



# A Complete Analysis of The Synthesis and Pharmacological Effects of Pyrazolone Derivatives

Justin Jacob Thomas<sup>1\*</sup>, Presanna kumaran P N<sup>2</sup>, Santhosh M Mathew<sup>3</sup>, Joshny Varghese<sup>4</sup> and Rincy Meriyam Varghese<sup>5</sup>

<sup>1\*,2,4,5</sup>Pushpagiri College of Pharmacy, Department of Pharmaceutical Chemistry, Thiruvalla, Kerala - 689107.

<sup>3</sup>Principal, Pushpagiri College of Pharmacy, Thiruvalla, Kerala - 689107.

Received: 12 Jan 2023 / Accepted: 10 March 2023/ Published online: 01 April 2023

\*Corresponding Author Email: [justinjthomas353@gmail.com](mailto:justinjthomas353@gmail.com)

## Abstract

Pyrazolone is a five membered lactam ring, containing two nitrogen and one ketonic group in its structure. Pyrazolone's possesses anti-microbial, anti-fungal, antioxidant, anti-inflammatory, cytotoxicity, analgesic, anti-pyretic and anti-depressant activities. They also serve as precursors for dyes, pigments, pesticides, and chelating agents. Generally, the condensation of hydrazines with  $\beta$ -ketoester compounds is the classical method for the synthesis of pyrazolones, followed by reaction with various benzaldehyde derivatives. It is an exciting area of pharmaceutical chemistry to research the biological evaluation of pyrazolone derivatives. This review article provides information about different synthetic schemes and biological activities of various pyrazolone derivatives.

## Keywords

Pyrazolone, Knorr condensation, Phenyl hydrazine, Ethyl Acetoacetate, Biological Activity.

\*\*\*\*\*

## INTRODUCTION:

The synthesis of heterocycles with nitrogen atoms has received a lot of interest recently due to its significance in biology and medicine, including ontology study. They are abundant in nature and necessary for survival. Numerous investigations have been conducted on pyrazolone derivatives because of their potential biological activity in various ways. It is possible to consider the use of pyrazolone as an intermediary in the synthesis of several biologically active cyclic molecules. Growing interest in the study of pyrazolone derivatives has recently been shown by chemists and biologists due to their production and bioactivity. Based on numerous literature studies, it was shown that pyrazolone compounds with methyl and phenyl substitutions have important pharmacological effects. Pyrazolone is a 5-

membered heterocycle containing two adjacent nitrogen atoms. It can be viewed as a derivative of pyrazole possessing an additional carbonyl (C=O) group. The first synthesis of pyrazolones was reported in 1883 by Ludwig Knorr, via a condensation reaction between ethyl acetoacetate and phenyl hydrazine. The electrophilic substitution at the C-4 position of pyrazolones is an effective synthetic route for the construction of pyrazolones linked with chiral groups and 4-disubstituted pyrazolones. Medicinal chemistry research has synthesized drug-like pyrazolone candidates with several medicinal features including antimicrobial, antitumor, central nervous system effect, anti-inflammatory activities and so on. For instance, a number of pyrazolone medications, including phenazone, propyphenazone, ampyrone, and metamizole, are effective analgesics

and antipyretics. One of these, 3-methyl-1-phenyl-2-pyrazolin-5-one (edaravone), a well-known pyrazolone derivative, has been utilised in clinical studies as a commercial medication for brain and cardiac ischemia. Among the pyrazoles, Crizotinib, Cefoselis, and Celebrex (celecoxib) are medications used to treat rheumatoid arthritis and osteoarthritis, respectively. Antipyrine I was one of the earliest synthetic organic compounds with a pyrazolone nucleus that was employed as a significant medicine. Many pyrazolones are also commonly used as analgesic, antipyretic, and anti-inflammatory medications. Examples include amino phenazone II, propyphenazone III, and famorofazone. Additionally,

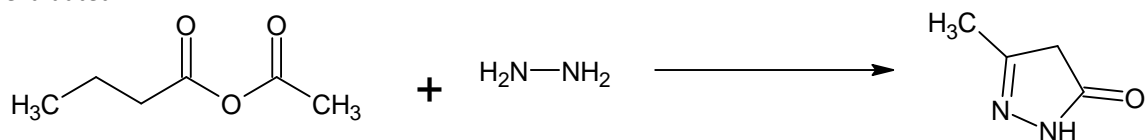
many pyrazolones were discovered to have strong anti-inflammatory activity. Moreover, the use of pyrazolone derivatives in the production of herbicides, liquid crystals, and dyes has grown significantly along with their relevance. As a result, research into the pyrazolones' synthetic chemistry has attracted a lot of attention. Based on Structure Activity Relationship, medicinal chemists synthesized a plenty of analogues for multiple targets. This review is a concise and critical account focusing on the synthesis based on the synthesis of nucleus and a multicomponent approach was also explained. Pharmacological activity such as antimicrobial, antidepressant, anti-inflammatory, antioxidant etc.

## MATERIALS AND METHODS:

### SYNTHESIS OF PYRAZOLONES:

#### 1. Synthesis of basic pyrazolone nucleus:

Parajulii *et al* synthesised pyrazolone derivatives using phenyl hydrazine and ethyl acetoacetate with substituted benzaldehyde (Figure 1). Antimicrobial and cytotoxic activity of the synthesized derivatives were evaluated.<sup>(1)</sup>



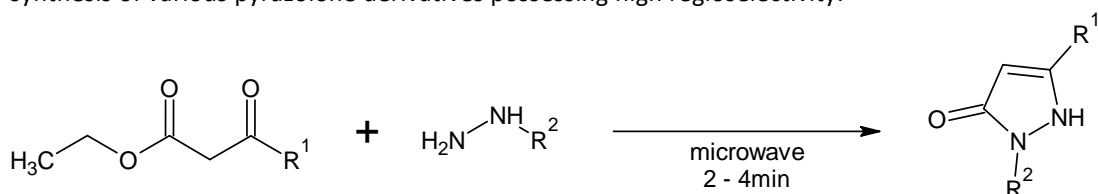
Ethyl acetoacetate

Hydrazine hydrate

3-methyl pyrazol-5-one

Figure 1: Scheme 1

J. Braz *et al* synthesised pyrazolone derivatives using microwave irradiation method. The reaction between  $\beta$ -keto ester with substituted or unsubstituted hydrazine (Figure 2) provides a one pot approach for the synthesis of various pyrazolone derivatives possessing high regioselectivity.<sup>(2)</sup>



beta- keto ester

hydrazine

pyrazolone derivative

Figure 2: Scheme 2

Brana *et al*, used ethyl ester, acyl chloride and hydrazines for the synthesis of bis aryl pyrazolone (Figure 3) and growth inhibitory activity of the developed compound was evaluated.<sup>(3)</sup>

