ejpmr, 2020,7(6), 270-278

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

PYRAZOLES AS THERAPEUTICS AGENTS: A REVIEW

Pratik Ugale*, Nirmala Shinde and Sachin Bhosale

Department of Pharmaceutical Chemistry, S.M.B.T. College of Pharmacy, Nandi Hills, Dhamangaon. Tah: Igatpuri, Dist: Nashik (MH) India.

***Corresponding Author: Pratik Ugale**

Department of Pharmaceutical Chemistry, S.M.B.T. College of Pharmacy, Nandi Hills, Dhamangaon. Tah: Igatpuri, Dist: Nashik (MH) India.

Article Received on 15/04/2020 **Article Revised on 05/05/2020** **Article Accepted on 26/05/2020**

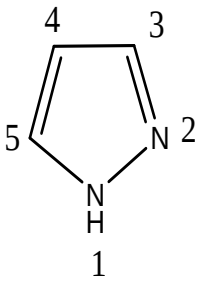
ABSTRACT

Pyrazole are potent medicinal scaffolds and possesses a broad spectrum of biological activities. This review focusses on the various pharmacological activities shown by different synthesized pyrazoles and their derivatives. This supplement may assist the medicinal chemists to generate new leads containing pyrazole nucleus with high efficacy.

KEYWORDS: Pyrazole, anticancer, antibacterial, antifungal, anthelmintic, antioxidant.

Pyrazoles

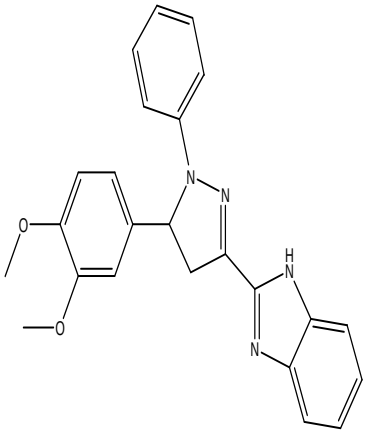
Pyrazoles is a class of simple organic compound with the formula $C_3H_3N_2H$ and containing two nitrogen atoms and three carbon atom in adjacent positions. It has number of pharmacological effect on human being and generally they are classify as alkaloids. In 1959, the first natural pyrazole, 1- pyrazolyl-alanine, was isolated from seeds of watermelons.[1,2]



Pyrazole (1)

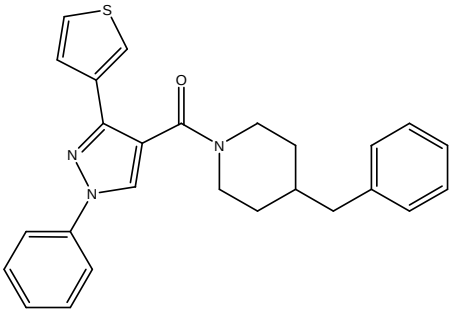
Pyrazole with anticancer potential

A series of pyrazole derivative were prepared by using chalcone derivatives through cyclocondensation using Phenyl hydrazine or Hydrazine hydrate as intermediate. The pyrazole derivatives were selected for five dose screening of anticancer activity at NCI (National cancer Institute). From the series of compounds, (2-[5-(3,4-dimethoxyphenyl)-1-phenyl-4,5-dihydro-1H-3-pyrazolyl]-1H-benzimidazole found to be more active.[3]

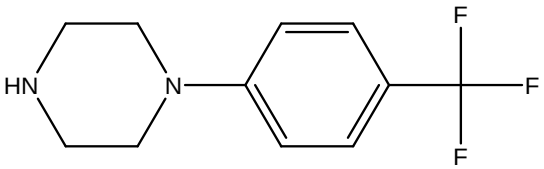


2-[5-(3,4-dimethoxyphenyl)-1-phenyl-4,5-dihydro-1H-3-pyrazolyl]-1H-benzimidazole (2)

The series of 1,3-diarylpyraole derivatives containing thiophene were synthesized and confirmed by spectral studies followed by screening for anticancer activity using MIT assay against MCF7, MDA-MB-231, HeLa, Raji, and HL60 human cancer cells. From the series of synthesized compounds, (4-Benzyl-piperidin- 1-yl)-(1-phenyl-3-thiophen-3-yl-1H-pyrazol-4-yl)-methanone showed highest growth of inhibition against Rajiand HL60 cancer cells. 4-trifluoromethylphenyl piperazine showed potent activity on Rajiand HL60 cancer cell lines.[4]

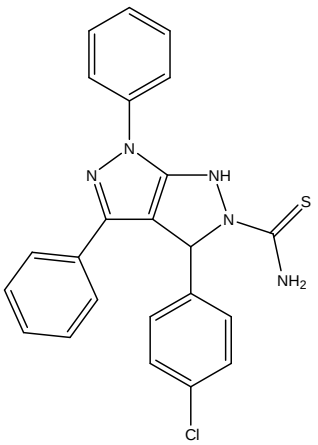


(4-Benzyl-piperidin- 1-yl)-(1-phenyl-3-thiophen-3-yl-1H-pyrazol-4-yl)-methanone **(3)**

