and to induce apoptosis [25]. A novel 2′-(2 ′′- 4 ′′- dinitrophenyl)-5α-cholestano [5,7-cd] pyrazoline (12) was investigated to govern the anti-tumor action in contrast to the HeLa cell line. This compound was screened by using the MTT cell viability assay and has a potent promising activity in the prevention of Human cervical cancer [26]. Using the MTT assay, the anti-cervical cancer potency of the steroidal pyrazoline cholest-5-en-7-one (13) was assessed against the HeLa cancer cell line using 5-FU and Doxorubicin as standard and 8-chloro-3-(1*H*-indol-3-yl)-2-phenyl-2,3,3a,4-tetrahydro[1]benzothiopyrano[4,3-*c*]pyrazole was found to be a potent anti-neoplastic compound with significant IC_{50} value [27]. A series of 3-(1H-indol-3-yl)-2,3,3a,4-tetrahydrothiochromeno[4,3-c]pyrazole derivatives were synthesized by Song *et al*., 2020[28] and tested their efficacy as topoisomerase II selective inhibitors. These substances have a higher IC_{50} value and demonstrate strong action against the cervical cancer cell line HeLa, according to the studies. Further, 6,8-dichloro-3-(1*H*-indol-3-yl)-2-phenyl-2,3,3a,4-tetrahydro[1]benzothiopyrano[4,3-*c*]pyrazole (14) and 6,8-dichloro-3-(1*H*-indol-3-yl)-2-phenyl-2,3,3a,4-tetrahydro[1]benzothiopyrano[4,3-*c*]pyrazole (15) induced G2/M phase cell cycle arresting and promising anti-cervical cancer activity via promoting apoptosis. These compounds also showed specific inhibitory effects towards topoisomerase II. DNA unwinding and cleavage reaction assays demonstrated that these compounds were a non-interactive topo II catalytic inhibitor, which agreed with the docking findings [28]. Yu *et al*., 2014 [29] tested a series of 4-(5-(Benzo[d][1,3]dioxol-5-yl)-3-(trifluoromethyl)-4,5-

dihydro-1H-pyrazol-1-yl)benzenesulfonamide (16) for cytotoxicity using the ELISA and Inhibitory assays. The chemical exhibited strong action towards the HeLa cells, according to the findings. This compound showed better inhibitory potential, QSAR also performed and found to be the inhibitor ofthe COX-2/B-Raf pathway [29]. The structures of compounds (1–15), which were previously described, are shown in figure 2, while compound (16) is shown in figure 3.

Pyrazoline Derivatives against Breast Cancer

The series of novel pyrazoline-containing compounds was designed and cytotoxicity against breast cancer was assessed using molecular docking studies with tamoxifen and erlotinib as standards. The study revealed that 5-(4-chlorophenyl)-1,3-diphenyl-4,5-dihydropyrazole (17) was established as most dynamic against P450, 4-(2-chlorophenyl)-2-(4-chlorophenyl)-1-phenyl-2,3-dihydropyrazole (18) was active against EGFR and 2,4-bis(2-chlorophenyl)-1-phenyl-2,3-dihydropyrazole (19) had exhibited higher potential against VEGFR1 and VEGFR2. The given compounds were also found to be exhibiting good pharmacokinetic properties and were predicted to be non-toxic [30]. 8-[1-(4-Chloro phenyl sulfonyl)-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl]-7-methoxy-2H-chromen-2-one (20) was created and assessed for its capability to prevent the development of breast cancer cells (MCF-7) using the SRB assay; the results showed that it was an effective candidate. Also, it was proved that it can efficiently inhibit the PI3K Isoforms [11]. Lv *et al*., 2011[31] designed thiazolyl-pyrazoline derivatives and evaluated its anti-proliferative activity against the MCF-7 cancer cell line. Among different derivatives, 4-(4-chlorophenyl)-2-(3-(3,4-dimethylphenyl)-5-(4-fluorophenyl)-4,5-dihydro-1H-pyrazol-1-yl)thiazole (21) has potent anti-breast cancer activity. According to the molecular docking studies, it was found to be having high potency as EGFR Kinase inhibitor and will exerts the potential towards the ATP binding site [31]. (5-(benzo(d)[1,3]dioxol-5-yl)-3-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)(3,4,5-tri methoxyphenylmethanone (22) was investigated for its potent anti-proliferative activity against the MCF-7 breast cancer cell line using MTT assay. Also, this compound induces the accumulation of cells in the G2/M phase of the cell cycle and promotes apoptosis [32]. Anticancer prospective of Bis-pyrazoline (23) was investigated against the MCF-7 cells using the MTT technique, compared with the standard 5-Fluorouracil. This compound was found to be potent against breast cancer and also found to be inhibiting the VEGFR2 Tyrosine Kinase receptor [33]. Rabou *et al*., 2018 [33] tested a series of bis-N-thioamide pyrazolines for the investigation of cytotoxicity using the MTT assay. They have possessed promising efficacy towards MCF-7 cells. Among the established derivatives, 1,4-bis (5-methyl-4-(5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-1H-1,2,3-triazol-1-yl)benzene (24) has exhibited significant activity. The molecular docking studies were also carried out and found to have significant inhibitory potential against VEGFR Tyrosine Kinase enzyme [33]. 1-[3-(5-bromo thiophen-2-yl)-5-(4-methoxy phenyl)-4,5-dihydro-1H-pyrazol-1-yl] ethanone (25) was synthesized by the process of condensation. Anti-cancer investigations on breast cancer cell line MCF-7 using Doxorubicin as the standard drug was evaluated by SRB assay and found to be more active [34].

