WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 11, 544-556. Review Article ISSN 2277– 7105

A REVIEW ON NEWLY SYNTHESIZE PYRAZOLE BASED COMPOUNDS & IT'S PHARMACOLOGICAL ACTIVITY

Jaiswal Shivam*, Gupta Kumar Sujeet, BhumikaYogi, Rudrapratap Singh, Ram Sevak Varma and Amitdiwedi

Hygia Institute of Pharmaceutical Education and Research (Pharmaceutical Chemistry Department), Sitapur Hardoi Bypass Road, Opposite Sahara City Homes, Prabandh Nagar, Lucknow Pin Code 226020 (Uttar Pradesh) India.

Article Received on
01 August 2020,
Revised on 22 August 2020,
Accepted on 12 Sept. 2020,
DOI: 10.20959/wjpr202011-18740

***Corresponding Author**
Jaiswal Shivam
Hygia Institute of Pharmaceutical Education and Research (Pharmaceutical Chemistry Department), Sitapur Hardoi Bypass Road, Opposite Sahara City Homes, Prabandh Nagar, Lucknow Pin Code 226020 (Uttar Pradesh) India.

ABSTRACT

Pyrazole is a hetero cyclic with five member ring compound it has minimum one hetero atom like O,S,N. Pyrazole is multilateral lead compound for designing new biological activities of compound by modification of substitute of pyrazole like Bactericidal, Fungicidal, Anticonvalsant, Antiviral, Anti-inflammatory, Anti diabetic, Anticancer, Anti-tumor, Anti-microbial & Carbonic anhydrase an Acetylcholinesterase inhibitors Activities by using of different bioassay. All pyrazole derivatives determine via different spectrometrical methods such that Ultra-violet, Infra-red, FTIR, NMR, MASS spectrometric technique and identified the different compounds and their different biological activity. In this article described many model such that carragennan induced rat paw edema model and also describe the more potent compounds structure. Given data describe that pyrazole being five memebered heterocyclic have pharmacological action. Result of various derivaties of various substitute pyrazole are reviewed in present article. Different types methods for synthesizing pyrazole derivatives and pharmacological action are discussed after studying many research paper.

KEYWORDS: Pyrazole, Antiinflammatory, Antibacterial, AntiDiabetic, Antitumor, Antiviral, Anti cancer.

NTRODUCTION

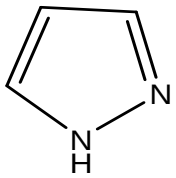
Organic Compound which have all carbon atom in cyclic ring know as carbocyclic compound. Although two or more then two or may be single hetero atom such as nitrozen, oxyzen, sulphur are include in cyclic compound known as heterocyclic compound.

Heterocycles exist as three, four, five, six and multimembered ring. Heterocyclic compound may be classified into aliphatic and aromatic. Nitrozen, oxyzen and sulphur is main hetero atoms & hetero cyclic ring bearing another heteroatoms are also known. The name hetero cyclic compound is due to presence of hetero atom in cyclic ring.

Hetero cyclic compound are such as furan, pyran both are having oxygen hetero atom and pyrrole, pyridine, piperidine having nitrogen hetero atom. some other hetero compound like thiophene, thiopyron having sulphur hetero atom. these are single hetero atom cantaining compound.[15]

PYRAZOLE

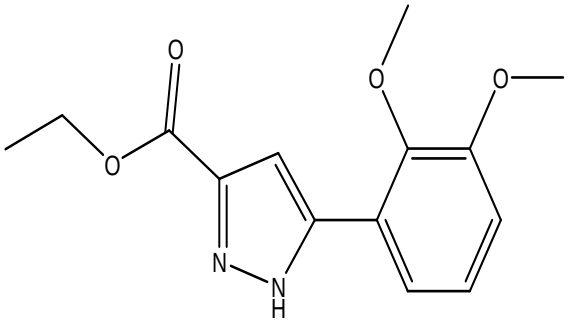
"LUDWING KNORR" is chemist which gives the name pyrazole. Pyrazole is a five membered ring compound. Pyrazole contain 3 carbon, and 2 adjacent nitrogen hetero atom in 5 membered ring. Pyrazole having no of carbon so its a organic compound with $C_3H_4N_2$ chemical formula. Pyrazole is a weak base. Pyrazole also known as 1,2-diazole.pyrazole is a alkaloid in nature.



