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ANTIOXIDANT POTENTIAL OF PYRAZOLINES SYNTHESIZED VIA GREEN CHEMISTRY METHODS

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Abstract

In the chemical and pharmaceutical sectors, pyrazolines are the most significant class of chemicals and are thought to be the most promising molecules for the development of novel pharmaceuticals. In terms of response time and energy consumption, green technologies like the microwave and grinding techniques have been found to be superior to the conventional way. The pyrazoline derivatives, 2a-i and 3a-i, were produced by microwave irradiation as well as conventional heating. 1H NMR, 13C NMR, IR, and mass spectrum studies were used to describe the produced compounds. The antioxidant capacity of pyrazoline derivatives made using green chemistry techniques is examined in this work. For synthesis, standard heating, microwave irradiation, and grinding methods were applied using synthetic-grade starting materials obtained from Sigma Aldrich. The produced compounds were characterized using spectroscopic techniques like 1H, 13C, and FTIR. Using the DPPH radical scavenging method, the compounds' antioxidant activity was evaluated, and the efficacy was estimated by calculating the IC50 values.

Keywords: *Pyrazoline derivatives, green chemistry methods, Conventional heating, Microwave irradiation, Grinding techniques*

1. INTRODUCTION

Nitrogen fills in as the hetero component in the huge five-part heterocyclic atom known as pyrazoline. Various mixtures of pyrazoline show huge pharmacological properties. Various natural exercises, including antitumor1 and calming properties,2 MAO-B inhibition3, and antioxidant4 action, have been connected to pyrazoline and its derivatives. Applications for pyrazoline derivatives incorporate dyestuffs, agrochemicals, and scientific reagents.5. Similarly, mixtures of subbed furan/thiophene additionally show vital natural action, including antimicrobial, anticancer, antioxidant, and HIV-1 combination hindrances. 6-10. In light of these discoveries, and as a feature of a persistent undertaking to find physiologically dynamic heterocycles, an original series of N-acetyl pyrazolines with an arylfuran/arylthiophene moiety have been synthesized and introduced here. The antioxidant limit of these synthetic substances was surveyed. Looking at two or three the examined mixtures to the business standard, butylated hydroxytoluene (BHT), significant antioxidant movement was noticed.

The investigation of heterocyclic chemistry is significant to the study of restorative chemistry. They can likewise be fundamental or acidic. The heterocyclic moiety is available in a larger part

of pharmacologically bioactive atoms as a result of their critical qualities. In medicinal chemistry, azoheterocycles are important and frequently used. Some examples of these are pyrimidines (like zidovudine), pyrazoles (like febuxostat), quinolines (like chloroquine), indoles (like fluoxetine), diazepines (like lorazepam), and pyridines (like sulfasalazine).

Manageable chemistry, or "green chemistry," utilizes synthetic cycles and synthetics with a lower natural effect. Decreased byproducts, non-harmful parts, and expanded effectiveness might be remembered for the utilization and creation of these substances. In green chemistry, the dissolvable decides most of the cycle's natural presentation, alongside its impacts on cost, wellbeing, and wellbeing. Consequently, the dissolvable is an essential part that should be considered in a green convention. However most natural atoms are not adequately dissolvable in water, it is a particularly engaging dissolvable choice. Involving ethanol as the response medium is a completely OK substitute since it is an economical, biorenewable ware with less ecological gamble and insignificant damage to people. Because of worries over dissolvable free conditions and heterocyclic chemistry, conventions using clean techniques have arisen as an option for pyrazole planning. Zhang and partners have concocted an eco-accommodating and powerful method for the effortless combination of pyrazoles under mechanochemical ballmilling conditions. Furthermore, there are various advantages to utilizing sonochemistry or microwaves in natural combination, including more significant returns, less difficult stir up, cleaner responses, and very speedy response times. The most recent improvements in the combination of pyrazoles with antioxidant attributes are introduced here as a feature of the creators' continuous exploration on heterocyclic mixtures and green chemistry.

Various natural and pharmacological impacts, including antibacterial, antihepatotoxic, mitigating, antioxidant, and anticancer properties, are shown by antioxidant substances. A few methodologies in view of different pathways can be utilized to assess a substance's antioxidant movement.

1.1.Pyrazolines and Antioxidant Activity

Because of its many pharmacological characteristics, pyrazolines, a type of heterocyclic compounds with a five-membered ring including two carbon atoms and three nitrogen atoms, have attracted a lot of interest in medicinal chemistry. These substances have a wide range of biological actions, such as antioxidant, antibacterial, anticancer, and anti-inflammatory properties. Given the critical role that antioxidants play in reducing oxidative stress-related disorders and the aging process, their antioxidant potential has emerged as one area of particular attention among these.