The antiproliferative potential of the series of novel synthetic pyrazolines were assessed by using SRB assay. Among the tested compounds,1-(5-(4-Chlorophenyl)-3-(4-ethoxyphenyl)-4,5- dihydropyrazol-1-yl)ethanone (26) showed better activitywith significant IC_{50} value and provided the relationship between structure and activity for the design of anti proliferative agents [35]. Using the MTT assay towards MCF-7 cancer cells, investigators looked into the antiproliferative potential of a number of 5-substituted aryl-2-pyrazoline derivatives. Among them, 1-(2, 4-di-nitro phenyl)-5-(4-chloro phenyl)-3-(4- methoxy phenyl)-2-pyrazoline (27) and 1-(2,4-di-nitro phenyl)-5-(4-N,N-di-methyl amino phenyl)-3-(4-methoxy phenyl)-pyrazoline (28) remained as the effective compounds with better IC_{50} values. To identify the most effective binding mode and supportive mechanism, these compounds were docked with the Epidermal growth factor receptor (EGFR) and found to be potent EGFR inhibitors with better binding affinities [36]. The anticancer potential of 3-(4-methoxyphenyl)-5-substituted phenyl-2-pyrazoline-1-carbothioamide derivatives was screened by using SRB assay. 3-(4-Methoxyphenyl) -5-phenyl-2-pyrazoline-1-carbothioamide (29), 5-(3-Methoxyphenyl)-3-(4-methoxyphenyl)-2-pyrazoline-1-carbothioamide(30),5-(4-Chlorophenyl)-3(4methoxyphenyl)-2-pyrazoline-1-carbothioamide(31) and 3-(4-Methoxyphenyl) -5-(p-tolyl) -2-pyrazoline1-carbothioamide (32) have significant anti-cancer activity against the MCF-7 breast cancer cell line and observed an EGFR inhibitory activity [37]. The structures of compounds (17–30), which were previously described, are shown in figure 3, while

compounds (31) and (32) are shown in figure 3. To determine the efficacy of an array of new pyrazoline derivatives bearing naphthalin through inhibiting cell proliferation in the MCF-7 cells, researchers used the MTT assay in conjunction with inhibitory assays such as the EGFR/HER-2, HER-3, VEGFR-2, FAK, and BCATM protein assays. Among them, 3-(3,4-Dichlorophenyl)-5-(naphthalen-2-yl)-4,5- dihydro-1H-pyrazole-1-carbothioamide (33) has a better IC_{50} value and is devoted to have EGFR/HER-2 inhibitory activity [38]. Employing the MTT colorimetric technique, a battery of new pyrazolines was tested towards the anti-cancer potential against MCF-7 cells. Among the tested derivatives, 1-(2,4-dinitrophenyl)-3-((7-propylnaphthalen-1-yl)methoxy)-4,5-dihydro-1H-pyrazole-5-carboxylic acid (34) has high IC_{50} value. According to the molecular docking studies, this compound was found to act upon the ER-α receptor [39]. (E)-5-(4-Methoxyphenyl)-3-(4-methoxystyryl)-4,5-dihydro-1H-pyrazole-1-carboxamide (35), (E)-3-Phenyl-5-styryl-4,5-dihydro-1H-pyrazole-1-carbothioamide (36), (E)-3-(4-Chlorophenyl)-1-phenyl-5-styryl-4,5-dihydro-1H-pyrazole (37) and E)-1-(4-Methoxyphenyl)-3-phenyl-5-styryl-4,5-dihydro-1H-pyrazole (38) were prepared and found to be having promising cytotoxicity against the breast cancer cell line MCF-7, determined by the MTT assay with a standard reference staurosporine. According to the molecular docking investigations, these compounds were devoted as effective EGFR inhibitors [40]. 2-[3,5-bis(4-chlorophenyl0-4,5-dihydro-1H-pyrazol-1-yl]-5-(2-methoxybenzylidene)-1,3-thiazol-4(5H)-one (39) was prepared by Khalil *et al*., 2012 [41]. This compound was found to be a potent anti-cancer compound against the MCF-7 cancer cell line, compared with the standard Doxorubicin, determined using SRB assay [41]. The antiproliferative efficacy of the thiazolyl-pyrazolines was evaluated via MTT assay against the MCF-7 cell line (breast cancer). Based on the molecular docking and *in vitro* investigations, 1-(4-(4-Cyanophenyl)thiazol-2-yl)-3-(4- morpholinophenyl)-5-(4-chlorophenyl)-2-pyrazoline (40) and 1-(4-(4-Cyanophenyl)thiazol-2-yl)-3-(4- piperidinophenyl)-5-(4-chlorophenyl)-2-pyrazoline (41) was identified as the potent molecules, which has significant inhibitory potential, along with high affinity towards the ATP binding sites of EGFR and HER-2 [42].

2-(5-(Benzo[d][1,3]dioxol-5-yl)-3-(4-bromophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-4-(4-bromophenyl)thiazole (42) was found to have potent anti-proliferative activity against the MCF-7 cancer cell line with better IC_{50} value. This compound was also found to be inhibiting the HER2 receptor, determined by the molecular docking studies [43]. Jasril *et al*., 2020 tested a pyrazoline analog against an MCF-7 cell line, evaluated using the MTT assay technique. 5-(4-fluorophenyl)-3-(naphthalen-1-yl)-4,5-dihydro-1*H*-pyrazole (43) was estimated as highly effective and it was evidenced that the compound has hydrogen bonding interactions with Arg 791 and also a hydrophobic interaction with His 790, estimated via molecular docking studies [44]. A novel pyrazoline derivative, 5-(4-fluorophenyl)-3-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole (44) was tested for its cytotoxic potential towards the MDA-MB-231 cell line and has found to possessing promising anti-cancer efficacy, which was evaluated by Scratch-wound and Transwell assays. It induces apoptosis via arresting the G0/G1 phase cell cycle [45]. 1-(2-93,5-diphenyl-4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethyl) imidazolidine-2,4-dione (45) has a promising anti-cancer potential against the MCF-7 cells, assessed by the MTT cell viability technique. This compound has a potent possession in breast cancer activity. Studies conducted using *in vitro* methods revealed increased DNA damage, Caspase activation, Cell cycle arrest in the G0/G1 phase and a decrease in the expression of the anti-apoptotic protein BCL-2 [46]. The structures of compounds (33–45), which were previously described, are shown in figure 4. A novel steroidal glycoside pyrazoline functionalhybrid,4-((17-(5-(2-chloro-4-methylphenyl)-4,5-dihydro-1H-pyrazol-3-yl)-8,14-dihydroxy-3((2R,4S,5R,6R)5-(((1S,3S)-4-hydroxy-3-methylcyclohexyl)oxy)-4methoxy6methyltetrahydro2Hpyran2yl)10,13dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-12-yl)oxy)benzoyl chloride (46) was prepared and evaluated for cytotoxicity against the MCF-7 cell line and the compound exhibited promising potential with potent IC_{50} value [47]. 4-(5-(4-chlorophenyl)-3-(pyridine-2-yl)-4,5-dihydro-1H-pyrazol-1-yl) benzene sulfonamide (47) acts as an effective agent towards the MCF-7 breast and MDA-MB-468 triple negative breast cancer cell lines. According to the molecular docking studies, this compound has a high docking score against the PARP1 and acts as potent PARP1 antagonist [48]. A series of new pyrazoline hybrids were efficiently synthesized by Kumari *et al*., 2020 [7]. (2R,3S,4R,5R,6S)-2-(hydroxymethyl)-6-((5-(5-nitro-1H-indol-3-yl)isoxazol-3-yl)methyl)tetrahydro-2H-pyran-3,4,5-triol (48) was found to be potent promising anti-cancer compound against the MCF-7, MDA-MB-453 and MDA-MB-231 breast cancer cell lines, assessed by the MTT assay. The molecular docking findings also agreed with the results of the MTT assay [7]. The structures of compounds (46–48), which were previously described, are shown in figure 5.