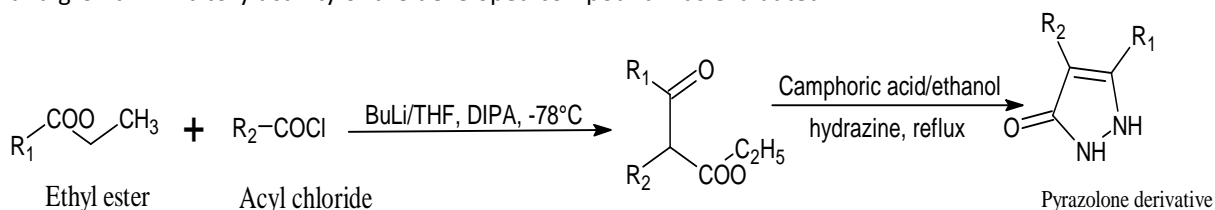


Figure 3: Scheme 3

Azim F. *et. al*, prepared fused pyrazolone derivatives by the reaction between ethyl acetoacetate and hydrazine hydrate. The obtained pyrazolone then treated with aromatic aldehydes to obtain benzylidene

derivatives of pyrazolone (Figure 4). The synthesized compounds were proved to exhibit moderate antibacterial and antioxidant properties.<sup>(4)</sup>

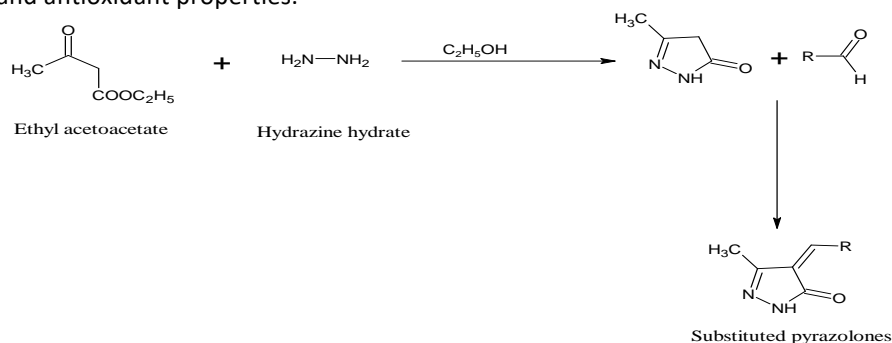


Figure 4: Scheme 4

Min *et al*, constructed an efficient method by the condensation of hydrazine derivatives with beta-keto esters (Figure 5) in water catalysed by tungstophosphoric acid for the formation of pyrazolone.<sup>(5)</sup>

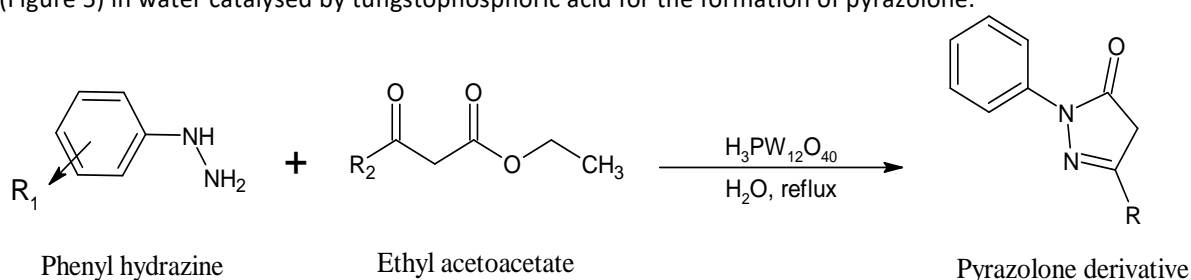


Figure 5: Scheme 5

Aliye Gediz Erturk and Hilal Omerustaoglu synthesized a series of substituted-5-pyrazolone which is substituted with different aldehyde derivatives through Vilsmeier- Haack reaction (Figure 7). The synthesized compounds were investigated for cytotoxic and antioxidant effects.<sup>(6)</sup>

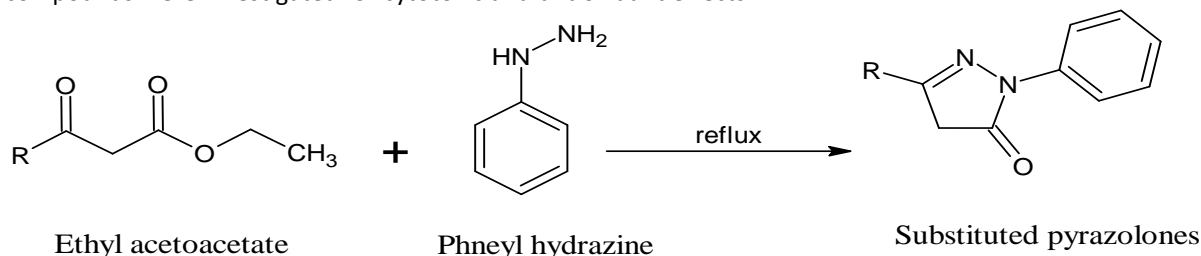


Figure 6: Scheme 6

M.M. Mojtahedi *et al*, developed a method for the rapid formation of pyrazolone by the condensation of hydrazine derivatives with various beta-keto ester (Figure 7) in solvent free conditions using microwave irradiation.<sup>(7)</sup>

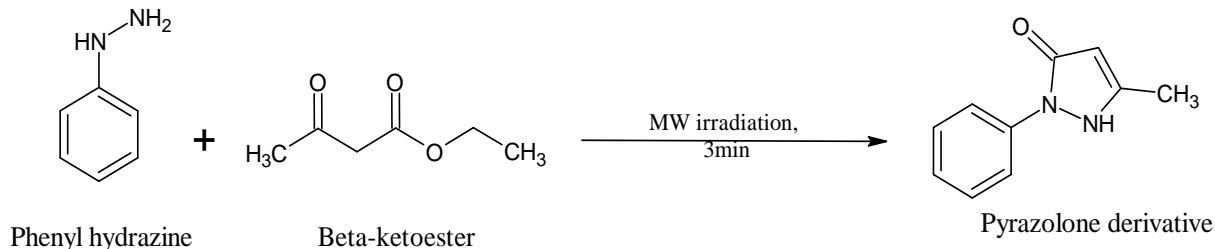


Figure 7: Scheme 7

Naik and Malik *et al*, prepared 3-methyl-phenylpyrazol-5-one and its derivatives with the usage of phenyl hydrazine, ethyl acetoacetate and its derivatives (Figure 8). Both the reactants were

refluxed to provide the crude pyrazolone derivatives. The obtained pyrazolone derivative was allowed to react with methyl amine with the aid of methanol to

form 3-methyl-1-phenyl pyrazolone-5-methylamine and its derivatives.

