INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Research Article

Microwave Assisted Synthesis and Evaluation of Pyrrole Derivative

Jadhav Asmita*, Dr. Malpani Suraj, Dr. Dharashive Vishweshwar

Department of Pharmaceutical Chemistry, Shivlingeshwar College of Pharmacy, Almala

ARTICLE INFO
Published: 08 July 2026
Keywords:
Pyrrole derivatives, Microwave-assisted synthesis, Molecular docking, Antibacterial activity, Spectral characterization
DOI:
10.5281/zenodo.21261458

ABSTRACT

Pyrrole derivatives are important heterocyclic compounds with significant biological activities. In the present study, pyrrole derivatives were synthesized using microwave-assisted Paal–Knorr synthesis and characterized using FTIR, UV, LC-MS, 1H NMR and 13C NMR studies. Antibacterial activity against Staphylococcus aureus and molecular docking studies were performed.

INTRODUCTION

Heterocyclic compounds represent an important class of organic molecules due to their broad applications in medicinal chemistry and pharmaceutical sciences. Among nitrogen-containing heterocycles, pyrrole has gained considerable attention because of its unique structural characteristics and diverse biological activities. Pyrrole (C_4H_5N) is a five-membered aromatic heterocyclic compound containing one nitrogen atom, where the lone pair of electrons contributes to aromatic stabilization according to Hückel's rule [1]. The electron-rich nature of pyrrole makes it highly reactive toward electrophilic substitution reactions, especially at C-2 and C-5 positions.

Pyrrole derivatives occur naturally in several biologically important molecules such as heme, chlorophyll, vitamin B12, and cytochromes, indicating their significance in essential physiological functions [2]. Owing to these properties, pyrrole has become an important pharmacophore in medicinal chemistry.

Pyrrole derivatives possess a wide spectrum of biological activities including antimicrobial, anti-inflammatory, antioxidant, antiviral, anticancer, anticonvulsant, and antihypertensive effects [3].

***Corresponding Author:** Jadhav Asmita
Address: *Department of Pharmaceutical Chemistry, Shivlingeshwar College of Pharmacy, Almala*
Email ✉: Jadhavasmita645gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The biological activity of pyrrole compounds mainly depends upon the nature and position of substituents attached to the pyrrole ring. Structural modifications at various positions influence pharmacokinetic properties, receptor binding affinity, and biological selectivity [4].

Several clinically important drugs contain pyrrole or pyrrole-related scaffolds such as Atorvastatin, Sunitinib, Ketorolac, and Tolmetin, demonstrating the pharmaceutical significance of this nucleus [5]. Among various synthetic methods available for pyrrole synthesis, the Paal–Knorr synthesis is one of the most commonly used methods involving cyclization of 1,4-dicarbonyl compounds with primary amines or ammonia [6].

Recently, the development of environmentally friendly synthetic approaches has attracted significant interest in medicinal chemistry research. Microwave-Assisted Organic Synthesis (MAOS) has emerged as an efficient green chemistry technique due to its ability to reduce reaction time, improve yield, minimize solvent use, and decrease energy consumption [7]. Microwave-assisted synthesis of pyrrole derivatives has shown considerable advantages over conventional heating methods by providing rapid and efficient synthesis under eco-friendly conditions.

Molecular docking has also become an important computational approach in drug discovery for predicting ligand–receptor interactions and evaluating binding affinity. It provides useful information regarding molecular interactions and helps in identifying compounds with potential biological activity [8].

Therefore, pyrrole derivatives synthesized using microwave-assisted approaches represent promising candidates for the development of novel biologically active compounds with improved pharmacological potential.

MATERIALS AND METHODS

Pyrrole derivatives were synthesized by microwave-assisted Paal–Knorr synthesis using corresponding amines and diketones. Synthesized compounds were purified and analyzed by TLC and spectroscopic techniques.

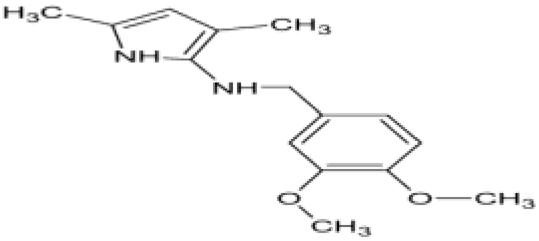
Synthesized Compounds

N-(3,4-dimethoxybenzyl)-2,5-dimethylpyrrole

Analytical Results

The synthesized compounds showed acceptable melting point, Rf value and percentage yield (75–76%). Spectral studies confirmed successful synthesis.

Table no.1:-Analytical description of N-(3,4-dimethoxybenzyl)-2,5-dimethylpyrrole

Parameter	Property
Chemical name	N-(3,4-dimethoxybenzyl)-2,5-dimethylpyrrole
Molecular formula	$C_{15}H_{19}NO_2$
Structure	
Molecular weight	245.32 g/mol

Physical state	Solid
Appearance	Off-white to pale yellow crystalline powder*
Odor	Characteristic
Solubility	Soluble in methanol, ethanol, chloroform, DMSO; sparingly soluble in water*
Nature	Aromatic heterocyclic compound
Melting point	110-115ºc
Rf value (TLC)	0.48
Microwave irradiation synthesis % yield	75%

RESULTS AND DISCUSSION

Spectral Characterization

FTIR confirmed functional groups, UV confirmed aromatic conjugation, LC-MS verified molecular mass, while 1H and 13C NMR confirmed proton and carbon environments.