pyrazole shows more biological activities. when pyrazole ring with celecoxib nucleus then gives anti inflamentory. Pyrazole also gives other biological activity such as anti pyretic. These anti pyretic activity is first synthetic activity. pyrazole used in treatment of Rheumatic artheitis. different derivative of pyrazole gives different biological activity like anti fungle, anti diabetic etc.[13]

1. Pyrazole as an Anti-inflammatory activity

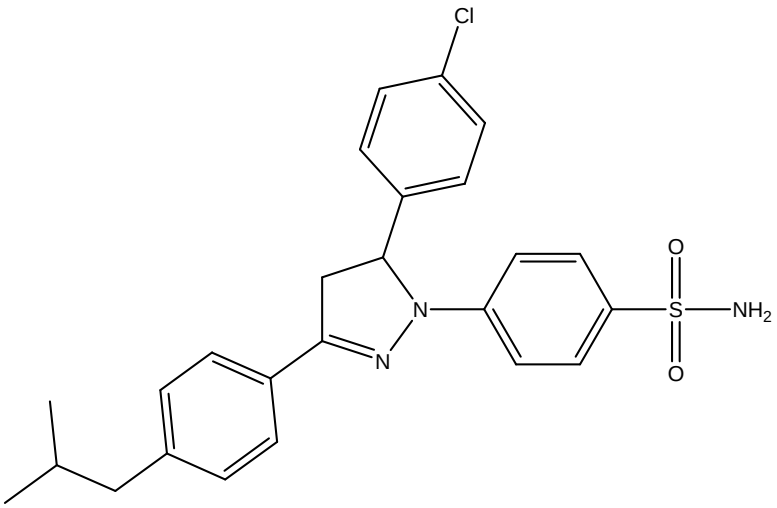
Gupta K.Sujeet, *etal (*2018) were synthesized a novel series of 5-(substitututed)-1pyrazole-3-carboxylate (1a-1j) derivatives of pyrazole by di oxalate reaction with acetophenone for evaluating Antiinflammatory activity via carrageenan-induced inflammation in rat paw edema model. All newly compound had confermed by FTIR, ^{1}HNMR, Infrared, Mass spectra & elemental analysis. Anti-inflammatory activity reveales That Ethyl 5-(3,4-di methoxyphenyl) 1H-pyrazole-3-carboxylate(1f) & ethyl5-(2,3-dimethoxyphenyl-1H-pyrazole-3-carboxylate (1e) shows more potent compounds as anti inflammatory activity.[1]



[1]

1.2 Pyrazole as an Anti-inflammatory activity

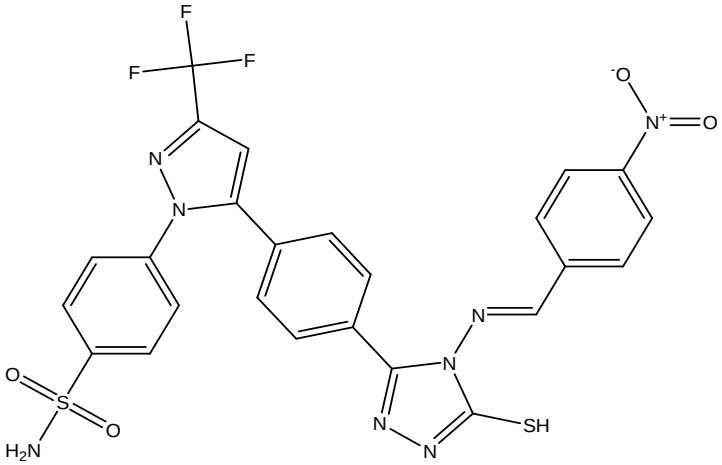
Abdellatif Khaled R.A, *et al* (2015)were synthesized a novel chain of 1,3,5-triaryl-4,5-dihydro-1H-pyrazole derivatives (2a–2p) synthesize through aldolcondensation of ¾-nitroacetophenones by way of suitably Aldehyde substitute then cyclized & produced chalcones with 4-methanesulfonyl phenyl hydrazine hydrochloride. Every new formed compounds had screened for its cyclo oxygenase (COX)inhibition, anti-inflammatory activity and ulcerogenic problem. Every compounds had morepotent inhibitors for COX-2 than COX-1. Various compounds exhibited well anti-inflammatoryactivity. By the using of COX-1/COX-2 Inhibition colorimtric assy. Compound were charectrized by NMR, IR Mass spectrometry. Compound (2i) was more potent compound then celecoxib compound.[2]