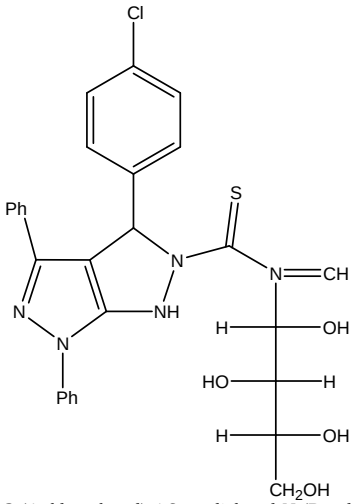


4-trifluoromethylphenyl piperazine **(4)**

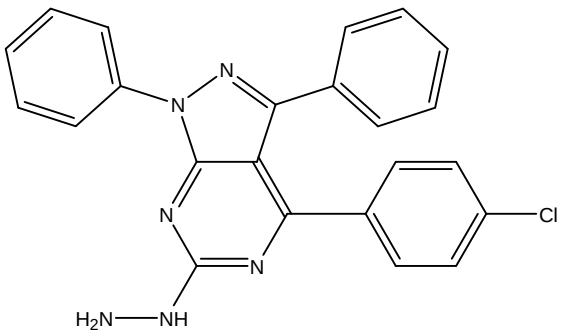
By the reaction of 4-(4-Chlorobenzylidene)-2,5-diphenyl-2,3-dihydro-3H-pyrazol-3-one 3a and 4-(3,4-dimethoxybenzylidene) -5-phenyl-2,3-dihydro-3H-pyrazol-3-one 3b with phenylhydrazine, thiosemicarbazide, hydroxylamine hydrochloride, ethyl acetoacetate, diethylmalonate, malononitrile, ethyl cyanoacetate, and thiourea, fused pyrazole derivatives were prepared. New S-, O-, and N-glycoside derivativeswere then prepared by reacting with cyclic and acyclic sugars.The compounds were screenened for antitumor activity against the human breast cancer cells (MCF-7). Four of the new compounds showed IC50 values less than those of the positive control, indicating that these four compounds (5), (6), (7), and (8) are better anticancer agents than doxorubicin.[5]



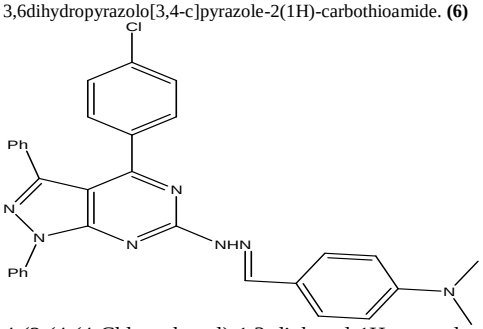
3-(4-Chlorophenyl)-4,6-diphenyl-3,6-dihydropyrazolo[3,4-c] pyrazole-2(1H)-carbothioamide **(5)**



3-(4-chlorophenyl)-4,6 diphenyl-N-(D-xyloteritolylidene)-3,6dihydropyrazolo[3,4-c]pyrazole-2(1H)-carbothioamide. **(6)**

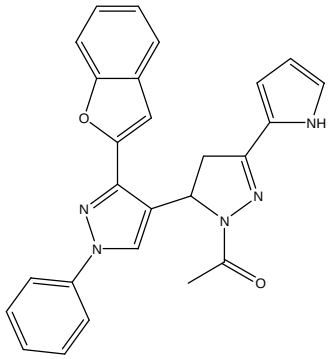


4-(4-Chlorophenyl)-6-hydrazinyl-1,3-diphenyl-1H-pyrazolo [3, 4-d]pyrimidine (7)



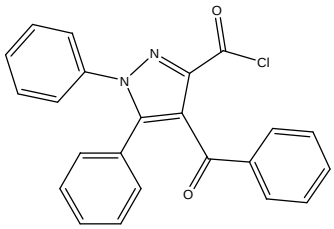
4-(2-(4-(4-Chlorophenyl)-1,3-diphenyl-1H-pyrazolo [3,4-d] pyrimidin-6yl) hydrazono)methyl-N,N-dimethylaniline **(8)**

Design and synthesis of novel benzofuran-pyrazole hybrids was carried out and among the series of compounds, Eight compounds were tested for anticancer activity at NCI(USA). Compound showed notable growth inhibitory activity in contradiction of Leukemia CCRF-CEM, MOLT-4, Lung Cancer HOP-92, Colon Cancer HCC-2998, CNS Cancer SNB-75, Melanoma SK-MEL-2, Ovarian Cancer IGROV1, Renal Cancer 786-0, RXF 393, Breast Cancer HS 578T and T-47D (GI50: 1.00 – 2.71 µM).[6]



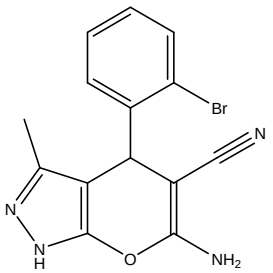
1-(5-(3-(Benzofuran-2-yl)-1-phenyl-1H-pyrazol-4-yl)-4,5-dihydro-3-(1Hpyrrol-2-yl)pyrazol-1-yl)ethanone (9)

