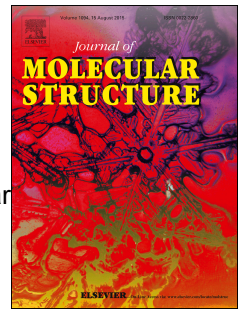
# Accepted Manuscript

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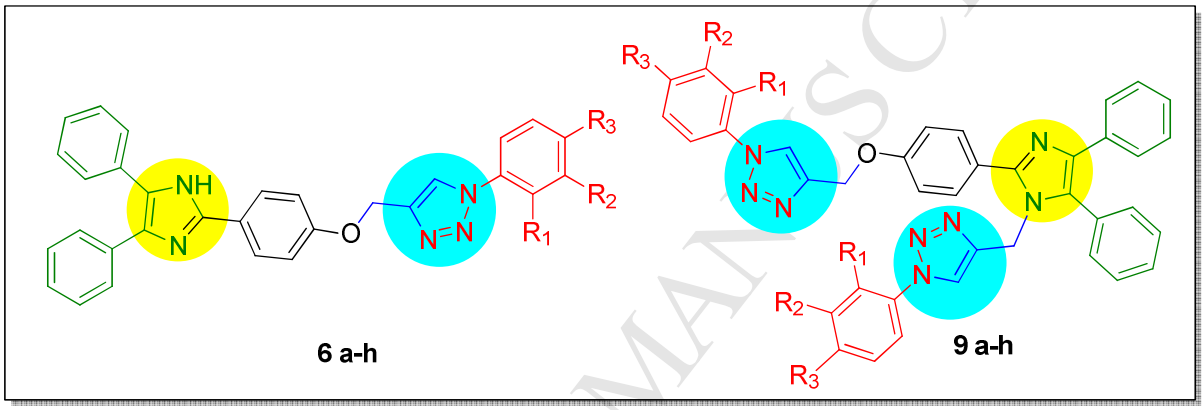

# Design and synthesis of imidazolo-1, 2 ,3-triazoles hybrid compounds by microwave-assisted method: Evaluation as an antioxidant and antimicrobial agents and molecular docking studies

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**Abstract:**

The present manuscript describes synthesis of a new class of antimicrobial and antioxidant agents (imidazole linked 1,2,3-triazole hybrid compounds) and screened for their *in-vitro* studies for antimicrobial and antioxidant activity. In the present investigation, We have developed a simple and convenient method to design and synthesize imidazole linked mono-triazole (6) as well as imidazole linked bis-triazole (9**)** derivatives by using the click reaction followed by multi component reaction for compounds (6) and *vice-versa* for the synthesis of compounds (9**)**. The reactions were carried out by two different techniques, conventional heating and microwave irradiation. Microwave irradiation method offers excellent yields, lesser reaction times and environmental friendly reactions. These compounds were studied for their antimicrobial, antioxidant and molecular docking studies using Schrodinger suite. For their *in-vitro* antimicrobial activity against gram-positive, gram-negative strains; preliminary results indicated that some target compounds exhibited promising antimicrobial potency especially **6c, 6h, 9d, 9e** and **9h**. Further these compounds were tested for their *in-vitro* antioxidant activity using four different methods few of them are exhibited excellent antioxidant activity especially **6d, 6h, 9a, 9c, 9e, 9f, 9h**. In addition these compounds activity relationship were further supported by *in-silico* molecular docking studies some of the active compounds **6c, 6h, 9d** and **9e** showed maximum dock score.

**Key words:** Imidazole, 1, 2, 3-triazole, anti-microbial, anti-oxidant, and molecular docking**.**

## 1. Introduction:

Imidazole and triazole derivatives are widely used as an important class for many natural and synthetic compounds to displace diverse range of biological activities. Due to their biological importance of Imidazole and triazole derivatives widely used for many clinical applications such as mainly antimicrobial[1], anti-inflammatory,[2] antioxidant agent,[3] anticancer,[4] antipyretic,[5] anticonvulsant,[6] antidepressant,[7] antimalarial,[8] antitumor,[9] antiviral,[10] (Fig.1). In the present manuscript synthesis the biological studies of Imidazole and triazole derivatives were mainly involved in antimicrobial and antioxidant studies. The antimicrobial agents are the basic medicines for human and animal health, and are considered as "miracle drugs" to treat infections caused by microorganisms, fungi, parasites, and viruses. Antimicrobial susceptibility testing can be used for drug discovery, epidemiology and prediction of therapeutic outcome. In meanwhile, antioxidants that can scavenge reactive chemical element species is also of economical worth in preventing the diseases like autoimmune, cardiovascular and neurovascular diseases.

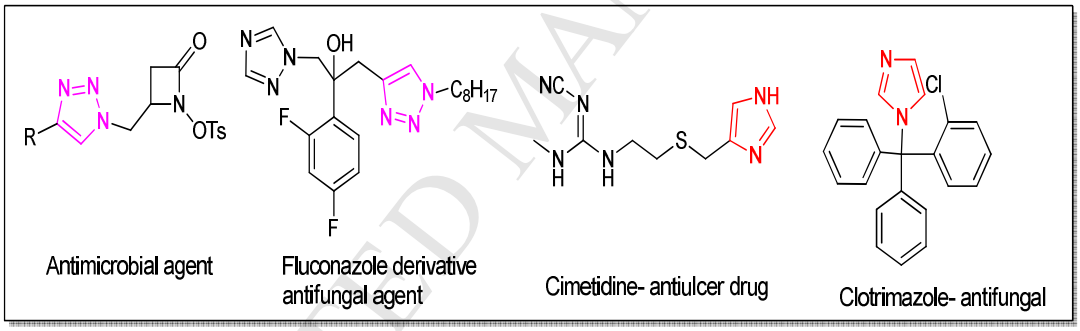



**Figure. 1**

These health risks encourages us to develop and modification of antioxidant, antimicrobial agents for developing a convenient method for the synthesis of imidazole linked 1, 2, 3-triazole hybrids with high potency, low toxicity and broad spectrum. Therefore, the synthesis of imidazole linked 1,2,3-triazole hybrid compounds in the pursuit of novel and potential compounds to become a new drugs for antimicrobial, antioxidant agents. In the present investigation, we have designed and synthesized imidazole linked mono-triazole (**6a-h**) as well as imidazole linked bis-triazole (**9a-h)** derivatives by using the click reaction followed by multi component reaction (MCR) for compounds (**6a-h**) and *vice-versa* for compounds (**9a-h)**. The reactions were carried out by two different techniques, conventional heating and microwave irradiation.Microwave irradiation method offers excellent yields, lesser the reaction times and environmental friendly reactions. These compounds were studied for their

antimicrobial, antioxidant and molecular docking studies using Schrodinger suite. For their *in-vitro* antimicrobial activity against gram-positive, gram-negative strains; preliminary results indicated that some target compounds exhibited promising antimicrobial potency especially **6c, 6h, 9d, 9e** and **9h**. Further these compounds were tested for their *in-vitro* antioxidant activity using four different methods few of them are exhibited excellent antioxidant activity especially **6d, 6h, 9a, 9c, 9e, 9f, 9h**. In addition these compounds activity relationship were further supported by *in-silico* molecular docking studies some of the active compounds **6c, 6h, 9d** and **9e** showed maximum dock score.

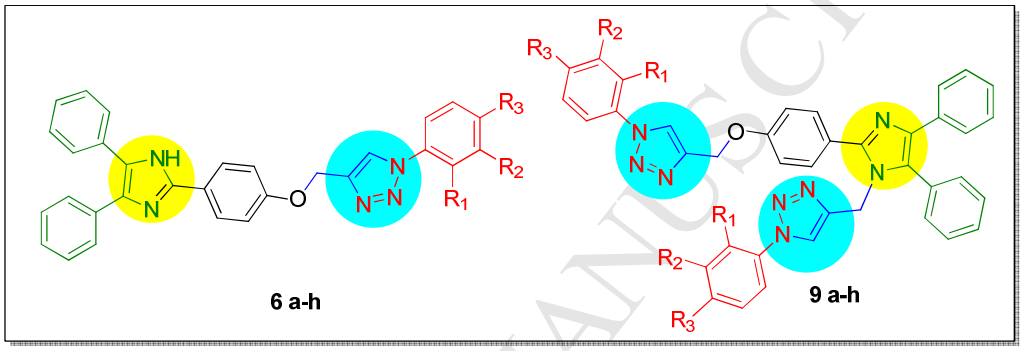
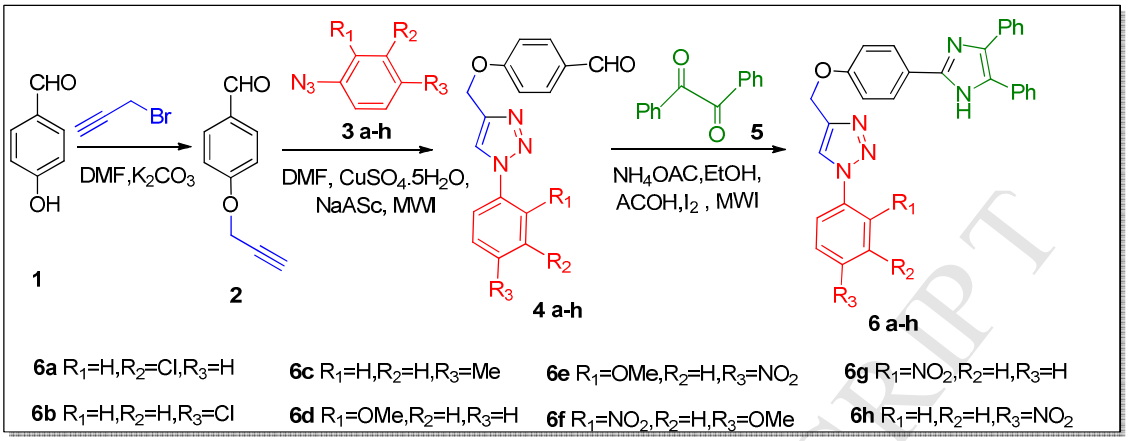