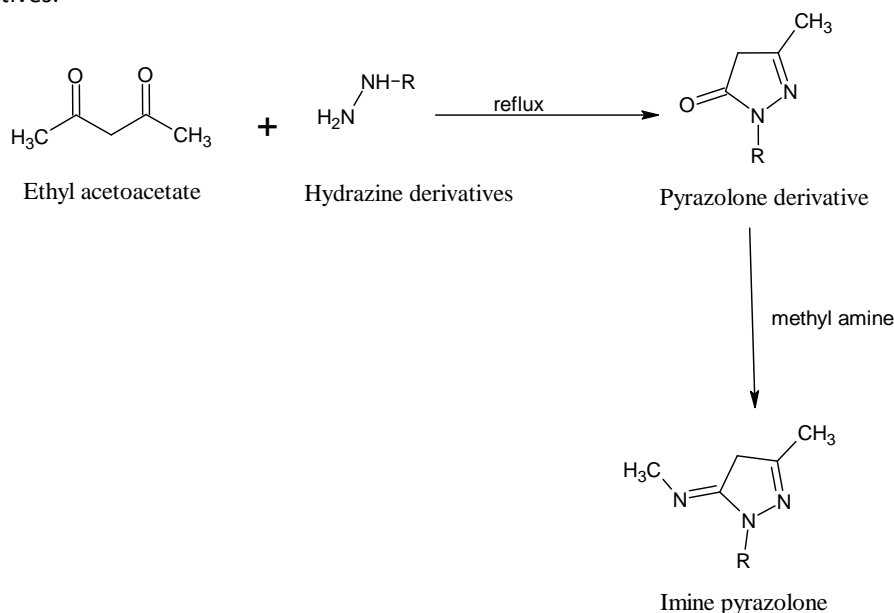


Figure 8: Scheme 8

Nedjar-Kolli B *et al*, used 2 distinct processes to create a sequence of pyrazolone derivatives, which were more effective. One was using a Keggin type heteropoly acid and the other was the reaction between 3-acetyldihydrofuran-2-one and

thiosemicarbazide derivatives in ethanol (Figure 9) which could also occur without the aid of a catalyst. *In-vitro* anti-bacterial property of the generated compounds was investigated against potent bacterial strains.<sup>(8)</sup>

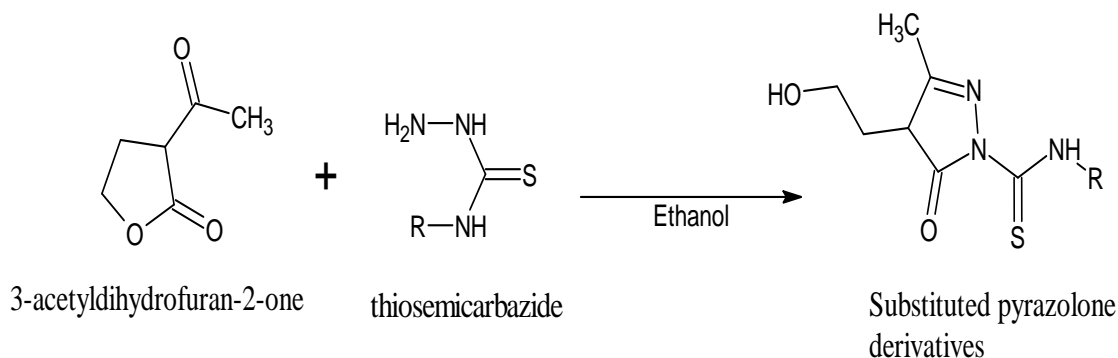
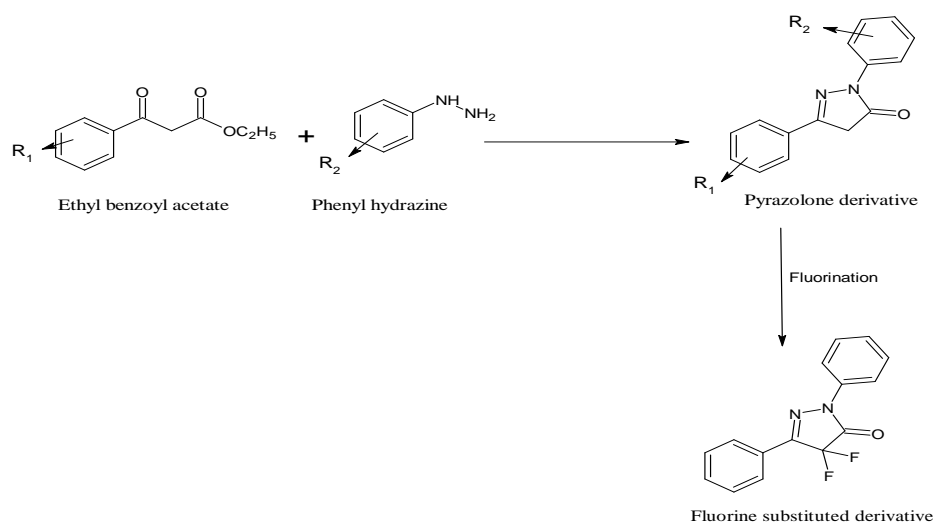


Figure 9: Scheme 9

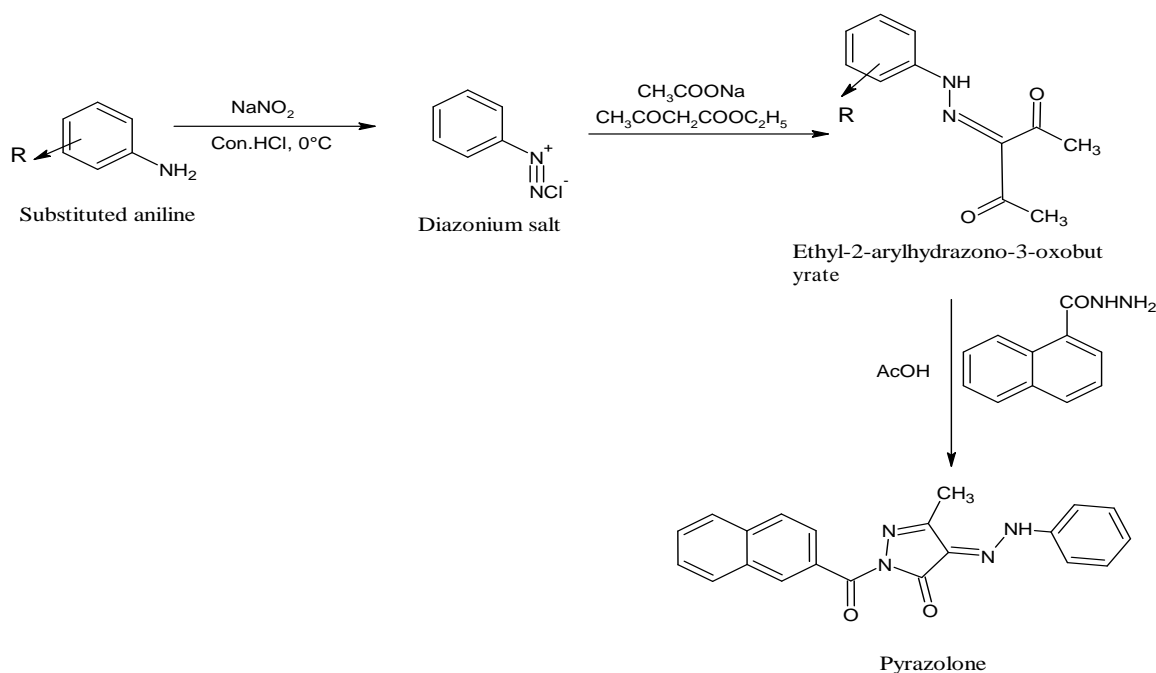
Joseph L. Howard *et al*, put forwarded a methodical procedure for sequentially executing two solventless reactions by multistep mechanochemistry, thereby magnifying the solvent savings. When compared to processes that use solvents, solventless mechanochemical synthesis represents a technique with better sustainability criteria. The consequence