Pyrazoline Derivatives Against Colorectal Cancer

3-Anthracen-9-yl-5-phenyl-4,5-dihydro-1H-pyrazole (49), 3-Anthracen-9-yl-5-(4-chloro-phenyl)-4,5-dihydro-1H pyrazole (50), 3-Anthracen-9-yl-5-p-tolyl-4,5-dihydro-1H-pyrazole (51) and 3-Anthracen-9-yl-5-(3-chloro-phenyl)-4,5-dihydro-1H pyrazole (52) were evaluated and identified as promising anti-cancer compounds against the HCT-116 cell line, escorted by better IC_{50} values. These compounds were screened by using an MTT assay using curcumin as a standard [13]. 3-(5′-chloro-2′-hydroxy-4′,6′-dimethylphenyl)-5-(4-(N,N-dimethylamino)phenyl)-1-(p-sulfamylphenyl) —pyrazoline (53) was evaluated for anti-cancer activity against COLO 205 cell line and found to be a potent against the treatment of colorectal cancer [49]. 1,3-Diphenyl-4-(4-fluoro phenyl)-5-(4-fluoro benzoyl) pyrazoline (54) and 4-(4-Fluoro phenyl)-5-(4-methoxy benzoyl)-1-phenyl-3-(styryl) pyrazoline (55) were prepared and their potency against the HT29 cell line was assessed using the SRB assay. The produced compound was found to be a promising anti-colon cancer compound with better IC_{50} value [50]. 1,3,5-triaryl-2-pyrazoline (56) was prepared and gauged for its colon cancer efficacy against the HCT116 cells using the SRB assay. 1-(4-bromophenyl)-4-(4-fluorophenyl)-3-phenylimidazolidine was found to be more potent, yielding a more favorable IC_{50}value. It showed a better structural and molecular features, related to its biological activity [51]. The HCT 15 cell line was used to assess the cytotoxic potential of many new pyrazoline derivatives through the use of the ATPase test and the DNA-Topo II cleavable complex assay. Among the tested derivatives, Benzo [d] thiazol-2-yl-(3-(4-chloro phenyl)-5-(4-methoxy phenyl)-4,5-dihydro-1H-pyrazol-1-yl) methanone (57) showed a better IC_{50} value. The endogenous topo mediated DNA relaxation studies were also performed, it indicated that this compound can effectively inhibited endogenous topo-mediated pBR322 plasmid relaxation than the standard etoposide [52]. 2-[5-(4-Fluorophenyl)-3-(4-tolyl)-4,5-dihydropyrazol-1-yl]-1-methyl-6-oxo-4-phenyl-1,6- dihydropyrimidine-5-carbonitrile (58) and 2-[3-(4-Chlorophenyl)-5-(4-methoxyphenyl)-4,5-dihydropyrazol-1-yl]-1-methyl-6-oxo-4-phenyl-1,6-dihydropyrimidine-5-carbonitrile (59) was appraised using the HT 29 colon cancer cell line by Cell Titer Glo technique. From this assay, these compounds were found to possess potent anti-proliferative activity [53]. The structures of compounds (49-58), which were previously described, are shown in figure 5, while the compound (59) is shown in figure 6.

Using the Sulforhodamine B assay, novel 17 -pyrazolinyl derivatives of pregnenolone were explored to appraise their cytotoxic action towards HT-29 and HCT-15 cell lines. 1-(5-(3-Fluorophenyl)-4,5-dihydro-3-((10R,13S)2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3-hydroxy-10,13-dimethyl-1H-cyclopenta[a]phenanthren 17-yl)pyrazol-1-yl)ethenone(60),1-(5-(4-Fluorophenyl)-4,5-dihydro-3- ((10R,13S)2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3-hydroxy-10,13-dimethyl-1H-cyclopenta[a]phenanthren-17- yl) pyrazol-1-yl) ethenone (61), 1-(4,5-Dihydro-3-((10R,13S)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3-hydroxy-10,13dimethylcyclopenta [a] phenanthren -17- yl) -5-o-tolylpyrazol-1-yl) ethenone (62), 1- (4,5-Dihydro-3-((10R,13S)-2,3,4,7,8,9, 10,11,12, 13,14,15,16, 17-tetradecahydro-3-hydroxy-10,13-dimethyl-1H-cyclopenta[a]phenanthren-17-yl)-5-m-tolylpyrazol-1-yl) ethenone (63), 1-(4,5-Dihydro-3-((10R,13S)-2,3,4,7,8,9,10,11,12,13,14,15,16,17- tetradecahydro-3-hydroxy-10,13-dimethyl-1H-cyclopenta[a]phenanthren-17-yl)-5-(4-methoxyphenyl) pyrazol-1-yl)ethenone (64) and 1-(5-(2-Chlorophenyl)-4,5-dihydro-3-((10R,13S)- 2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3- hydroxy-10,13-dimethyl-1H-cyclopenta[a] phenanthren-17-yl) pyrazol-1-yl)ethenone (65) presented substantial anti-cancer action towards the tested colon cancer cells [54]. 2-(5-(Benzo [d][1,3]dioxol -5-yl)-3-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazol-1-yl)-4-(4substitued phenyl)thiazole (66) was produced by Mansour *et al.*,2019 [55] and tested their promising anti-proliferative activity against HCT -116 cancer cell line. This potent compound was screened by *in vitro* methods with a better IC_{50} value [55]. An innovative thiazolone-containing compound encompassing a pyrazoline moiety was screened by using a cytotoxicity assay. 5-(4-Hydroxy-3,5-dimethoxybenzylidene)-2-[5-(2-hydroxyphenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl]-1,3-thiazol-4(5H)-one (67) has significant anti-cancer activity against selective influence on HT 29 (colon cancer cell line) [56]. The anti-proliferative activity of N-acetyl and N-formyl pyrazoline derivatives was evaluated using the SRB assay against the HCT-15 cell line.5-(4-Chlorophenyl)-3-[4-(7-chloroquinolin-4-ylamino) phenyl]-4,5-dihydro-1H-pyrazole-1-carbaldehyde(68), 5-(4-Chlorophenyl)-3-[3-(7-chloroquinolin-4-ylamino) phenyl]-4,5-dihydro-1H-pyrazole-1-carbaldehyde (69), 3-[3-(7-Chloroquinolin-4-ylamino)phenyl]-5-phenyl-4,5- dihydro-1H-pyrazole-1-carbaldehyde (70), 3-[3-(7-Chloroquinolin-4-ylamino) phenyl]-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazole-1-carbaldehyde (71) and 3-[3-(7-Chloroquinolin-4-ylamino)phenyl]-5-(3,4,5-trimetho-xyphenyl)-4,5-dihydro-1H-pyrazole-1-carbaldehyde (72) were found to possess potent anti-proliferative compounds for the colon