N-(3,4-dimethoxybenzyl)-2,5-dimethylpyrrol

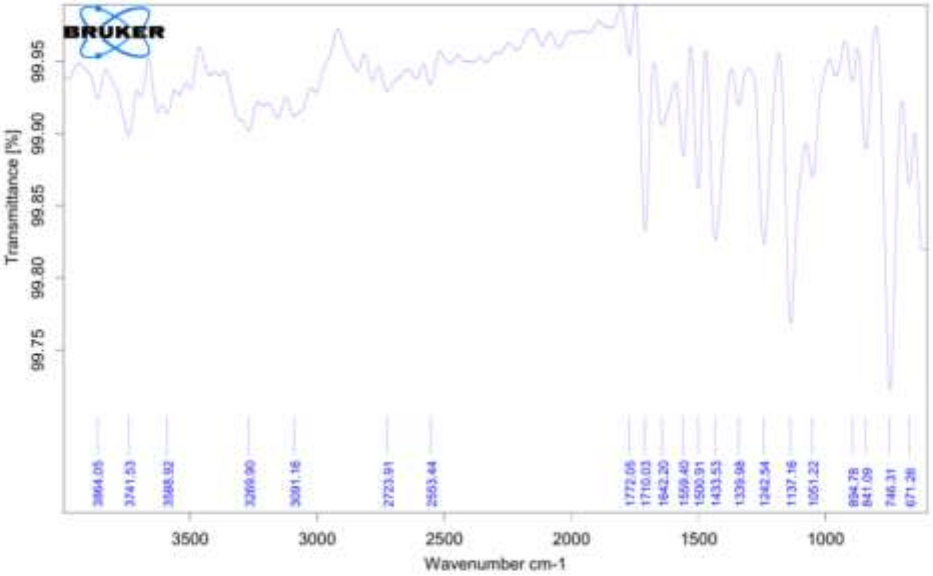


Fig..no.1:- IR spectra of 3,4-dimethoxybenzylamine

Table .no.2:-IR spectra of 3,4-dimethoxybenzylamine interpretation

Peak (cm⁻¹)	Functional Group	Interpretation
3269	N–H stretching	Indicates presence of primary amine group
3091	Aromatic C–H stretching	Confirms aromatic ring
1559	N–H bending	Confirms amino group
1500	Aromatic C=C stretching	Indicates aromatic structure
1242	Ar–O–CH_3 stretching	Indicates methoxy group
1137	C–O stretching	Confirms ether linkage
1051	C–O stretching	Supports presence of methoxy group

Discussion:

The FTIR spectrum of the synthesized compound showed characteristic absorption peaks corresponding to the expected functional groups. The peak at 3269 cm⁻¹ confirmed N–H stretching of the primary amine group. Aromatic C–H stretching was observed at 3091 cm⁻¹, while the peak at 1500 cm⁻¹ confirmed aromatic C=C stretching. Peaks at 1242, 1137 and 1051 cm⁻¹ indicated the presence of methoxy and C–O groups. The observed peaks supported the proposed structure of the synthesized compound.

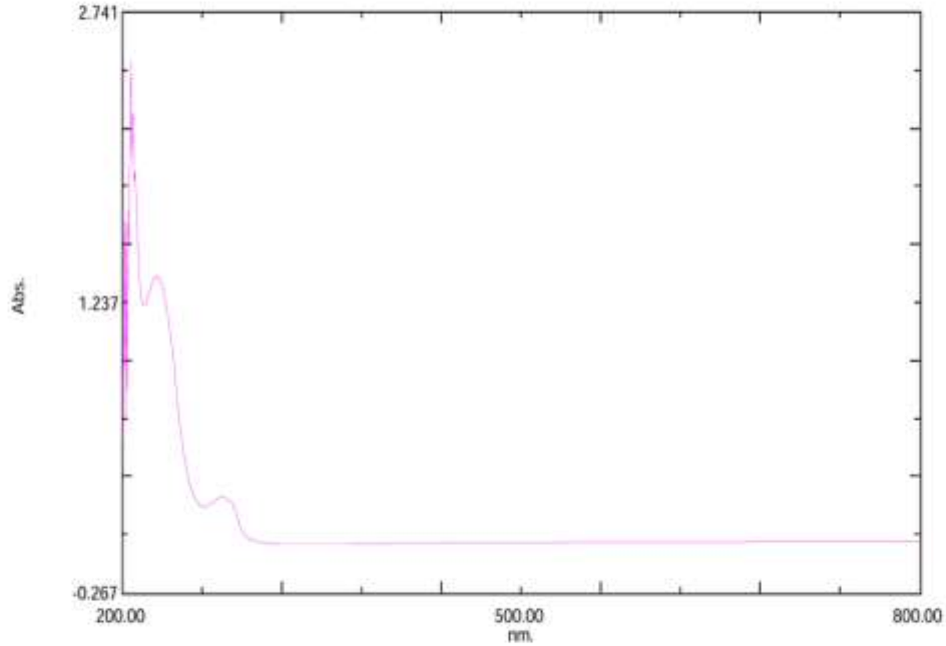


Fig.no2:- UV spectrum of 3,4-dimethoxybenzylamine

Table.no.3:- UV spectrum of 3,4-dimethoxybenzylamine Interpretation

Wavelength (nm)	Assignment	Interpretation
205–210	$\pi \rightarrow \pi^*$ transition	Indicates presence of aromatic ring system
225–240	Conjugated absorption band	Confirms conjugation within the molecule
290–310	$n \rightarrow \pi^*$ transition	Indicates presence of heteroatom-containing groups