Pyrazolines have antioxidant properties because they can scavenge reactive oxygen species and prevent oxidative damage to biomolecules like proteins, DNA, and lipids. The pyrazoline structure's electron-donating groups, which have the ability to efficiently neutralize free radicals and stop the chain processes linked to oxidative stress, are thought to be responsible for this function. The pyrazoline moiety functions as a hydrogen or electron donor, respectively, to stabilize reactive intermediates and stop the spread of radicals.

The kind and location of substituents on the pyrazoline ring, as well as the existence of functional groups that alter electron density and resonance stabilization, all have an impact on the antioxidant activity of pyrazolines. Electron-rich aromatic or heteroaromatic substituents are frequently added to structures in an effort to increase their antioxidant efficacy. These additions can increase the molecule's ability to donate electrons and increase its effectiveness in scavenging free radicals. Furthermore, pyrazoline derivatives' stereochemistry may influence their antioxidant activity; some configurations may be more effective than others because of improved molecular interactions and conformational stability.

Pyrazolines are being investigated as possible antioxidant agents because they are important because they guard against diseases caused by oxidative damage and maintain cellular homeostasis. Researchers hope to create new pyrazoline derivatives with enhanced efficacy, selectivity, and safety profiles for use in treating disorders linked to oxidative stress by clarifying the structure-activity relationships governing their antioxidant properties and utilizing green chemistry methodologies for their synthesis.

1.2.Principles of Green Chemistry in Synthesis

Sustainable chemistry, or "green chemistry," is the application of a set of guidelines designed to minimize the negative effects of chemical reactions on the environment while enhancing their effectiveness and safety. Applying green chemistry concepts to the synthesis of pyrazolines entails using creative approaches and techniques that minimize or completely do away with the use of dangerous chemicals, solvents, and byproducts, therefore encouraging sustainability all the way through the synthetic process.

The use of environmentally benign, renewable, and non-toxic reagents and solvents is a cornerstone of green chemistry. During the process of synthesizing pyrazolines, it can be necessary to substitute conventional organic solvents like dichloromethane or chloroform with more environmentally friendly options like water or solvents produced from renewable resources. Furthermore, whenever feasible, green chemistry promotes the use of catalytic processes rather than stoichiometric reactions since they can effectively aid in bond formation, encourage selective transformations, and reduce waste production.

Waste minimization and atom economy, which entail creating synthetic pathways that optimize the incorporation of starting materials into the finished product and reduce the formation of undesired byproducts, are important components of green chemistry. This can be done in the synthesis of pyrazolines by using multicomponent methods or cascade reactions that facilitate the simultaneous production of many bonds in a single operation, simplifying the synthetic process and lessening its overall environmental impact.

In addition, green chemistry places a strong emphasis on process intensification and energy efficiency to lower the energy usage and environmental effect of chemical reactions. This could include improving reaction conditions to reduce energy input and maximize resource usage, as well as using alternative energy sources like microwave or ultrasonic irradiation to speed up reaction rates and increase product yields. Furthermore, by lowering solvent volumes, reaction durations, and waste generation, process intensification strategies including solid-phase synthesis

and continuous flow chemistry might improve the sustainability of pyrazoline synthesis even more.

1.3.Research Objectives

- To use synthetic-grade starting materials obtained from Sigma Aldrich to synthesis pyrazoline derivatives by green chemistry procedures, such as conventional heating, microwave irradiation, and grinding processes.
- to evaluate the produced compounds' purity and structure elucidation by characterizing them using spectroscopic techniques including FTIR, Mass, and 1H, 13C NMR.
- To assess the synthesized pyrazoline derivatives' antioxidant capacity using the DPPH radical scavenging method, figuring out IC50 values to measure their effectiveness as antioxidants and possible uses in therapeutic treatments.

2. LITERATURE REVIEW

Achutha et al. (2020) developed a sustainable process for the synthesis of pyrazoline carbothioamides and then assessed the compounds' effectiveness as antioxidants and antimicrobials. The study demonstrated the compounds' aptitude to fight microbiological infections and their capacity to scavenge free radicals, indicating possible uses in medications and functional foods.

Dhonnar et al. (2023) produced 1,3,5-trisubstituted 2-pyrazolines using a PEG-mediated synthesis method, and then looked into their possible antioxidant, antibacterial, and antifungal effects. They conducted a thorough investigation to see how well these chemicals worked against bacterial and fungal strains as well as how well they might reduce oxidative stress using antioxidant assays. This study offers insightful information about the complex pharmacological properties of 1,3,5-trisubstituted 2-pyrazolines, indicating a range of potential therapeutic uses.

Muchtaridi, M. (2021) This article will go over the fact that it is so significant to enhance the blend response conditions by representing various union boundaries to deliver the ideal natural item results utilizing customary techniques. Utilizing PubChem, Chemspider Google Researcher, Exploration Door, Science Direct, and Elsevier, a writing search was done, and the union of pyrazolines was picked in view of the physicochemical profile, response system, and combination method.

