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Original Article

Synthesis, Therapeutic Potential, Quantum Studies and Molecular Properties of Amino Acid Fused 1,3,4-Oxadiazole Derivatives as an Unnatural Amino Acids

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ABSTRACT

Background: In present study 1,3,4-oxadiazole derivatives with iso-sterically fused amino acids was attempted to synthesize. As variety of chemical reactions that 1, 3 and 4-oxadiazole molecules can experience, it made them very useful for searching of molecule altogether its high advantaged structure having enormous biological potential. Heterocyclic ring fusion has yielded compounds with a diverse array of biological functions. In the biological system, amino acids are important. With the hope that adding amino acids to an oxadiazole scaffold may result in new molecules that are potentially referred to as unnatural amino acids, this experiment helps to synthesize substances. It is possible to create novel hormones, enzymes and medications using unconventional amino acids. **Materials and Methods:** Derivatives were tried to synthesize from two methods, conventional as well as new microwave method in order to find out highest yielding method. Microwave method also referred to as "green chemistry" because it uses no external energy sources to produce any harmful fumes, gases, or heat. The synthesised compounds were analysed for their therapeutic potential, molecular properties and quantum studies. **Results:** "Method B" i.e., microwave used method found to be produce high yield. Synthesised derivatives of fused amino acids with 1,3,4-oxadiazole were said to be unnatural amino acids. The compound(s) were analysed using UV, IR, Mass and NMR spectral data. Synthesized compound(s) were experienced for *in vitro* DPPH activity with quantum studies, antibacterial potential and anti-fungal activity and found that compound 1A and 1B to have promising activity. **Conclusion:** The synthesis of fused amino acids is a field of recent study that is gaining interest. Study provides preparation of fused oxadiazole as an Unnatural amino acid and for its similar compound(s). The findings might make a significant contribution to the future development of innovative medicinal medications.

Keywords: Unnatural amino acids, Oxadiazole, Microwave synthesis, Scavenging activity, Amino acids, Quantum Studies, Molecular Properties.

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INTRODUCTION

Medicinal chemists have recently become interested in heterocyclic systems because of their fascinating nitrogen and oxygen content. This can be attributed to both the extraordinary efficacy of the systems and the vast array of biological functions that consume nitrogen and oxygen. Numerous significant derivatives that are used therapeutically that contain pyrazoles include aminopyran, Novalgina and other commonly prescribed NSAIDs.[1] Among their many biological activities are antifungal, anti-malarial and hypertensive qualities for imidazole and triazole, respectively.[2] This theory states that the potent antibacterial properties of oxadiazoles have drawn a lot of attention.[3,4]

The oxadiazole nucleus has been demonstrated to be a promising target for drug research due to its high level of bioactivity. As a result, for a considerable amount of effort and research, the synthesis of 1,3,4-oxadiazole and its conversion have been the focus of attention. It has been used to find molecules with the 1,3,4-oxadiazole ring, which is an essential part of medicinal chemistry and has significant biological effects, including antibacterial,[5-8] antituberculosis,[9-11] anticancer,[12] anti-inflammatory,[13,14] antiparasitic,[15] and antihyperglycemic drug.[16] Additionally, chemicals with antibacterial and antiparasitic qualities have been identified using this method. Furthermore, it has been demonstrated that it can trigger cell apoptosis.[17]

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At least 1.27 million deaths in 2019 can be attributed to antibiotic resistance; however, it is more likely that up to 5 million deaths will result from the disease. The well-being of every person on the earth is now in a challenging situation as a result.[18] Microbes such as bacteria, fungi and other organisms can become resistant to the effects of antimicrobial medications, a phenomenon known as antimicrobial resistance.[19] This gives the idea that the germs are still alive and well even after being eliminated. There is still a need for novel antimicrobial medications, despite the fact that a growing number of diseases are becoming resistant to the treatments that are already accessible everywhere. Furthermore, there is a serious risk to human health from bacteria that have evolved to be resistant to the effects of numerous drugs. Utilizing genomes may assist in identifying novel therapeutic targets, enhancing currently available antibiotics and-most importantly-discovering novel antimicrobial therapies.[20-22]