Interpretation:

The UV–Visible spectrum of the synthesized compound showed characteristic absorption peaks in the ultraviolet region. The absorption peak observed around 205–210 nm was attributed to $\pi \rightarrow \pi^*$ electronic transition of the aromatic ring system. A broad absorption band observed around 225–240 nm indicated the presence of conjugation in the molecule. The absorption peak around 290–310 nm was assigned to $n \rightarrow \pi^*$ electronic transition associated with heteroatom-containing functional groups.

Discussion:

The UV–Visible spectral study of the synthesized compound revealed characteristic absorption bands corresponding to different electronic transitions within the molecule. The observed absorption peaks confirmed the presence of aromatic and conjugated systems in the synthesized compound. The obtained spectral data were found to be in agreement with the proposed molecular structure and indicated successful synthesis of the compound.

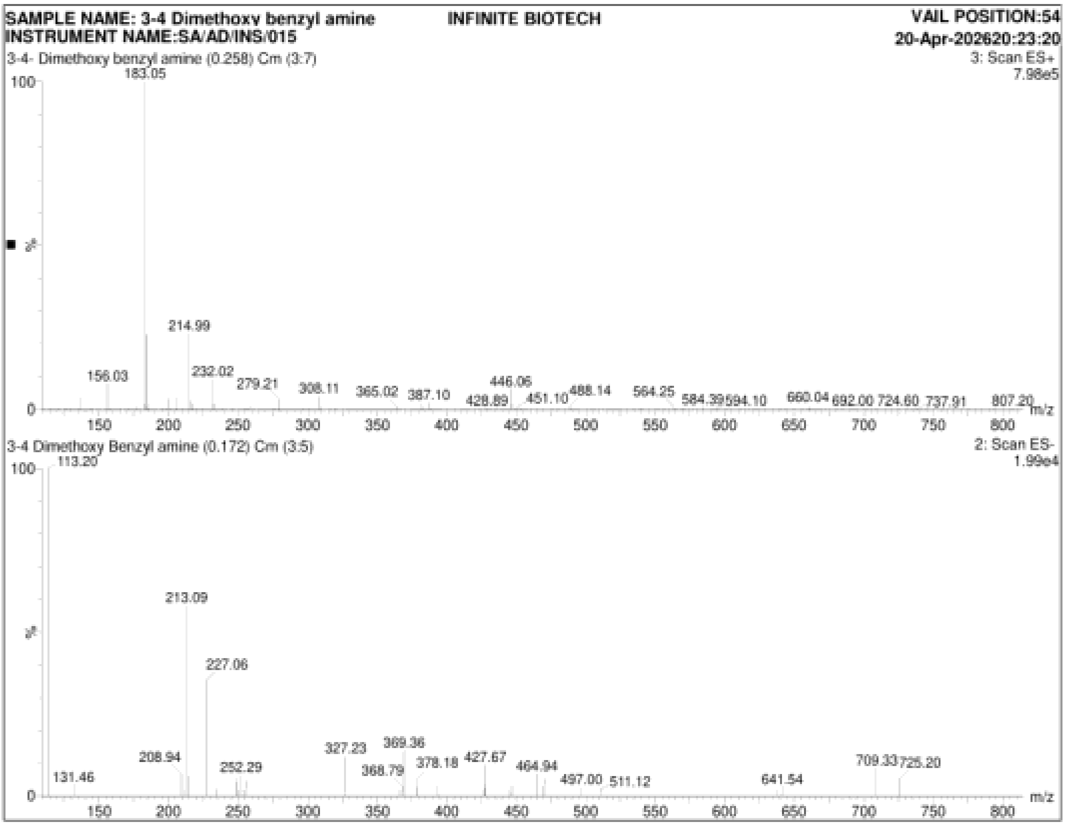


Fig.no.3:-Mass spectrum of 3,4-dimethoxybenzylamine

Table.no.4:-Mass spectrum of 3,4-dimethoxybenzylamine Interpretation

m/z Value	Fragment / Ion	Interpretation
183.05 $[M+H]^+$	Molecular ion peak	Corresponds to protonated molecular ion of synthesized compound
182.05	Molecular mass (M)	Indicates molecular weight of compound

Interpretation:

The mass spectrum of the synthesized compound showed a prominent molecular ion peak at m/z 183.05 $[M+H]^+$, corresponding to the protonated molecular ion of the compound. The observed peak indicated a molecular weight of approximately 182.05 g/mol. The obtained molecular ion peak confirmed the expected molecular mass of the synthesized compound.

Discussion:

The LC–MS spectrum showed a characteristic molecular ion peak corresponding to the synthesized compound. The molecular ion peak observed at m/z 183.05 $[M+H]^+$ matched the theoretical molecular weight of the proposed structure. The absence of significant additional peaks suggested good purity of the synthesized compound. The obtained spectral data supported the successful synthesis and structural confirmation of the compound.