cancer therapy [57]. The structures of compounds (60-69), which were previously described, are shown in figure 6, whereas the compounds (70-72) in figure 7.

The potency of a variety of 1-acyl-2-pyrazoline derivatives towards the HCT-1 cell line was studied. The repressive impact of the derivatives that were synthesized was appraised via the MTT assay. Among them, (2-(2,3-Dimethyl phenyl amino)phenyl) (4,5-dihydro-5- (4-methoxyphenyl)-3-phenylpyrazo-1-yl) methanone (73), 1-(4,5-Dihydro-3,5-diphenylpyrazol-1-yl)-2-(4-isobutyl phenyl) propan-1-one (74) and 1-(4,5-Dihydro-5-(4-methoxyphenyl)-3-phenylpyrazol-1-yl) 2-(4-isobutyl phenyl)propan-1-one (75) was found to be possessing potent and promising activity [58]. A series of N-acyl derivatives of ferrocenyl pyrazoline was tested via MTT assay and the compound (76) was a potent anti-cancer agent against HCT-116 human colorectal cancer cells [59]. A novel pyrazoline derivatives was efficiently synthesized and gauged for their antiproliferative action towards the HCT-116 colorectal cancer cell line using Sulforhodamine B assay. Among them, 1-(3-(4-(benzyloxy)phenyl)-5-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-1-yl) ethenone (77) and 1-(3-(4-(benzyloxy)phenyl)-5-(4-fluorophenyl)-4,5-dihydro-1H- pyrazol-1-yl) ethenone (78) was identified to be the potent candidates. The binding interaction of compounds with proteins (RCSB PDB ID: 1M17 and 5ZTO) has been studied. According to the molecular docking studies, it showed that the compounds can efficiently interacts with target proteins and also exhibited better binding affinities [60]. Using the MTT assay Tilekar *et al*., 2020 [61] assessed the anticancer potential of 1-(2-(3-9-fluorophenyl)-5-(p-tolyl)-4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethyl)pyrrolidine-2,5-dione (79) against the HT 29 colon cancer cell line. It was found to possessing potent activity and discovered to interfere with the growth phases in cell cycle analysis, causing the cell population to increase in the G_1/G_0 Phase and decrease in the G_2/M phase [61]. The structures of compounds (73-79), which were previously described, are shown in figure 7.

Pyrazoline Derivatives against Prostate Cancer

A variety of pyrazoline scaffolds were explored by to appraise their cytotoxicity against the PC-3 Prostate cancer cell line. 1-[5-(4-chlorophenyl)-3-(4-[(4-fluorophenyl)methoxy]phenyl)-4,5-dihydro-1*H*-pyrazol-1-yl]ethan-1-one (80), 5-(4-fluorophenyl)-3-(4-[(4-fluorophenyl)methoxy]phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide (81), 3-(4-[(4-fluorophenyl)methoxy]phenyl)-5-phenyl-4, 5-dihydro-1*H*-pyrazole (82) and 5-(4-chlorophenyl) -3- (4- [(4-fluoro phenyl)methoxy]phenyl)-4,5-dihydro-1*H*-pyrazole (83) have the promising anti-cancer activity and exhibits better IC_{50} value. Furthermore, the molecular docking analyses of these compounds with the EGFR and VEGFR ATP binding sites were performed and found to be potent EGFR inhibitor [15]. A series of pyrazoline derivatives were synthesized and evaluated their anti-proliferative activity against the PC-3 cancer cell line by using an MTT assay. (3-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-5-(4-dimethylamino-naphthalen-1-yl)-4,5 dihydro-pyrazole-1-carboxylic acid (4-chloro-phenyl)-amide (84), 3-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-5-(4-dimethylamino-naphthalen-1-yl)-4,5 dihydro-pyrazole-1-carbothioic acid amide (85), 1-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-3-4-dimethylamino-naphthalen-1-yl)-propenone (86),3-Benzofuran-2-yl-5-(4-dimethylamino-naphthalen-1-yl)-4,5-dihydro-pyrazole-1 carboxylic acid (4-chloro-phenyl)-amide (87) and 3-Benzofuran-2-yl-5-(4-dimethylamino-naphthalen-1-yl)-4,5-dihydro-pyrazole-1 carbothioic acid amide (88) were found be the significant anti-cancer compounds. According to molecular docking studies, these compounds can efficiently inhibit tubulin polymerization [62]. 3,5-diaryl N-acetyl pyrazolines (89) were synthesized and assessedtheir cytotoxicity against the PC-3 Prostate cancer cell lines using SRB assay and the tested compound exhibits the promising anti-neoplastic activity with better IC_{50} value [63]. The structures of compounds (80-89), which were previously described, are shown in figure 8. Using the Sulforhodamine B assay, we tested an assortment of pyrazoline derivatives for their cytotoxic effects on the DU145 prostate cancer cell line. (E)-3-(3-((1-(4-fluorobenzyl)-1H-1,2,3-triazol-4-yl)methoxyphenyl) -1- (3,4,5-trimethoxyphenyl) prop-2-en-1-one (90) was identified as an effective anti-neoplastic agent with a significant GI_{50} value. This compound was responsible for tubulin polymerization inhibition and cell accumulation in the G_2/M Phase [64]. A novel pyrazolines were prepared and evaluated their antiproliferative potential towards PC-3 cells using *in-vitro* SRB assay. Among those derivatives, 9-[(1,3-Diphenyl-4,5-dihydro-1H-pyrazol-5-yl)methyl]-6-piperidinyl-9H-purine (91) exhibits the compelling antiproliferative action and used in the prostate cancer therapy. This compound also revealed that it has high lipoxygenase inhibitory activity in combination with significant anti-thrombin activity, suggesting that this compound can effectively inhibits tumor growth and development [65]. Using the SRB assay method, 5-