Song, M. (2022) In this work, pyrazoline and eighteen pyrazole derivatives were consolidated, and the mixtures' mitigating and antibacterial properties were surveyed. Utilizing 1H NMR, 13C NMR, and HRMS, the objective mixtures were all synthesized with no issues and afterward described. Their mitigating impact was surveyed utilizing two models: an in vitro model delivered by lipopolysaccharide (LPS) to create cancer rot factor (TNF)- α, and an in vivo model brought about by xylene to cause ear edema. Utilizing the sequential weakening methodology, antimicrobial movement against various Gram-positive and Gram-negative microscopic organisms was evaluated. Most of the substances fundamentally smothered TNF-α articulation at a centralization of 20 μg/mL, as per pharmacological examinations. Intensifies 9b had a more elevated level of hindrance (66.4%) than the positive control prescription, dexamethasone (DXMS), when it came to the LPS-incited creation of TNF-α. Additionally, compounds 4b, 5a,

5b, 6b, and 9b showed inhibitory activity that was like that of DXMS. Compound 4a smothered edema in the xylene-actuated ear-edema model by 48.71%, which was more than DXMS's (47.18%) viability in such manner.

3. RESEARCH METHODLOGY

The review utilized a synthetic methodology to investigate the antioxidant limit of derivatives of pyrazoline created utilizing green chemistry techniques. The review utilized starting materials got from Sigma Aldrich and a combination of conventional heating, microwave irradiation, and grinding techniques to integrate pyrazoline derivatives. Actual constants and slight layer chromatography (attention) were used to screen the responses, and spectroscopic techniques like FTIR, Mass, and 1H, 13C NMR were utilized for characterization.

3.1.Data Collection:

Starting fixings and solvents were synthetic grade materials that were bought from Sigma Aldrich for every response. Each phase of the blend included the utilization of unmistakable dissolvable frameworks and response periods, which were all carried out all through the controlled responses. For each union method, data was recorded about the temperature, span, and groupings of reagents during the response.

3.2.Antioxidant Potential Analysis:

Utilizing the DPPH radical scavenging method, the antioxidant potential of the synthesized pyrazoline derivatives was surveyed. Methanol was utilized to create arrangements of the synthesized compounds at a centralization of 100 μg/mL. Simultaneously, a DPPH arrangement was made in methanol. Following 30 minutes of room temperature brooding, the absorbance of the response combination was estimated at 517 nm utilizing a Shimadzu UV spectrometer.

3.3.Materials:

Each response utilizes synthetic-grade starting fixings and solvents that are acquired from Sigma Aldrich. Slender layer chromatography (attention) and actual consistent were utilized to portray the virtue of the relative multitude of substances and fabricated items. With the utilization of a pre-covered tender loving care plate (Silica gel 60-120), each reaction was seen. For Step-1 mixtures, the dissolvable framework utilized was chloroform:methanol (8:2), and for Step-2 mixtures, chloroform:methanol (9:1). The got tender loving care plates were inspected in an iodine chamber and under a long UV light to search for spots. Utilizing a microwave from Labline Logical Instruments, all responses were led under microwave radiation. The designs of the delivered compounds were explained and affirmed by spectroscopic methods like FTIR, Mass, and 1H, 13C NMR.

3.4.Methods:

3.4.1. Traditional heating technique (1a–i): First step:

In a cone-shaped flagon with an appealing stirrer, mix 2.2 grams sodium hydroxide, 20 milliliters water, and 12.5 milliliters ethanol. Crushed ice around the cup. 43 million mol A nice stirrer was used to add 4.4 ml of acetophenone to the fluid above and mix it. Add 4.6 ml of subbed benzaldehyde (0.43mol) dropwise and maintain the blend temperature at 25 ◦C. The reaction mix was refrigerated temporarily. To promote the chalcone, the reaction mixture was diluted with 50

mL cold water and fermented with 10% aq. HCl. After separating and rinsing the resulting item in cool water until litmus-nonpartisan, 10 ml of cold amended soul was added. The object was recrystallized in methanol.

3.4.2. Method 1a-i for microwave irradiation: Step 1:

Utilizing tender loving care to screen the radiation, the blend was presented to 180 W for three minutes in a microwave broiler. From that point forward, 3N HCl (5 ml) was added to kill the combination. Following filtration, cold water was utilized to wash the item.

Step 2: The general process for creating derivatives of pyrazolines (2a-i, 3a-i) is as follows:

supplanted 2a-I/phenyl hydrazine hydrate with chalcone 1a-I (10 mmol) and INH (10 mmol, 1.37g). In the wake of dissolving in 10 milliliters of icy acidic corrosive, 3a-I refluxed for a day and a half. Attention followed the response's turn of events. In the wake of adding the mix to super cold water, sodium bicarbonate was utilized to kill it. In the event that important, a saline solution treatment was utilized to dispose of the tacky nature. By joining compound (1a-I) with isonicotinic corrosive hydrazide arrangement in frosty acidic corrosive.

