Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(6), 2816-2822 | ISSN:2251-6727

"Review on Biological Activities of Pyrazole Derivatives"

Kiran Balasaheb Kharad*

Department of Chemistry, Jijamata College of Science and Arts, Bhende Bk, Ahmednagar, Maharashtra, India – 414605. Affiliated to Savitribai Phule Pune University Pune.

(Received: 16 October 2024 Revised: 20 November 2024 Accepted: 02 December 2024)

KEYWORDS

Pyrazole, biological activities, anticancer, antimicrobial, anti-inflammatory, antiviral,

ABSTRACT:

A summary of the many different biological actions that are related with pyrazole moieties is provided in this review. Anticancer, antiviral, antibacterial, anti-inflammatory, anti-obesity, anticonvulsant, and antidepressant effects are some of the activities that are highlighted by this substance. The purpose of this review is to consolidate the findings from a variety of investigations that have been conducted on the biological effects of pyrazole compounds, as reported by researchers.

Graphical Abstract: -

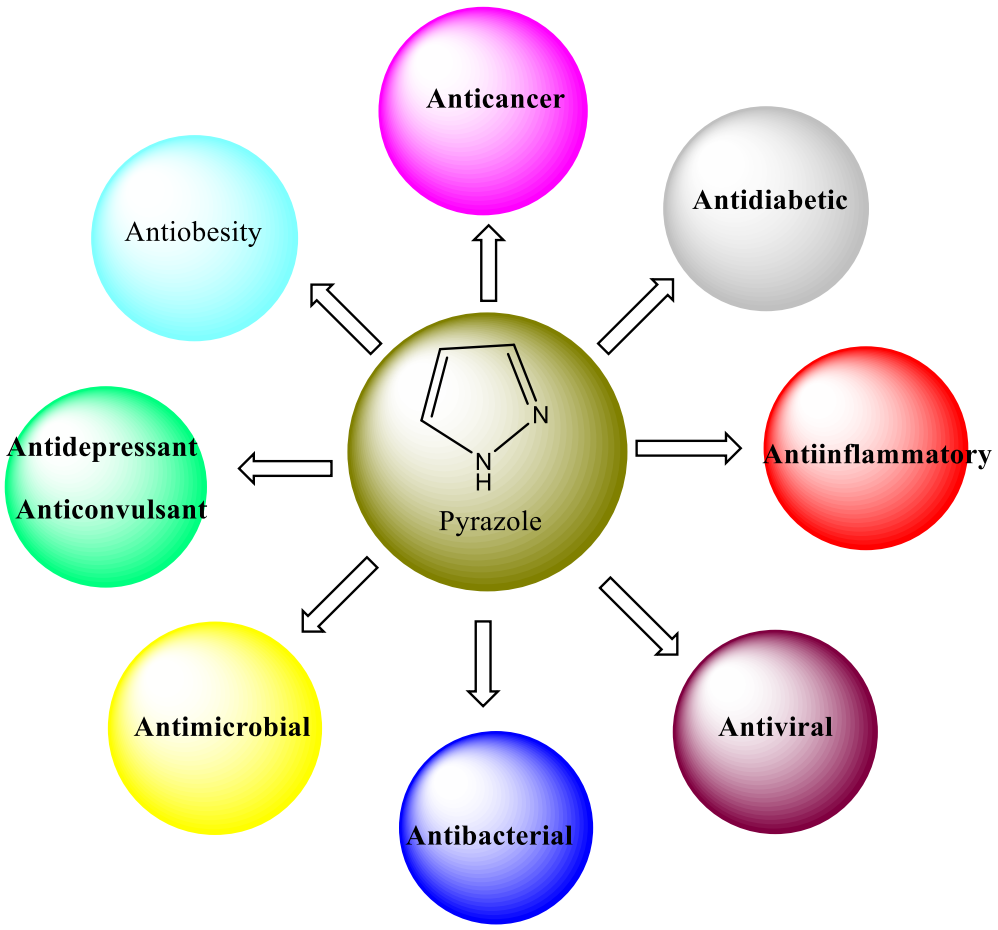


Figure- 14 Pyrazole contain different biological activities

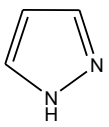
Journal of Chemical Health Risks

www.jchr.org

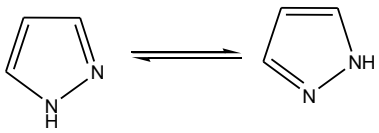
JCHR (2024) 14(6), 2816-2822 | ISSN:2251-6727