In several fields of chemistry, amino acids have long been crucial. Naturally, only 20 amino acids are used, but even a little alteration to one of these amino acids has resulted in an amazing diversity in terms of chemical structure and function. The likelihood of novel drugs, hormones and enzymes originating from non-proteogenic unnatural amino acids is fast rising along with their abundance.[23] Nevertheless, the development and optimization of drugs is especially interested in unnatural amino acids. The synthesis of unnatural amino acids is receiving increase attention. Though in past few years' researchers and organic chemists create several techniques for the same purpose, but a potent and selective medication candidate is still desperately needed. Therefore, the study involves the synthesis of iso-sterically fused amino acids with derivatives of substituted 1,3,4-oxadiazole, which were then assessed for their potential as antioxidants, antibacterials and antifungals. Moreover, quantum and molecular characteristics studies were performed to make sense of the *in vitro* and *in silico* data.

MATERIALS AND METHODS

Experimental

Solvents employed in the processes were first tried to distil and all of the compound(s) utilized in the investigation were of Laboratory Grade (LR). The open capillary method was used to calculate the physical data, including melting points. On silica gel TLC plates, the homogeneity of produced substances was evaluated. All compounds were subjected to Thin Layer Chromatography (TLC), which was periodically recorded and discovered to differ from the starting substance. Isosteric technique was used to synthesis all the compounds in accordance with the scheme design (Figure 1). For the reaction, a conventional (Method A) as well as a microwave (Method B) was used. For method B domestic microwave oven (IFB) was employed. Compounds' maximum absorption was measured using an SL210 UV spectrophotometer. Through a Thermos Nicolet IR 200 spectrophotometer, IR spectra were captured using the KBr disc technique. An Agilent 1100 series LC-MS used for mass spectra, while 400 MHz Bruker Advance II NMR Spectrometer used for 1H-NMR spectra.

Synthesis of (5-aryl-oxadiazole-2-amino) acetone (1)

Synthesis of compound (1): A combination of aryl-amino-oxadiazole with chloro- acetone was taken in round flask. In another round flask anhydrous potassium carbonate was taken with dry acetone and allows stirring for half an hour. Then the blend was transferred to round flask which was taken later. The reaction was allowed to reflux till the compound formed by checking the TLC time to time. It was filtered and recrystallized from suitable solvent to get the product.[24,25]

Synthesis of compound (2A to 2E): Synthesis of derivatives

All the compounds from 1A to 1E were synthesized by two methods for getting and comparing yield.[26] Form compounds A-E different amino acids were used, shown in Table 1.

Method A (Conventional Method)

The mixture of compound (1) and amino acid (1A to 1E) in 50 mL water stirred and heated under reflux till the compound formed by checking the TLC time to time. When the compound supposed to be formed the reaction was discontinued to heat more. After using toluene to distil out any remaining water from the process, the residue was triturated with acetone until it crystallized. Filtered and recrystallized with suitable solvent to get the compound.

Method B (Microwave method)

The mixture of synthesized compound (1) and amino acid (1A to 1E) in 25 mL water was added in a 100 mL open Erlenmeyer flask and irradiated carefully in domestic microwave with power 500 W for 5 min (5x60 sec) till the compound formed by checking the TLC after every 60 sec. Remained water was evaporated by distillation with toluene and the residue was triturated with acetone until it solidified. Filtered and recrystallized with suitable solvent to get the compound.

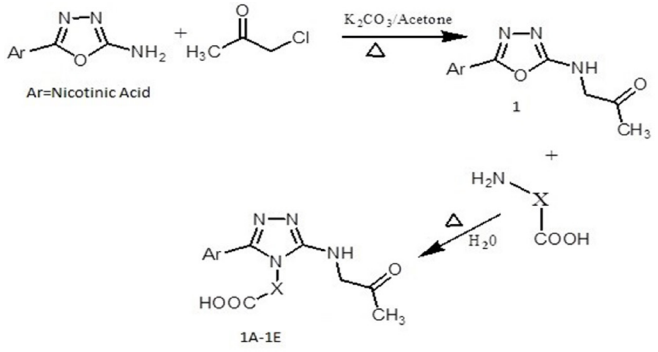


Figure 1: Scheme design.