[2]

1.3 Pyrazole as an Anti-inflammatory activity

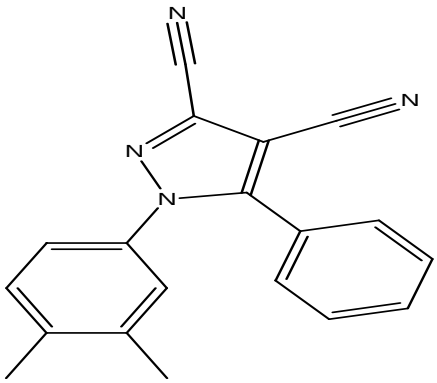
Ghulam Mustafa *et al* (2019) were synthesize a new chain of Pyrazole derivatives 4-{5-[4(4-amino-5-mercapto-4h-[1,2,4]trizol-3-yl)3-trifluoromrthyl-pyrazole-1-yl)-benzenesulfonamide (3a-3m) by oxidized CH_3 group of Celecoxib with aqueous potassium permanganate then made Ester via CH_3OH and evaluated for carbonic anhydrase (CA,)inhibitors against human which invalves many diseases like glaucoma, retinitis tumors, pigmentosa, epilepsy etc.(3f) compound shows more potent anti-inflammatory activity through use of Ratpaw oedema model *in vivo* compared celecoxib as standard. These new pyrazole derivatives structure are characterize by elementary analysis, Nuclear Magnetic Resonance, Infra-Red &Mass spectrometry.[3]



[3]

2. Pyrazole as Acetylcholinesterase and Carbonicanhydrase inhibitor

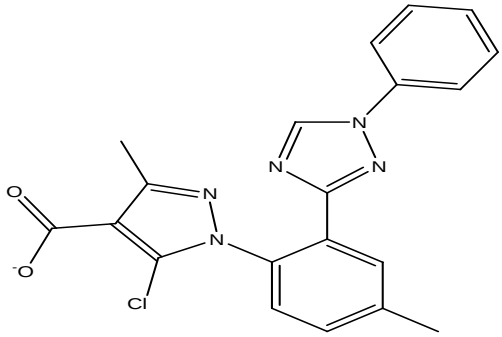
Turkan Fikret, *etal* (2019) were synthesized new chain of substitute Pyrazole compound (1-8 and 9a,b) by starting material pyrazole-3,4-dicarboxylic acid and studied Carbonic anhydrase & Acetylcholinestrase inhibitory activity. The characterization of synthesized compounds done via fundamental analysis, NMR, Infra-red, Mass spectrometry. These novel pyrazole derivatives come out as valuable inhibitor of carbonicanhydrase isoform (Hca I and II) & acetychlinestrase enzyme. Compound (5,4) were more potent against acetychlinestrase enzyme with K_i values 48.94 $\pm$ 9.63 and 55.93 $\pm$10.42 µM, respectively.[4]



[4]

3.1 Pyrazole as Antibacterial activity

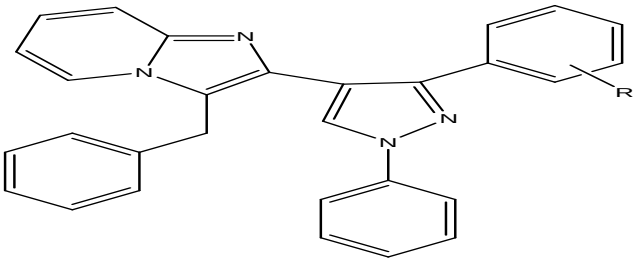
Ming-jie Chu, *etal*.(2019) were synthesized some novel triazole containing Pyrazole ester derivatives chain by Vilsmeier Haack reaction starting from phenylhydrazine and studied for their anti bacterial activity as topoisomerase II inhibitors. The Compound had Identify via elementalanalysis, FT-IR, NMR, Mass spectrometery. The antibacterial activity revels that compound 1-phenyl-1H-1,2,4-triazol-3-yl5-chloro-3-methyl-1-(p-tolyl)-1H-pyrazole-4-carboxylate (4d) having high potency & MIC values of 4µg/ ml, 2 µg/ ml, 1 µg/ ml and 0.5 µg/ ml in opposition to *Escherichia coli*, *Salmonella gallinarum*, *Listeria monocyogenes*, *Staphylococcus aureus* respectively & (4d)shows higher active topoisomeraseII (IC_{50}= 13.5microgram/ml) & topoisomerase IV (IC_{50}= 24.2microgram/ml) Inhibitory Activity by the vivo enzyme inhibition assay.[5]