Introduction: -

Pyrazole is a simple aromatic heterocyclic chemical molecule composed of a five-membered ring with three carbon atoms and two nitrogen atoms arranged next to one another (Figure 1). Its molecular formula is $C_3H_4N_2$. The term 'pyrazole' was first introduced by Ludwig Knorr in 1883. Pyrazole-based compounds exhibit diverse biological effects, including anticancer, anti-inflammatory, antimicrobial, and pain-relieving activities. Compounds containing pyrazole structures have distinctive properties that make them valuable in medicinal chemistry. Many pyrazole derivatives are used as pharmacophoric components in various drug molecules [1]. Pyrazole is a colorless crystalline compound that melts at 69–70°C and boils between 186–188°C, a property influenced by intermolecular hydrogen bonding. The compound exists in two tautomers that rapidly interconvert, making them non-separable (Figure 2). A detailed review of this heterocyclic class revealed that pyrazole-containing pharmacophores play a significant role in the development of bioactive agents in medicinal chemistry [2].



Pyrazole (Figure -1)



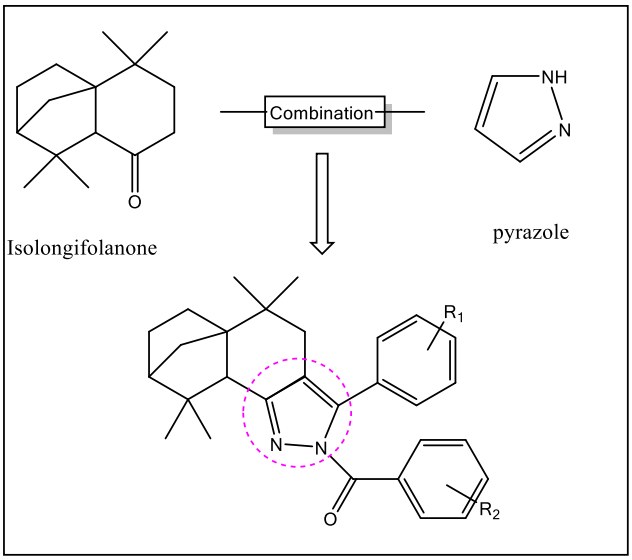
(Figure - 2)

Literature Review: -

This review primarily focuses on biologically active pyrazole compounds with significant therapeutic potential. Pyrazole-containing compounds are widely acknowledged for their notable biological activity and importance as heterocyclic structures in medicinal chemistry [3,4,5]. A review of existing studies demonstrates that pyrazole derivatives exhibit a wide range of pharmacological effects.

1) Anticancer Activity:

Cancer remains a major global health concern and is currently the second leading cause of death worldwide [6]. Several pyrazole derivatives have shown promising anticancer activity. In particular, isolongifolanone derivatives incorporating a pyrazole ring have been identified as potential candidates for anticancer therapy [7] (Figure-3).



(Figure- 3: Pyrazole ring containing isolongifolanone derivatives with antitumor activity.)

Pyrazole-pyrimidine compounds and their bioisosteres are heterocyclic structures known for a range of biological activities, including notable antitumor effects [8] (Figures 4, 5, 6). A series of 4-benzoyl-1,5-diphenyl-1H-pyrazole-3-carbonyl thiourea derivatives have demonstrated significant anticancer activity, making them promising candidates for the treatment of leukemia, liver cancer, and colon cancer [9] (Figure 7).

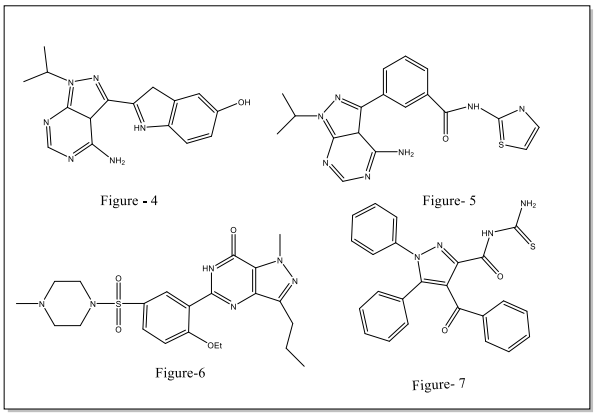


Figure - 4

Figure- 5

Figure-6

Figure- 7

2) Antimicrobial Activity:

The major diseases spread in the environment only because of microbes. Even in the hospital's intensive

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(6), 2816-2822 | ISSN:2251-6727

care units are polluted by microorganisms, specially, Gram-positive bacteria. Hence, there is a need to develop antibiotics which contain microbial-resistant agents. Hence, the current study aimed to develop prominent antimicrobial drug-related compounds. Heterocycles containing Pyrazole derivatives shows antimicrobial activity. A novel synthesized tri-substituted pyrazole derivatives shows measurable antimicrobial Activity [10] (Figure- 8, 9). A series of ethyl-1-(5- phenylfuran-2- carbonyl)-5-propyl-1H-pyrazole-3-carboxylate compounds which displayed significant fungicidal activity against various fungi, especially against P. infestans [11]. Pyrazoles are the class of azoles as antimicrobial agents due to the increasing resistance of pathogenic microbes to multiple drugs including ciprofloxacin [12].

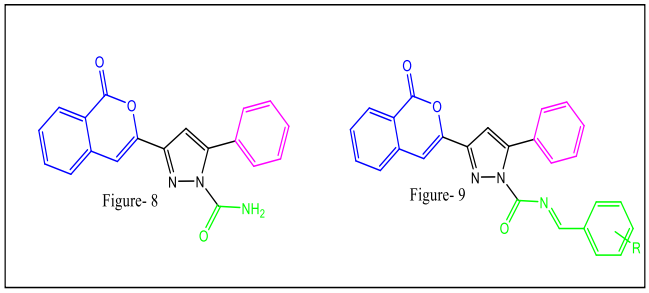


Figure- 8 Figure- 9

3) Anti-inflammatory Activity:

Pyrazole-based compounds, such as celecoxib, are well-known for their significant anti-inflammatory properties, making them valuable in the pharmaceutical industry [13] (Figure-10). Recent pyrazole derivatives, specifically compounds A, B, C, and D, have shown notable potency and selectivity against the COX-2 enzyme, exhibiting IC_{50} values of 39.4, 61.2, 38.7, and 39.1 nM, respectively. These compounds performed as well as or better than celecoxib in in vivo anti-inflammatory evaluations [14]. The development of pyrazole derivatives continues to offer great potential for advancing anti-inflammatory drug research.

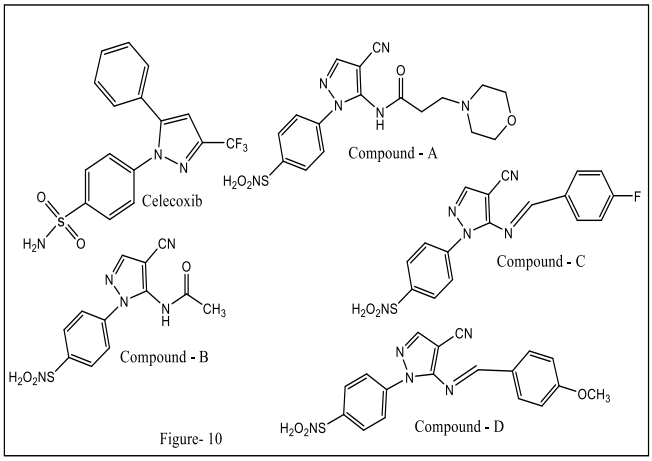


Figure- 10

4) Antidiabetic Activity:

Several pyrazole derivatives have demonstrated notable antidiabetic potential. Among the synthesized compounds, 2-(5-(1H-indol-3-yl)-3-phenyl-1H-pyrazol-1-yl)-4-(4-bromophenyl) thiazole demonstrated the most potent antihyperglycemic effect, recording an IC_{50} of 236.1 µg/mL. This activity was compared to the reference drug acarbose, which showed an IC_{50} of 171.8 µg/mL. Additionally, compounds E, F and G bearing fluoro, bromo, and hydroxyl substituents on the phenyl ring attached to the thiazole pyrazole core exhibited significant inhibitory activity [15] (Figure-11). Additionally, novel urea and thiourea derivatives were synthesized via reactions between pyrazoles and corresponding isocyanates or isothiocyanates. Subsequent cyclization of the thiourea intermediates produced cyclic structures, some of which displayed strong antimicrobial properties, while others demonstrated significant hypoglycemic effects.[16]