Compound 1: (5-aryl oxadiazole-2-amino) acetone (1)

λ_{max} (methanol): 241 nm; IR (KBr) cm^{-1}: 3309 (CH- aromatic in pyridine), 1551 (C=C and C=N ring in pyridine), 706 C-H (out of plane in pyridine), 1298 (C-C Str), 3383 (N-H Str), 3368 (N-N Str), 1648 (C=N Str), 1592 (C-O Str), 1591(C=O Str), 2874 (C-H-CH_3), ^{1}H NMR: δ 1.0-4.1 (s 2H Aromatic C-NH), 7.97-7.75 (s 1H CH), 8.55-8.59 (m 2H N-CH), δ3.9-4.0 (s 1H NH Sec amine), δ 3.8-3.9 (s 3H CH_3 Methoxy).

Compound 1A (S-isoleucine)

λ_{max} (methanol): 298nm; IR (KBr) cm^{-1}: 2962 (CH-aromatic in pyridine), 1562 (C=C and C=N- Str ring in pyridine), 706 (C-H Str out of plane in pyridine), 2538 and 1503 (Str O-H and C=O(COOH)), 3372 (N-H Str), 2877 (Str C-H in CH_3), 1417 (C-H in CH_2), 1596 (C-N Str), 1134 (C-C Str), 1108 (CHCOOH,C_2H_5 str), 1596 (N-N Str), ^{1}H NMR: δ 2.54-3.99 (d 2H -CHCOOH), 0.82-1.94 (m 9H C_4H_9), 7.30 (s 1H -NH), 7.85-9.00 (s 4H Pyridine).

Compound 1B (S-alanine)

λ_{max} (methanol): 242 nm; IR (KBr) cm^{-1}: 3074 (Str CH-aromatic in pyridine), 1594 (C=C and C=N Str ring in pyridine), 706 (C-H Str out of plane in pyridine), 2806 and 1622 (Str O-H and C=O(COOH)), 2985 (Str N-H), 2806 (Stretching C-H in CH_3), 1458 (Str C-H in CH_2), 855 (C-N Str), 1309 (Str C-C in CH_2COOH), 1551 (Str N-N), ^{1}H NMR: δ 1.91-2.50 (d 2H -CHCOOH), 3.40-3.77 (s 3H -CH_3), 7.35 (s 1H -NH), 7.86-9.00 (s 4H Pyridine).

Compound 1C (S-tryptophane)

λ_{max} (methanol): 239 nm; IR (KBr) cm^{-1}: 3048 (CH- Str aromatic in pyridine), 1458 (C=C and C=N Str ring in pyridine), 743 (C-H Str out of plane in pyridine), 2527 and 1559 (O-H and C=O Str in COOH), 3402 (Str N-H), 2966 (Str C-H), 847 (Str in C-N), 1659 (Str C=N(indole)), 1112 (Str C-C in CH_2COOH), 1585 (Str N-N), ^{1}H NMR: δ 7.03 (s 1H -NH), 11.13 (s 1H -COOH), 2.51-3.92 (m 3H CH,CH_2), 6.93-7.93 (s 5H Indole), 7.61-9.02 (s 4H Pyridine).

Compound 1D (2-aminoacetic acid)

λ_{max} (methanol): 249 nm; IR (KBr) cm^{-1}: 3022 (Str CH aromatic in pyridine), 1439 (Str C=C and C=N ring in pyridine), 687 (Str C-H out of plane in pyridine), 3007 and 1499 (Str O-H and C=O in COOH), 3096 (Str N-H), 2873 (Str C-H in CH_3), 1048 (Str C-N), 1391 (Str C-C in CH_2COOH), 1518 (Str N-N), ^{1}H NMR: δ 2.50-2.51 (d 3H CHCOOH), 3.58 (s 1H -H), 7.26 (s 1H -NH), 7.26-9.04 (s 4H Pyridine).