**Figure 2:** Compounds (**6a-h**) and (**9a-h**)

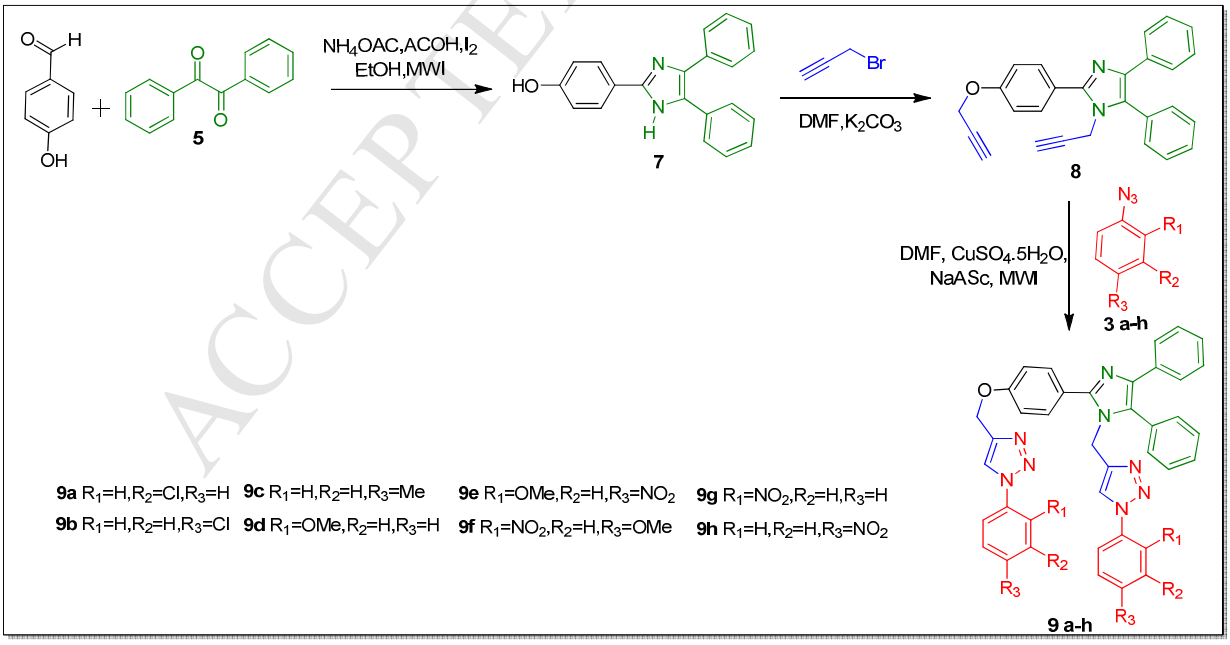
## 2. Results and discussion:

**2.1 Synthesis of imidazole linked 1,2,3-triazole compounds:** We have developed a simple and convenient method for the synthesis of imidazole linked 1,2,3-triazole compounds (**6a-h** & **9a-h**) in two different methods. Compounds which contains triazole and imidazole ring (**6a-h)** (Fig. 2), synthesis first started with proporgylation of 4-hydroxy benzaldehyde **(1)** and then click reaction with aryl azides **(3a-h)** at terminal alkyne position obtained triazole ring of 4-hydroxy benzaldehyde compounds (**4a-h)**, and performed one-pot multi component reaction for condensation of benzil (**5**), benzaldehyde of compounds (**4a-h)** and ammonium acetate in presence of ethanol, acetic acid in iodine under the microwave irradiation method afforded our targeted compounds (**6a-h) (**Scheme-1), respectively, in good to excellent yields.




**Scheme 1: Synthesis of compounds (6a-h)**

**2.2 Synthesis of compounds (9a-h):** In this current method, we have fallowed our previous synthetic route of *vice versa* for the synthesis of compounds (**9a-h**). In this method synthesis first started with one-pot multi component reaction of 4-hydroxy benzaldehyde **(1)**, benzil (**5**) and ammonium acetate in presence of ethanol, acetic acid in iodine under microwave methods offered compounds **(7)** followed by proporgylation of compound **(7)** and bis proporgylation takes place at position of free O-H and N-H groups yielded to bis-propargylated compound **(8)** which on further click reaction of aryl azides **(3a-h)** with bis-propargylated compound **(8)** in this final reaction observed compounds with imidazole linked bis-triazole compounds **(9a-h)** (Scheme-2), respectively, in good to excellent yields.




**Scheme 2: Synthesis of compounds (9a-h)**

## 2.3 Biological activity

In view of various biological and pharmacological importance of various series of imidazoles and 1, 2, 3-triazoles, it is felt worthy to evaluate **(6a-h & 9a-h)** derivatives for attainable activities. These compounds thus were screened for antimicrobial, antioxidant and molecular docking studies using Schrodinger suite. The details of these studies along with the observations were recorded in tables.

### 2.3.1. Antimicrobial activity

The antimicrobial activities of all the synthesized imidazole-1,2,3-triazole hybrid derivatives **(6a-h & 9a-h)** were tested all the synthesized molecules and find the MIC values against 6 microbial strains: *S. aureus*, *B. cereus* ;*E. coli* , *P.vulgaris*; *A. fumigates* and *C.albicans*. The results from the analysis of antimicrobial effects measured as (MIC) Minimum Inhibitory concentrations which are summarized in Table 1. All tested compounds showed good MIC values (1 mg /mL), against gram +ve and gram -ve bacteria compared to the reference drug ampicillin (100µg /mL). The tested compounds showed sensible to glorious antimicrobial activities against the strains, similar to the quality drug Ampicillin and fluconazole as shown in Table 1. Out of the various compounds tested, compounds **6c**, **6h**, **9d, 9e** and **9h** inhibited microrobial growth very effectively compared to others in the series with MIC values ranging from 8.86 to 33.25µg/mL. The best potent anti-bacterial and anti-fungal compounds **9d** ($R_1$=$OCH_3$)**,** and **9e** ($R_1$=$OCH_3$, $R_3$=$NO_2$ respectively). It was observed that the presence of the 9d $R_1$= OMe, 9e $R_1$=OMe, $R_3$= $NO_2$ $R_1$and $R_3$ position of the 1-phenyl-1*H*-[1, 2, 3] triazol-4-ylcore brought about an enhancement of the antimicrobial potency. moreover **6h** ($R_3$=$NO_2$)**, 6c** ($R_3$=$CH_3$)**,** showed good activity, **9h** ($R_3$=$NO_2$)showed moderate activity antibacterial and antifungal activity and remaining compounds showed poor activity .It can be concluded that all the synthesized imidazole-1,2,3-triazole hybrid derivatives **(6a-h & 9a-h ) 9d, 9e**showed excellent activity than compounds **6h**, **6c** showed good activity compared to **9h**.