[5]

3.2 Bactericidal activity

Paul awolade, *etal* (2019) were synthesized new chain of Pyrazole –imidazole [1,2-a]pyridine (5a,6a-6r) by One Pot three component reaction. The synthesize compound were screening for bactericidal activity in vitro in opposition to methicillin-resistant *Staphylococcus aureus*(Gram-positive bacteria) & *Klebsiella pneumoniae*, *Salmonella typhimurium*, *Pseudomonasaeruginosa*, *Escherichia coli* (Gram-negative bacteria) exhibit more bactericidal potent activity with minimum bactericidal concentration in compared with ciproflaxacine as reference. All newly shythesized compound were characterized by IR, NMR, Mass spectrometry technique. Compound (6d) exhibit large-scale bactericidal activity with MBC values less than 2.50 µg/ml against all bacterial strain thus, a possible beat compounds for large-scale antibacterial.[6]

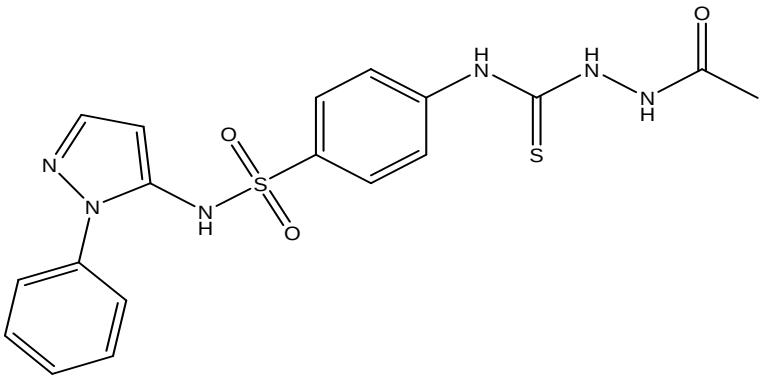


[6]

Compound	R
6b	diOCH_3
6d	4-F
6e	2-OH

4. Pyrazole as Anti cancer activity

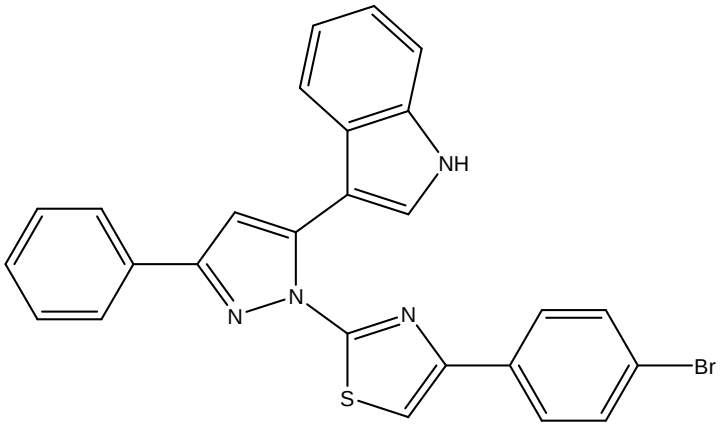
El Gaby *et al* (2017) have synthesized new chain of pyrazole derivatives(1-10) by the 4-isothiocynato-(1-phenyl-1H-Pyrazole-5-yl)benzene sulfonamide use as starting material & evaluate for their anti cancer activity in opposition to *Ehrlich ascites carcinoma cells (EAC)* through *in vitro.* All novel synthesized compounds were comfirmed via spectroscopical Infra-red, NMR, Mass spectrometry, elementary analysis. Compound(7) 2-acetyl-N-(4-(N-(1-phenyl-1H-pyrazol-5-yl)sulfamoyl)phenyl)hydrazinecarbothioamide with IC_{50} value (2.14 µg/ml) exhibited high anti cancer activity compare with doxorubicin IC_{50} value (43.6 µg/ml) as standard drug.[7]