Compound 1E (3-aminopropanonic acid)

λ_{max} (methanol): 254 nm; IR (KBr) cm^{-1}: 2966 (Str CH aromatic in pyridine), 1555 (Str C=C and C=N ring in pyridine), 706 (Str C-H out of plane in pyridine), 2571 and 1585 (O-H and C=O in COOH), 3379 (Str N-H), 2880 (Str C-H in CH_3), 1417 (C-H in CH), 1383 (Str C-H in CH), 844 (Str C-N), 1339 (Str C-C in CHCOOH), 2929 (Str N-N), ^{1}H NMR: δ 1.91-2.50 (d 2H -CHCOOH), 3.40-3.77 (s 3H -CH_3), 7.35 (s 1H -NH), 7.86-9.00 (s 4H Pyridine).

Screening of Antibacterial Activity against Bacteria[27]

The process of screening involves determining the concentration of various derivatives. Drug plates were made by combining compounds at varying concentrations with various sterile nutritional agar media. *Escherichia coli* and *Staphylococcus aureus* were taken for the screening. On the drug plates with varying concentrations of chemicals, each microorganism was spot-injected. The plates were then incubated at 37°C for a minimum of 24 hr and a maximum of 72 hr. It was determined after 24 hr whether there had been any bacterial growth on the various plates. In accordance with NCCLS (National Committee for Laboratory Standards) recommendations, the compounds' Minimum Inhibitory Concentration (MIC) was ascertained against the bacterial strains.

Table 1: Physiochemical Properties of compounds and fused amino acids.

Comp.	Amino Acid Attached	Molecular Formula	Molecular weight	Yield (g)		MP (°C)	Solubility
				Method A	Method B		
1	--	$C_{10}H_{10}N_4O_2$	218.21	11.1	-	155-158	ACN
1A	S-isoleucine	$C_{16}H_{21}N_5O_3$	275.31	2.2	2.4	180-185	ACN
1B	S-alanine	$C_{13}H_{15}N_5O_3$	233.23	2.1	2.3	185-190	ACN
1C	S-tryptophane	$C_{19}H_{19}N_5O_4$	381.39	1.8	2.2	190-192	DCM
1D	2-aminoacetic acid	$C_{12}H_{13}N_5O_3$	219.2	2.0	2.8	175-180	Water
1E	3-amino propanoic acid	$C_{13}H_{15}N_5O_3$	289.29	2.3	2.5	180-180	Ethanol

Screening of antifungal activity against fungi[28]

Drug plates and varied sterile dextrose agar media were created, along with various compounds of varying concentrations. Strains of *Aspergillus niger* and *Candida albicans* were used. The plates were then cultured for fungus for a further seven days at 22°C. Different plates were examined to determine whether fungi had grown or not after being incubated for 24 hr. According to NCCLS criteria, the extract's Minimum Inhibitory Concentration (MIC) was evaluated for a variety of fungus strains (National Committee for Laboratory Standards).

Free radical scavenging assays

Diphenyl-Picrylhydrazyl radical scavenging (DPPH) assay was used to calculate the impact of standard medication and produced compound(s) on the DPPH radical. 1 mL of a chemical in methanol containing 0.02-0.1 mg of the sample was combined with 1 mL of a solution of 0.135 mM DPPH in methanol. After completely overtaxing the produced solution and leaving it in the dark for 30 min, it was measured at 517 nm using ascorbic acid as a reference.[29]

Computational Studies

Density Functional Theory

All energy values of the Lowest Unoccupied Molecular Orbitals (LUMO) and Highest Occupied Molecular Orbitals (HOMO) were computed by the GAMESS (General Atomic and Molecular Electronic Structure System) software.[30] In the calculation of simple energy, the Becke's three-parameter hybrid functional, the Lee-Yang-Parr correlation (B3LYP) functional[31] and the 6-31G (d, p) basis set were used in these molecular systems in gas phase, considering the neutral and singlet structures. The Hickel method[32] generated an initial estimate of molecular orbitals and electronic density. Consequently, the Self-Consistent Field (SCF) convergence was attributed by the Restricted Hartree-Fock (RHF) method,[31] which was limited to 30 iteration cycles