**Table 1:** Minimum inhibition showing antimicrobial activities of the compounds compared with reference drugs, results given in µg/ml sample

| Compounds | *S. aureus* | *B. cereus* | *E. coli* | *P. vulgaris* | *A. fumigatus* | *C. albicans* |
|---|---|---|---|---|---|---|
| 6a | 45.78 | 40.9 | 32.12 | 43.85 | 46.32 | 35.7 |
| 6b | 49.23 | 42.71 | 31.23 | 35.29 | 51.83 | 39.01 |
| **6c** | **18.21** | **14.25** | **15.62** | **11.58** | **29.25** | **33.25** |
| 6d | 31.37 | 35.75 | 31.5 | 25.65 | 37.95 | 31.75 |
| 6e | 100 | 78.4 | 71.29 | 81.11 | 121.39 | 105.47 |
| 6f | 38.72 | 29.56 | 32.78 | 29.76 | 38.73 | 39.5 |
| 6g | 75.78 | 65.71 | 88.5 | 66.85 | 74.5 | 83.7 |
| **6h** | **15.45** | **13.3** | **9.78** | **23.75** | **28.85** | **31.9** |
| 9a | 77.35 | 80.91 | 79.37 | 89.92 | 65.73 | 65.81 |
| 9b | 72.5 | 73.76 | 66.85 | 75.75 | 80.83 | 69.5 |
| 9c | 45.47 | 37.72 | 41.35 | 41.75 | 35.5 | 40.33 |
| **9d** | **13.78** | **17.89** | **25.5** | **31.75** | **19.75** | **23.65** |
| **9e** | **16.13** | **9.41** | **8.86** | **9.63** | **20.35** | **21.86** |
| 9f | 45.75 | 36.95 | 57.91 | 40.5 | 42.41 | 35.67 |
| 9g | 75.76 | 68.5 | 73.79 | 70.79 | 65.75 | 73.9 |
| **9h** | **30.79** | **33.83** | **32.38** | **35.78** | **31.63** | **28.2** |
| Ampicillin | 15.5 | 8.35 | 10.75 | 9.45 | - | - |
| Fluconazole | - | - | - | - | 21.65 | 25.3 |

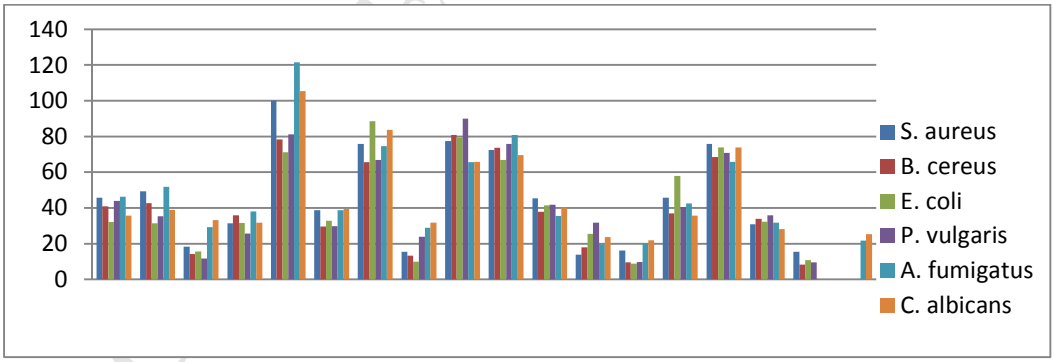



**Fig. 3** Graphical representation of MICs of compounds **6a-h** and **9a-h**

## 2.3.2 Antioxidant activity:

### 2.3.2.1 DPPH radical scavenging activity:

The antioxidant activity of all synthesized compounds were measured against 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical. Compound **9e** ($R_1$=$OCH_3$, $R_3$=$NO_2$ respectively) was the excellent

radical scavenger with associate % of inhibition worth of 250µg/mL. Furthermore compound **9c** ($R_3$=$CH_3$) showed a best radical scavenging activity with % of inhibition at 250µg/mL. Compounds **6h, 9h** ($R_3$=$NO_2$) conjointly showed good scavenging activities with 10, 50, 100, 250µg/mL

**Table 2:** DPPH radical scavenging activity analysis of **6a-h** and **9a-h**

| Compounds | 10µg | 50µg | 100µg | 250 µg |
|---|---|---|---|---|
| Standard | 85 | 89 | 93 | 97 |
| 6a | 57 | 71 | 81 | 94 |
| 6b | 49 | 55 | 59 | 63 |
| 6c | 42 | 53 | 65 | 69 |
| 6d | 53 | 59 | 64 | 93 |
| 6e | 35 | 42 | 55 | 63 |
| 6f | 44 | 61 | 79 | 90 |
| 6g | 41 | 49 | 53 | 61 |
| **6h** | **67** | **75** | **83** | **91** |
| 9a | 55 | 63 | 71 | 87 |
| 9b | 60 | 69 | 76 | 89 |
| **9c** | **69** | **78** | **81** | **95** |
| 9d | 48 | 67 | 79 | 85 |
| **9e** | **71** | **79** | **85** | **96** |
| 9f | 33 | 44 | 55 | 61 |
| 9g | 41 | 47 | 59 | 62 |
| **9h** | **66** | **74** | **81** | **90** |

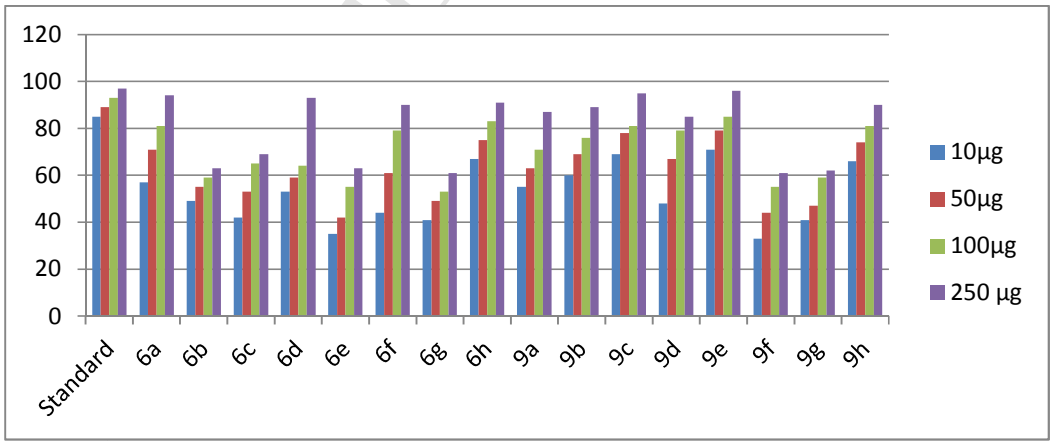



**Fig. 4** Graphical representation of DPPH radical scavenging activity of compounds **6a-h** and **9a-h**

### 2.3.2.2 Hydrogen peroxide radical scavenging activity

Hydrogen peroxide produces hydroxyl radicals in cells. Scavenging of these radicals by the test drug is used as a test for antioxidant activity. Compounds **9c** ($R_3$=$CH_3$), **9h** ($R_1$=$NO_2$, $R_3$= OMe), was the strongest radical scavenger with associate % of inhibition worth of 250µg/mL. Furthermore compound **6f, 6b** showed a good radical scavenging activity with % of inhibition at250µg/mL.

**Table 3:** Hydrogen peroxide radical scavenging activity of **6a-h** and **9a-h**

| Compounds | 10µg | 50µg | 100µg | 250µg |
|---|---|---|---|---|
| Standard | 83 | 91 | 95 | 98 |
| 6a | 49 | 67 | 75 | 87 |
| 6b | 59 | 73 | 81 | 92 |
| 6c | 40 | 49 | 55 | 57 |
| 6d | 47 | 65 | 72 | 89 |
| 6e | 31 | 43 | 49 | 56 |
| 6f | 52 | 73 | 81 | 92 |
| 6g | 35 | 43 | 51 | 63 |
| 6h | 57 | 68 | 75 | 88 |
| 9a | 51 | 63 | 78 | 91 |
| 9b | 54 | 71 | 82 | 90 |
| **9c** | **71** | **88** | **91** | **96** |
| 9d | 57 | 73 | 85 | 94 |
| 9e | 37 | 45 | 52 | 59 |
| **9f** | **65** | **78** | **86** | **94** |
| 9g | 38 | 45 | 53 | 55 |
| 9h | 57 | 65 | 78 | 86 |

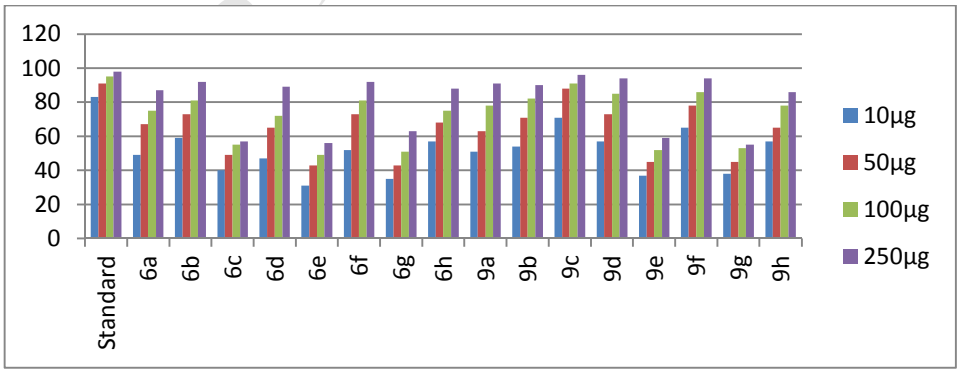



**Fig. 5** Graphical representation of Hydrogen peroxide radical scavenging activity of compounds **6a-h** and **9a-h**

### 2.3.2.3 Nitric oxide scavenging activity assay

Nitric oxide radical scavenging activity was determined according to the method reported by Garratt. Sodium nitroprusside in aqueous solution at physiological pH spontaneously generates nitric oxide, which interacts with oxygen to produce nitrite ions. Compound **6h** ($R_3$=$NO_2$) was the excellent nitric oxide radical scavenger with associate % of inhibition worth of 250µg /mL. Furthermore compound **9a** ($R_2$=Cl), **9c** ($R_3$=$CH_3$), **9h** ($R_3$=$NO_2$) showed a good nitric oxide radical scavenging activity with % of inhibition at seventy four 250µg/mL.