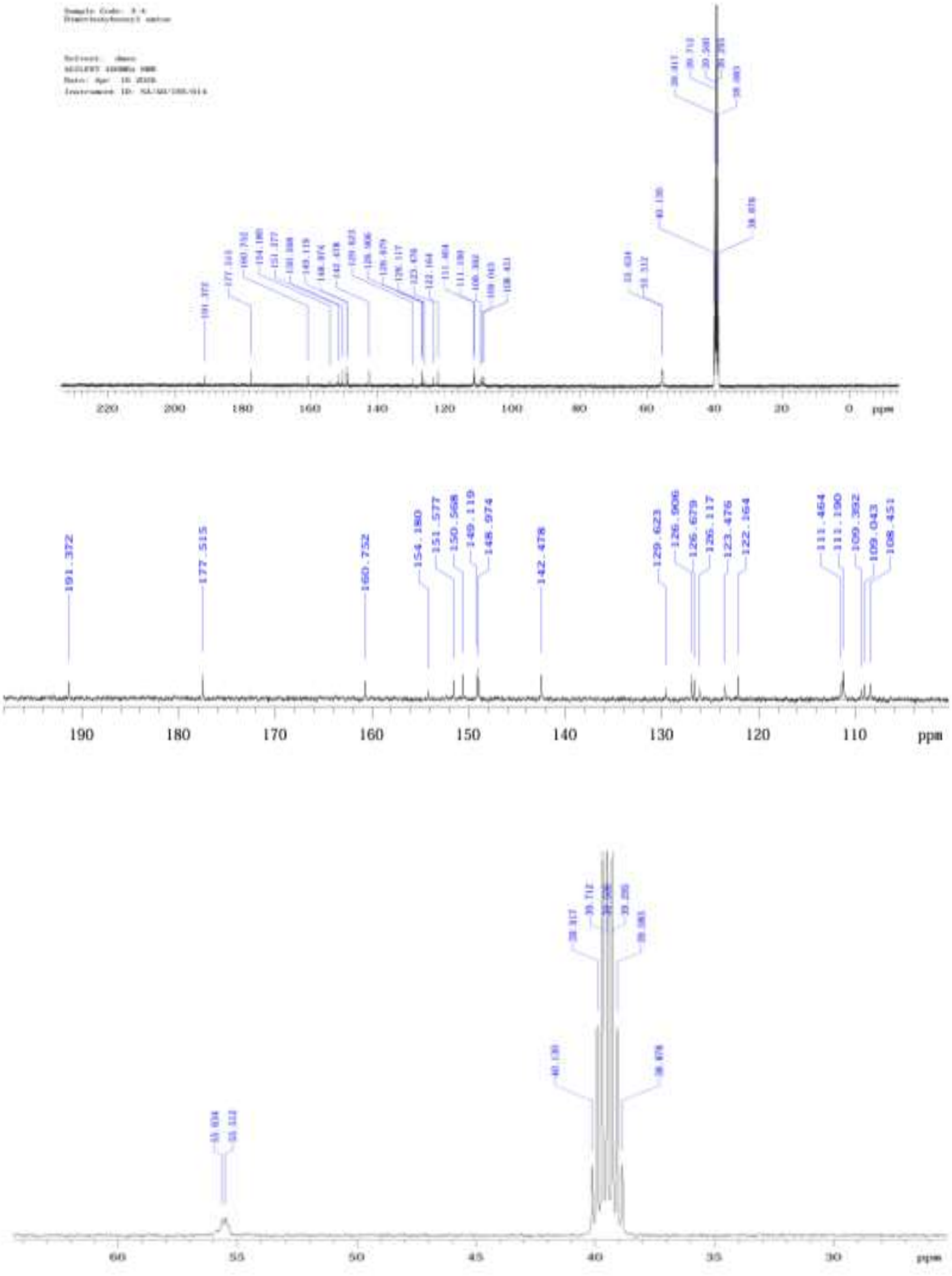


Fig.no.4:-Carbon 13 NMR spectrum of 3,4-dimethoxybenzylamine

Table.no.5:-Carbon 13 NMR spectrum of 3,4-dimethoxybenzylamine Interpretation

Chemical Shift (δ ppm)	Carbon Assignment	Interpretation
148–161	Methoxy substituted aromatic carbons	Indicates aromatic carbons attached to electronegative oxygen atoms
108–129	Aromatic carbons	Confirms presence of aromatic ring carbons
55.5	OCH_3 carbons	Indicates methoxy carbon atoms
~40	Benzylic CH_2 carbon	Indicates methylene carbon attached to aromatic system