of this was the creation of a two-step, one-jar technique for heterocycle synthesis and subsequent fluorination (Figure 10), which had been successfully used across a variety of substrates and produced 12 difluorinated pyrazolone's in moderate to good yields.<sup>(9)</sup>


**Figure 10: Scheme 10**

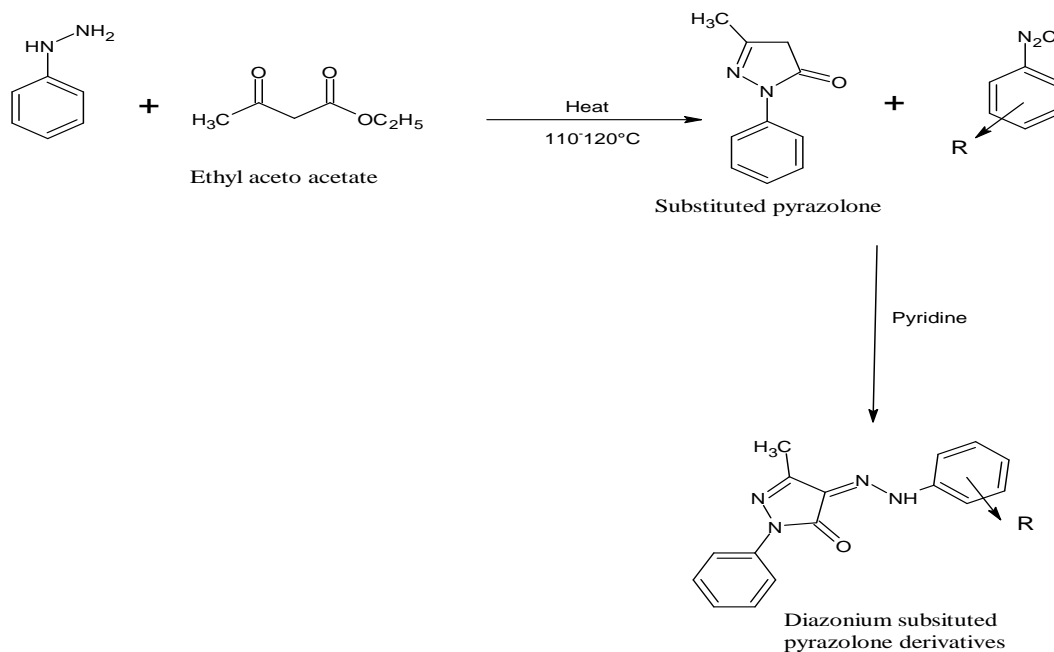
Vijay Kumar Merugumolu and Revanasiddappa Bistuvalli Chandrashekarappa *et al*, developed diazonium chlorides by diazotizing substituted anilines with  $\text{NaNO}_2$  and strong hydrochloric acid at  $0^\circ\text{C}$ . Ethyl-2-arylhydrazono-3-oxobutyrate were produced by combining substituted aryl diazonium

chlorides with ethyl acetoacetate in methanol, which reacted with naphthoic carbohydrazide to create pyrazolone derivative (Figure 11). The synthesized compound was examined for anti-depressant activity with the aid of tail suspension test and forced swimming test.<sup>(10)</sup>

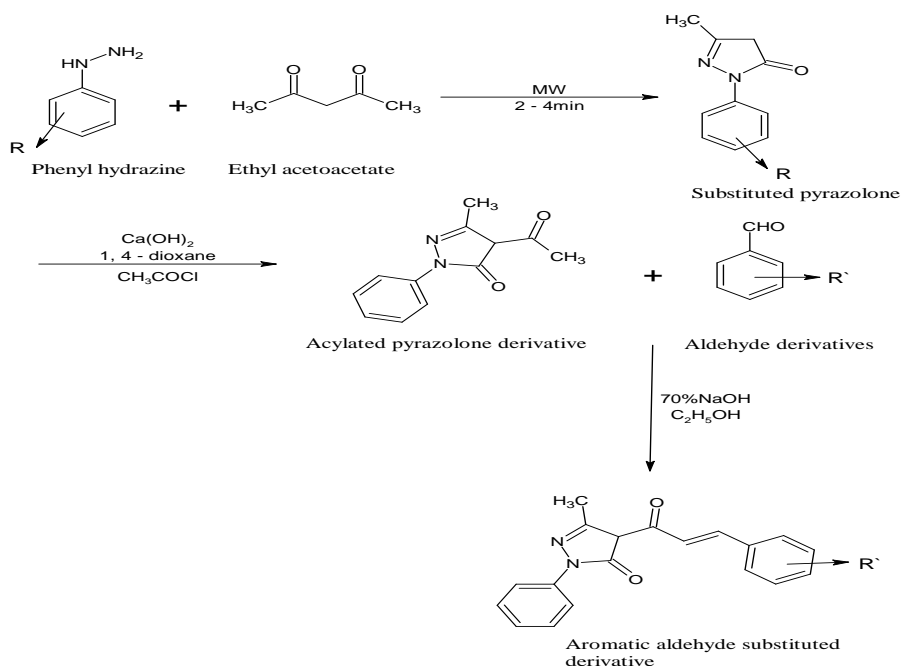

**Figure 11: Scheme 11**

Alam *et al*, reported an approach for successfully synthesising pyrazolone and the structures were verified using the findings from various spectral data (Figure 12). The proposed activities like anti-

inflammatory, analgesic, and antimicrobial properties were determined using *in-silico* studies.<sup>(11)</sup>


**Figure 12: Scheme 12**

R.V. Antre *et al*, created novel pyrazolone inflammatory, analgesic, and antipyretic compounds (Figure 13) that might be used as anti-medicines.<sup>(12)</sup>


**Figure 13: Scheme 13**

Amol Gadakh *et al*, described an effective synthesis of pyrazolone substituted with fluorine, and Knoevenagel condensation of the resulting compounds with various carbaldehydes with the aid of various conventional and non-conventional synthetic procedure (Figure 14).<sup>(13)</sup>