Anticancer activities of novel synthesized organic based compound acyl thiourea was studied. A pyrazole ring containing in the acyl thiourea derivatives were obtained with good yield through one pot reactiom of 4-benzoyl-1, 5-diphenyl-1H-pyrazole-3-carbonyl chloride with ammonium thiocyanate and various amines. The structure of synthesized were confirmed by spectral studies. The anticancer activities of compound were evaluated on human colon, liver and leukemia cancer cell lines. Cell culture studies have demonstrated significant toxicity of the compounds on the cell lines, and the levels of toxicity have altered in the presence of various side groups. These results showed that novel pyrazolyl acyl thioureas derived compounds may be utilized for cancer treatment.[7]

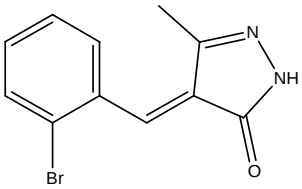


4-benzoyl-1, 5-diphenyl-1H-pyrazole-3-carbonyl chloride (10)

EGFR and VEGFR-2 speak to promising focuses for malignant growth treatment as they are significant in tumor improvement just as in angiogenesis and metastasis. In this work, 6-amino-4-(2-bromophenyl)- 3-methyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile 1 and (E)- 4-(2-Bromobenzylidene)- 5-methyl-2,4-dihydro-3H-pyrazol-3-one 11 were chosen as beginning materials to orchestrate diverse melded pyrazole subsidiaries.[8]

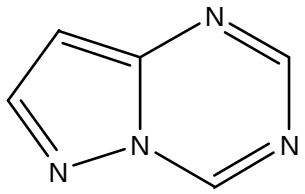


6-amino-4-(2-bromophenyl)-3-methyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (11)

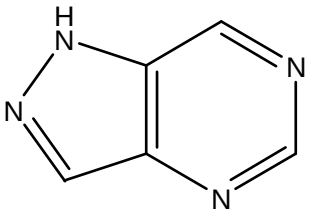


4-(2-Bromobenzylidene)-5-methyl-2,4-dihydro-3H-pyrazol-3-one (12)

Roscovitine is a pan-selective CDKs inhibitor with multiple effects on cell proliferation, cell cycle progression and/or induction of apoptosis in cancer cells. By incorporating the 3-aminopyrazole scaffold, pyrazolo[1,5-a]-1,3,5-triazine and pyrazolo[4,3-d]pyrimidine derivatives were designed and synthesized as roscovitine bioisosters and demonstrated to be potent cyclin-dependent kinases inhibitors with antiproliferative activity.[9]



, pyrazolo[1,5-a]-1,3,5-triazine (13)

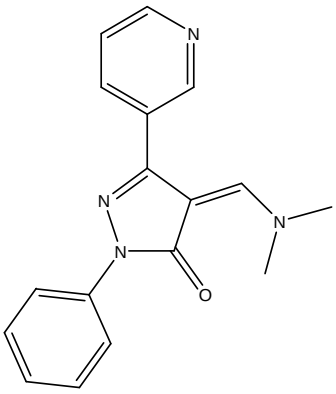


pyrazolo[4,3-d]pyrimidine (14)

Pyrazoles with Antimicrobial potential

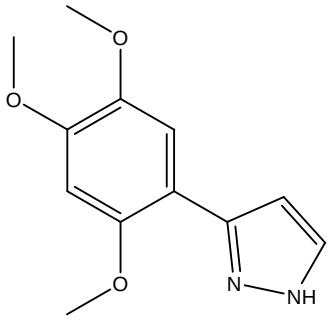
By the cyclization of aryl chalcones and hydrazine hydrate with 1H-pyrazole, aryl-aryl 1H pyrazoles have been synthesized in presence of $SOCl_2$. The synthesized compounds were characterized by spectral data. The hammett constants, F and R parameters were correlated with spectral data and the effect of substituent on the spectral frequencies have been studied from statistical analyses. The method of Bauer-Kirby studied the antimicrobial activity of all synthesized pyrazoline compound.

The synthesis of some new pyrazolopyridines from 4-(dimethylaminomethylene)-1-phenyl-3-(pyridine-3-yl)-1Hpyrazol-5(4H)-one was investigated. Among the synthesized compounds, exhibited remarkable antimicrobial activity against Escherichia coli, Enterobacter cloacae, and Serratia with inhibition zone diameter of 19, 19, and 17 nm (at 10 mg/ml sample concentration), respectively. Developed three series of thiazole-substituted pyrazole derivatives and investigated their antimicrobial potency. The result highlighted that compound exhibited strong activity against all the tested organism. However, compound showed good action against S. aureus with inhibition values of 24.41–27.13 mm (at 128 μg/ml). Introduction of F, Cl, Br, and NO2 groups to the phenyl ring enhanced antibacterial and antifungal capability.[10]



4-(dimethylaminomethylene)-1-phenyl-3-(pyridine-3-yl)-1Hpyrazol-5(4H)-one (15)