INDEX FREQUENCY PPM HEIGHT

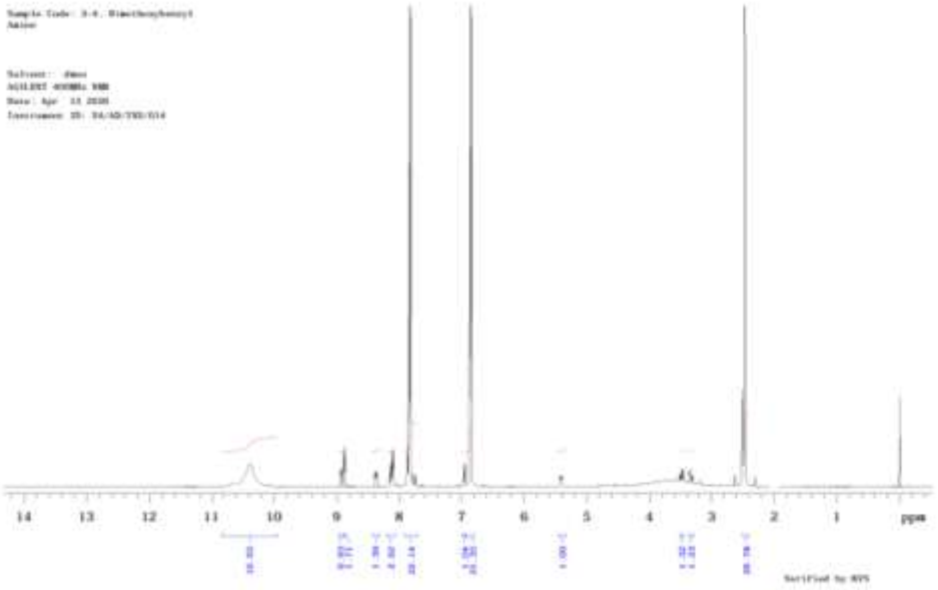
1 19239.9 191.372 3.7 2 17846.8 177.515 5.6 3 16161.4 160.752 4.0 4 15500.7 154.180 1.9 5 15239.0 151.577 4.0 6 15137.6 150.568 5.5 7 14991.8 149.119 6.9 8 14977.4 148.974 4.7 9 14324.3 142.478 5.4 10 13031.9 129.623 2.4 11 12758.7 126.906 5.4 12 12735.8 126.679 4.3 13 12679.4 126.117 2.5 14 12413.9 123.476 3.1 15 12281.9 122.164 5.1 16 11206.1 111.464 4.2 17 11178.7 111.190 6.2 18 10997.9 109.392 2.1 19 10962.8 109.043 3.3 20 10903.3 108.451 3.3 21 5593.2 55.634 5.5 22 5581.0 55.512 5.8 23 4034.5 40.130 24.8 24 4013.2 39.917 75.0 25 3992.6 39.712 149.4 26 3971.2 39.500 174.4 27 3950.6 39.295 148.6 28 3929.2 39.083 74.4 29 3908.6 38.878 24.

Interpretation:

The ^{13}C NMR spectrum showed signals corresponding to different carbon environments present in the synthesized compound. Signals in the region of δ 148–161 ppm were assigned to methoxy substituted aromatic carbons due to deshielding caused by oxygen atoms. Signals between δ 108–129 ppm corresponded to aromatic ring carbons. The signal at δ 55.5 ppm indicated methoxy carbon atoms, while the signal around δ 40 ppm was assigned to benzylic CH_2 carbon.

Discussion:

The ^{13}C NMR spectrum displayed characteristic carbon signals at expected chemical shift regions. The presence of aromatic carbons, methoxy carbons and benzylic carbon atoms confirmed the structural features of the synthesized compound. The observed chemical shifts were found to be in agreement with the proposed molecular structure and supported successful synthesis of the compound.