[7]

5. Pyrazole as Anti diabetic activity

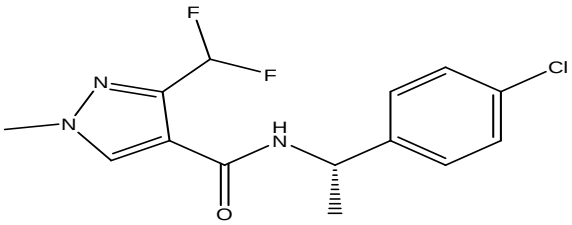
T. V. Sravanthi, *etal* (2017) were synthesized a new chain of substituted Pyrazole derivative (7a-7f) by three step reaction and evaluated for thir anti hyperglycemic activity against α-amylase and α-glucosidase enzymes all synthesized compound were characterize by spectroscopy UV, Infra-red, Nuclear magnetic resonance, Mass spectrometry and elementary analysis. the compound (7f) is shows high anti hyper glycemic activity (IC50 = 236.1 µg/m Ltrough comparing (acarbose, IC_{50} = 171.8µg/mL). as standard drug *In vitro.*[8]



[8]

6. Antifungle activity

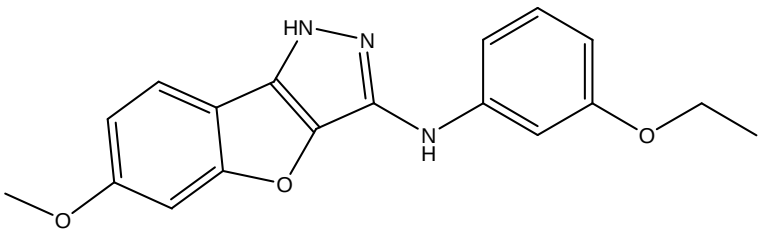
Xing-Hai Liu et al (2019) were synthesize a Novel chain of Pyrazole carboxamide derivatives (A_1-A_{27}) via using many synthesis method. in this series the starting material was trifluoroacetoacetate and studied for their anti fungle activity. the final compound pyrazole acyl amide derivative be characterize by ^{1}HNMR ^{13}NMR and mass spectrometry. The antifungal activity of pyrazole acylamide compound A1-A27 against in *Alternaria salani, Gibberella zeae, Botrytis cinerea. Phytophthora infestans.* A_{14}, A_{15} highly active against *C.arachidicola, S. sclerotiorum.* (A14) was elected as delegate compound *in vitro* Inhibitory activity test against SDH.[9]



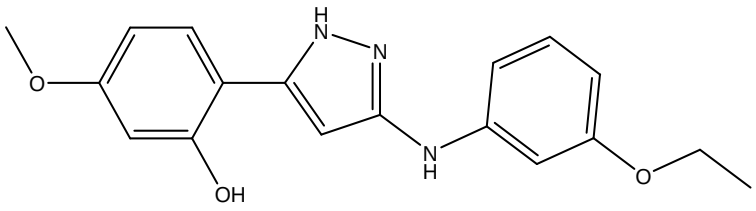
[9]

7. Pyrazole as Antitumor activity

Ying-jie Cui et al (2019) were synthesized and design two novel series of benzofuropyrazole (8a-e) and pyrazole (9a-e) derivative by Hoesch reaction starting from resorcinol and studied for their antitumor activity as inhibitory-activity against human erythroleukemia K562 cell, human lung cancer A549 cell, human breast cancer MCF-7 Cell via MTT Assay and *in vitro* tubulin polymerization inhibitory activity assay. The synthesize compounds were determined by analytical technique like ^{1}HNMR, ^{13}C-NMR and mass spectrometry. Antitumor activity revels that the compound **(8a)** has highest potency, GI_{50} of 0.26 and 0.19 µM respectively of ABT-71 & another benzofuropyrazoles shows modest or puny activity. 9**a** and **9b** both are highly active against the K 562 and A549 cell.[10]