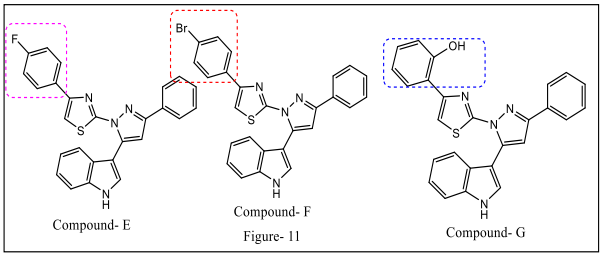


Figure- 11

5) Anticonvulsant and Antidepressant Activity:

Mohamed Abdel Aziz and other in 2009, synthesized new derivatives of a series of pyrazole and shown their potential anticonvulsant and antidepressant properties. Compounds 4a and 4b (Figure-12) demonstrated antidepressant effects in the tail suspension test, while

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(6), 2816-2822 | ISSN:2251-6727

derivatives 11a, 11b, and 11d (Figure-13) exhibited anticonvulsant activity in mice using the PTZ-induced seizure model [17].

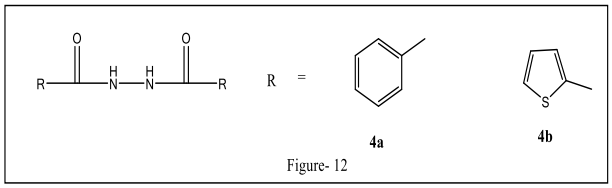


Figure- 12

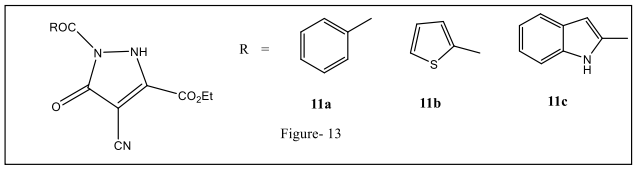
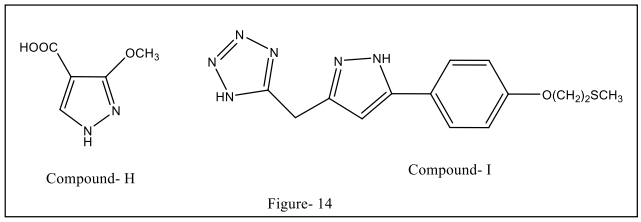


Figure- 13

6) Anti-obesity Activity:

Obesity significantly increases the risk of developing several chronic conditions, including type 2 diabetes, coronary artery disease, stroke, non-alcoholic fatty liver disease, sleep apnea, osteoarthritis, and specific types of cancer [18] (Figure-14). Cottineau et al. synthesized a novel series of substituted pyrazole-4-carboxylic acids and assessed their potential antidiabetic properties. Among the compounds tested, compound H demonstrated the most promising hypoglycemic effect [19] (Figure-14). Sharon et al. developed a novel series of 5-[(5-aryl-1H-pyrazol-3-yl) methyl]-1H-tetrazoles and investigated their antihyperglycemic effects in vivo. Among the compounds tested, compound I showed a 24.6% reduction in blood glucose levels at a dose of 100 mg/kg [20]. Several pyrazole-based derivatives have also demonstrated anti-obesity activity, as pyrazole is recognized as a key pharmacophore with a wide range of biological effects [21].



Compound- H Compound- I

Figure- 14

7) Antibacterial Activity:

coumarin-pyrazole carboxamide derivatives shows antibacterial activity against Staphylococcus aureus, Listeria monocytogenes, Escherichia coli and Salmonella, indicating that most of compounds exhibited moderate to potent antibacterial activities. [22] pyrazole present in quinoline-pyrazole hybrid derivatives shows antibacterial activity against three common pathogenic bacterial strains Staphylococcus aureus, Escherichia coli and Pseudomonas aeruginosa. [23] A pyrazole, triazole based benzohydrazones containing 4-chloro (compound – J) and 4-nitro (compound – K) derivatives showed significant broad spectrum of antibacterial activities against both Gram-positive (Staphylococcus aureus and Bacillus cereus) and Gram-negative (Escherichia coli and Pseudomonas aeruginosa) bacteria.[24] (Figure – 15)