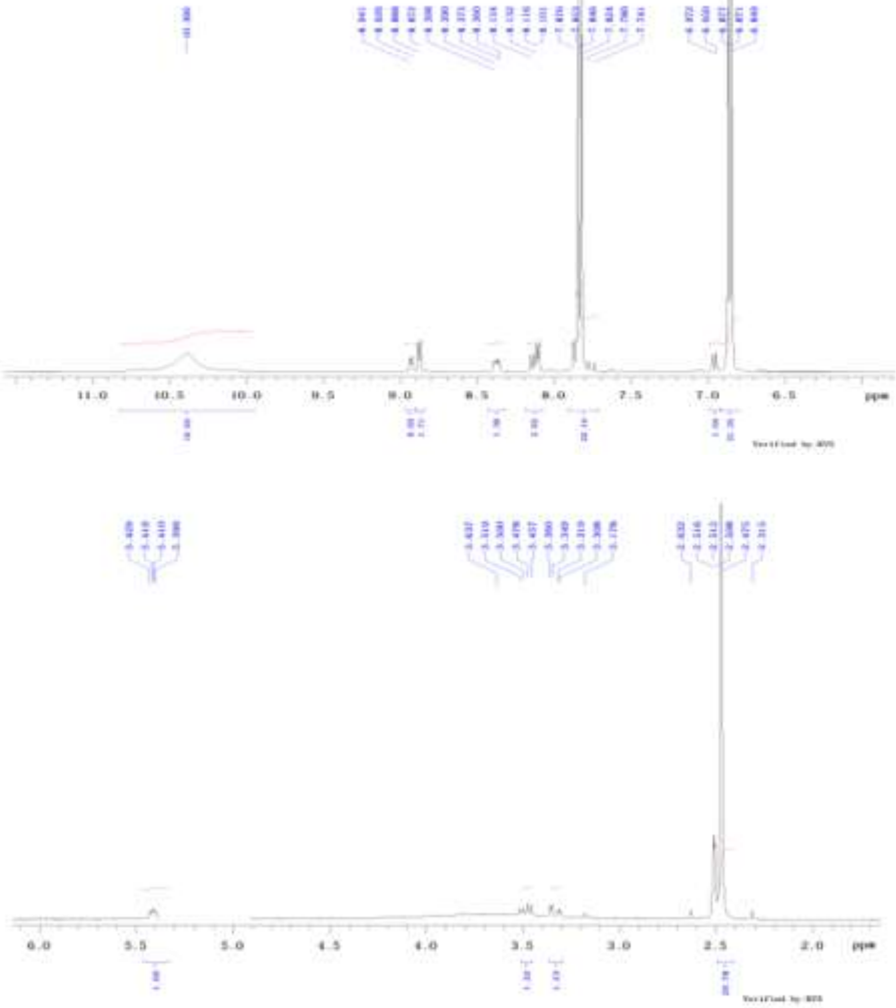


Fig.no.5:-H1 NMR spectroscopy of 3,4-dimethoxybenzylamine

Table.no.6:-H1 NMR spectroscopy of 3,4-dimethoxybenzylamine Interpretation

Chemical Shift (δ ppm)	Proton Assignment	Interpretation
6.84–6.97	Aromatic protons	Indicates aromatic hydrogen atoms
3.45–3.64	$CH_2–NH_2$	Indicates methylene group attached to amino group
~3.8	OCH_3	Indicates methoxy groups
5.39–5.43	NH_2 protons	Confirms amino protons

INDEX FREQUENCY PPM HEIGHT

1 4154.4 10.390 6.6 2 3574.8 8.941 4.8 3 3568.7 8.926 5.5 4 3553.5 8.888 10.2 5 3547.2 8.872 11.7 6 3357.9 8.398 3.2 7 3354.7 8.390 4.0 8 3348.4 8.375 4.6 9 3342.5 8.360 4.2 10 3260.1 8.154 5.9 11 3251.5 8.132 6.6 12 3245.2 8.116 10.2 13 3238.8 8.101 10.3 14 3149.1 7.876 11.5 15 3140.0 7.853 28.9 16 3137.1 7.846 140.5 17 3128.3 7.824 154.3 18 3110.7 7.780 3.9 19 3095.0 7.741 3.2 20 2787.4 6.972 6.3 21 2778.6 6.950 6.6 22 2749.8 6.877 26.7 23 2747.1 6.871 147.8 24 2738.3 6.849 147.7 25 2170.7 5.429 2.7 26 2166.6 5.419 3.4 27 2163.1 5.410 3.3 28 2158.7 5.399 3.0 29 1454.2 3.637 1.9 30 1407.0 3.519 3.9 31 1399.2 3.500 3.8 32 1390.4 3.478 5.1 INDEX FREQUENCY PPM HEIGHT 33 1382.3 3.457 5.0 34 1343.5 3.360 4.8 35 1339.1 3.349 5.0 36 1326.8 3.319 3.3 37 1322.4

3.308 3.3 38 1270.6 3.178 2.1 39 1052.5 2.632 3.3 40 1006.0 2.516 19.7 41 1004.3 2.512 27.9 42 1002.6 2.508 25.1 43 989.6 2.475 570.1 44 925.6 2.315 3.2 45 -0.0 -0.000 25.

Discussion:

The ^{1}H NMR spectrum showed characteristic proton signals corresponding to the synthesized compound. Signals in the region of δ 6.84–6.97 ppm indicated aromatic protons. The signal at δ 3.45–3.64 ppm confirmed CH_2 attached to the amino group. The signal observed around δ 3.8 ppm indicated methoxy groups, while signals at δ 5.39–5.43 ppm represented NH_2 protons. The obtained signals were in agreement with the expected structure.

Antibacterial Activity

The compounds showed moderate antibacterial activity against Staphylococcus aureus. 3,4-dimethoxybenzyl derivative showed highest inhibition (19 mm) among synthesized compounds

Table No.7:- Antibacterial activity of test compound against S. *aureus*

SR. NO	SAMPLES	ZONE IN DIAMETER (mm)
1	Control	00
2	Standard (Streptomycin)	26
3	3,4-dimethoxybenzyl	19
4	Benzyl amine	15
5	Phenyl amine	18

Image Activity:

Conclusion of the study:

The antibacterial activity against *Staphylococcus aureus* was evaluated using the zone of inhibition method, where the control showed no inhibition (0 mm), confirming the reliability of the assay. The standard antibiotic, Streptomycin, exhibited a strong inhibition zone of 26 mm, indicating high antibacterial efficacy. Among the test compounds, 3,4-dimethoxybenzyl showed the highest activity with a zone of 19 mm, followed by phenyl amine (18 mm) and benzyl amine (15 mm). Although all test compounds demonstrated lower activity compared to the standard Streptomycin, their measurable inhibition zones indicate moderate antibacterial potential against *Staphylococcus aureus*. Overall, 3,4-dimethoxybenzyl was found to be the most effective among the tested compounds.

N-(3,4-dimethoxybenzyl)-2,5-dimethylpyrrole

Molecular Docking and ADME

Docking score ranged from −3.94 to −4.72 kcal/mol. Compound A.J.3 showed strongest binding affinity with MMGBSA value of −38.86 kcal/mol and passed Lipinski parameters.