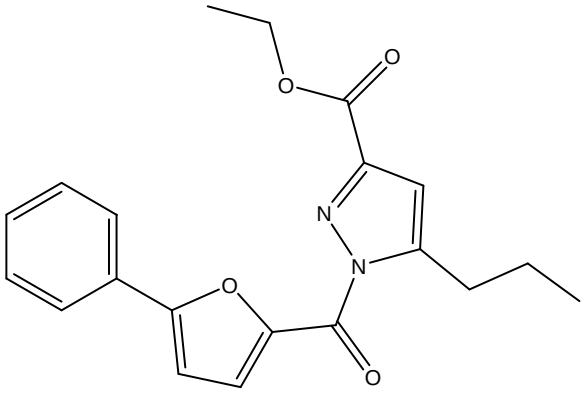
[10]



[11]

8. Pyrazole as Anti fungal activity

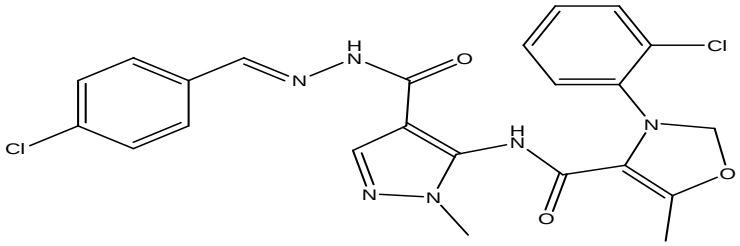
Muhammad Adnan *et al* (2019) were synthesize new chain of newr derivatives of pyrazole cantaining 5phenyl-2-furan by using Meerwein arylation method and catalized decomposition dizonium salt and evaluated for their fungicidal activity in opposition to *Phytophthora capsici*, *phytophthora infestance*, *Rhizoctonia solani*, *Botrytiscinerea*, and *Fusarium oxysporum in vitro* & *in vivo*. Compound ethyl-1-5-phenylfuran-2-carbonyl)-5-propyl-1H-pyrazole-3-carboxylate ethyl-1-(5-phenylfuran-2-carbonyl)-5-propyl-1*H*-pyrazole-3-carboxylate shows high antifungal activity in opposition to specially *Phytophthora infestans.* All newly synthesized compounds were Identify via analytical technique like ^{1}H Nuclear magnetic resonance, ^{13}C NMR, MassSpectrometry, elementary analysis and method of X-ray single crystal diffraction.[11]



[12]

9. Pyrazole as Anti viral activity

Zaibo Yang, *etal* (2018) were synthesize new chain Pyrazolehydrazole derivatives (10a-10r) cantaining an isoxazole moiety by half - leaf method bioassay and evaluated antiviral activity in opposition to *Tobacco mosaic virus* (TMV) *in vitro.* All newly synthesize compounds be identify via Infra-red, ^{1}H NMR, ^{13}C NMR and elementaryanalysis. This series were five step with yields of 85.9-91.2%. the compounds (10c,10q) were shows good antiviral avtivity in vivo and the compound (10a) shows better anti viral activity in compare to Ningnanmycin as reference drug.[13]



[13]

CONCLUSION

Pyrazole moity and its various derivative, various method, assay and different pharmacological action are studied and discussed in this article. This article mainly focus on various derivatives, various substitute of pyrazole exhibited varieties of pharmacological activities. Such as compound (4d) 1-phenyl-1H1-1,2,4-triazole-3-yl5-chloro-3-methyl-1(p-toly)-1H-pyrazol-4-carboxylate is higher active with MIC value of 4µg/ml, 2 µg/ ml, 1 µg/ ml and 0.5 µg/ ml in opposition to *Listeria monocyogenes*, *E. coli*, *Staphylococcus aureus*, *Salmonella gallinarum* in that order and shows the highly active topoisomeraseII (IC_{50}= 13.5 microgram milliliter) and topoisomerase IV (IC_{50}= 24.2 microgram/milliliter)inhibitors-activities by the vivo enzyme inhibition assay. The other compound that Ethyl5-(3,4-di methoxyphenyl)-1H-pyrazole-3-carboxylate (1f) and Ethyl5-(2,3-dimethoxyphenyl)-1*H*-pyrazole-3-carboxylate (1e) shows more potent compounds as anti inflammatory activity. Various other activity shows via other derivatives likes anti diabetic, anticonvalsant, antiviral activity, antimicrobial etc all the studied derivative produces various activities in previous years as well as still to use in future for discover and modification of new biological active molecules.