Likewise, compounds (1a-I) containing 2.5 mmol of phenyl hydrazine were added to an open pyrex vessel, and the response was then presented to microwave radiation for the appropriate measure of time (3-5 minutes) until attention checked that the response had finished. Following consummation, the response combination was permitted to cool to room temperature prior to being added to 50 milliliters of cold water. In the wake of being sifted, dried, and recrystallized from methanol, the strong was gotten.

3.4.3. The general procedure for synthesizing pyrazoline derivatives

The indistinguishable cycle framed in microwave union. Stage 2: Mixtures 2a-I were made by adding Compound 1a-I, then, at that point, consolidating it with frigid acidic corrosive, isoniconic corrosive hydrazide hydrate (0.02mol), and processing for a couple of moments. Attention was utilized to screen the response's decision. The strong, which had a light greenish-yellow tone, was isolated.

Moreover, comp. 1a-I was joined with phenyl hydrazine hydrate to make comp. 3a-I. The 3a-I union was entirely pummeled for a few minutes at room temperature in an open mortar utilizing a pestle. This response combination was blended in with acidic corrosive (0.001 mmol), and grinding was finished for a couple of moments while tender loving care followed the response's fruition. The strong, which had a pale greenish-yellow tone, isolated. The subsequent strong was isolated from the ethanol by Buchner filtration and recrystallization in the wake of being weakened with cold water. This delivered the pyrazoline subsidiary.

4. DATA ANALYSIS

4.1.Antioxidant Activity:

In methanol, the DPPH free radical displays a constant violet shading. When joined with decreasing or antioxidant synthetic compounds, it changes tone to yellow or dismal. These radicals can change into stable diamagnetic particles (yellow) by tolerating the odd electron or hydrogen from the antioxidant. The arrangement of synthesized intensifies has been made by dissolving in 100 µg/ml of methanol to identify the antioxidant action. In equal, a DPPH

arrangement was made in an alternate compartment, and the presence of a stable free radical (violet tone) made the arrangement show its most extreme absorbance at 517 nm. Subsequent to adding 4 ml of each test synthetic to 4 ml of DPPH arrangement, the combination was let to remain at room temperature for 30 minutes. A Shimadzu UV spectrometer was utilized to distinguish absorbance at 517 nm. Furthermore, standard and clear absorbances were adjusted. Ascorbic corrosive derivatives' antioxidant movement was determined by changing the absorbance in the recipe.

$$Percentage\ inhibition = \frac{Absorbance\ of\ control - Absorbance\ of\ Sample}{Absorbance\ of\ Control}$$

DPPH method: The DPPH examines incredible reproducibility and short investigation time make it an extraordinary method for surveying the antioxidant movement of as of late synthesized compounds. At the point when the antioxidant particle gives the DPPH free radical an electron, the absorbance decreases. Most of the substances displayed solid antioxidant capacity. as opposed to ascorbic corrosive, the reference. Table 1 shows the synthetic substances' enemy of oxidant action.

Table 1: Pyrazoline derivatives' antioxidant activity (IC50 in µg/mL)

Sr.no.	Comp. code	% Inhibition				
		6 µg/ml	11 µg/ml	16 µg/ml	21 µg/ml	IC50 µg/ml
1	3p	20.48	35.52	80.12	85.96	10.43
2	3q	35.93	42.71	69.93	84.15	10.86
3	3r	19.65	38.88	63.10	76.05	12.64
4	3s	28.55	39.73	60.12	87.46	11.64
5	3t	24.53	44.89	71.63	77.96	11.69
6	3u	30.76	43.51	78.99	88.62	10.49
7	3v	28.96	39.75	73.39	89.23	10.77
Std.	Ascorbic acid	39.00	55.86	72.41	92.94	9.45