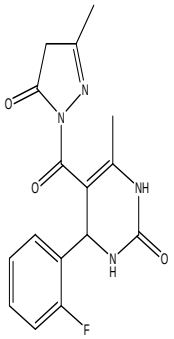
Enaminones are chemical compounds consisting of an amino group linked through a C=C to a carbonyl group. They are versatile synthetic intermediates that combine the ambident nucleophilicity of enamines with the ambident electrophilicity of enones. They are typical push-pull ethylenes in which the amine group pushes and the carbonyl pulls electron density. They carbonyl group, conjugated to the enamine moiety, gives this system enough stability to be easily prepared, isolated, and stored under atmospheric conditions at room temperature. Enaminones are the attractive intermediates for the synthesis of therapeutically active heterocycles such as quinolines, dibenzodiazepines, pyridinones, pyrazoles, oxazoles, and tetrahydrobenzoxazines.[11]



3-(2,4,5-Trimethoxyphenyl)-1H-pyrazole (16)

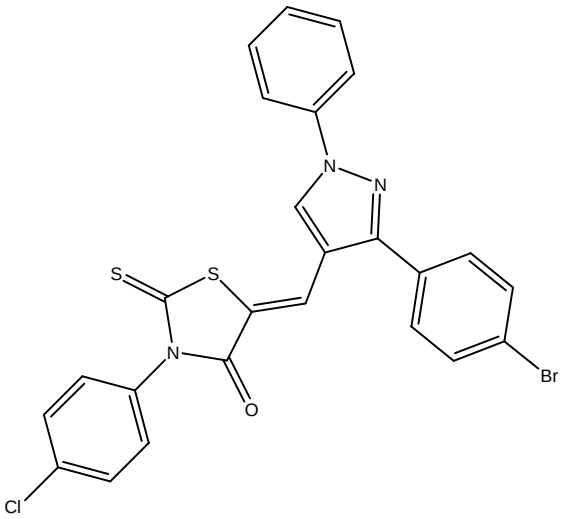
Proceeding with progress in the treatment of numerous diseases is currently compromised by the expanding number of pathogens impervious to antimicrobial medications. There is a need to the two stewards the utilization of existing medications better and to grow new helpful antimicrobials. The pyrazole ring is present as a core in a variety of prominent drugs such as

celecoxib, sildenafil, difenamizole, ionazolac and pyrazofurin.[12]



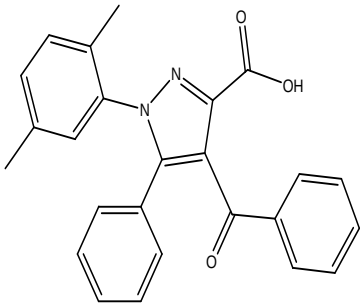
4-(2-fluorophenyl)-6-methyl-5-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazole-1-carbonyl)-3,4-dihydropyrimidin-2(1H)-one (17)

Microbial diseases have emerged as a main origin of morbidity and often as suppressor of immune power over the past two decades. Microbes are responsible for several poisonous syndromes and prevalent epidemics in human civilizations. Microbial diseases such as plague, diphtheria, typhoid, cholera, pneumonia and tuberculosis have taken high toll of humanity in recent pasts. In present times, many of the accessible antimicrobial drugs are poisonous and create recurrence of diseases because they are bacteriostatic and not bactericides.[13]



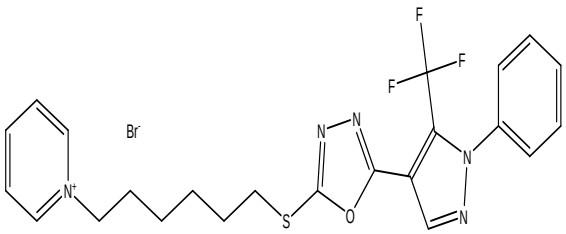
5-((3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)-3-(4-chlorophenyl)-2-thioxothiazolidin-4-one (18)

Common anti-toxin mixes utilized in the treatment and avoidance of bacterial disease have gotten essential for the ebb and flow human services framework, helping and supplementing the regular resistant framework against microbial pathogens. Notwithstanding, on the grounds that traditional anti-infection agents are regularly manhandled/abused to treat microbial diseases, a few microorganisms have created protection from a portion of these anti-infection agents. So the clinical networks are looked in a major issue with antimicrobial and anti-toxin obstruction.[14]



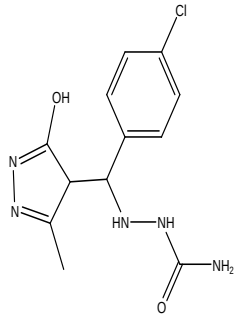
4-Benzoyl-1-(2,5-dimethylphenyl)-5-phenyl-1H-pyrazole-3-carboxylic acid (19)

a progression of pyridinium-custom fitted 5-trifluoromethylpyrazoles containing 1,3,4-oxadiazole moieties were developed through coupling key pharmaceutical pieces of pyridinium, pyrazole, and 1,3,4-oxadiazole platforms in single sub-atomic engineering. Antimicrobial results proposed that this sort of mixes showed critical exercises against three kinds of pathogenic microbes and six contagious strains in vitro. The negligible EC50 estimations of planned mixes against Xanthomonas oryzae pv. oryzae, Ralstonia solanacearum, and Xanthomonas axonopodis pv. citri could reach to 0.467, 1.04, and 0.600 lg/mL, separately, through tuning and improving N-substituents, crossing over iota, and alkyl length of the tailor.[15]



1-(6-((5-(1-phenyl-5-(trifluoromethyl)-1H-pyrazol-4-yl)-1,3,4-oxadiazol-2-yl)thio)hexyl)pyridinium bromide (20)