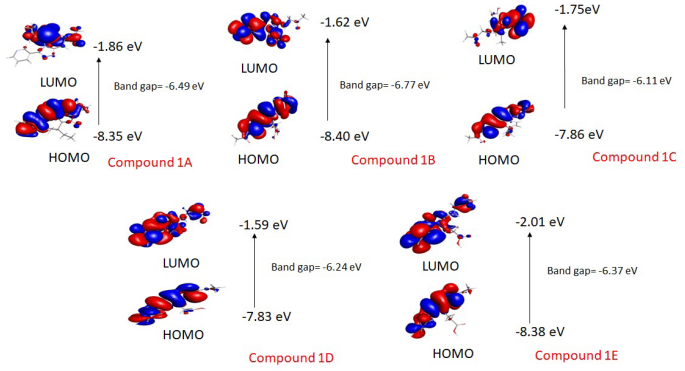


Figure 2: HOMO and LUMO potentials of the synthesized derivatives (1A-1E).

Molecular Properties and Pharmacokinetics

Mol-inspiration Chemo-informatics was used for calculating Octanol-Water Partition Coefficient (mi log P), number of atoms (n atoms), Topological Polar Surface Area (TPSA), Molecular Weight (MW), Hydrogen Bond Donors (HBD) and Hydrogen Bond Acceptors (HBA), Rotatable Bonds (NRB), Molecular Volume and Lipinski RO5 violations. The Swiss ADME tool which is available in http://www.swissadme.ch was used to check the bioavailability radar and assess various qualities like lipophilicity, drug similarities, medicinal chemistry and pharmacokinetics.

RESULTS

Compound (1) was synthesized from the conventional method, whereas compounds 1A, 1B, 1C, 1D, 1E were synthesized by two methods Method A and Method B, which gives different yields, A comparison of yields is shown in Table 1. Reaction completion time done by checking the reaction mixture after every 15 min for method A and after 60 sec for method B through TLC analysis and the gap was maintained and found suitable, details are shown in Table 2.

All synthesized compound(s) were subjected to anti-bacterial, anti-fungal and free radical scavenging assay. The results are shown in Table 3.

The E_{HOMO} and E_{LUMO}, respectively, represent the molecule's ability to give and receive electron density. All compounds' band gaps and HOMO and LUMO potentials are displayed in Figure 2.

In order to assess each compound's pharmacokinetic profile, physicochemical and topological parameters were estimated and listed in Figure 3. The parameters were calculated using the Swiss ADME web tool, it provides an interactive and user-friendly

Table 2: Reaction completion time.

Compound(s)	Reaction completion time*	
1	7 hr 15 min (reflux)	
	Method A	Method B
1A	2.0 hr	500 W (5X60 Sec)
1B	1.40 hr	500 W (5X60 Sec)
1C	1.30 hr	500 W (5X60 Sec)
1D	1.25 hr	500 W (5X60 Sec)
1E	2 hr	500 W (5X60 Sec)

*Reaction completion time done by checking the reaction mixture after every 15 min (Method A) and 60 sec (Method B) through TLC analysis.