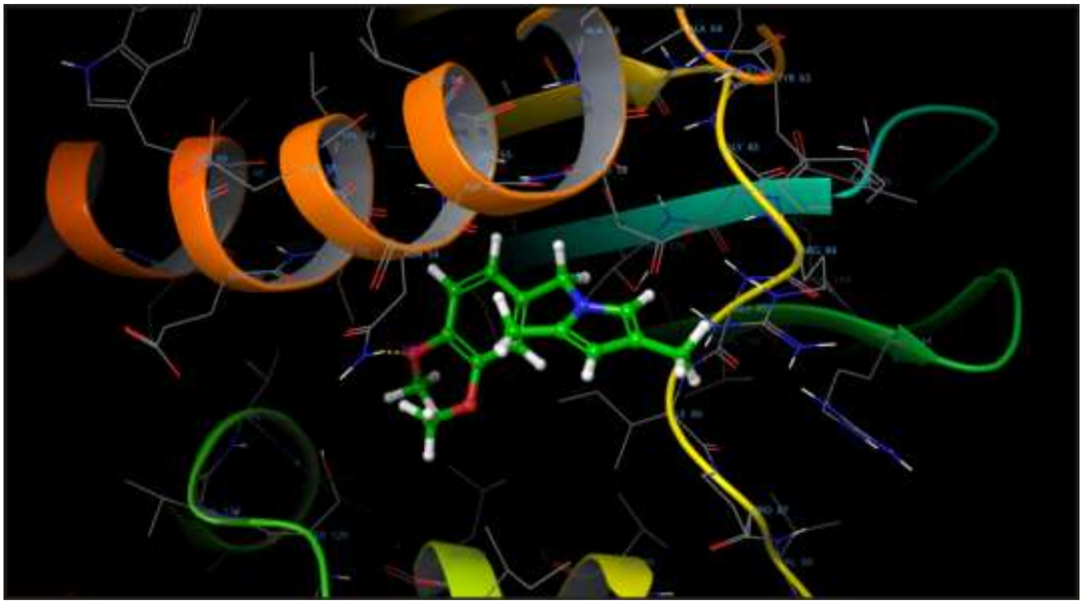


Fig.no.6:- 3D binding pose of N-(3,4-dimethoxybenzyl)-2,5-dimethylpyrrole

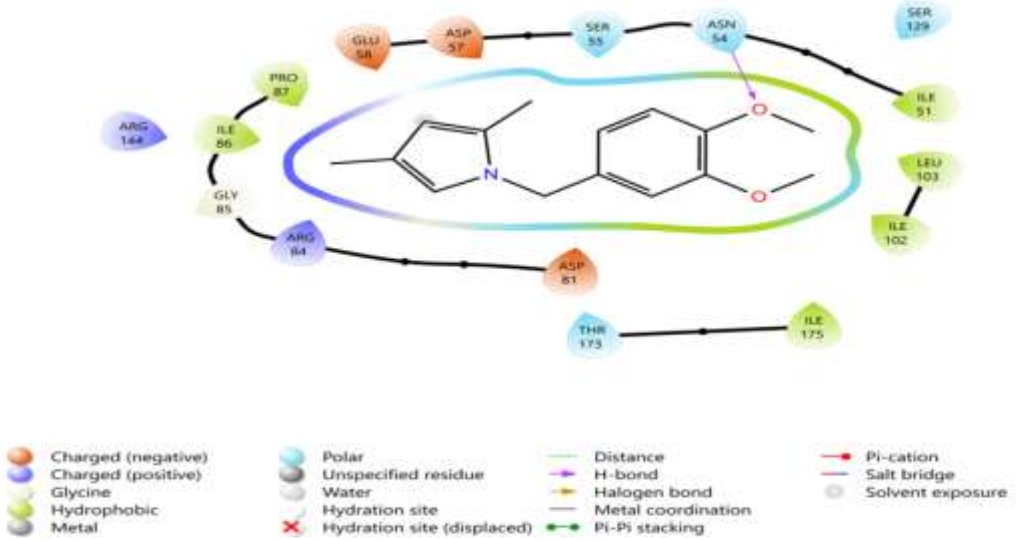


Fig.no.7:- 2D interaction diagram of N-(3,4-dimethoxybenzyl)-2,5-dimethylpyrro

Table no.8:-Molecular Docking and MM-GBSA Results

Compound Code	Docking Score (kcal/mol)	MMGBSA Binding Energy (kcal/mol)	Human Oral Absorption (%)	Lipinski Rule
A.J.3	-4.72	-38.86	100	Passed

Interpretation

The molecular docking results indicated that the synthesized pyrrole derivative exhibited favorable interaction with the target receptor protein. Compound A.J.3 showed a docking score of −4.72 kcal/mol, indicating good receptor binding affinity and stronger interaction with the active site residues.

The MMGBSA binding energy value further supported the docking result. Compound A.J.3 displayed a ΔG bind value of −38.86 kcal/mol, suggesting higher binding stability with the receptor protein.

The ADME study predicted that compound A.J.3 possesses 100% human oral absorption and satisfied Lipinski's Rule of Five, indicating favorable drug-likeness properties and supporting its potential as a bioactive molecule for further investigation.