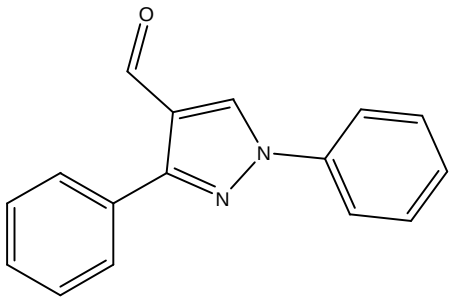
Business accessible pyrazole moiety, for example, Celecoxib is strong COX-2 inhibitor. Some different instances of pyrazole subsidiaries as NSAID are ramifenazone, Lonazolac (NSAID)) and Rimonabant. Compound (phenylbutazone) is a non stereoidal sedate Pyrazofurin is capability of antiviral movement, HCV infection. In ebb and flow inquire about, Anti-incendiary medication has been utilized most noticeable research regions. New Antiinflammatory drugs are recently utilized in clinical research, a portion of the medications still not effectively and excruciating symptoms.[16]



2-[(4-chlorophenyl)(3-hydroxy-5-methyl-4H-pyrazol-4-yl)methyl]hydrazinecarboxamide (21)

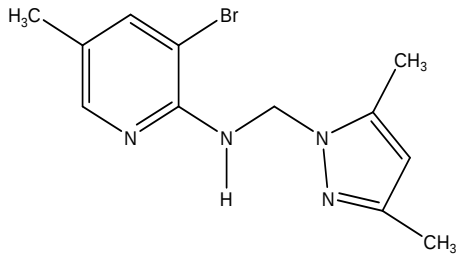
Pyrazole as antioxidant potential

Phenothiazines represent a key motif in heterocyclic chemistry and occupy a prime place in medicinal chemistry due to their competence to exhibit a wide range of pharmacological activities. Furthermore, pyrazole ring is present as the core in a varietyof leading drugs such as Celebrex,[15] Viagra,[16] or rimonabant. Moreover, 4-aminoantipyrine is used for the protection against oxidative stress as well as prophylactic of some diseases including cancer, and these are important directions in medicine and biochemistry.[17]



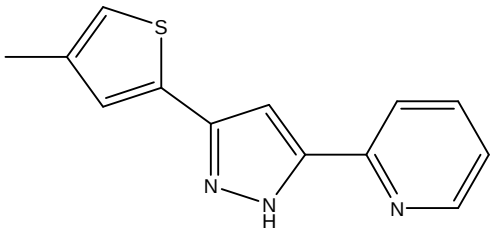
1,3-
diphenyl-1H-pyrazole-4-carbaldehyde (22)

Pyrazoles and their subordinates speak to a significant class of aggravates that find broad use in the pharmaceutical industry. Mixes containing a pyrazole theme are being created in a wide scope of remedial territories including metabolic, CNS (Central Nervous System) and oncological sicknesses, Antiinflammatory operators, for example, Celebrex, and Viagra.[18]



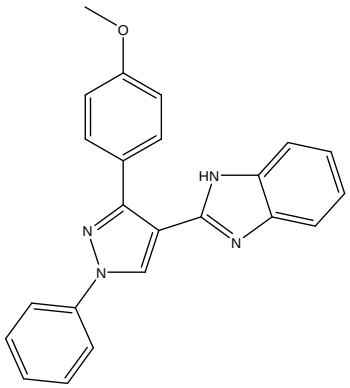
(3-Bromo-5-methyl-pyridin-2-yl)-(3,5-dimethyl-pyrazol-1-ylmethyl)-amine (23)

2-Pyrazolines and 2-pyrazole, electronrich nitrogen containing heterocyclic frameworks, assume a significant job in a few organic and pharmacological activities. The blended 3,5-disubtituted-2-pyrazoline and pyrazole subordinates were assessed in vitro for their xanthine oxidase (XO) inhibitory exercises, with the vast majority of the explored mixes being demonstrated to be strong inhibitors of cow-like milk XO.[19]



3-(4-methylthiophen-2-yl)-5-(2-pyridinyl)pyrazole (24)

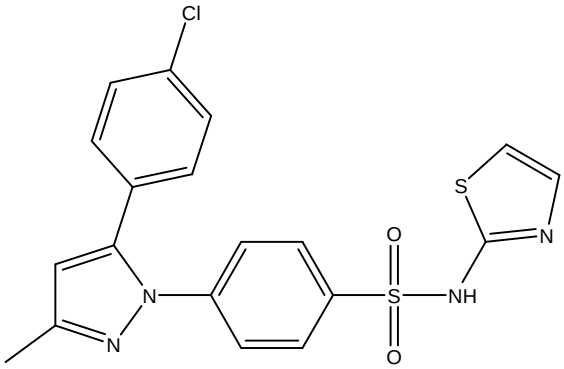
The basic heterocyclic moieties play a pivotal role in regulation of macromolecular targets in the living systems. Molecular structure is the most influential factor In understanding of several biological pathways and in the design and synthesis of therapeutical and pharmacological agents for the cure of various diseases. Synthesis of 2-(pyrazol-4-yl)benzimidazoles via condensation of 1,2-diaminobenzene with pyrazole-4-carbaldehydes requires an oxidative reagent such as H_2O_2 to generate benzimidazole nucleus. These aspects have motivated us to design and synthesize various N-substituted benzimidazoles bearing pyrazole ring at position 2 of the benzimidazole ring and screen them for the exhibition of antioxidant activity.[20]