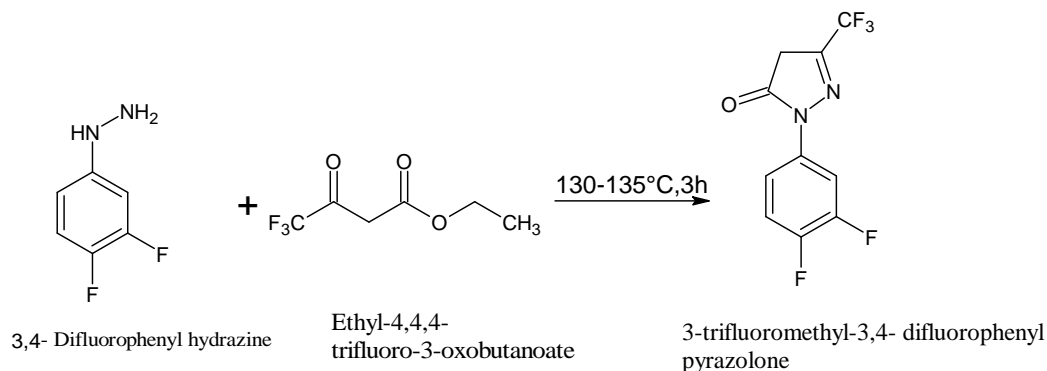


Figure 14: Scheme 14

Hari Pado Devnath and Md. Rabiul Islam *et al*, subjected ciprofloxacin to react with hydrazine derivatives, three pyrazolone compounds with pyrazole ring extensions were obtained (Figure 15).

IR and  $^1\text{H-NMR}$  spectral analyses were done to characterise all the products. Compared to ciprofloxacin, these compounds were found more cytotoxic to brine shrimp nauplii. <sup>(14)</sup>

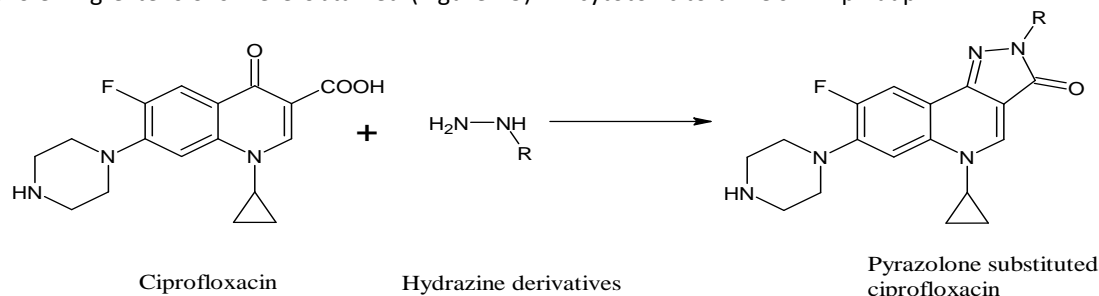


Figure 15: Scheme 15

### 1. Multicomponent approach for the synthesis of pyrazolone nucleus:

Vanita M *et al*, created pyrazolone derivatives (Figure 16) and tested for their anti-inflammatory activity. <sup>(15)</sup>

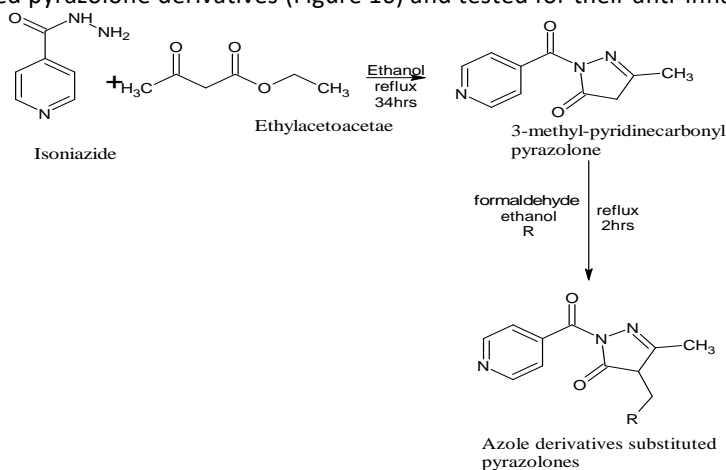


Figure 16: Scheme 16

Tu *et al*. synthesized arylidene pyrazolone using acetylene dicarboxylates, phenyl hydrazine and aryl aldehydes (Figure 17). <sup>(3)</sup>

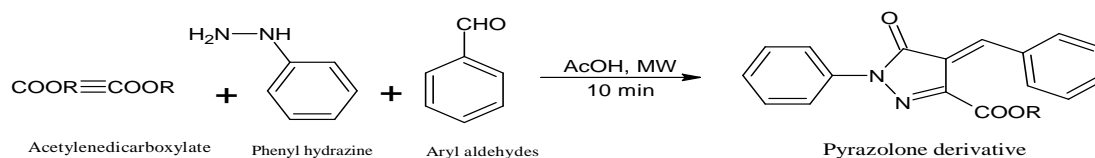


Figure 17: Scheme 17

Gupta *et al*, described the synthesis of a series of potent 4-chloro-3-methyl-N-substituted pyrazolone using the reaction between thiosemicarbazide and

ethyl-2-chloroacetate in DMF (Figure 18). The resultant compounds were examined for antifungal activity using disc diffusion techniques.<sup>(16)</sup>

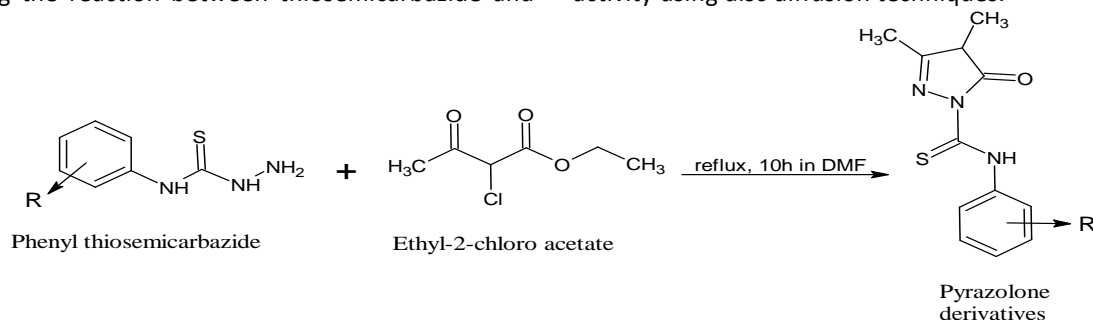


Figure 18: Scheme 18

#### APPLICATIONS OF SUBSTITUTED PYRAZOLONE DERIVATIVES:

##### ANTI-MICROBIAL

Parajuli *et al.*,<sup>(1)</sup> synthesized pyrazolone derivatives and were evaluated for anti-microbial and

cytotoxicity activity. The results of the studies showed that compound **1a**, **1b** (Figure 19) showed more anti-bacterial activity and **1b** showed prominent cytotoxic activity.