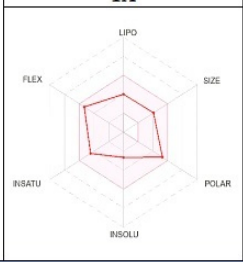
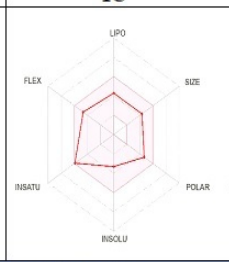
MOLECULAR PROPERTIES					
	1A	**1B**	**1C**	**1D**	**1E**
Bioavailability Radar					
Physicochemical Properties					
Num. heavy atoms	24	21	26	20	21
Num. atom. heavy atoms	11	11	17	11	11
Fraction Csp3	0.44	0.31	0.26	0.25	0.31
Num. rotatable bonds	8	6	7	6	7
Num. H-bond acceptors	6	6	5	6	6
Num. H-bond donors	2	2	2	2	2
Molar Refractivity	89.44	75.02	99.76	70.21	75.02
TPSA	110.00 Å²	110.00 Å²	92.93 Å²	110.00 Å²	110.00 Å²
Lipophilicity					
Log $P_{o/w}$ (iLOGP)	1.30	1.30	1.77	0.90	1.32
Log $P_{o/w}$ (XLOGP3)	1.51	0.18	2.02	-0.22	-0.48
Log $P_{o/w}$ (WLOGP)	1.82	0.80	2.66	0.23	0.62
Log $P_{o/w}$ (MLOGP)	0.42	-0.35	1.22	-0.22	0.06
Log $P_{o/w}$ (SILICOS-IT)	1.29	0.31	2.37	0.11	0.48
Consensus Log $P_{o/w}$	1.27	0.45	2.01	0.16	0.40
Pharmacokinetics					
GI absorption	High	High	High	High	High
BBB permeant	No	No	No	No	No
P-gp substrate	Yes	No	Yes	No	No
CYP1A2 inhibitor	No	No	No	No	No
CYP2C19 inhibitor	No	No	Yes	No	No
CYP2C9 inhibitor	No	No	No	No	No
CYP2D6 inhibitor	No	No	Yes	No	No
CYP3A4 inhibitor	No	No	Yes	No	No
Log K_p (skin permeation)	-7.25 cm/s	-7.94 cm/s	-7.01 cm/s	-8.14 cm/s	-8.41 cm/s
Drug likeness					
Lipinski	Yes; 0 violation	Yes; 0 violation	Yes; 0 violation	Yes; 0 violation	Yes; 0 violation
Ghose	Yes	Yes	Yes	Yes	Yes
Veber	Yes	Yes	Yes	Yes	Yes
Egan	Yes	Yes	Yes	Yes	Yes
Muegge	Yes	Yes	Yes	Yes	Yes
Bioavailability Score	0.56	0.56	0.55	0.56	0.56
Medicinal Chemistry					
PAINS	0 alert	0 alert	0 alert	0 alert	0 alert
Brenk	0 alert	0 alert	0 alert	0 alert	0 alert
Lead likeness	Yes	Yes	Yes	Yes	Yes
Synthetic accessibility	3.79	3.24	3.47	2.69	2.77

Figure 3: Molecular Properties and Pharmacokinetics of synthesized compounds (1A-1E).

Table 3: Results of activity of antimicrobial, antifungal and free radical scavenging activity.

Compound	Zone of inhibition (mm)						DPPH free radical scavenging Activity				
	Bacterial Stain				Fungal Stain						
	S. aureus (gram positive)		*E. coli* (gram negative)		*A. niger*	*C. albicans*					
Concentrations	100 µg/mL	50 µg/mL	100 µg/mL	50 µg/mL			0.02	0.04	0.06	0.08	0.1
1A	21	11	20	10	20	18	45.43	52.23	67.49	74.79	83.58
1B	26	13	21	10	21	19	33.83	55.38	64.67	77.33	81.44
1C	19	10	19	09	10	07	31.67	34.99	40.96	48.42	51.74
1D	11	12	14	05	14	11	38.47	40.13	58.70	63.34	67.99
1E	21	10	14	06	16	12	25.53	32.00	34.16	41.62	54.39
Ciprofloxacin	32	17	28	14	-	-	-	-	-	-	-
Itraconazole	-	-	-	-	30	28	-	-	-	-	-
Ascorbic acid	-	-	-	-	-	-	74.62%	77.94%	81.09%	83.58%	80.76%

visualization tool, multi-molecule calculation, many input methods, and the ability to see and store results for individual molecules.

DISCUSSION

Chemistry

With the method, a high yield or nearly the same yield was achieved in a noticeably shorter amount of time (5-15 min). A unique series of substituted amino acids in 1,3,4-oxadiazole derivatives were produced as an Unnatural amino acid as a result of the scheme. Scheme shows the connection of five distinct amino acids listed in Table 1. To represent the process of unnatural amino acid production involved in the final step of target molecule synthesis. When groups like -NH_2 and -OH are present, which donate electrons, the electron donation state may develop. The inclusion of electron-withdrawing groups like -NO_2 and -Cl can enhance the final compound yield, although this could lead to a drop in the yield of the final product. It was found that aryl acids belonging to the electron-releasing group (-OCH_3, -OH) accelerated the process more rapidly than those belonging to the electron-withdrawing group (-NO_2, -Cl). Table 1 summarizes the synthesized compounds' physiochemical characteristics. When the total yield of all the synthesized compounds was compared between Method A and Method B, it was found to be good. To find out how pure the produced chemicals were, a TLC analysis was performed. Using mass spectrometers, 1H-NMR, and IR, the structural properties of the generated compounds were verified. The band gap is the difference between the two energy levels which provides a molecular reactivity estimate. The reactivity of the molecule is inversely related to the distance between those energy levels. Compounds 1A and 1b were found to be more reactive and have more band gaps as compared to other compounds. Thus, both showed good activity in free radical scavenging assay by DPPH. The Bioavailability Radar data yields a graphical representation of a compound's drug-likeness. For all criteria, Compounds 1A and 1B are within the ideal range. Furthermore, 1A and 1B exhibit favorable synthetic accessibility and medicinal chemistry, all of which are critical for medication. Additionally, both have significant blood-brain barrier permeability and Gastrointestinal absorption (GI).