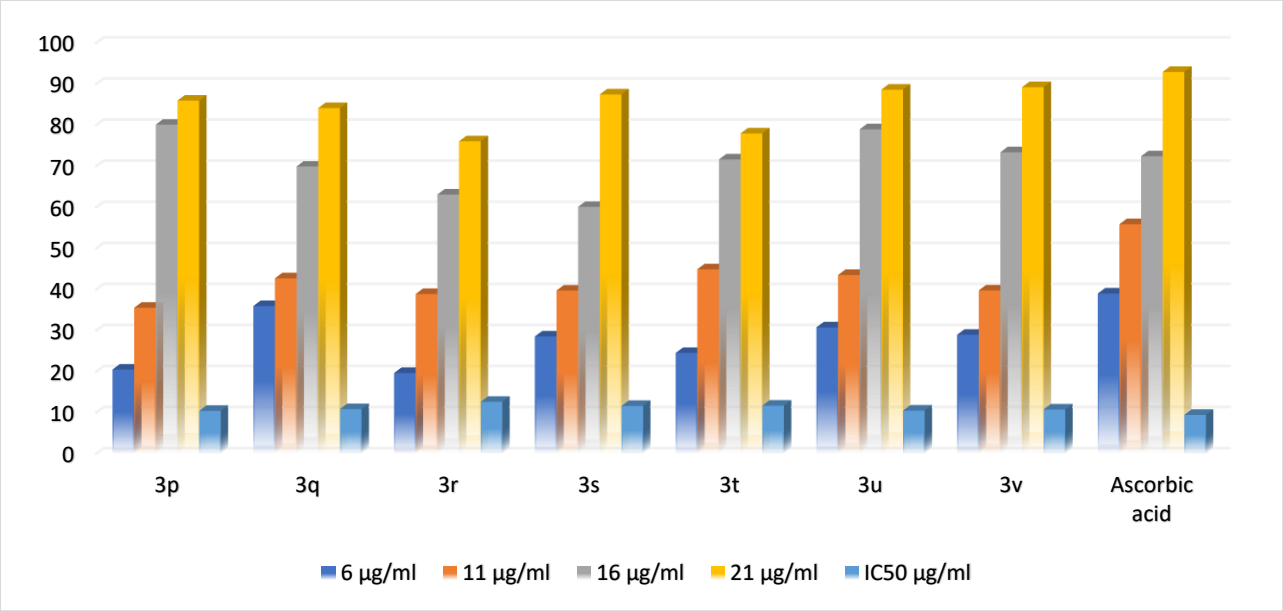

Figure 1: Pyrazoline derivatives' antioxidant activity (IC50 in µg/mL)

Table 1 displays the pyrazoline derivatives' antioxidant activity as well as their IC50 values in µg/mL at different concentrations (6 µg/mL, 11 µg/mL, 16 µg/mL, and 21 µg/mL) based on their inhibition percentage. The concentration-dependent inhibition percentages of pyrazoline derivatives 3p, 3q, 3r, 3s, 3t, 3u, and 3v varied, with IC50 values ranging from 10.43 µg/mL to 12.64 µg/mL. At every measured concentration, compound 3q exhibited the highest percentage of inhibition among the rest. With an IC50 value of 9.45 µg/mL, standard ascorbic acid had larger inhibition percentages at all concentrations when compared to the majority of pyrazoline derivatives, demonstrating its superior antioxidant activity.

4.2.**Antimicrobial activity:**

Using a changed agar scattering test strategy, all integrated mixtures were considered for their antibacterial properties in contrast to Escherichia coli and Staphylococcus aureus. Streptomycin was utilized as the positive control. The temperature and term of hatching for antibacterial movement were 37°C for an entire day. The zone of hindrance is utilized to communicate antimicrobial movement results. Table 3 shows the result of the synthetic mixtures' movement. Compounds are sorted as profoundly dynamic, decently dynamic, less dynamic, and least dynamic in view of the ZOI esteem in millimeters. Compound 3b showed the greatest action against E. Coli and Staphylococcus aureus, individually, as indicated by the investigation of antibacterial screening. Intensifies 3a and 3e had great generally speaking viability against microorganisms that were Gram negative and Gram positive. Table 3 showed the synthetics that were synthesized and their antimicrobial movement.

Table 2: The antibacterial properties of derivatives of pyrazolines

Microorganisms	Zone of inhibition (mm) of compunds	
Compunds Code	Gram (-) E. Coli (mm)	Gram (+) S.aureus (mm)
2p	12	11