(benzo[d][1,3]dioxol-5-yl)-3-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazole-1-carbothioamide (92) was investigated for its promising anti-tumor activity against the DU-145 prostate cancer cell line. Also, it was found to exhibit a superior GI_{50} value against the tested cancer cell line [16]. A furan-based N-acetyl pyrazoline derivative was produced and evaluated for potent proliferative efficacy on PC-3 cells using DNA intercalation assay. 1-[3-(2,5-dimethylthiophen-3-yl)-5-(2-nitro phenyl)-4,5-dihydropyrazol-1H-1-yl]ethenone (93), 1-[3-(2,5-dimethylthiophen-3-yl)-5-(4-nitro phenyl)-4,5-dihydropyrazol-1-1H-yl] ethenone (94) and 1-[3-(2,5-dimethylfuran-3-yl)-5-(5-hydroxy-2-nitrophenyl)-4,5-dihydro-pyrazol-1H-1-yl]ethenone (95) were found to be significant anti-cancer compounds. The apoptotic effect using Topo II decatenation assay was determined and found to arrest the cell cycle at the G_1 phase [66]. The structures of compounds (90-95), which were previously described, are shown in figure 9.

Pyrazoline Derivatives against Lung Cancer

The MTT assay was used to evaluate the anti-cancer activity of pyrazoline-linked carboxamide derivatives that were developed and tested against the A549 human non-small-cell lung tumor cell line. Among them,3′-[4-(Benzyloxy)phenyl]-1′-phenyl-5-(pyridin-3-yl)-3,4-dihydro 1′H,2H-[3,4′-bipyrazole]-2-carboxamide (96) and 3′-[4-(Benzyloxy)phenyl]-1′-phenyl-5-(pyridin-4-yl)-3,4-dihydro1′H,2H-[3,4′-bipyrazole]-2-carboxamide (97) exhibits the promising anti-neoplastic activity. These compounds efficiently binds to the ATP binding site of EGFR Kinase like the erlotinib standard drug, determined according to the molecular docking studies [14]. The anti-lung cancer activity of a variety of pyrazolines was tested using the Cell titer Glo assay method on the A549 cancer cell line. These pyrazolines were made via a cyclocondensation technique. Among them, 2-[5-(4-Methoxyphenyl)-3-phenyl-4,5-dihydropyrazol-1-yl]-1-methyl-6-oxo-4-phenyl-1,6-dihydropyrimidine-5-carbonitrile (98) was found to be a potent anti-cancer compound with better IC_{50} value [53]. N-acetyl-5-ferrocenyl-3-(2-thienyl)-2-pyrazoline (99) was synthesized and evaluated by the methyl thiazol tetrazolium assay. This compound has been confirmed as a potent anti-cancer agent to prevent lung cancer by acting against the A549 cancer cell line [67]. A novel thienopyrimidine containing pyrazoline unit was prepared and appraised its potency towards the A549 cells using the MTT assay. N1-(2-(5-(4-Methoxyphenyl) -3-phenyl-4, 5-dihydro-1H-pyrazol-1-yl) thieno [2,3-d]pyrimidin-4-yl) -N1,N2,N2 trimethylethane-1,2 diamine (100) was identified as an effective anti-proliferative candidate. Furthermore, it was found to have better inhibitory potential against the P13K α\mTOR protein kinase. Annexin V-FITC/PI staining also revealed that this compound can induces apoptosis [68]. The structures of compounds (96-100), which were previously described, are shown in figure 9.

Using the MTT assay, we evaluated the potential anti-cancer activity of N-formyl derivatives that were developed and synthesized by the cyclization procedure against the A549 cells. 3-(4-chlorophenyl)-5-(4-(dimethylamino)phenyl)-4,5-dihydro-1H- pyrazole-1-carbaldehyde (101) and 3-(4-bromophenyl)-5-(4-(dimethylamino)phenyl)-4,5-dihydro-1H-pyrazole-1-carbaldehyde (102) were found to be the Topo-isomerase II inhibitor. Also, the molecular dynamics simulation studies revealed the stability of the complexes [69]. A series of pyrazoline analogues were prepared and assessed for *in vitro* anti-cancer activity towards A549 small cell lung cancer cell line. Among them, 5-(4-Fluorophenyl)-N-(naphthalen-1-yl)-3-(3,4,5 trimethoxyphenyl)-4,5-dihydro-1H-pyrazole-1-carbothioamide (103), 5-(4-(Methylthio)phenyl)-N-(naphthalen-1-yl)-3-(3,4,5 trimethoxyphenyl) -4,5- dihydro-1H-pyrazole-1-carbothioamide (104) and 5-(4-Methoxyphenyl)-N-(naphthalen-1-yl)-3-(3,4,5trimethoxyphenyl)-4,5-dihydro-1H-pyrazole-1-carbothioamide (105) have revealed a promising anti-cancer activity with better GI_{50} values [70]. A novel thiazole containing pyrazoline compounds was designed and screened for cytotoxicity towards the A549 cell line (NSCLC) by using both lactate dehydrogenase assay as well as SRB assay method. 2-(3-(4-chlorophenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-4-(pyridin-4-yl)thiazole (106) was found to be the potent anti-neoplastic agent and also inhibits the activity of mTOR via FKBP12, which can be reversed by 3BDO, an mTOR activator and autophagy inhibitor [71]. 1-acetyl-3-(2-thienyl)-5-aryl-2-pyrazoline derivatives were tested and assessed for their anti-cancer action towards the A549 cells consuming MTT assay. Among them, 1-[5-(4-methylphenyl)-3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazol-1-yl]ethan-1-one (107), 1-[5-(4-bromophenyl)-3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazol-1-yl]ethan-1-one (108) and1-(5-(benzo[d][1,3]dioxol-5-yl)-3-(thiophen-2-yl)-4,5-dihydro-1H-pyrazol-1-yl)ethanone (109) were found to be promising anti-cancer agents. It was also revealed that these

compounds can indices apoptosis via caspase-3 activation [72]. The structures of compounds (101-107), which were previously described, are shown in figure 10, whereas the compounds (108 and 109) in figure 11.