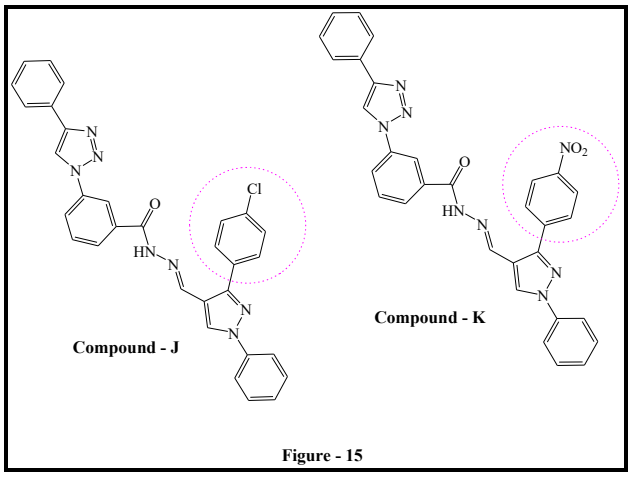


Figure - 15

8) Antiviral Activity:

Pyrazole derivative containing oxime ester group have good anti-TMV bioactivity. [25] A new heterocyclic compound is formed from pyrazole and thiazole containing moieties which is actively antivirus agent. [26] Various pyrazole derivatives were synthesized by reacting 5-chloro-4-formyl-3-methyl-1-phenylpyrazole with selected nitrogen- and carbon-based nucleophiles. The synthesized compounds were evaluated for their antiviral efficacy against NDV, showing that hydrazone derivative compound L and thiazolidinedione compound M provided complete protection with no mortality, and pyrazolopyrimidine derivative compound N offered 95% protection.[27] (Figure – 16)

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(6), 2816-2822 | ISSN:2251-6727

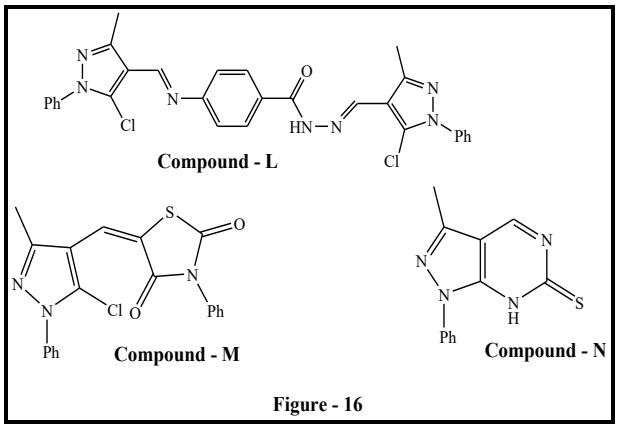


Figure - 16

Conclusion: -

The literature reviewed above indicates that pyrazole compounds and their derivatives exhibit a broad range of biological activities. This review summarized the findings of various researchers on the pharmacological properties of synthesized pyrazole compounds. Further studies are needed to explore additional therapeutic potential of pyrazoles, especially for diseases that present significant challenges in medical treatment.

Acknowledgement: -

The author is thankful to the Principal and Head of the Department, Jijamata College of Science and Arts, Bhende Bk, Tahshil - Newasa, Dist.- Ahmednagar, Maharashtra, India, for providing infrastructure for research. The author is also thankful to Dr. Sadhana D. Mhaske, Head of the Department, Dadapatil Rajale Arts and Science College, Adinathnagar, Tahshil – Pathardi, Dist.- Ahmednagar, Maharashtra, India and Dr. Sushama J. Takate, Department of Chemistry, New Arts Commerce and Science College, Ahmednagar, Maharashtra, India for guidance, help, encouragement, and support. I also thank my friend Mr. Mahesh S. Jangale, Department of Chemistry, Arts, Commerce and Science College Sonai, Tahshil - Newasa, Dist.- Ahmednagar, Maharashtra, India for his support and help.