2q	17	14
2r	14.6	8
2s	10.6	10.6
2t	16.6	11.8
Streptomycin	20	23

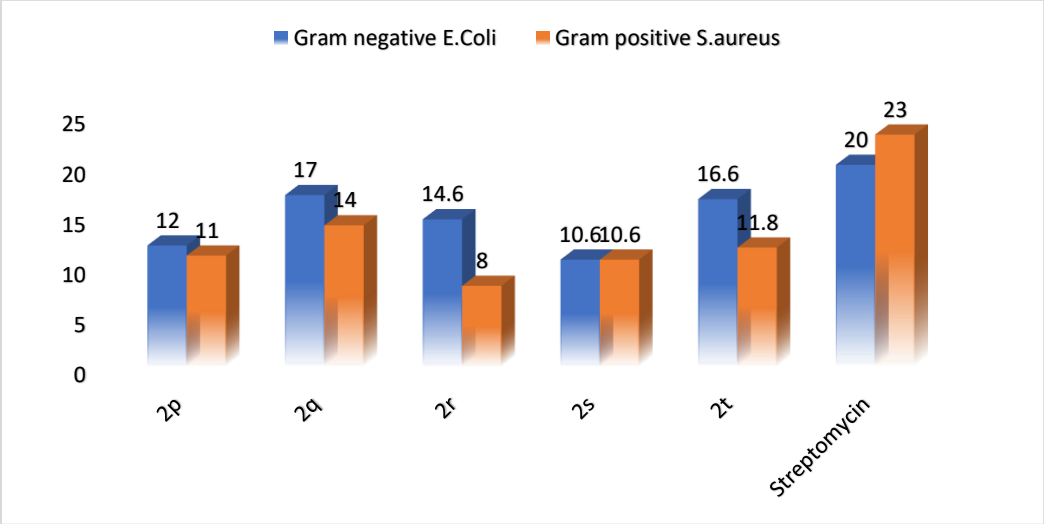

Figure 2: The antibacterial properties of derivatives of pyrazolines

Table 2 illustrates the millimetre-scale inhibitory zone of different pyrazoline derivatives against Gram-positive Staphylococcus aureus and Gram-negative Escherichia coli bacteria. Compounds 2p, 2q, 2r, 2s, and 2t inhibited E. coli from 10.6 to 17 mm and S. aureus from 8 to 14 mm. The chemical with the greatest S. aureus and E. coli inhibitory zone was 2q.

5. CONCLUSION

Chalcones were used to create a number of new heterocyclic derivatives with pyrazoline rings. IR, 1H NMR, 13C NMR, and mass spectrometry were used in the structural elucidation process. In the biological examination, antibacterial, anti-inflammatory, and antioxidant activity screens were performed. When compared to traditional synthetic methods, microwave synthesis produced greater yields in a considerably shorter amount of time. It is clear from the synthetic derivatives that the antioxidant activity results in the evaluation using standards shown moderate to good activity. To sum up, this research clarifies the antioxidant capacity of pyrazoline derivatives produced using green chemical techniques. By using the DPPH radical scavenging method to determine their IC50 values, the synthesized compounds showed considerable antioxidant activity. The chemicals' effectiveness points to their possible use in antioxidant therapy. The importance of green chemistry methods in ecologically friendly and sustainable synthetic methodologies is highlighted by their usage in synthesis.

REFERENCES

1. Achutha, D. K., Vagish, C. B., Renuka, N., Lokeshwari, D. M., & Kariyappa, A. K. (2020). Green synthesis of novel pyrazoline carbothioamides: A potent antimicrobial and antioxidant agents. Chemical Data Collections, 28, 100445.

2. B. S. Holla, B. Kalluraya, S. N. Shetty, Indian J. Heterocycl. Chem. 2 (1992) 61 17. N. Vinutha, M. S. Kumar, V. H. S. Jois, K. Balakrishna, N. K. Lokanath, D. Revannasiddaiah, Acta Crystallogr., E 69 (2013) o1528.
3. Dhonnar, S. L., Jagdale, B. S., Adole, V. A., & Sadgir, N. V. (2023). PEG-mediated synthesis, antibacterial, antifungal and antioxidant studies of some new 1, 3, 5-trisubstituted 2-pyrazolines. Molecular Diversity, 27(6), 2441-2452.
4. Gschwendt M, Kielbassa K, Kittstein W, Marks F. Tyrosine phosphorylation and stimulation of protein kinase porcine spleen by src in vitro Dependence on the activated state of protein kinase C8. 1994;347:85–9.
5. Hayes, B.L. Microwave Synthesis - Chemistry at the speed of light, 1st ed.; CEM: USA, 2002
6. J. J. Harnett, M. Auguet, I. Viossat, C. Dolo, D. Bigg, P.-E Chabrier, Bioorg. Med. Chem. Lett. 12 (2002) 1439
7. John R, Sukumarana K, Kuttana G, Raob MNA, Subbarajuc V, Kuttana R. CANCER Anticancer and antioxidant activity of synthetic chalcones and related compounds. 1995;97:33–7.
8. Joshi DR, Adhikari N. GREEN CHEMISTRY: BEGINNING , RECENT PROGRESS , AND FUTURE GREEN CHEMISTRY: BEGINNING , RECENT PROGRESS , AND. 2019; July. https://doi.org/10.20959/wjpps20197- 14208.
9. K. S. Girisha, B. Kallurya, Synth. Commun. 42 (2012) 3097 14. K. S. Girisha, B. Kallurya, J. H. S. Vidyahsree, Indian J. Chem., B 51 (2013) 1767
10. K. V. Sujith, B. Kalluraya, A. Adhikari, K. Vijayanarayana, Med. Chem. Res. 21 (2012) 543
11. Kalirajan, R.; Muralidharan, V.; Jubie, S., Gowramma, B.; Gomathy, S.; Sankar, S.; Elango, K. Synthesis of some novel pyrazole-substituted 9-anilinoacridine derivatives and evaluation for their antioxidant and cytotoxic activities. J. Heterocyclic Chem., 2012, 49(4), 748-754.
12. L. I. Mensor, F. S. Menezes, G. G. Leitao, A. S. Reis, T. Don Santos, C. S. Coube, S. Leitao, Phytother. Res. 15 (2001)127
13. Nithinchandra, B. Kalluraya, S. Aamir, A. R. Shabaraya, Eur. J. Med. Chem. 54 (2012) 597
14. Noroozi-Pesyan N, Khalafy J, Malekpoor Z. Can be azo dyes obtained by grinding under solvent-free conditions? J Chinese Chem Soc. 2009;56:1018–27.
15. Praceka, M. S., Megantara, S., Maharani, R., & Muchtaridi, M. (2021). Comparison of various synthesis methods and synthesis parameters of pyrazoline derivates. Journal of Advanced Pharmaceutical Technology & Research, 12(4), 321-326.
16. Rangaswamy, J.; Kumar, H.V.; Harini, S.T.; Naik, N. Synthesis of benzofuran based 1,3,5-substituted pyrazole derivatives: As a new class of potent antioxidants and antimicrobials-A novel accost to amend biocompatibility. Bioorg. Med. Chem. Lett., 2012, 22(14), 4773-4777.