**Table 4:** Nitric oxide radical scavenging activity of **6a-h** and **9a-h**

| | **10µg** | **50µg** | **100µg** | **250µg** |
|---|---|---|---|---|
| **Standard** | 81 | 86 | 91 | 96 |
| 6a | 49 | 55 | 63 | 78 |
| 6b | 54 | 69 | 75 | 89 |
| 6c | 31 | 37 | 44 | 51 |
| 6d | 56 | 68 | 79 | 85 |
| 6e | 29 | 36 | 41 | 47 |
| 6f | 48 | 56 | 67 | 74 |
| 6g | 23 | 32 | 39 | 43 |
| **6h** | **61** | **77** | **86** | **95** |
| **9a** | **65** | **75** | **82** | **89** |
| 9b | 57 | 69 | 79 | 87 |
| **9c** | **68** | **79** | **88** | **91** |
| 9d | 57 | 68 | 75 | 88 |
| 9e | 25 | 37 | 42 | 46 |
| 9f | 48 | 55 | 67 | 78 |
| 9g | 21 | 27 | 33 | 39 |
| **9h** | **67** | **65** | **77** | **86** |

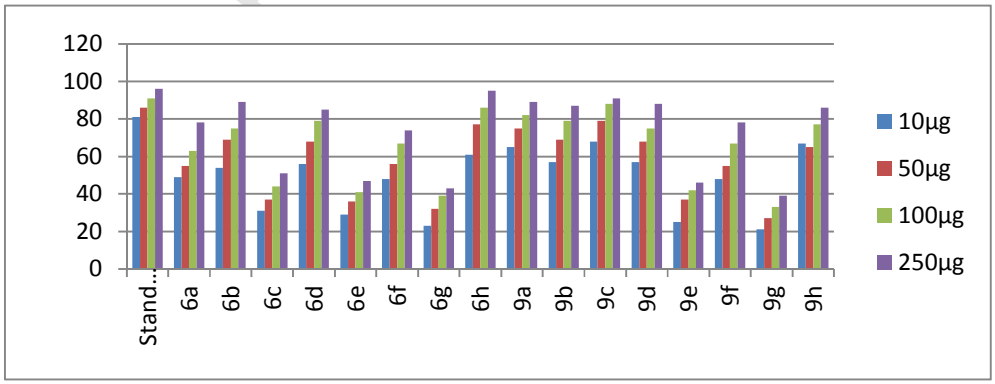



Fig6: Graphical representation of **Nitric** oxide radical scavenging activity of Compounds **6a-h** and **9a-h**

### 2.3.2.4 Reducing power assay (FRAP)

The synthesized compounds (0.75 ml) at various concentrations was mixed with 0.75 mL of phosphate buffer (0.2 M ,pH 6.6) and 0.75 mL of potassium hexacyanoferrate [$K_3Fe(CN)_6$] (1%, w/v), followed by incubating at 50$^oC$ in a water bath for 20 min. The absorbance at 700 nm was measured as the reducing power. Higher absorbance of the reaction mixture indicated greater reducing power. Compound **9c** ($R_3$=$CH_3$ is substituted phenyl ring) was the excellent Reducing power assay% of inhibition worth of 250µg /mL. Further compounds **6d** ($R_1$=$OCH_3$), **9d** ($R_1$=$OCH_3$), **9h** ($R_3$=$NO_2$) showed good Reducing power assay with % of inhibition at 250µg/mL.

**Table 5:** FRAP oxide radical scavenging activityof**6a-h** and **9a-h**

| | 10µg | 50µg | 100µg | 250µg |
|---|---|---|---|---|
| Standard | 88 | 92 | 95 | 99 |
| 6a | 47 | 64 | 78 | 87 |
| 6b | 51 | 67 | 79 | 93 |
| 6c | 31 | 39 | 43 | 47 |
| **6d** | **63** | **77** | **83** | **92** |
| 6e | 22 | 27 | 32 | 38 |
| 6f | 57 | 68 | 77 | 85 |
| 6g | 27 | 33 | 40 | 45 |
| **6h** | 49 | 58 | 69 | 87 |
| **9a** | 56 | 63 | 75 | 89 |
| 9b | 49 | 58 | 67 | 85 |
| **9c** | **65** | **71** | **84** | **97** |
| 9d | **64** | **79** | **86** | **91** |
| 9e | 30 | 37 | 45 | 50 |
| 9f | 45 | 53 | 62 | 85 |
| 9g | 31 | 39 | 43 | 48 |
| **9h** | **60** | **69** | **78** | **87** |

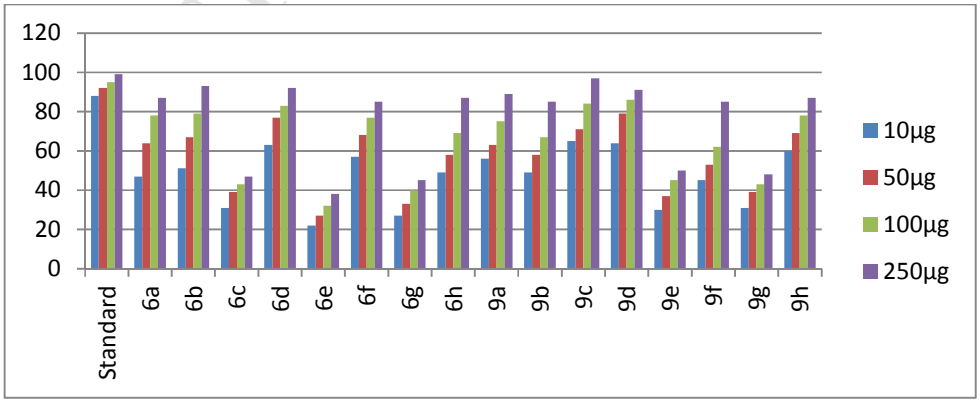



**Fig 7**: Graphical representation of FRAP oxide radical scavenging activity of Compounds **6a-h** and **9a-h**

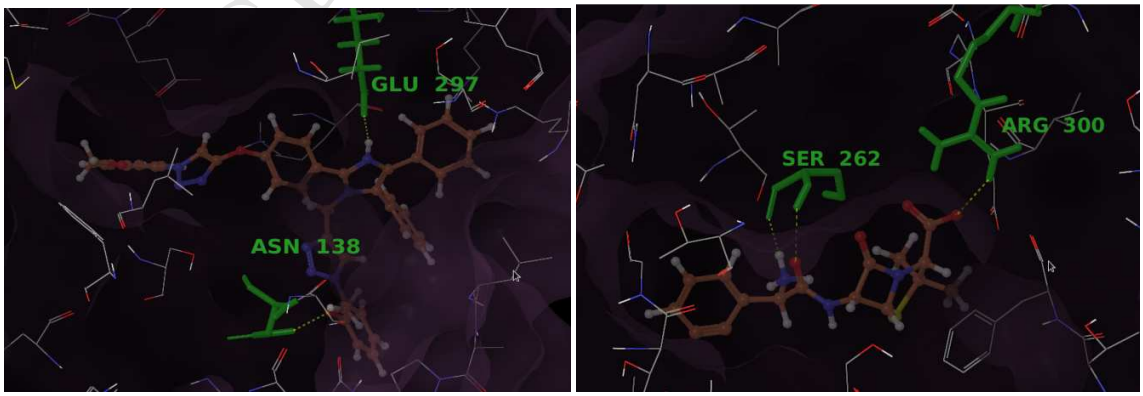
### 2.3.2.5 *In-Silico* Molecular Docking Studies:

Considering the results obtained from antimicrobial study, it was thought worthy to perform molecular docking studies by substantiating the *in-vivo* results with *in-silico* studies**.** The comparative docking of Penicillin binding protein 4and *E.coli* Penicillin Binding Protein 6with compounds 6c, 9d, 6h, and 9e and the standard Ampicillin exhibited good affinity.