2-[3-(4-Methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl]-1H-benzimidazole (25)

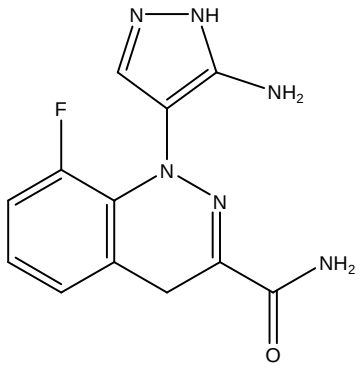
Pyrazole with anti-inflammatory potential

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used for the treatment of pain and inflammation by counteracting the cyclooxygenase enzymes (COX). However, long-term therapy may cause gastrointestinal complications ranging from stomach irritation to life-threatening gastrointestinal ulceration and bleeding. Therefore, it is important to find new anti-inflammatory drugs with a potential for clinical use and not associated with adverse effects. Pyrazole derivatives represent an important class of heterocycles due to their highly pronounced biological and pharmacological activities.[21]



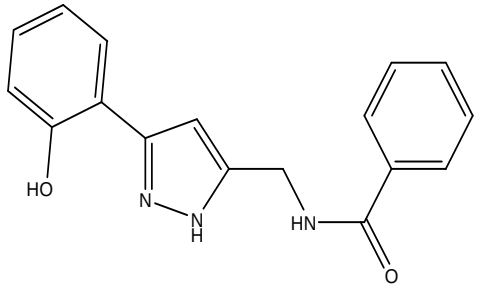
4-[5-(4-Chlorophenyl)-3-methyl-1H-pyrazol-1-yl]-N-(2-thiazolyl)benzenesulfonamide (26)

Pyrazole subsidiaries have a long history of utilization in agrochemicals and pharmaceutical industry as herbicides and dynamic pharmaceuticals. The ongoing accomplishment of pyrazole COX-2 inhibitor has additionally featured the significance of these heterocycles in therapeutic science. A methodical examination of this class of heterocyclic lead uncovered that pyrazole containing pharmacoactive operators assume significant job in restorative science. The commonness of pyrazole centers in naturally dynamic atoms has animated the requirement for rich furthermore, effective approaches to make these heterocyclic lead. The treatment of torment keeps on being the subject of significant pharmaceutical and clinical research. Microbial contaminations regularly produce agony and irritation. Chemotherapeutic, pain relieving and calming drugs are endorsed all the while in ordinary practice.[22]



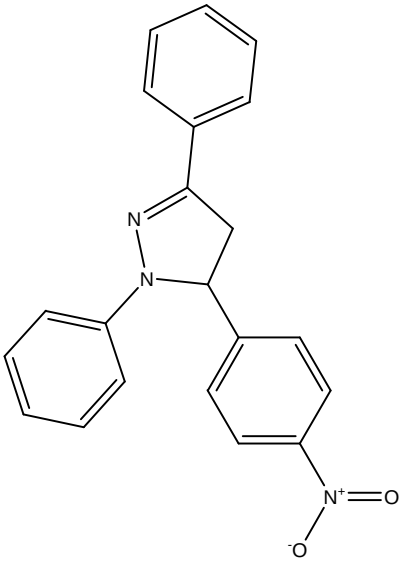
8-Fluoro-4(-5-amino-pyrazole) cinnoline-3-carboxamide (27)

The treatment of aggravation includes balancing the cyclooxygenase protein and incendiary arbiters by non-steroidal mitigating drugs (NSAIDs). Essentially, a drawn out treatment prompts a few entanglements; especially gastrointestinal which include ulceration and draining. These medications in truth restrain the cyclooxygenase - 1 (COX-1), which catalyzes the arrangement of arachidonic corrosive (AA) to prostaglandins H2 (PGH2) exhaustively alongside COX-2 out of a couple of cases, because of absence of selectivity. Concealment of thromboxane A2 (TXA2) creation and hindrance of platelet collection are different characteristics of NSAIDs.[23]



N-((3-(2-hydroxyphenyl)-1H-pyrazol-5-yl)methyl)benzamide (28)

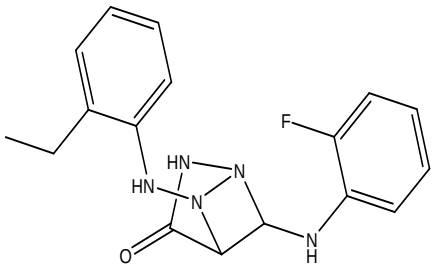
In the current examination, the chalcone intermediates are blended by Claisen-Schmidt buildup response among acetanilide and suitable fragrant aldehydes. Further, these chalcone intermediates were cyclized with phenylhydrazine in frosty acidic corrosive to give new pyrazolines subordinates utilizing ultrasonic illumination with better returns in lesser time. All the integrated subordinates are described by their TLC, Physical consistent, FTIR, and 1H NMR. The Chalcone intermediates were screened for their antimicrobial movement while cyclized pyrazolines subordinates were screened looking for potential mitigating mixes. The compound 4c had indicated great potential for calming action.[24]