Pharmacology

Human digestive tracts are often home to *E. coli*, a kind of bacteria. In addition to food poisoning, this bacterium may also cause other ailments. Numerous diseases, such as septic arthritis, staphylococcal endocarditis, and pneumonia, have been associated with S. aureus. Consequently, the likelihood that these infections may negatively impact people's health is high. Studies were carried out to confirm the idea that many of the recently synthesized derivatives of amino acid fused-1,3,4-oxadiazole had antibacterial activity. The compounds 1A and 1B, which had the maximum activity when compared to all of the other compounds, were the most effective against these pathogens.

Every one of the produced compounds was tested to see if it had any antifungal action against A. Niger and Candida albicans. To achieve this, an average inhibition zone for each component was found. The control was the medication itraconazole. Maximum activity against *A. Niger* and *Candida albicans* was demonstrated by the molecules 1A and 1B, but at a lower efficacy than the standard. When tested against the fungi under investigation, the antifungal activity of the remaining chemicals ranged from moderate to poor. These compounds have higher levels of activity due to the amino substituent attached to the moiety associated with the oxadiazole ring than other compounds with structurally similar structures. Results predict that biological activity was higher when an electron donor group (-OCH_3, -OH, or -NH_2) was present in the ring. Our studies are under a previous study which stated 1,3,4-oxadiazoles, a heterocyclic five-membered

ring plays a vital role in developing newer medicinal compounds for treating various biological activities, such as the proliferation of cells, tuberculosis, allergy, viral diseases.[33-35]

CONCLUSION

Modern technologies in chemistry like green synthesis are more valuable in addition to traditional chemical synthesis methods. The above-mentioned method(s) promise the synthesis of amino acid(s) fused 1,3,4-Oxadiazole derivatives as an unnatural amino acid with an improved yield. Structures were confirmed by IR, NMR, and UV analysis. The compound(s) were evaluated by known methods against standard compounds. *In vitro* studies like the determination of molecular properties with their quantum studies were done to establish a relation with produced results. Without a doubt, this new synthetic approach to creating unnatural amino acids with oxadiazoles will continue to pave the way for peptidomimetic research and, by extension, the development of new drugs. In the future, compounds may be tested further for potential hepatoprotective and anticancer effects.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

UAA's: Unnatural Amino Acids; **UV:** Ultraviolet; **DPPH:** 2,2-diphenyl-1-picrylhyrazyl; **nm.:** Nanometre; **TLC:** Thin Layer Chromatography; **IR:** Infra-Red; **KBr:** Potassium Bromide; **MHz:** Megahertz; **NMR:** Nuclear Magnetic Resonance; **DMSO:** Dimethyl-sulfoxide; **mL:** Milliliter; **mM:** Millimolar; **Abs:** Absorption; **Str:** Stretching.

SUMMARY

In this study, oxadiazole derivatives as an unnatural amino acid were attempted to synthesized, followed by the determination of molecular properties, quantum studies, and correlated activities. Amino acids have an essential role in the biological system. In the hopes of creating novel compounds that might be referred to as "unnatural amino acids," amino acids are iso-sterically attached to an oxadiazole scaffold. The microwave method yielded the highest results and all synthesized compounds showed optimum activity with justified quantum studies and molecular properties. The study promotes the expanding field of unnatural amino acid synthesis and provides a simple procedure for making these derivatives and related substances. The results may play a significant role in the future development of newer therapeutic medications.

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