Pyrazoline Derivatives against Liver Cancer

The MTT assay was used to explore a range of anthracenyl pyrazoline derivatives. 3-Anthracen-9-yl-5-(3-nitro-phenyl)-4,5-dihydro-1H-pyrazole (110), 3-Anthracen-9-yl-5-furan-2-yl-4,5-dihydro-1H-pyrazole (111), 3-Anthracen-9-yl-5-(3,4,5-trimethoxy-phenyl)-4,5-dihydro-1H-pyrazole (112) and 3-Anthracen-9-yl-5-93,4-dimethoxy-phenyl)-4,5-dihydro-1H-pyrazole (113) revealed that they have a significant cytotoxic activity in HepG2 cells with better IC_{50} values [13]. A novel pyrazoline coumarins were produced and investigated for anti-proliferative action towards the HepG2 hepatocellular cancer cell line by using MTT assay. 7-methoxy-8-(5-[4-(methylthio)phenyl]-4,5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (114) showed better anti-cancer activity. The apoptotic potential was determined by Annexin V FITC/PI staining and it shows that this compound can effectively induce apoptosis [73]. A series of isolongifolanone pyrazoline derivatives were prepared and assessed their anti-proliferative potential against the HepG2 cells. The compounds were also screened via both apoptosis assay as well as MTT assay using Etoposide, 5-Fluorouracil as a controlled drug. The MTT assay showed that 3-(4-methoxyphenyl)-N,5,5,9,9-pentamethyl-4,5,7,8,9,9a-hexahydro-5a,8-methanobenzo[g]indazole-2(6H)-carbothioamide (115) was identified to be a potent candidate against liver cancer. Also, this compound potently induces apoptosis in HepG2 cells by enhancing intracellular reactive oxygen species [74]. In order to determine whether or not these pyrazolines had any anti-cancer effects, we used the MTT assay on the HepG2 cells. 3-(3-[4-Chlorophenyl]-5-[4-(trifluoromethyl)phenyl]-4,5-dihydropyrazol-1-yl)-6-phenylpyridazine (116) was found to be promising anti-cancer compound and exhibits equal apoptotic and necrotic properties [75]. Benzo[b]thiophen-2-yl-[5-(4-hydroxy-3,5-dimethoxy-phenyl)-3-(2-hydroxy-phenyl)-4,5-dihydro-pyrazol-1-yl]-methanone (117) was established as a promising agent against the HepG2 cells with significantly better IC_{50} value and compared using cisplatin as a controlled drug. It significantly arrested the cell cycle in the G2\M phase and induced apoptosis, as determined via the cell cycle analysis and apoptosis/necrosis evaluation [76]. The structures of compounds (110-117), which were previously described, are shown in figure 11.

Pyrazoline Derivatives against Ovarian Cancer

Utilizing the sulforhodamine B assay, an array of N-acetyl and N-formyl-pyrazoline derivatives were produced through the cyclocondensation technique and tested on the OVCAR-3 and ADR-RES cell lines, which comprise an ovarian cancer panel. Among the tested compounds, 5-(4-Chlorophenyl)-3-[4-(7-chloroquinolin-4-ylamino) phenyl]-4,5-dihydro-1H-pyrazole-1-carbaldehyde (118), 5-(4-Chlorophenyl)-3-[3-(7-chloroquinolin-4-ylamino) phenyl]-4,5-dihydro-1H-pyrazole-1-carbaldehyde (119), 3-[3-(7-Chloroquinolin-4-ylamino)phenyl]-5-phenyl-4,5 dihydro-1H-pyrazole-1-carbaldehyde (120), 3-[3-(7-Chloroquinolin-4-ylamino)phenyl]-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazole-1-carbaldehyde (121) and 3-[3-(7-Chloroquinolin-4-ylamino)phenyl]-5-(3,4,5-trimethoxyphenyl)-4,5-dihydro-1H-pyrazole-1-carbaldehyde (122) revealed the promising anti-tumor activity against the tested cell lines with significant IC_{50} values [57]. A novel steroidal glycoside pyrazoline functional hybrid, 17-(5-(2-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl) -8,14-dihydroxy-3- ((4-((5-hydroxy-4-methoxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)-5 methoxy-3-methyl tetrahydro-2H-pyran-2-yl)oxy)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-12-yl benzoate (123) was synthesized and appraised its antiproliferative action towards the OVCAR-3 cells by using cell viability assay and Lactate dehydrogenase assay. The tested compound was found to be potent anti-cancer agent and possess higher growth inhibitory potential than the cisplatin standard drug [47]. The structures of compounds (118 and 119), which were previously described, are shown in figure 11, whereas the compounds (120-123) are shown in figure 12.

CONCLUSION

A five-membered heterocyclic structure containing nitrogen, pyrazoline is well-known in medicinal chemistry. This adaptable structure, which is semi-saturated, offers a distinct spatial configuration that enables different patterns of substitution to have significant pharmacological effects. These effects can include anticancer, antitrypanosomal,

antimicrobial, anti-inflammatory, analgesic, antidiabetic, antiviral, antiepileptic, etc., as well a selective activity, such as MAO inhibitory, cannabinoid CB1 receptor antagonist and NOS inhibitory activity. The chemical reactivity of pyrazolines has led to their eager modification to fabricate a wide assortment of lead moieties, which in turn have produced innovative therapeutic candidates for the management of many disorders. In this present review, we have comprehensively reviewed the various anticancer activities of the pyrazoline derivatives, with special reference to cervical, breast, colorectal, prostate, lung, liver and ovarian cancers. Additionally, these compounds could act upon several stages of the cell cycle, induce apoptosis, and decrease cell growth, ATP binding, and caspase activation. They can also inhibit various proteins, enzymes and receptors, including Epidermal growth factor receptors, Vascular endothelial growth factor receptors, Tumor necrosis factor, Estrogen receptors, Human Epidermal receptors, Tyrosine kinase and Janus kinase receptors. Thus, we trust that this paper will be helpful for budding researchers and medicinal chemists seeking their research toward the designing and development of pyrazoline derivatives and developing novel derivatives with different pharmacological properties. Hence, these pyrazoline derivatives will be utilized further in the management of several ailments.