CONCLUSION

The present molecular docking and ADME study demonstrated that the synthesized pyrrole derivatives possess promising receptor binding characteristics and acceptable drug-likeness properties. Compound A.J.3 exhibited comparatively better binding affinity and stability among the tested compounds and may serve as a potential lead compound for further biological investigation.

REFERENCES

1. Joule JA, Mills K. Heterocyclic Chemistry. 5th ed. Wiley-Blackwell; 2010.
2. Gilchrist TL. Heterocyclic Chemistry. 3rd ed. Longman Scientific and Technical; 1997.
3. Sharma V, Kumar P, Pathak D. Biological importance of pyrrole derivatives: A review. J Heterocycl Chem. 2010;47:491–502.
4. Patil PO, Bari SB, Firke SD, Deshmukh PK, Donda ST, Patil DA. Review on synthesis and biological activities of pyrrole derivatives. J Pharm Res. 2013;7:123–129.
5. Kumar D, Sundaree S, Johnson EO, Shah K. An overview of pyrrole derivatives as therapeutic agents. Eur J Med Chem. 2009;44:3805–3813.
6. Paal C. Synthesis of substituted pyrrole compounds. Ber Dtsch Chem Ges. 1885;18:367–371.
7. Kappe CO. Controlled microwave heating in modern organic synthesis. Angew Chem Int Ed. 2004;43:6250–6284.
8. Morris GM, Lim-Wilby M. Molecular docking methods and applications in drug discovery. Methods Mol Biol. 2008;443:365–382
9. Katritzky AR, Ramsden CA, Scriven EFV, Taylor RJK. Comprehensive Heterocyclic Chemistry III. Oxford: Elsevier; 2008.
10. Gupta RR, Kumar M, Gupta V. Heterocyclic Chemistry. New Delhi: Springer; 2013.
11. Kaur R, Rani V, Abbot V. Pyrrole: A resourceful small molecule in key medicinal hetero-aromatics. Asian J Pharm Clin Res. 2017;10(6):20–32.
12. Khajuria R, Dham S, Kapoor KK. Synthesis and biological activity of pyrrole derivatives: A review. Int J Pharm Sci Res. 2016;7(4):1458–1468.
13. Knorr L. Synthese von Pyrrolderivaten. Ber Dtsch Chem Ges. 1884;17:2863–2870.
14. Lidstrom P, Tierney J, Wathey B, Westman J. Microwave assisted organic synthesis—a review. Tetrahedron. 2001;57(45):9225–9283.
15. Kappe CO, Dallinger D. Microwave-assisted synthesis in medicinal chemistry. Nat Rev Drug Discov. 2006;5(1):51–63.
16. Varma RS. Solvent-free organic syntheses using microwave irradiation. Green Chem. 1999;1(1):43–55.
17. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery. Adv Drug Deliv Rev. 2001;46(1–3):3–26.
18. Veber DF, Johnson SR, Cheng HY, Smith BR, Ward KW, Kopple KD. Molecular properties affecting oral bioavailability. J Med Chem. 2002;45(12):2615–2623.
19. Morris GM, Huey R, Lindstrom W, Sanner MF, Belew RK, Goodsell DS, et al. AutoDock4 and AutoDockTools4: Automated docking with selective receptor

flexibility. J Comput Chem. 2009;30(16):2785–2791.

20. Trott O, Olson AJ. AutoDock Vina: Improving docking speed and accuracy. J Comput Chem. 2010;31(2):455–461.
21. Daina A, Michielin O, Zoete V. SwissADME: A free web tool to evaluate pharmacokinetics and drug-likeness. Sci Rep. 2017;7:42717.
22. Wermuth CG. The Practice of Medicinal Chemistry. 4th ed. London: Academic Press; 2015.
23. Silver LL. Challenges of antibacterial discovery. Clin Microbiol Rev. 2011;24(1):71–109.
24. Bauer AW, Kirby WM, Sherris JC, Turck M. Antibiotic susceptibility testing by standard single disk method. Am J Clin Pathol. 1966;45(4):493–496.
25. Patrick GL. An Introduction to Medicinal Chemistry. 6th ed. Oxford: Oxford University Press; 2017.
26. Rang HP, Ritter JM, Flower RJ, Henderson G. Rang and Dale's Pharmacology. 8th ed. Edinburgh: Elsevier; 2016.
27. Wilson CO, Gisvold O, Doerge RF. Textbook of Organic Medicinal and Pharmaceutical Chemistry. Philadelphia: Lippincott Williams & Wilkins; 2011.
28. Subramaniam S, Kirubakaran P, Saravanan R. Design, synthesis and biological evaluation of pyrrole derivatives as antimicrobial agents. Eur J Med Chem. 2012;54:618–625.
29. Kumar D, Kumar NM, Ghosh S. Recent advances in pyrrole derivatives and their pharmacological activities. Eur J Med Chem. 2018;157:138–165.
30. Gupta AK, Sharma S, Gupta A. Pyrrole derivatives and their biological significance: A review. Int J Pharm Sci Rev Res. 2015;31(2):180–190.

HOW TO CITE: Jadhav Asmita, Dr. Malpani Suraj, Dr. Dharashive Vishweshwar, Microwave Assisted Synthesis and Evaluation of Pyrrole Derivative, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 7, 1607-1618. https://doi.org/10.5281/zenodo.21261458