**Table 6**: Dock score of synthesized molecules **6a-h and 9a-h**from Glide Docking**:**

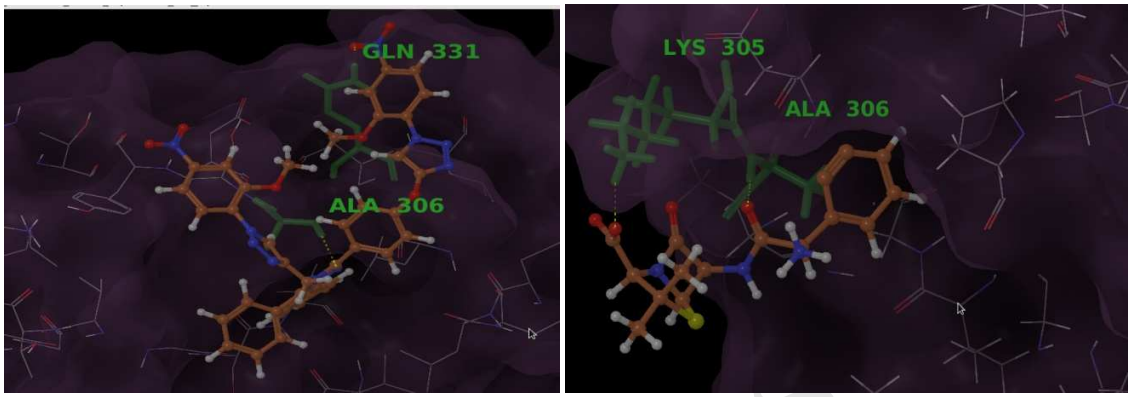
| compounds | *Staphylococcus aureus* PDB ID:3HUN | *Escherichia coli* PDB ID:3ITA |
|---|---|---|
| | **Dock score (K cal/mol)** | **Dock score (K cal/mol)** |
| **6a** | -3.660 | -3.101 |
| **6b** | -3.471 | -2.785 |
| **6c** | **-6.131** | -3.043 |
| **6d** | -3.570 | -2.470 |
| **6e** | -4.077 | -3.092 |
| **6f** | -3.667 | -2.958 |
| **6g** | -3.458 | -2.351 |
| **6h** | -3.546 | **-4.224** |
| **9a** | -4.484 | -3.367 |
| **9b** | -4.289 | -2.836 |
| **9c** | -3.767 | -3.090 |
| **9d** | **-7.148** | -2.900 |
| **9e** | -4.385 | **-4.396** |
| **9f** | -4.347 | -2.814 |
| **9g** | -4.518 | -3.272 |
| **9h** | -3.923 | -3.181 |
| **Ampicillin** | **-7.730** | **-4.883** |

**Fig. 8** Docked pose of **9d**(a) and **Ampicillin** (b) in the protein active site. Showing the hydrogen bond interaction (yellow lines) with GLU 297, ASN 138 and ARG 300, SER 262 respectively in *Staphylococcus aureus* (PDB.ID-3HUN).




**(a)** **(b)**

**Fig. 9** Docked pose of **9e** (a) and **Ampicillin** (b) in the protein active site. Showing the hydrogen bond interaction (yellow lines) with ALA 306, GLN 331 and ALA 306 , LYS 305respectively in *E.Coli* (PDB.ID3ITA).




**(a)** **(b)**

**Figure 10:** Docked pose **6c** (a) and **6h** (b) in the protein active site of Staphylococcus aureus (PDB.ID-3HUN), E.coli (PDB.ID-3ITA) respectively

**(a)** **(b)**

## 3. Conclusions:

In conclusion, we have synthesized a novel series of imidazole based 1,2,3-riazole moites by using click reaction followed by MCR and *vice versa* starting from 4-hydroxy benzaldehyde and all the newly synthesized compounds were confirmed by $^{1}$H NMR $^{13}$C NMR, IR and mass spectra. *in- vitro* antioxidant and anti-microbial activity evaluation showed that most of the synthesized imidazole -1,2,3-triazole hybrids exhibited good to excellent activity. These results clearly shows that imidazol-1,2,3 -triazole motifs have biological significance further optimization of these identified compounds

as well as their structural modifications are in progress in order to enhance the efficacy against above activities. Microwave irradiation method was the best method as compared with conventional heating method, because it offered excellent yields, reduced the reaction times and also environmental friendly reactions.

## 4. Experimental:

### 4.1 General experimental methods:

All the reactions were performed in oven dried apparatus. Reactions were monitored by thin layer chromatography (TLC) on silica gel plates (60 $F_{254}$), visualizing with ultraviolet light/ iodine vapours, column chromatography was performed on silica gel (60-120 mesh) using distilled hexane and ethyl acetate solvents.$^{1}$H NMR and $^{13}$C NMR spectra were determined in $CDCl_3$ and some of in DMSO by using 400 and 100 MHz spectrometers respectively (Instrument Bruker Avance II 400MHz). Mass spectra were recorded on QSTAR XL GCMS mass spectrometer. Infrared spectra were recorded on a shimadzu FT-IR-8400s spectrometer. Melting points were determined in open glass capillary tube on a Gallen-Kamp MFB-595 apparatus and were uncorrected.

**4.2.1** General procedure for the preparation of **4-((1-aryl-1H-1,2,3-triazole)methoxy) benzaldehydes ( 4a-h):**

The synthesis of above compounds **(4a-h)** compounds we started with 4-hydroxy –benzaldehyde **(1)** was propargylated by propargyl bromide in dry DMF and dry $K_2CO_3$ 25-30 $^{o}$C under stirring affording the o-propargylated benzaldehyde (**2**) in high yields. The o-propargylated benzaldehyde **(2)** were reacted with different aryl azides **(3a-h)** using Click reaction in $CuSO_4 \cdot 5H_2O$, Sodium ascorbate to form 1,2,3-triazole containing benzaldehyde**(4a-h)** was done according to the previous [11].

**4.2.2** General procedure for the preparation of **4-((4-(4,5-diphenyl-1H-imidazol-2-yl)phenoxy)methyl)-1-aryl-1H-1,2,3-triazoles (6a-h)** using the click followed by MCR reaction**:**

The synthesis of title compounds **(6a-h)** was performed in two different techniques (Scheme-**1**):

**a. Conventional method:**

The synthesis of title compounds **(6a-h)** (Scheme-**1**):To a stirred mixture of 4-((1-aryl-1H-1,2,3-triazol-4-yl)methoxy) benzaldehydes **(4a-h)** (0.2 mmol), benzil (**5**) (0.2 mmol) and ammonium acetate (0.8 mmol) in 5 ml ethanol taken in a 100 ml round bottomed flasks catalytic amounts of

Iodine and acetic acid were added simultaneously. The reaction vessels were fitted to a reflux condensers and refluxed at 80°C for 4-5 hours. The completion of reactions were monitored by TLC. After the completion of reactions the contents of the flasks were cooled to room temperature and dropped in a 100 ml beakers containing crushed ice. Solids obtained at the bottom was filtered under buchner funnel and dried in vacuum at reduced pressure to yield crude compounds which were purified by column chromatography using hexane/ ethyl acetate (1:3 v/v) to afford 4-((4-(4,5-diphenyl-1H-imidazol-2-yl)phenoxy)methyl)-1-aryl-1H-1,2,3-triazoles **(6a-h)** gave moderate yields 60- 64%.

**b. Microwave method:**

To the mixture of 4-((1-aryl-1H-1,2,3-triazol-4-yl)methoxy)benzaldehydes **(4a-h)** (0.2 mmol), benzil (**5**) (0.2 mmol) and ammonium acetate (0.8 mmol) in 5 ml ethanol taken in a 100 ml beakers catalytic amounts of Iodine and acetic acid were added and treated under microwave irradiation at 180 W for 3-5 min. The completions of reactions were monitored by TLC at regular intervals of 30 sec. After the completion of reactions the contents of the flasks were cooled to room temperature and dropped in a 100 ml beakers containing crushed ice. Solids obtained at the bottom was filtered under buchner funnel and dried in vacuum at reduced pressure to yield crude compounds which were purified by column chromatography using hexane/ ethyl acetate (1:3 v/v) to afford **4-((4-(4,5-diphenyl-1H-imidazol-2-yl)phenoxy)methyl)-1-aryl-1H-1,2,3-triazoles (6a-h)** gave excellent yields 90-95%

Comparison of the result obtained under conventional heating method and microwave irradiation is presented in **Table 7**

**Table 7**: Yields of compounds under conventional heating and microwave irradiation methods

| Compound Number | Conventional heating (A) | | Microwave irradiation (B) | |
|---|---|---|---|---|
| | Time (hr) | Yield (%) | Time (min) | Yield (%) |
| **6a** | 4 | 62 | 3 | 90 |
| **6b** | 4 | 60 | 5 | 94 |
| **6c** | 5 | 60 | 3 | 92 |
| **6d** | 4 | 63 | 4 | 95 |
| **6e** | 5 | 62 | 4 | 93 |
| **6f** | 5 | 61 | 5 | 95 |
| **6g** | 4 | 64 | 4 | 90 |
| **6h** | 4 | 62 | 3 | 92 |

**4.2.3** General experimental procedure for the synthesis of **4-(4,5-diphenyl-1H-imidazol-2-yl)phenol (7):**

One-pot multi component reaction proceeds with 4-hydroxy benzaldehyde **(1),**benzil (**5)**, ammonium acetate in presence of ethanol, acetic acid in iodine mixture under microwave activation at 180 W for 3-5 min afford for the target compound **(7)** according to the known procedure from the previous reports[12].