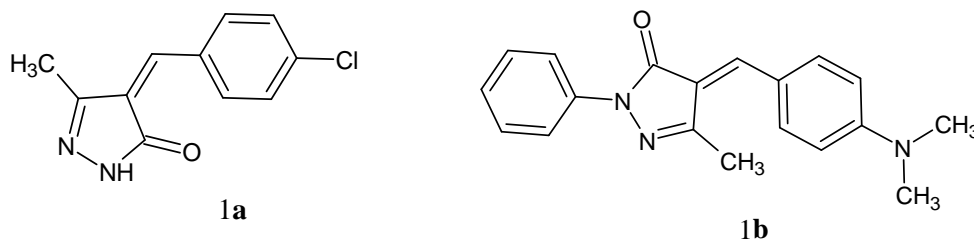


Figure 19: 1a and 1b

Azim F. *et. al*<sup>(4)</sup> conducted antibacterial assay for the synthesized pyrazolone derivatives using paper disc diffusion method. From the synthesized compounds,

derivatives **2a** and **2b** (Figure 20) were found to be more active against the tested organism.



Figure 20: 2a and 2b

Nedjar-Kolli B *et al.*<sup>(8)</sup> screened the synthesized pyrazolone derivatives for their *in-vitro* anti-bacterial

activity and compounds **3a** and **3b** (Figure 21, Table 1) were found to be active.

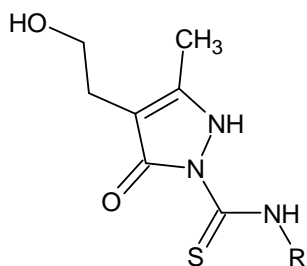


Figure 21: 3a and 3b

NO.	R
3a	-CH <sub>3</sub>
3b	-C <sub>2</sub> H <sub>5</sub>

Table 1



Alam *et al.*<sup>(11)</sup> investigated the anti-bacterial activity of the synthesized derivatives using dilution technique in which ciprofloxacin was taken as the standard. From the compounds under evaluation,

derivatives **4a**, **4b**, **4c** (Figure 22, Table 2) and **4d** showed prominent activity towards the tested microorganisms.

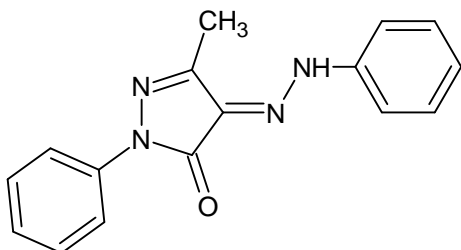


Figure 22: 4a, 4b, 4c and 4d

NO.	R
4a	4 -F
4b	2 -OCH <sub>3</sub>
4c	2 -Cl
4d	4 -Cl

Table 2

#### ANTI-FUNGAL

Gupta *et al.*<sup>(16)</sup> tested the synthesized compounds for anti-fungal activity using fluconazole as standard.

Among the evaluated compounds **5a**, **5b**, **5c** and **5d** (Figure 23, Table 3) were found to exhibit more activity.

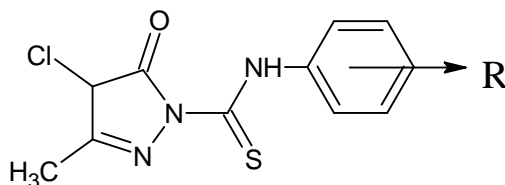


Figure 23: 5a, 5b, 5c, 5d and 5e

NO.	R
5a	3 -CH <sub>3</sub>
5b	4 -CH <sub>3</sub>
5c	3 -OCH <sub>3</sub>
5d	4 -OCH <sub>3</sub>

Table 3

#### CYTOTOXICITY

Aliye Gediz Erturk and Hilal Omerustaoglu *et al.*<sup>(6)</sup> evaluated the cytotoxic effect of the synthesized

pyrazolone derivatives and compound **6a** (Figure 24) turned to be more active.

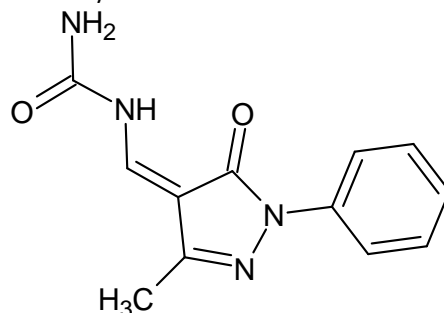


Figure 24: 6a

Hari Pado Devnath and Md. Rabiul Islam *et al.*<sup>(14)</sup> evaluated cytotoxic property by brine shrimp lethality bioassay using ciprofloxacin as standard.

From the evaluated compound, **7a** (Figure 25) showed prominent activity.

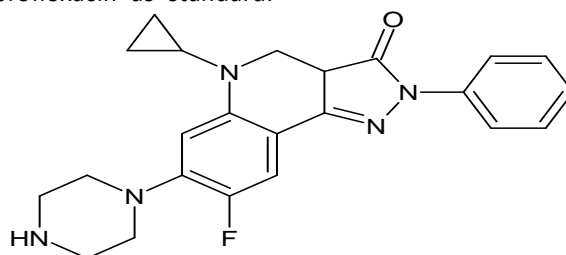


Figure 25: 7a

### ANTIOXIDANT

Azim F. *et al.*<sup>(4)</sup> synthesized various pyrazolone derivatives and screened for their antioxidant

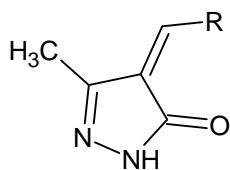


Figure 26: 7a and 7b

activity using DPPH free radical scavenging activity. Among the evaluated compounds, **7a** and **7b** (Figure 26, Table 4) were found to be more active.

NO.	R
7a	-C <sub>6</sub> H <sub>5</sub>
7b	-C <sub>6</sub> H <sub>5</sub> -CH <sub>2</sub> =CH <sub>2</sub>

Table 4

### ANTI-INFLAMMATORY

Julee P. Soni, Dhruvo Jyoti Sen *et al.*<sup>(6)</sup> prepared pyrazolone derivatives and observed their anti-inflammatory activity in comparison with celecoxib.

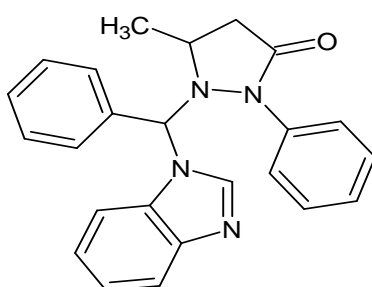


Figure 27: 8a

The anti-inflammatory activity was evaluated by carrageenan induced inflammation method and compound **8a** (Figure 27) was found to be more potent.