References: -

[1] Alka Chauhan, P. K. Sharma, Niranjan Kaushik, Pyrazole: A Versatile Moiety, International Journal of ChemTech Research, (2011), Vol.3, No.1, pp 11-17, ISSN : 0974-4290

[2] Md. Jahangir Alam, Ozair Alam , Perwaiz Alam , Mohd Javed Naim, A Review on Pyrazole chemical entity and Biological Activity , International Journal of Pharma Sciences and Research (IJPSR), 2015

[3] Y.-G. Zheng, J.-A. Wang, L. Meng, X. Pei, L. Zhang, L. An, C.-L. Li, Y.-L. Miao, Design, Synthesis, Biological Activity Evaluation of 3-(4-Phenyl-1H-Imidazol-2-yl)-1H-Pyrazole Derivatives as Potent JAK 2/3 and Aurora A/B Kinases Multi-targeted Inhibitors, European Journal of Medicinal Chemistry, **https://doi.org/10.1016/j.ejmech.2020.112934.**

[4] Jéssica Venância Faria , Percilene Fazolin Vegi , Ana Gabriella Carvalho Miguita, Maurício Silva dos Santos , Nubia Boechat , Alice Maria Rolim Bernardino, "Recently reported biological activities of pyrazole compound" *Bioorganic & Medicinal Chemistry* 25 , **2017** , 5891–5903. https://doi.org/10.1016/j.bmc.2017.09.035

[5] Ş.Güniz Küçükgüzel , Sevil Şenkardeş, "Recent advance in bioactive pyrazole" European Journal of Medicinal Chemistry, Volume 97, pages 786-815, (2015) https://doi.org/10.1016/j.ejmech.2014.11.059

[6] Jacques Ferlay , Isabelle Soerjomataram , Rajesh Dikshit , Sultan Eser, Colin Mathers , Marise Rebelo , Donald Maxwell Parkin, David Forman and Freddie Bray, Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012, International Journal of Cancer, 136, E359–E386 (2015) DOI: 10.1002/ijc.29210,

[7] A Yunyun Wang, Wei Shi, Chenliang Wu, Lin Wan, Yuxun Zhao, Chenglong Zhang, Wen Gu, Shifa Wang, Pyrazole ring-containing isolongifolanone derivatives as potential CDK2 inhibitors: Evaluation of anticancer activity and investigation of action mechanism, Biomedicine & Pharmacotherapy,(2021),139,111663 https://doi.org/10.1016/j.biopha.2021.111663

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(6), 2816-2822 | ISSN:2251-6727

[8] Shi, J. B., Tang, W. J., qi, X. B., Li, R., & Liu, X. H. (2015). Novel pyrazole-5-carboxamide and pyrazole–pyrimidine derivatives: Synthesis and anticancer activity. European Journal of Medicinal Chemistry, (2015), 90, 889–896. https://doi.org/10.1016/j.ejmech.2014.12.013

[9] Valentina Anuta, George Mihai Nitulescu, Cristina Elena Dinu-Pîrvu and Octavian Tudorel Olaru, Biopharmaceutical Profiling of New Antitumor Pyrazole Derivatives, Molecules **2014**, 19, 16381-16401. **https://doi.org/10.3390/molecules191016381**

[10] Guda Mallikarjuna Reddy, Jarem Raul Garcia, Gutha Yuvaraja, Munagapati Venkata Subbaiah, Jet-Chau Wen, Design, synthesis of tri-substituted pyrazole derivatives as promising antimicrobial agents and investigation of structure activity relationships, 2020, DOI: 10.1002/jhet.3952

[11] Ahmed W, Yan X, Hu D, Adnan M, Tang R-Y & Cui Z-N, *Bioorg Med Chem*, 27(19), **2019**, 115048. https://doi.org/10.1016/j.bmc.2019.115048

[12] Shubhangi, Kumar N, Kanagaraj R, Lal K & Paul A K, *J Mol Structure*, 1195, **2019**, 435-450. https://doi.org/10.1016/j.molstruc.2019.05.125

[13] Baumann, M.; Baxendale, I.R.; Ley, S.V.; Nikbin, N. An overview of the key routes to the bestselling 5- membered ring heterocyclic pharmaceuticals. Beilstein J. Org. Chem. **2011**, 7, 442–495. https://doi.org/10.3762/bjoc.7.57

[14] Hassan, G. S., Abdel Rahman, D. E., Abdelmajeed, E. A., Refaey, R. H., Alaraby Salem, M., & Nissan, Y. M. (2019). New pyrazole derivatives: Synthesis, anti-inflammatory activity, cycloxygenase inhibition assay and evaluation of mPGES. European Journal of Medicinal Chemistry, 171, 332–342. doi:10.1016/j.ejmech.2019.03.052

[15] Sravanthi, T. V., Sajitha Lulu, S., Vino, S., Jayasri, M. A., Mohanapriya, A., & Manju, S. L. (2017). Synthesis, docking, and evaluation of novel thiazoles for potent antidiabetic activity. Medicinal Chemistry Research, 26(6), 1306–1315. doi:10.1007/s00044-017-1851-8