**4.2.4** General experimental procedure for the synthesis of **4,5-diphenyl-1-(prop-2-yn-1-yl)-2-(4-(prop-2-yn-1-yloxy)phenyl)-1H-imidazole (8):**

To a well stirred suspension of dry (4 equivalents/ 12.7mmol) $K_2CO_3$ in 10 ml DMF, was added a solution of (1 equivalent/ 3.02 mmol) 4-(4,5-diphenyl-1H-imidazol-2-yl)phenol **(7)**in DMF(5 ml). After the reaction was stirred for 30 min, a solution of 3-bromoprop-1-yne ( 80% in toluene) (2.4 equivalents/ 7.6mmol) was added in a drop wise manner and the mixture was stirred at room temperature for 8 hours and the progress of the reaction was monitored by TLC. After the completion of reactions 50 ml of ice cold water was added to the residue, the solid separated, filtered and washed with excess of water and dried in vacuum to obtain the pure 4,5-diphenyl-1-(prop-2-yn-1-yl)-2-(4-(prop-2-yn-1-yloxy)phenyl)-1H-imidazole **(8)** gave high yields (%) 90,mp 235-237$^oC$; $^1H$ NMR (400 MHz, DMSO) δ 7.88 (m, 2H), 7.55-7.45 (m, 6H), 7.23-7.10 (m, 6H), 4.76 (d, $J$ = 2.32 Hz, 2H, $OCH_2$), 4.47 (d, $J$ = 2.44 Hz, 2H, N-$CH_2$), 2.55 (t, , $J$ = 2.32 Hz, 1H, -CH), 2.45 (t, $J$ = 2.44 Hz, 1H, -CH).

**4.2.5** General experimental procedure for the synthesis of **4-((4-(4,5-diphenyl-1-((1-phenyl-1H-1,2,3-triazol-4-yl)methyl)-1H-imidazol-2-yl)phenoxy)methyl)-1-phenyl-1H-1,2,3-triazol derivatives (9a-h)**

The synthesis of title compounds **(9a-h)** was performed in two different techniques (Scheme-**2**):

**a. Conventional method**:

To a mixture of aryl azides **(3a-h)** (0.52 mmol) and 4,5-diphenyl-1-(prop-2-yn-1-yl)-2-(4-(prop-2-yn-1-yloxy)phenyl)-1H-imidazole **(8)** ( 0.26 mmol) in DMF/ water ( 3:1 v/v) (5 ml), 10 mol% $CuSO_4 \cdot 5H_2O$ and 10 mol% sodium ascorbate were added and stirred for 4 hr at 50°C. After completion of reaction (as indicated by TLC), the resulting mixture was added to crushed ice taken in a beaker. The solid separated was filtered and dried under reduced pressure in vacumm. The crude product thus obtained was purified by column chromatography hexane/ ethyl acetate (2:3 v/v) to afford pure 4-((4-(4,5-diphenyl-1-((1-phenyl-1H-1,2,3-triazol-4-yl)methyl)-1H-imidazol-2-yl)phenoxy)methyl)-1-phenyl-1H-1,2,3-triazole derivatives **(9a-h).** gave moderate yields (%) 60- 65.

**b. Microwave irradiation method:**

To a mixture of aryl azides **(3a-h)** (0.52 mmol) and 4,5-diphenyl-1-(prop-2-yn-1-yl)-2-(4-(prop-2-yn-1-yloxy)phenyl)-1H-imidazole **(8)** ( 0.26 mmol) in DMF/ water ( 3:1 v/v) (5 ml), 10 mol% $CuSO_4 \cdot 5H_2O$ and 10 mol% sodium ascorbate were added and subjected to microwave irradiation at 100 W for 2-3 min at regular intervals of 20 sec each. The reaction was monitored by TLC and after completion of reaction the resulting mixture was added to crushed ice taken in a beaker. The solid separated was filtered and dried under reduced pressure in vacuum. The crude product thus obtained was purified by column chromatography hexane/ ethyl acetate (2:3 v/v) to afford pure4-((4-(4,5-diphenyl-1-((1-phenyl-1H-1,2,3-triazol-4-yl)methyl)-1H-imidazol-2-yl)phenoxy)methyl)-1-phenyl-1H-1,2,3-triazole derivatives **(9a-h)** gave high yields (%) 80-90.

Comparison of the result obtained under conventional heating method and microwave irradiation is presented in **Table 8.**

**Table 8**: Conventional heating and microwave irradiation optimization for the synthesis of title compounds **9a-h.**

| Compound Number | Conventional heating (A) | | Microwave irradiation (B) | |
|---|---|---|---|---|
| | Time (hr) | Yield (%) | Time (min) | Yield (%) |
| **9a** | 4 | 61 | 3 | 87 |
| **9b** | 4 | 63 | 5 | 90 |
| **9c** | 5 | 63 | 3 | 82 |
| **9d** | 4 | 65 | 4 | 86 |
| **9e** | 5 | 65 | 4 | 90 |
| **9f** | 5 | 64 | 5 | 85 |
| **9g** | 4 | 60 | 4 | 86 |
| **9h** | 4 | 61 | 3 | 89 |

### 4.3 Biological activities:

#### 4.3.1. Antimicrobial activity

The antimicrobial activities of all the synthesized imidazole-1,23-triazole hybrid derivatives were tested by the presence or absence of inhibition zones and zone diameter against 6 microbial strains: gram-positive bacterium (*S. Aureus* ATCC 6538P, *B. cereus* ATCC 11778); two gram-negative bacteria (*E. coli* ATCC 853, *P.vulgaris* ATCC 7829, *Aspergillus fumigatus* (ATCC 13073), one yeast (*Candida albicans* NRRL Y-477). The results from the analysis of antimicrobial effects square measure summarized in Table1. The compounds were compared with the quality antibacterial Ampicillin and also the yeast/antifungal drug Fluconazole. The Minimum Inhibitory concentration (MIC) of all compounds was conjointly screened as listed in Table1. All tested compounds showed high MIC 1 mg /mL, against gram-positive and gram-negative bacterium compared to the reference drug Ampicillin (100 µg /mL). It was found that compounds **6c, 6d, 6f, 9d,9e, 9f**showed variable medicinal drug activity against gram-positive and Gram-negative bacterium. The best potent molecules showed good MIC values (**9d, 6h***S. aureus),(***9e, 6h***B. cereus),(***9e, 6h***E. coli),(***9e,6c***P.Vulgaris)*. All synthesized compounds were screened for the antifungal activity against two fungal stains A. *fumigates, C.albicans*. Among all tested compounds, compound **9d** and **9e** showed significant activity against both tested fungal pathogens with MIC values 100 µg/mL, remaining synthesized compounds almost inactive against tested fungal pathogens strain square measure tabulated in Table1.

#### 4.3.2 Antioxidant activity:

**a. DPPH radical scavenging activity:**

The antioxidant activity of all synthesized compounds **(6a-h)** and **(9a-h)** were measured against 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical. The DPPH procedure is one among the foremost effective strategies for evaluating the concentration of radical scavenging materials active by a chain-breaking mechanism. Briefly, 0.1 mM solution of DPPH was prepared in ethanol and 0.5 mL of this solution was added 1.5 mL of synthesised solution in ethanol at different concentrations (10-250 µg/mL).These solutions were vortexed thoroughly and incubated in dark. A half hour later, the absorbance was measured at 517 nm against blank samples. Lower absorbance of the reaction mixture indicates higher DPPH free radical scavenging activity. A standard curve was prepared using different concentrations of DPPH. The capability to scavenge the DPPH radical was calculated using the following equation-%

of Inhibition = ($A_0$ - $A_b$) / $A_0$ 100.Where $A_C$ is the absorbance of the control which contains DPPH solution and $A_S$ is the absorbance in the presence of synthesized solution. The results of DPPH method were tabulated in **table-2**.Compound **9e** was the excellent radical scavenger with associate % of inhibition worth of 250µg/mL. Furthermore compound **9c** showed a best radical scavenging activity with % of inhibition at 250µg/mL. Compounds **6h, 9h** conjointly showed good scavenging activities with 10, 50, 100, 250µg/mL.