Alam *et al.*<sup>(11)</sup> synthesized derivatives and evaluated the anti-inflammatory activity and compounds **9a** and **9b** (Figure 29, Table 5) were found to be active.

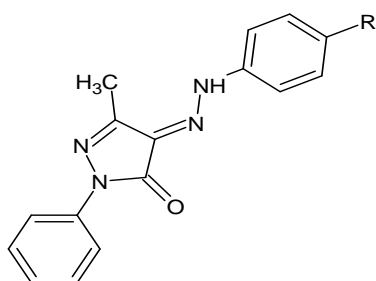


Figure 28: 9a and 9b

NO.	R
9a	4-F
9b	4-Cl

Table: 5

Vanita M *et al.*<sup>(11)</sup> synthesized and evaluated the anti-inflammatory activity of the pyrazolone derivatives. Compounds **10a** and **10b** (Figure 29, Table 6) showed better result when compared to standard aspirin.

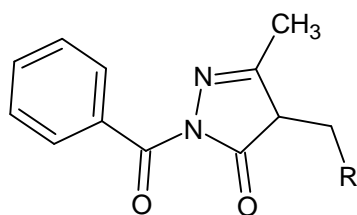


Figure 29: 10a and 10b

NO.	R
10a	NH <sub>2</sub>
10b	NH <sub>2</sub>

Table 6

R.V. Antre *et al*<sup>(12)</sup> developed various pyrazolone derivatives and explored their anti-inflammatory activity using carrageenan induced paw edema with indomethacin as standard. From the evaluated compounds, **11a** and **11b** (Figure 30, Table 7) turned to be more active.

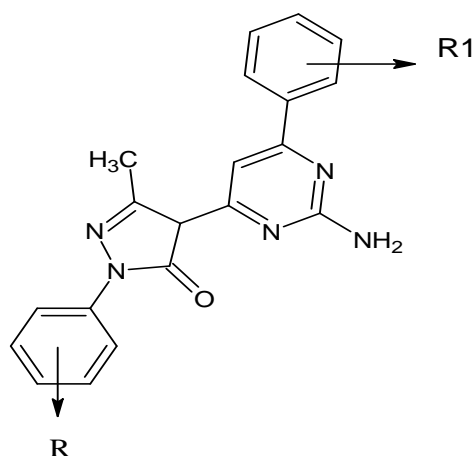


Figure 30: 11a and 11b

NO.	R	R <sub>1</sub>
11a	H	4-OH, 3-OCH <sub>3</sub>
11b	H	4-OCH <sub>3</sub>

Table 7

#### ANTI-DEPRESSANT

Vijay Kumar Merugumolu and Revanasiddappa Bistuvalli Chandrashekarappa *et al*<sup>(10)</sup> reported the synthesis of pyrazolone derivatives and examined their anti-depressant activity with the aid of forced

swim test and tail suspension test giving imipramine as standard drug. Among the investigated compounds, **12a** and **12b** (Figure 31, Table 8) showed more activity.

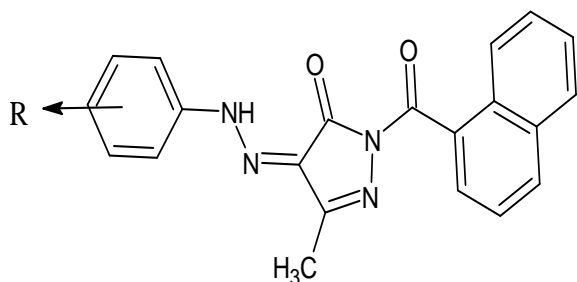


Figure 31: 12a and 12b

NO.	R
12f	3,4 -(CH <sub>3</sub> ) <sub>2</sub>
12g	3,4 -(Cl) <sub>2</sub>

Table 8

#### ANALGESIC AND ANTI-PYRETIC

R.V. Antre *et al*<sup>(12)</sup> produced various derivatives and explained the analgesic activity of the compounds using Eddy's hot plate method as diclofenac sodium as standard. Derivatives **13a** and **13b** (Figure 32,

Table 9) showed significant anti-pyretic and analgesic activity.

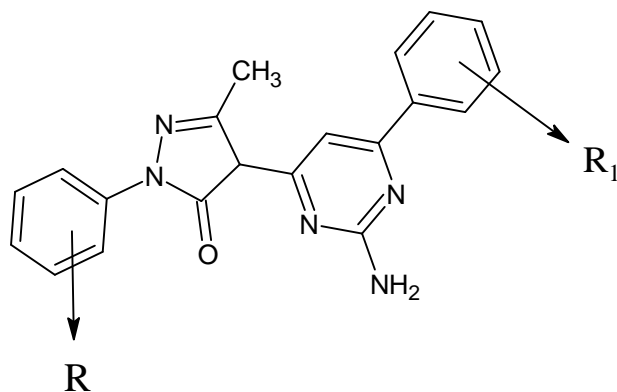


Figure 32: 13a and 13b

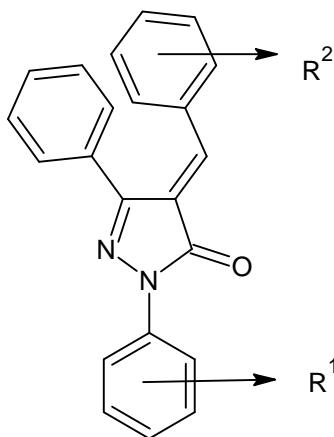
NO	R	R <sub>1</sub>
13a	H	-4 OH 3 -OCH <sub>3</sub>
13b	H	-4 -OCH <sub>3</sub>

Table 9

### ANTI-VIRAL

Ramajayam *et al.*<sup>(18)</sup> From the preliminary inquiry, it was found that molecules containing a substituent R<sub>2</sub> as carboxyl group and R<sub>1</sub> substitution with halogens, cyano, and nitro groups and showed significant

inhibition of SARS-CoV 3CLpro. Among the developed derivatives, compound **14a** (Figure 33) substituted with cyano group at 4<sup>th</sup> position showed maximum inhibitory activity.



R<sup>1</sup> = 4-CN      R<sup>2</sup> = 4-COOH

### CONCLUSION:

Pyrazolones are one of the most important and explored compounds among diverse fused heterocycles having multiple biological activities. Being a versatile molecule with immense biological significance, pyrazolone derivatives are being developed for several pathological screening including antimicrobial, CNS effect, anti-inflammatory, antioxidant, antipyretic activities since long. Different synthetic methods and pharmacological activities were disclosed in this review. These data will be helpful to explore novel pyrazolone analogues for the challenging pathophysiological conditions.