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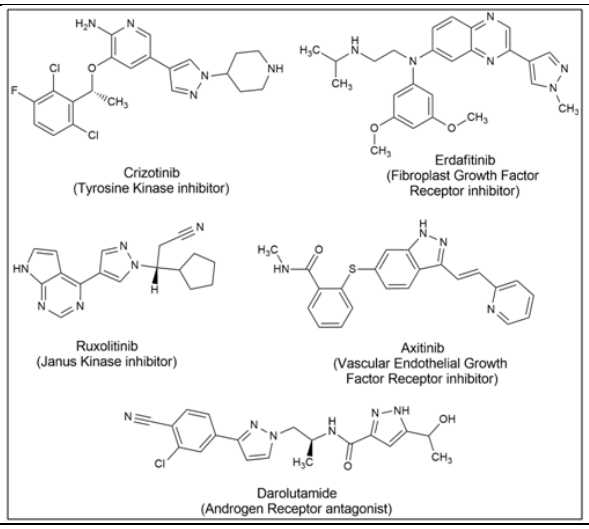

Figure 1: Biologically important FDA-approved anticancer drugs bearing pyrazoline moiety

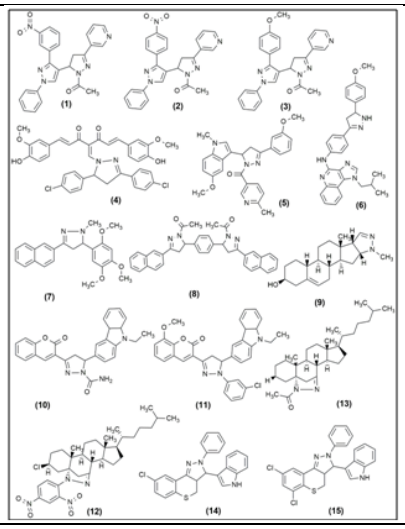

Figure 2: Structures of the compounds against cervical cancer

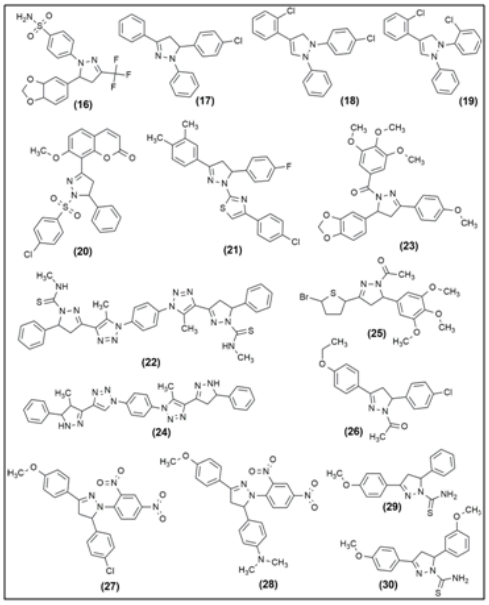

Figure 3: Structures of the compounds against cervical (compound 16) and breast cancer (17-30)

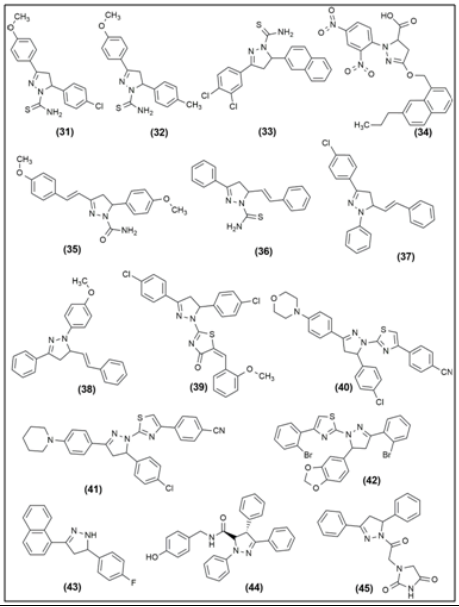

Figure 4: Structures of the compounds against breast cancer

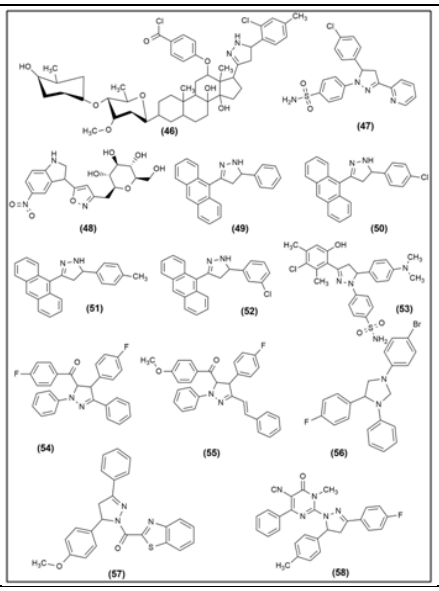

Figure 5: Structures of the compounds against breast adenocarcinoma (compounds 46-48) and colorectal cancer