17. Toda F. Solid State Organic Chemistry : Efficient Reactions ,. Acc Chem Res. 1995;28:480–6.
18. Yan, R., Huang, X., Deng, X., & Song, M. (2022). Synthesis and activity evaluation of some pyrazole–pyrazoline derivatives as dual anti-inflammatory and antimicrobial agents. Polycyclic Aromatic Compounds, 42(8), 5006-5019.
19. Zangade S, Mokle S, Vibhute A, Vibhute Y. An Efficient and Operationally Simple Synthesis of Some New Chalcones by An Efficient and Operationally Simple Synthesis of Some New Chalcones by Using. 2017; May. https://doi.org/10.4172/2150-3494.1000011.
20. Zangade SB, Mokle SS, Shinde AT, Yeshwant B. Green Chemistry Letters and Reviews An atom efficient , green synthesis of 2-pyrazoline derivatives under solvent-free conditions using grinding technique. 2013;8253.
21. Mandal S, Vishvakarma P. Nanoemulgel: A Smarter Topical Lipidic Emulsion-based Nanocarrier. Indian J of Pharmaceutical Education and Research. 2023;57(3s):s481-s498.
22. Mandal S, Jaiswal DV, Shiva K. A review on marketed Carica papaya leaf extract (CPLE) supplements for the treatment of dengue fever with thrombocytopenia and its drawback. International Journal of Pharmaceutical Research. 2020 Jul;12(3).
23. Mandal S, Bhumika K, Kumar M, Hak J, Vishvakarma P, Sharma UK. A Novel Approach on Micro Sponges Drug Delivery System: Method of Preparations, Application, and its Future Prospective. Indian J of Pharmaceutical Education and Research. 2024;58(1):45-63.
24. Mishra, N., Alagusundaram, M., Sinha, A., Jain, A. V., Kenia, H., Mandal, S., & Sharma, M. (2024). Analytical Method, Development and Validation for Evaluating Repaglinide Efficacy in Type Ii Diabetes Mellitus Management: a Pharmaceutical Perspective. Community Practitioner, 21(2), 29–37. https://doi.org/10.5281/zenodo.10642768
25. Singh, M., Aparna, T. N., Vasanthi, S., Mandal, S., Nemade, L. S., Bali, S., & Kar, N. R. (2024). Enhancement and Evaluation of Soursop (Annona Muricata L.) Leaf Extract in Nanoemulgel: a Comprehensive Study Investigating Its Optimized Formulation and Anti-Acne Potential Against Propionibacterium Acnes, Staphylococcus Aureus, and Staphylococcus Epidermidis Bacteria. Community Practitioner, 21(1), 102–115. https://doi.org/10.5281/zenodo.10570746
26. Khalilullah, H., Balan, P., Jain, A. V., & Mandal, S. (n.d.). EUPATORIUM REBAUDIANUM BERTONI (STEVIA): INVESTIGATING ITS ANTI-INFLAMMATORY POTENTIAL VIA CYCLOOXYGENASE AND LIPOOXYGENASE ENZYME INHIBITION - A COMPREHENSIVE MOLECULAR DOCKING AND ADMET. Community Practitioner, 21(03), 118–128. https://doi.org/10.5281/zenodo.10811642
27. Mandal, S. (n.d.). GENTAMICIN SULPHATE BASED OPHTHALMIC NANOEMULGEL : FORMULATION AND EVALUATION , UNRAVELLING A PARADIGM SHIFT IN NOVEL PHARMACEUTICAL DELIVERY SYSTEMS.