### DISCUSSION:

More than any other heterocyclic nucleus, pyrazolone derivatives play a significant role in the pharmaceutical and other agricultural industries. Because the scaffold and naturally occurring nucleotides are fundamentally identical, they can easily form complexes with a variety of target locations and receptors. (3) As a result, compounds made from the pyrazolone ring system are effective against a wide range of human diseases, such as cancer, hypertension, diabetes, infections from bacteria or viruses, inflammation, gastroenteritis, neurological disorders, and more. We have discussed numerous synthetic methods for creating pyrazolone derivatives in this paper. These kinds of synthetic procedures are carried out employing a number of catalysts, environmentally friendly solvents, under separate headings including synthesis of basic nucleus and multicomponent strategies for the synthesis. Anti-microbial activity(1) of the derivatives

is produced when the nucleus is substituted with benzyl group(1), dimethyl amino derivatives(4), substituted hydroxy derivatives(8) and phenyl hydrazine derivatives.(11). Antioxidant(4), anti-fungal(16) and cytotoxic activity(6) are produced when the nucleus is substituted with sulphonyl(4), hydrazines(16), piperazine(16), alkyl group derivatives(6). When the scaffold is substituted with phenyl hydrazine(11), benzoyl group, piperidine<sup>(11)</sup> and different aldehyde derivatives<sup>(18)</sup> result in anti-inflammatory<sup>(11)</sup>, anti-depressant<sup>(10)</sup>, and anti-viral activities<sup>(18)</sup>. In this article, different synthetic approaches for obtaining pyrazolone nucleus and a variety of biological activities of were discussed.

### AUTHORS CONTRIBUTION:

Conceptualizing, Dr. Presannakumaran P N; resources, Justin Jacob Thomas, Rincy Meriyam Varghese, Joshny Varghese; writing- original draft preparation, Justin Jacob Thomas; writing – review and editing, Joshny Varghese, Rincy Meriyam Varghese; supervision- Dr.Santhosh.M. Mathew and Dr. Presannakumaran P N; All authors have read and agreed to the published version of the manuscript.

### CONFLICTS OF INTEREST:

Conflict of interest declared none.

### REFERENCES

1. Parajuli R, Banerjee J, Khanal H. Synthesis of some pyrazolone derivatives and evaluation of its antibacterial and cytotoxic activity. *Oriental Journal of Chemistry*. 2015;31(4):2099–106.
2. Pal S, Mareddy J, Suneetha Devi N. High Speed Synthesis of Pyrazolones using Microwave-Assisted

- Neat Reaction Technology. Vol. 19, J. Braz. Chem. Soc. 2008.
3. Dhawan S, Narang R, Khatik GL, Chopra HK, Nayak SK. Strategies for chemical synthesis of pyrazolone derivatives and their bio-significance. Available online [www.jocpr.com](http://www.jocpr.com) Journal of Chemical and Pharmaceutical Research [Internet]. 2016;8(5):969–81. Available from: [www.jocpr.com](http://www.jocpr.com)
  4. Azim F, Nadeem H, Imran M, Naz S, Ihsan-Ul-Haq, Muhammad N, et al. Synthesis, characterization and biological evaluation of novel 3-methyl-5-pyrazolone derivatives. Journal of Medicinal and Chemical Sciences. 2021 Dec 1;4(1):42–52.
  5. Min ZL, Hu XM. Tungstophosphoric acid-catalyzed synthesis of pyrazolones in water. Asian Journal of Chemistry. 2013;25(13):7290–2.
  6. Erturk AG, Omerustaoglu H. Synthesis and cytotoxic evaluation of some substituted 5-pyrazolones and their urea derivatives. Molecules. 2020 Feb 18;25(4).
  7. Mojtahedi MM, Jalali MR, Abaee MS, Bolourtchian M. MICROWAVE-ASSISTED SYNTHESIS OF SUBSTITUTED PYRAZOLONES UNDER SOLVENT-FREE CONDITIONS.
  8. Boumediene H. INTERNATIONAL JOURNAL OF PHARMACEUTICAL, CHEMICAL AND BIOLOGICAL SCIENCES A CATALYTIC METHOD FOR THE SYNTHESIS OF PYRAZOLONE DERIVATIVES USING HETEROPOLYACIDS AND STUDY OF THE ANTI-BACTERIAL ACTIVITY. IJPCBS [Internet]. 2013(3):732–7. Available from: [www.ijpcbs.com](http://www.ijpcbs.com)
  9. Howard JL, Nicholson W, Sagatov Y, Browne DL. One-pot multistep mechanochemical synthesis of fluorinated pyrazolones. Beilstein Journal of Organic Chemistry. 2017 Sep 14; 13:1950–6.
  10. Merugumolu VK, Chandrashekarappa RB. Synthesis and anti-depressant evaluation of novel pyrazolone derivatives. Bangladesh J Pharmacol. 2016;11(2):558–63.
  11. Alam MA, Alam MM, Zaman MS, Khan A, Akhter M. 65 SYNTHESIS, IN-SILICO STUDIES, OF NEW SUBSTITUTED PYRAZOLONE BASED HYDRAZONE DERIVATIVES AND THEIR BIOLOGICAL ACTIVITIES. Vol. 2, International Journal of Pharmaceutical Chemistry and Analysis.
  12. Antre R v., Cendilkumar A, Goli D, Andhale GS, Oswal RJ. Microwave assisted synthesis of novel pyrazolone derivatives attached to a pyrimidine moiety and evaluation of their anti-inflammatory, analgesic and antipyretic activities. Saudi Pharmaceutical Journal. 2011 Oct;19(4):233–43.
  13. Pandit C, Rindhe SS, Karale B. Synthesis of Novel Multifluorinated Pyrazolone-5-one Derivatives via Conventional and Non-conventional Methods Amol Gadakh (Corresponding author). Int J Chem [Internet]. 2010;2(2). Available from: [www.ccsenet.org/ijc](http://www.ccsenet.org/ijc)
  14. Devnath HP, Islam R. Synthesis of some pyrazolone derivatives from ciprofloxacin and study of their cytotoxicity. Bangladesh J Pharmacol. 2010;5(1):30–4.
  15. Marvaniya V, Marvaniya H, Tiwari D, Patel S, Kaur R. Synthesis and anti-inflammatory activity of some pyrazolone derivatives [Internet]. Vol. 5, Int. J. of Allied Med. Sci. and Clin. Research. Available from: [www.ijamscr.com](http://www.ijamscr.com)
  16. Gupta P, Gupta JK. Synthesis and In-vitro Antifungal Evaluation of 5- Pyrazolones. Open Chemistry Journal. 2016 May 10;3(1):17–24.
  17. Soni JP, Sen J, Modh KM. Structure activity relationship studies of synthesised pyrazolone derivatives of imidazole, benzimidazole and benzotriazole moiety for anti-inflammatory activity. J Appl Pharm Sci. 2011(04):115–20.
  18. Ramajayam R, Tan KP, Liu HG, Liang PH. Synthesis and evaluation of pyrazolone compounds as SARS-coronavirus 3C-like protease inhibitors. Bioorg Med Chem. 2010 Nov 15;18(22):7849–54.