**b. Hydrogen peroxide radical scavenging activity**

1ml of (10-250µg/ml) test drug/standard (Ascorbic acid) was added to 0.6ml of Hydrogen peroxide solution (PharmaTech labs, Hyderabad) in phosphate buffer (PH-7.4). After incubating for10 minutes at 37$^o$C the absorbance was measured at 230nm.Corresponding blanks were taken. The experiment was performed in triplicate. The absorbance of hydrogen peroxide in phosphate buffer as control was measured at 230nm. The scavenging effect (%) was measured using equation (1).Hydrogen peroxide produces hydroxyl radicals in cells. Scavenging of these radicals by the test drug is used as a test for antioxidant activity. The reduction of these radicals is seen by the decreased absorbance at 230nm with increasing concentration of the test drug. % of Inhibition = 100 ($A_0$ - $A_b$) / $A_0$ Compounds **9c, 9f** was the strongest radical scavenger with associate % of inhibition worth of 250µg/mL. Furthermore compound **6f, 6b** showed a good radical scavenging activity with % of inhibition at 250µg/mL. The results of $H_2O_2$ method were given in **table-3.**

**c. Nitric oxide scavenging activity assay**

Nitric oxide radical scavenging activity was determined according to the method reported by Garratt. Sodium nitroprusside in aqueous solution at physiological pH spontaneously generates nitric oxide, which interacts with oxygen to produce nitrite ions. 2 mL of 10 mM sodium nitroprusside in 0.5 mL phosphate buffer saline (pH 7.4) was mixed with 0.5 mL of test solution at various concentrations and the mixture incubated at 25$^o$C for 150 min. From the incubated mixture 0.5 mL was taken out and added into 1.0 mL sulfanilic acid reagent (33% in 20% glacial acetic acid) and incubated at room temperature for 5 min. Finally, 1.0 mL naphthyl ethylene diamine dihydrochloride (0.1% w/v) was mixed and incubated at room temperature for 30 min before measuring the absorbance at 540 nm was measured with a spectrophotometer. The nitric oxide radicals scavenging activity was calculated.

% of Inhibition = (A0 - Ab) / A0 100. The results of Nitric oxide method were tabulated in **table-4**.

Compound **6h** was the excellent nitric oxide radical scavenger with associate % of inhibition worth of 250µg /mL. Furthermore compound **9c, 9a, 9h** showed a good nitric oxide radical scavenging activity with % of inhibition at seventy four 250µg/mL.

**d. Reducing power assay (FRAP)**

The synthesised compounds (0.75 ml) at various concentrations was mixed with 0.75 mL of phosphate buffer (0.2 M, pH 6.6) and 0.75 mL of potassium hexacyanoferrate [$K_3Fe(CN)_6$] (1%, w/v), followed by incubating at 50°C in a water bath for 20 min. The reaction was stopped by adding 0.75 mL of trichloroacetic acid (TCA) solution (10%) and then centrifuged at 3000 r/min for 10 min. 1.5 ml of the supernatant was mixed with 1.5 mL of distilled water and 0.1 mL of ferric chloride ($FeCl_3$)solution (0.1%, w/v) for 10 min. The absorbance at 700 nm was measured as the reducing power. Higher absorbance of the reaction mixture indicated greater reducing power. % of Inhibition = 100 ($A_0$ - $A_b$) / $A_0$. Higher absorbance of the reaction mixture indicated greater reducing power. The results of FRAP method were tabulated in **table-5**.Compound **9c** was the excellent Reducing power assay% of inhibition worth of 250µg /mL. Further compounds **6d, 9d, 9h** showed good Reducing power assay with % of inhibition at 250µg/mL.

**4.3.3*In Silico* Molecular Docking Studies:**

The synthesized molecules of series **6a-h** and **9a-h** were selected for performing molecular docking studies by using Schrödinger's molecular docking software. Molecules were built in maestro build panel and prepared by Lig prep 2.3[13]module by applying default parameters. Crystal structures of *Staphylococcus aureus.* Penicillin binding protein 4and *E.coli* Penicillin Binding Protein 6 (pdb id: 3HUN[14] 3ITA[15]were downloaded from protein data bank (www.rcsb.org). The protein was prepared using protein preparation wizard of Schrödinger's molecular docking software, in this target preparation, all water molecules were removed and hydrogen atoms were added to the target. Grid was generated around the active site of the protein by selecting the co-crystalized ligand. Receptor van der Waals scaling for the nonpolar atoms was kept 0.9[16]Low energy conformation of the ligands were selected and docked into the grid using extra precision (XP) docking [17].Dock score and energy of each ligand was analysed for interactions with the receptor.

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**Spectral data:**

**1-(3-chlorophenyl)-4-((4-(4,5-diphenyl-1H-imidazol-2-yl)phenoxy)methyl)-1H-1,2,3-triazole(6a)**

Yield 90%, mp: 135-138 $^{o}$C; Rf = 0.40 (EtOAc:n-Hexane 2:3); IR (KBr): 3061, 1595,1490, 1026, 833, cm–1;$^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.88 (d, *J* = 8.8 Hz, 2H), 7.80 (t, *J* = 1.9 Hz, 1H), 7.67 – 7.54 (m, 5H), 7.45 (m, 2H), 7.37 – 7.28 (m, 6H), 7.08 (d, *J* = 8.8 Hz, 2H), 5.33 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 158.0, 145.9, 144.8, 137.6, 135.6, 130.8, 129.0,128.5, 127.8, 127.3, 127.0, 121.0, 120.8, 118.5, 115.0, 61.8; LC-MS m/z: 504[M+H]+; Anal. Calcd for $C_{30}H_{22}ClN_5O$:C, 71.49; H, 4.40; N, 13.90, Found: C, 71.40; H, 4.38; N, 13.85.

**1-(4-chlorophenyl)-4-((4-(4,5-diphenyl-1H-imidazol-2-yl)phenoxy)methyl)-1H-1,2,3-triazole(6b)**

Yield 94%, mp: 135-138 $^{o}$C; Rf = 0.40 (EtOAc:n-Hexane 2:3); IR (KBr): 3070, 1606,1498, 1051, 835, cm–1;$^{1}$H NMR (400 MHz, DMSO) δ 12.53 (s, 1H), 9.02 (s, 1H), 8.05 (d, *J* = 8.8 Hz, 2H), 7.98 (d, *J* = 8.9 Hz, 2H), 7.70 (d, *J* = 8.8 Hz, 2H), 7.55-7.3 (m,12H), 5.32 (s, 2H).$^{13}$C NMR (101 MHz, DMSO) δ163.0, 150.4,148.8 141.7, 140.3, 140.2, , 137.9 , 137.1, 136.1, 134.7, 133.5, 133.2,131.9, 128.5, 127.9, 126.7, 119.8, 66.0. LC-MS m/z: 504[M+H]+; Anal. Calcd for $C_{30}H_{22}ClN_5O$:C, 71.49; H, 4.40; N, 13.90; Found: C, 71.40; H, 4.38; N, 13.85.

**4-((4-(4,5-diphenyl-1H-imidazol-2-yl)phenoxy)methyl)-1-(p-tolyl)-1H-1,2,3-triazole(6c)**

Yield 92%, mp: 195-197 $^{o}$C; Rf = 0.5 (EtOAc:n-Hexane 2:3); IR (KBr): 3053, 1608, 1494, 1243, 1026 cm–1;$^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.85 (d, *J* = 8.5 Hz, 2H), 7.57 (m, 6H), 7.30 (m, 8H), 7.04 (d, *J* = 8.5 Hz, 2H), 5.27 (s, 2H), 2.42 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 158.7,139.1, 130.2, 129.9, 129.0, 128.5, 127.8, 127.3,126.9, 123.3, 121.0,120.5 115.1, 62.0, 21.1; LC-MS m/z: 484 [M+H]+; Anal. Calcd for $C_{31}H_{25}N_5O$: C, 77.00; H, 5.21; N, 14.48; Found: C, 76.92; H, 5.17; N, 14.41.