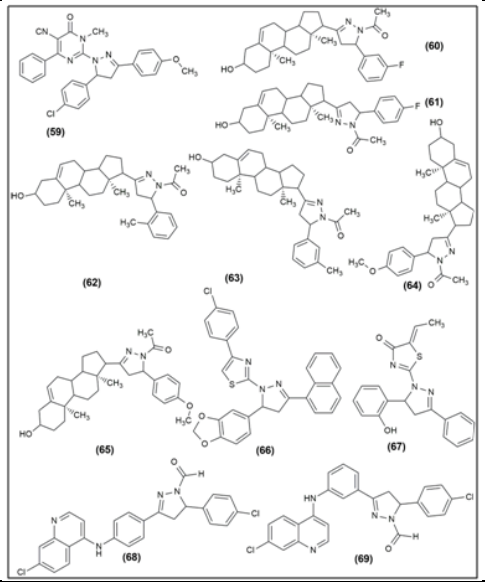

Figure 6: Structures of the compounds against colorectal cancer

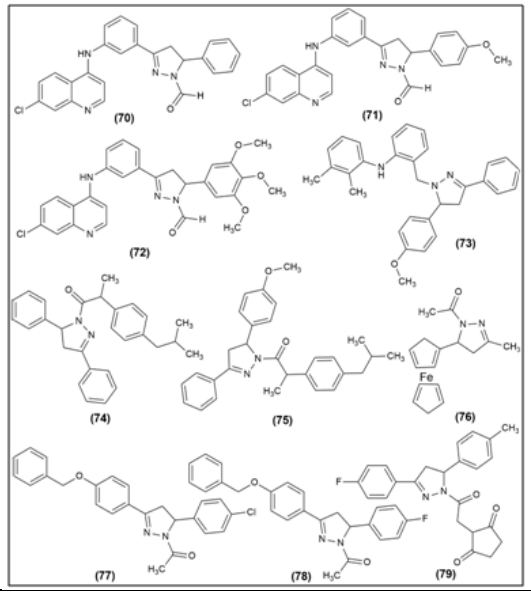

Figure 7: Structures of the compounds against colorectal cancer

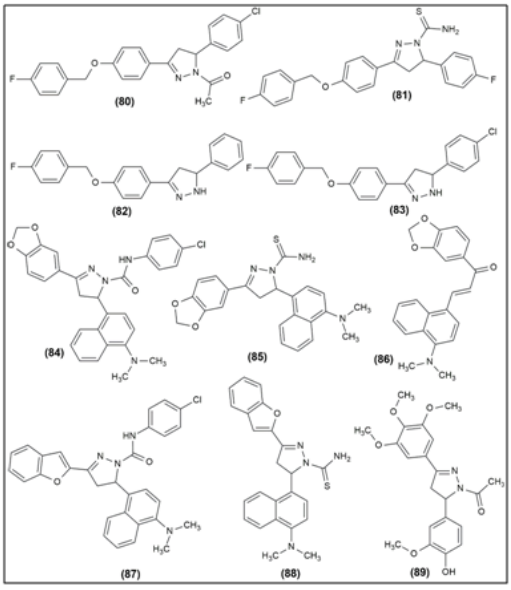

Figure 8: Structures of the compounds against prostate cancer

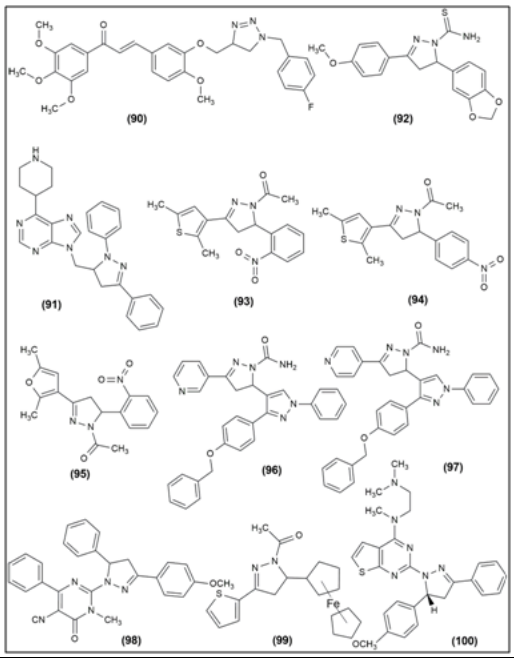

Figure 9: Structures of the compounds against prostate cancer (compounds 90-95) and Lung cancer (compounds 96-100)

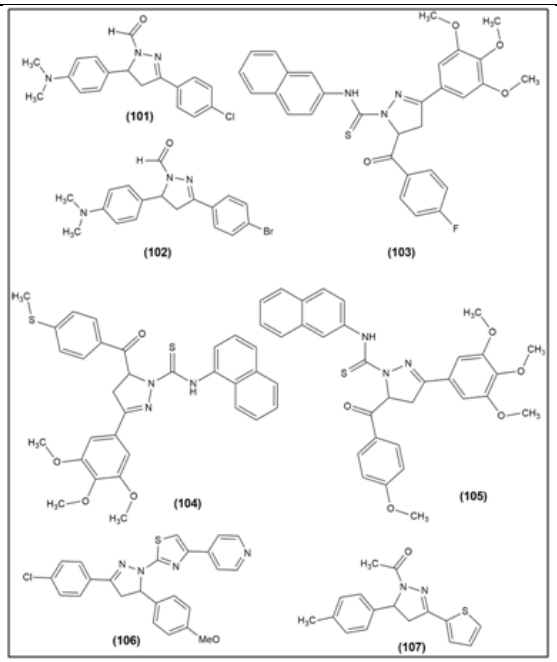

Figure 10: Structures of the compounds against lung cancer

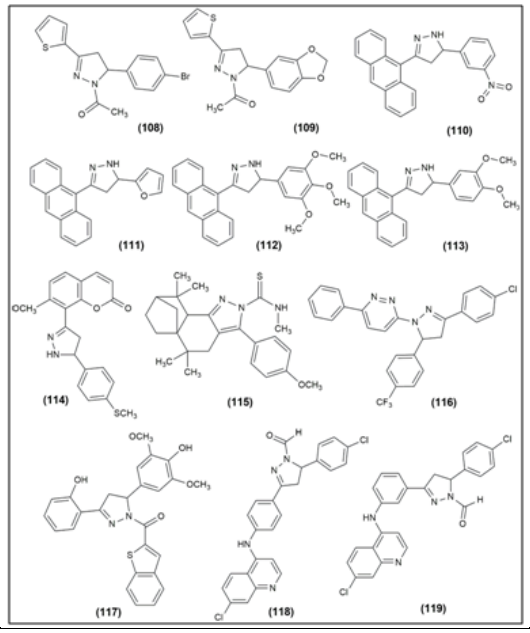

Figure 11: Structures of the compounds against lung cancer (compounds 108 and 109), liver cancer (compounds 110-117) and ovarian cancer (118 and 119)

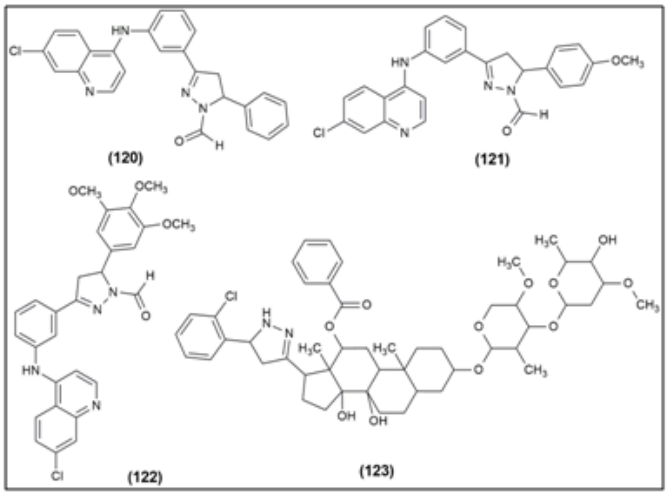

Figure 12: Structures of the compounds against ovarian cancer