1,3-diphenyl-5-(4-nitrophenyl)-4,5-dihydro-1H-pyrazole (29)

Non-steroidal anti-inflammatory drugs (NSAIDs) comprise a heterogeneous group of medications, with analgesic, antipyretic and anti-inflammatory activity. They act as inhibitors of prostaglandin synthesis through non-selective inhibition of COX enzymes but as a side effect they cause mucosal damage, ulceration and ulcer complication. Moreover, several pyrazole derivatives were reported as anti-inflammatory in addition to pyrazolo pyridine derivatives were synthesized and investigated for their anti-inflammatory agents and were

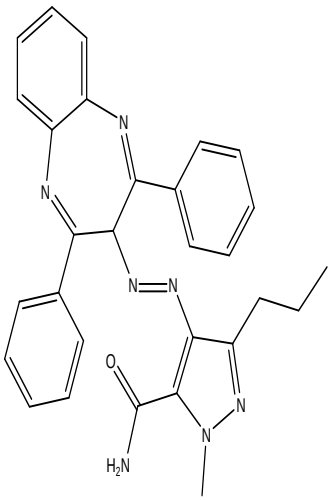
recognized as promising multi-potent anti-inflammatory agents.[25]



4-(2-(2-Ethylphenyl)hydrazono)-3-((2-fluorophenyl)amino)-1Hpyrazol-5(4H)-one (30)

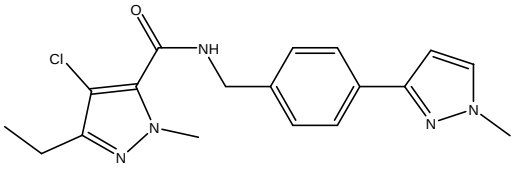
Pyrazole with Anthelmintic potential

Benzodiazepines have stood out as a significant class of heterocyclic mixes in the field of medications and pharmaceuticals. These mixes are broadly utilized as anticonvulsant, hostile to tension, pain relieving, soothing, energizer also, sleep inducing agents,1 just as mitigating operators .Our advantage laid in the combination the pyrazole moiety containing 1,5-benzodiazepines, as pyrazoles are known to have noteworthy pharmacological properties.[26]



4-[(2,4-Diphenyl-3H-1,5-benzodiazepin-3-yl)azo]-1-methyl-3-propyl-1H-pyrazole-5-carboxamide (31)

Anthelmintic resistance imposes a huge burden on global animal healthcare, particularly livestock, with significant negative socioeconomic impacts. This burden is caused by the excessive and uncontrolled use of marketed anthelmintics and the induced genetic change in parasite populations. Since the ground-breaking discovery of monepantel as a novel class of anthelmintic in 2008, there has been no new commercial chemical entity with potent anthelmintic activity approved for the control of parasitic worms in livestock. In addition, resistance has also been reported for monepantel as well as moxidectin, another anthelmintic agent for the treatment of haemonchosis. Therefore, a sustained effort to discover and develop novel anthelmintics is an essential component of the battle against drug resistance.[27]



4-Chloro-3-ethyl-1-methyl-N-(4-(1-methyl-1H-pyrazol-3-yl)-benzyl)-1H-pyrazole-5-carboxamide (32)

REFERENCES

1. Pyrazole: Wikipedia https://www.google.com/search?sxsrf=ALeKk0061ya1X9H0g1b1kbJtX CQ4QYXtaQ%3A1588749055103&source=hp&ei=_2KyXuyfBMaS9QOT3pDQCQ&q=pyrazole&oq=pyrazole&gs_lcp=CgZwc3ktYWIQAzIECCMQJzIECCMQJzIECCMQJzIFCAAQkQIyBAgAEEMyAggAMgQIABBDMgQIABBDMgIIADICCAA6BwgjEOoCECc6BQgAEIMBUMUDWPsQYOIVaAJwAHgAgAGNA4gBqg2SAQcwLjUuMi4xmAEAoAEBqgEHZ3dzLXdperABCg&sclient=psyab&ved=0ahUKEwism8K4157pAhVGSX0KHRMvBJoQ4dUDCAc&uact=5.
2. Mahadik KR, Kuchekar BS, Deshmukh KR. Concies pharmaceutical organice chemistry, 6th edition; 2013, p.p -1-10.
3. Shaharyar M*, Abdullah MM, Bakht MA, Majeed J. Pyrazoline Bearing Benzimidazole: Search for anticancer agent. European Journal of Medicinal Chemistry, 2010; (45): 114-119.
4. Inceler N*, Yilmaz A, Baytas SN. Synthesis of ester and amide derivatives of 1-phenyl-3-(thiophen-3-yl)-1H-pyrazole-4-carboxylic acid and study of their anticancer activity. Medi Chem Res, 2013; (22): 3109-3118.
5. Nassar IF, Farargy AF, Abdelrazek FM*. Synthesis and anticancer activity of some new Fused Pyrazoles and their Glycoside derivatives, J. Heterocyclic Chem, 2018; 00(00).
6. EI-Karim SA, Anwar MM*, Mohamed NA, Naser T. Design, synthesis, biological evaluation and molecular docking studies of novel benzofuran-pyrazole derivatives as anticancer agents. Bioorganic chemistry, 2015; (63): 1-12.
7. Koca I*, Ozgur A, Coksun KA, Tutar Y. Synthesis and anticancer activity of acyl thioureas bearing pyrazole moiety, Bioorganic & medicinal chemistry, 2013; 3859-3865.
8. Saleh NM, EI- Gazzer MG, Othman RA. Novel Anticancer fused pyrazole derivatives as EGFR & VEGFR -2 Dual TK inhibitors, Front. Chem, 2020; 7: 917.
9. Nitulescu GM*, Draghici C, Olaru OT. New Potential Antitumor Pyrazole Derivatives:Synthesis and Cytotoxic Evaluation. Int. J. mol. Sci, 2013; (14): 21805-21818.
10. Ardiansah B* A Recent Update: Antimicrobial Agents Containing Pyrazole Nucleus, Asian journal of pharmaceutical and clinical research, 2018; 11(12): 88-94.