[16] Faidallah, H. M., Khan, K. A., & Asiri, A. M. (2011). Synthesis and biological evaluation of new 3-trifluoromethylpyrazolesulfonyl-urea and thiourea derivatives as antidiabetic and antimicrobial agents. Journal of Fluorine Chemistry, 132(2), 131–137. doi:10.1016/j.jfluchem.2010.12.009

[17] Abdel-Aziz, M., Abuo-Rahma, G. E.-D. A., & Hassan, A. A. (2009). Synthesis of novel pyrazole derivatives and evaluation of their antidepressant and anticonvulsant activities. European Journal of Medicinal Chemistry, 44(9), 3480–3487. doi:10.1016/j.ejmech.2009.01.032

[18] Kopelman, P. G. Obesity as a medical problem. Nature 2000, 404, 635-643.

[19] Cottineau, B.; Toto, P.; Marot, C.; Pipaud, A.; Chenault, J. Synthesis and hypoglycemic evaluation of substituted pyrazole-4-carboxylic acids. Bioorg. Med. Chem. Lett. 2002, 12, 2105–2108. https://doi.org/10.1016/S0960-894X(02)00380-3

[20] Sharon, A.; Pratap, R.; Tiwari, P.; Srivastava, A.; Maulik, P.R.; Ram, V.J. Synthesis and in vivo antihyperglycemic activity of 5-(1H-pyrazol-3-yl) methyl-1H-tetrazoles. Bioorg. Med. Chem. Lett. 2005, 15, 2115–2117 https://doi.org/10.1016/j.bmcl.2005.02.060

[21] Karrouchi, K., Radi, S., Ramli, Y., Taoufik, J., Mabkhot, Y., Al-aizari Faiz, & Ansar, M. (2018). Synthesis and Pharmacological Activities of Pyrazole Derivatives: A Review. Molecules, 23(1), 134. doi:10.3390/molecules23010134

[22] H. Liu, Z.-L. Ren, W. Wang, J.-X. Gong, M.-J. Chu, Q.-W. Ma, J.-C. Wang, X.-H. Lv, Novel coumarin-pyrazole carboxamide derivatives as potential topoisomerase II inhibitors: Design, synthesis and antibacterial activity, European Journal of Medicinal Chemistry (2018), doi: 10.1016/j.ejmech.2018.07.059.

[23] Nagabhushana Nayak, Jurupula Ramprasad, Udayakumar Dalimba, Synthesis and antitubercular and antibacterial activity of some

active fluorine containing quinoline-pyrazole hybrid derivatives, Journal of Fluorine Chemistry http://dx.doi.org/10.1016/j.jfluchem.2016.01.011

[24] Sravanthi K, Snehalatha P, and Subhashini NJP, Microwave Assisted Green Synthesis of Pyrazole, 1, 2, 3- Triazole Based Novel Benzohydrazones and Their Antibacterial Activities, J. Heterocyclic Chem., 00, 00 (2017). https://doi.org/10.1002/jhet.3073

[25] Guiping Ouyang, Zhuo Chen, Xue-Jian Cai, Bao-An Song , Pinaki S. Bhadury, Song Yang, Lin-Hong Jin, Wei Xue, De-Yu Hu, Song Zeng, Synthesis and antiviral activity of novel pyrazole derivatives containing oxime esters group, Bioorganic & Medicinal Chemistry 16, 9699–9707 (2008) https://doi.org/10.1016/j.bmc.2008.09.070

[26] Osama I. El-Sabbagh, Mohamed M. Baraka, Samy M. Ibrahim, Christophe Pannecouque , Graciela Andrei, Robert Snoeck, Jan Balzarini, Adel A. Rashad, Synthesis and antiviral activity of new pyrazole and thiazole derivatives, European Journal of Medicinal Chemistry 44,3746–3753, (2009) https://doi.org/10.1016/j.ejmech.2009.03.038

[27] Ahmed El-Sewedy, Alaa R. I. Morsy, Eman A. El-Bordany, Naglaa F. H. Mahmoud, Safwa Z. Mohamed & Sayed K. Ramadan, Antiviral activity of newly synthesized pyrazole derivatives against Newcastle disease virus, scientific report, 15, Article number: 18745 (2025) https://doi.org/10.1038/s41598-025-03495-6.