ACKNOWLEDGEMENT

We are heartly thanks to all the staff of Hygia Institute of Pharmaceutical Education and Research Lucknow for their guidance in searching various articles and journals for completing my this review.

REFERENCES

1. Gupta kumar Sujeet, Khanal pratik, Yogi Bhumika, Sinha Anshuman Synthesis, Characterization of Ethyl 5-(substituted)-1*H*-pyrazole-3-carboxylate Derivative as Potent Anti-inflammatory Agents Anti-inflammatory & Anti-allergy Agent in Medicinal Chemistry journal of Bantham Science, 2018; 17(1): 32-38.

2. Abdellatif, R.A. Khaled, Mohamed A.Abdelgawad, Heba A.H.Elshemy Shahindas S.R.Alsayed synthesis and anti-inflammatory evaluation of new 1,3,5triaryl-4,5,-di hydro-1H-pyrazolederivatives possessing an amino sulphonyl pharmacophore pharmacal research journal of Pharma Research, 2015; 38(11): 1932-1942.
3. Gulam Mustafa, Andrea Angeli, Muhammad Zia –ur- Rehman, Nosheen Akbar,Saiqa Ishtiaq synthesis of novel derivatives4-{5-[4-4-amino-5-mercapto-4H-[1,2,4]triazole-3-yl)-3-trifluoromethyl-pyrazol-1-yl}-benzenesulfonamides and their anti-inflammatory potential European Journal of Medicinal Chemistry, 2019; 91: 103-110.
4. Fikret Turkan, Adnan Cetin, Parham Taslimi, Muhammet Karaman synthesis, biological evaluation and molecular docking of novel pyrazole derivatives as potent carbonic anhydrase and acetylcholinsterase inhibitors European Journal of Medicinal Chemistry, 2019; 86: 420-427.
5. Ming-Jie Chu, Wei Wang, Zi-Li Ren, Hao Liu, Xiang Cheng, Kai Mo, Li Wang Discovery of novel triazole –cantaining Pyrazole Ester derivatives as potential antibacterial agents journal of molecules, 2019; 24(7): 1311.
6. Oluwakemi Ebenezer, Paul Awolade, Nell Koorbanally, Parvesh Singh synthesis, antibacterial avtivity and molecular docking studies International journal of WILEY, 2019; 95(1): 162-173.
7. El– Gaby Mohammed S.A., Mustafa M. ghorab, Zainb H.Ismail synthesis ,structural characterization and anticancer evaluation of pyrazole derivatives national journal of Medicinal chemistry research, 2017; 27: 72-79.
8. T.V. Sravanthi, S.Sajitha Lulu, S.Vino, M.A. Jayasri, synthesis, docking, and evaluation of novel thiazole for potent antidiabetic activity International journal of Medicinal chemistry research, 2017; 26: 1306-1315.
9. Xing-Hal Liu, Li Qiao, Zhi-Wen Zhai, Peng-peng Cal, Charles L Cantrell novel 4-pyrazole carboxamide derivatives cantainig flexible chain motif: design synthesis and anti fungal activity journal of society chemical industry, 2019; 75(11): 2892-2900.
10. Ying-Jie Cui, Long-Qian Tang, Cheng-Mei Zhang synthesis of novel pyrazole derivatives and their tumor cell growth inhibitory activity journal of molecules, 2019; 24(2): 279.
11. Muhammad Adnan, Wasim Ahmed, Xiaojing Yan, Dekun Hu Ri –Yuan Tang synthesis and fungicidal activity of novel pyrazole derivatives containing 5-Phenyl-2-Furan European Journal of Medicinal Chemistry, 2019; 27(19): 115048.

12. Zaibo Yang, Pei Li Xiuhai Gan novel Pyrazole – Hydrazone Derivatives Containing an Isoxazole Moity: Design, Synthesis, and Antiviral Activity International Journal of Molecules, 2018; 23(7): 1798.
13. Sharma S.C. A Text Book of Organic Chemistry SHOBAN LAL & CO. Educational Publishers page no 979-983.
14. Abraham, J.D, 1998 Burgers Medicinal Chemistry and Drug Discovery, John wiley and sons, inc. New York, Fifteenth Edition, 6: 635-637.
15. Sabale p. et al synthesis and anti-tubercular activity of substitute phenyl pyrazole having Benzimidazole ring Research journal of pharmacy technology, 2018; 11(8): 3599-3608.