11. Bhat MA, Al-omar MA, Naglah AM, Khan AA. Enaminone-Derived Pyrazoles with Antimicrobial Activity. Hindawi journal of chemistry, 2019; 1-10.
12. Desai NC, Vaghani HV, Patel BY, Karkar TJ. Synthesis and Antimicrobial Activity of Fluorine Containing Pyrazole-clubbed Dihydropyrimidinones, Indian journal of pharmaceutical science, 2018; 80(2): 242-252.
13. Bhatt HB, Sharma S. Synthesis and antimicrobial activity of pyrazole nucleus containing 2-thioxothiazolidin-4-one derivatives. Arabian Journal of Chemistry, 2013; 10(2): S1590-S1596.
14. Cetin A, Bildiici I. A study on synthesis and antimicrobial activity of 4-acyl-pyrazoles. Journal of Saudi chemical society, 2018; 22(3): 279-296.
15. Zhou L, Wang PY, Zhou J, Shao WB, Fang HS, Yang S* Antimicrobial activities of pyridinium-tailored pyrazoles bearing 1,3,4-oxadiazole scaffolds. Journal of Saudi chemical society, 2017; 21: 852-860.
16. Kumar RS, Arif IA, Ahamed A, Idhayadhullah A. Anti-inflammatory and antimicrobial activities of novel pyrazole analogues. Saudi Journal of Biological science, 2015; 23(5): 614-620.
17. Hamama WS, Gouda MA, EI- Din HA, Zoorob HH. Synthesis and Antioxidant Activity of Some New Binary Pyrazoles Containing Core Phenothiazine Moiety. Journal of Heterocyclic chemistry, 2016; 54(2): 1369-1377.
18. Abrigach F, Khoutoul M, Merghache S, Oussaid A, Lamsayah M, Zarrouk A Benchat N, Touzani R. Der Pharma chemical, 2014; 6(3): 280-285.
19. Usta A, Balta N, ozakan M. Synthesis of some novel pyrazoline and pyrazole derivatives as potential *in vitro* anti-xanthine oxidase and antioxidant activities. Revue Roumaine de Chimie, 2018; 63(12): 1097-1105.
20. Bellam M, Gundluru M, Sarva S, Chandive S, Netala VR, Tartte V, Cirandur SR*. Synthesis and antioxidant activity of some new N-alkylated pyrazole-containing benzimidazoles. Chemistry of Heterocyclic compound, 2017; 53(2): 173-178.
21. Moghazy SM, Barsoum FF, Rahman HM, Marzouk AA. Medicinal Chemistry Research, 2012; 21: 1722–1733.
22. Pankaj M, Vikas S, Minu K, Abhishek S. Synthesis, Characterization and Antiinflammatory activity of Cinnolines (pyrazole) derivatives. IOSR Journal of Pharmacy and Biological Sciences, 2015; 10(6): 77-82.
23. Amdare MD, Jogdand KR, Kathane LL, Kuhite NG, Padole CD, Mahaptra DK. Synthesis of a Potential Anti-Inflammatory Pyrazole Derivative from Hippuric Acid as the Starting Material. Journal of Pharmaceutical, Chemical and Biological Sciences, 2017; 5(3): 216-220.
24. Sethiya JP, Bhavsar SP, Shahare HV. Synthesis Of Potential Anti-Inflammatory Pyrazoline Derivatives Under Ultrasonic Irradiation. International journal of pharmaceutical science and research, 2019; 10(7): 3290-3294.
25. Mohamed LW, Shaaban MA, Zaher AF, Alhamaky SM, Elsahar AM. Synthesis of new pyrazoles and pyrozolo [3,4-b] pyridines as anti-inflammatory agents by inhibition of COX-2 enzyme. Bioorganic chemistry, 2019; 83: 47-540.
26. Kumar R, Joshi YC. Synthesis and antimicrobial, antifungal and anthelmintic activities of 3*H*-1,5-benzodiazepine derivatives. Journal of Serbian chemical society, 2008; 73(10): 937-943.
27. Le TG, Kundu A, Ghoshal A. Novel 1-Methyl-1H-pyrazole-5-carboxamide Derivatives with Potent Anthelmintic Activity. Lournal of Medicinal Chemistry, 2019; 62: 3367-3380.