Community Practitioner, 21(03). https://doi.org/10.5281/zenodo.10811540

28. Mandal, S., Tyagi, P., Jain, A. V., & Yadav, P. (n.d.). Advanced Formulation and Comprehensive Pharmacological Evaluation of a Novel Topical Drug Delivery System for the Management and Therapeutic Intervention of Tinea Cruris (Jock Itch). Journal of Nursing, 71(03). https://doi.org/10.5281/zenodo.10811676
29. Pal N, Mandal S, Shiva K, Kumar B. Pharmacognostical, Phytochemical and Pharmacological Evaluation of Mallotus philippensis. Journal of Drug Delivery and Therapeutics. 2022 Sep 20;12(5):175-81.
30. Singh A, Mandal S. Ajwain (Trachyspermum ammi Linn): A review on Tremendous Herbal Plant with Various Pharmacological Activity. International Journal of Recent Advances in Multidisciplinary Topics. 2021 Jun 9;2(6):36-8.
31. Mandal S, Jaiswal V, Sagar MK, Kumar S. Formulation and evaluation of carica papaya nanoemulsion for treatment of dengue and thrombocytopenia. Plant Arch. 2021;21:1345-54.
32. Mandal S, Shiva K, Kumar KP, Goel S, Patel RK, Sharma S, Chaudhary R, Bhati A, Pal N, Dixit AK. Ocular drug delivery system (ODDS): Exploration the challenges and approaches to improve ODDS. Journal of Pharmaceutical and Biological Sciences. 2021 Jul 1;9(2):88-94.
33. Shiva K, Mandal S, Kumar S. Formulation and evaluation of topical antifungal gel of fluconazole using aloe vera gel. Int J Sci Res Develop. 2021;1:187-93.
34. Ali S, Farooqui NA, Ahmad S, Salman M, Mandal S. Catharanthus roseus (sadabahar): a brief study on medicinal plant having different pharmacological activities. Plant Archives. 2021;21(2):556-9.
35. Mandal S, Vishvakarma P, Verma M, Alam MS, Agrawal A, Mishra A. Solanum Nigrum Linn: An Analysis Of The Medicinal Properties Of The Plant. Journal of Pharmaceutical Negative Results. 2023 Jan 1:1595-600.
36. Vishvakarma P, Mandal S, Pandey J, Bhatt AK, Banerjee VB, Gupta JK. An Analysis Of The Most Recent Trends In Flavoring Herbal Medicines In Today's Market. Journal of Pharmaceutical Negative Results. 2022 Dec 31:9189-98.
37. Mandal S, Vishvakarma P, Mandal S. Future Aspects And Applications Of Nanoemulgel Formulation For Topical Lipophilic Drug Delivery. European Journal of Molecular & Clinical Medicine.;10(01):2023.
38. Chawla A, Mandal S, Vishvakarma P, Nile NP, Lokhande VN, Kakad VK, Chawla A. Ultra-Performance Liquid Chromatography (Uplc).
39. Mandal S, Raju D, Namdeo P, Patel A, Bhatt AK, Gupta JK, Haneef M, Vishvakarma P, Sharma UK. Development, characterization, and evaluation of rosa alba l extract-loaded phytosomes.
40. Mandal S, Goel S, Saxena M, Gupta P, Kumari J, Kumar P, Kumar M, Kumar R, Shiva K. Screening of catharanthus roseus stem extract for anti-ulcer potential in wistar rat.
41. Shiva K, Kaushik A, Irshad M, Sharma G, Mandal S. Evaluation and preparation: herbal gel containing thuja occidentalis and curcuma longa extracts.

42. Vishvakarma P, Kumari R, Vanmathi SM, Korni RD, Bhattacharya V, Jesudasan RE, Mandal S. Oral Delivery of Peptide and Protein Therapeutics: Challenges And Strategies. Journal of Experimental Zoology India. 2023 Jul 1;26(2).
43. Mishra, N., Alagusundaram, M., Sinha, A., Jain, A. V., Kenia, H., Mandal, S., & Sharma, M. (2024). Analytical Method, Development and Validation for Evaluating Repaglinide Efficacy in Type Ii Diabetes Mellitus Management: a Pharmaceutical Perspective. Community Practitioner, 21(2), 29–37. https://doi.org/10.5281/zenodo.10642768
44. Singh, M., Aparna, T. N., Vasanthi, S., Mandal, S., Nemade, L. S., Bali, S., & Kar, N. R. (2024). Enhancement and Evaluation of Soursop (Annona Muricata L.) Leaf Extract in Nanoemulgel: a Comprehensive Study Investigating Its Optimized Formulation and Anti-Acne Potential Against Propionibacterium Acnes, Staphylococcus Aureus, and Staphylococcus Epidermidis Bacteria. Community Practitioner, 21(1), 102–115. https://doi.org/10.5281/zenodo.10570746