**4-((4-(4,5-diphenyl-1H-imidazol-2-yl)phenoxy)methyl)-1-(2-methoxyphenyl)-1H-1,2,3-triazole(6d)**

Yield 95%, mp: 188-190$^{o}$C; Rf = 0.43 (EtOAc:n-Hexane 2:3); IR (KBr): 3055, 1610, 1496, 1246, 1028 cm–1;$^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.84 (d, *J* = 8.6 Hz, 2H), 7.55 (m, 6H), 7.30 (m, 8H), 7.01 (d, *J* = 8.7 Hz, 2H), 5.23 (s, 2H), 2.42 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 160.9,159.0 , 145.8 , 145.1 , 143.9 , 132.0 , 131.9,131.3,129.5,128.5, 128.0 , 127.7, 127.7 ,125.3 ,122.7, 119.3,115.1,110.8, 61.6 , 56.4; LC-MS m/z:500 [M+H]+; Anal. Calcd for$C_{31}H_{25}N_5O_2$: C, 74.53; H, 5.04; N, 14.02; Found: C, 74.49; H, 5.00; N, 14.00.

**4-((4-(4,5-diphenyl-1H-imidazol-2-yl)phenoxy)methyl)-1-(2-methoxy-4-nitrophenyl)-1H-1,2,3-triazole(6e)**

Yield 93%, mp: 105-108$^{o}$C; Rf = 0.4 (EtOAc:n-Hexane 2:3); IR (KBr): 3059, 1606, 1344, 1249, 1018 cm–1;$^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.16 (s1,H), 8.02 (d,*J* = 7.5 Hz, 2H2H), 7.88 (d, *J* = 8.5 Hz, 2H 2H), 7.75(d, *J* = 7.5 Hz, 2H), 7.5- 7.38 (m, 7H), 6.97 (d, *J* = 8.5 Hz, 2H), 5.21 (s, 2H), 4.04 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ150.6, 148.1,145.9, 145.6, 143.5 , 130.8 , 130.6, 130.3,128.6, 128.1 ,126.5, 126.4 ,125.3, 125.1, 116.6, 115.1,107.8,61.6,56.9; LC-MS m/z:545 [M+H]+; Anal. Calcd for$C_{31}H_{24}N_6O_4$: C, 68.37; H, 4.44; N, 15.43; Found: C, 68.29; H, 4.40; N, 15.36.

**4-((4-(4,5-diphenyl-1H-imidazol-2-yl)phenoxy)methyl)-1-(4-methoxy-2-nitrophenyl)-1H-1,2,3-triazole(6f)**

Yield 95%, mp: 148-151 $^{o}$C; Rf = 0.4 (EtOAc:n-Hexane 2:3); IR (KBr): 3080, 1612, 1541, 1238, 1029 cm–1;$^{1}$H NMR (400 MHz, $CDCl_3$) δ8.04(s, 1H),8.01(s, 1H), 7.09 (d, *J* = 7.5 Hz, 2H), 7.61-7.42(m,7H) 7.38-7.21(m,6H),6.91 (d, *J* = 7.1 Hz, 2H), 5.16 (s, 2H), 3.93 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 160.9, 159.0 , 145.8, 145.1, 143.9, 131.3, 129.5, 128.5, 128.0, 127.7 , 127.3, 125.3, 122.7,119.3, 115.1, 110.8,61.9,56.4; LC-MS m/z: 545 [M+H]+; Anal. Calcd for $C_{31}H_{24}N_6O_4$:C, 68.37; H, 4.44; N, 15.43; Found: C, 68.25; H, 4.33; N, 15.38.

**4-((4-(4,5-diphenyl-1H-imidazol-2-yl)phenoxy)methyl)-1-(2-nitrophenyl)-1H-1,2,3-triazole (6g)**

Yield 90%, mp: 148-150$^{o}$C; Rf = 0.5 (EtOAc:n-Hexane 2:3); IR (KBr): 3081, 1608, 1537, 1236, 1010 cm–1;$^{1}$H NMR (400 MHz, DMSO) δ 12.73 (s, 1H), 8.89 (s, 1H), 8.25 (d, *J* = 7.9 Hz, 2H), 8.06 (d, *J* = 8.6 Hz, 2H), 7.92 (m, 4H), 7.53 (d, *J* = 7.3 Hz, 4H), 7.42 – 7.20 (m, 7H), 5.34 (s, 2H). $^{13}$C NMR (101 MHz, DMSO) δ 158.2 , 145.4 , 144.0, 143.3 , 134.4 , 131.2 , 129.0 , 128.4,127.7,127.6 , 126.8 ,126.0 , 125.5 , 114.9 , 60.9; LC-MS m/z: 515 [M+H]+; Anal. Calcd for $C_{30}H_{22}N_6O_3$ ;C, 70.03; H, 4.31; N, 16.33;Found: C, 70.00; H, 4.26; N, 16.21.

**4-((4-(4,5-diphenyl-1H-imidazol-2-yl)phenoxy)methyl)-1-(4-nitrophenyl)-1H-1,2,3-triazole(6h)**

Yield92%, mp: 148-150$^{o}$C; Rf = 0.5 (EtOAc:n-Hexane 2:3); IR (KBr): 3082, 1602, 1529, 1246, 1045 cm–1;$^{1}$H H NMR (400 MHz, DMSO) δ 12.55 (s, 1H), 9.21 (s, 1H), 8.48 (d, *J* = 9.0 Hz, 2H), 8.27 (d, *J* = 9.0 Hz, 2H), 8.05 (d, *J* = 8.7 Hz, 2H), 7.25 (m, 11H), 5.36 (s, 2H).$^{13}$C NMR (101 MHz, DMSO) δ158.2 , 145.4 , 144.0, 143.3 , 134.4 , 131.2 , 129.0 , 128.4,127.7,127.6 , 126.8 ,126.0 , 125.5 , 114.9 , 60.9. ; LC-MS m/z: 515 [M+H]+; Anal. Calcd for $C_{30}H_{22}N_6O_3$ ;C, 70.03; H, 4.31; N, 16.33;Found: C, 70.00; H, 4.26; N, 16.21.

**1-(3-chlorophenyl)-4-((2-(4-((1-(3-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)phenyl)-4,5-diphenyl-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazole(9a)**

Yield 87%, mp: 188-190$^{o}$C; Rf = 0.3 (EtOAc:n-Hexane 2:3); IR (KBr): 1595, 1489, 1240, 1037, 837 cm–1;$^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.82 (m, 3H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.57 – 7.39 (m, 14H), 7.23 – 7.11 (m, 4H), 6.97 (s, 1H), 5.32 (s, 2H),5.26(s,2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 158.8 , 147.7,144.9,144.7 , 137.7, 137.4, 135.6 ,135.6, 134.0 , 131.2, 131.0 ,130.8, 129.1,129.0, 128.9, 128.1, 126.9 , 126.5 ,123.7, 120.9 - 120.1, 118.5 , 118.2 , 115.0, 61.9 , 40.4; LC-MS m/z: 695[M+H]+; Anal. Calcd for $C_{39}H_{28}Cl_2N_8O$; C,67.34, H, 4.06, N,16.11 Found; C, 67.29; H, 4.02; N, 16.08.

**1-(4-chlorophenyl)-4-((2-(4-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)phenyl)-4,5-diphenyl-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazole(9b)**

Yield 90%, mp: 222-225 $^{o}$C $^{0}$C-; Rf = 0.5 (EtOAc:n-Hexane 2:3); IR (KBr): 1593, 1504, 1249, 1041, 827 cm–1;$^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.82-7.80 (d, J=8.6Hz, 2H), 7.70-7.69 (d, J=8.8Hz, 2H), 7.53-7.43 (m, 11H), 7.36-7.34 (d, J=7.4Hz, 2H), 7.21-7.18 (m, 2H), 7.15-7.12(m, 3H), 6.95 (s, 1H), 5.34 (s, 2H), 5.27 (s, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ158.8, 147.6, 144.8,144.7, 138.0, 135.3, 135.1, 134.7, 134.1, 131.2, 131.0, 129.9, 129.1, 128.8, 128.1,126.9, 126.5,123.8, 121.7, 121.3,120.9,120.0, 115.0, 61.9, 40.4; LC-MS m/z:695 [M+H]+; Anal. Calcd for $C_{39}H_{28}C_{l2}N_8O$: C, 67.34; H, 4.06; N, 16.11;; Found: C, 67.30; H, 4.01; N, 16.06.

**4-((4-(4,5-diphenyl-1-((1-(p-tolyl)-1H-1,2,3-triazol-4-yl)methyl)-1H-imidazol-2-yl)phenoxy)methyl)-1-(p-tolyl)-1H-1,2,3-triazole(9c)**

Yield 82%, mp: 175-178$^{o}$C; Rf = 0.4 (EtOAc:n-Hexane 2:3); IR (KBr): 1596, 1519, 1242, 1026, 813 cm–1;$^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.82 (d, *J* = 8.5 Hz, 2H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 7.4 Hz, 2H), 7.45 – 7.31 (m, 11H), 7.19 (m, 5H), 6.97 (s, 1H), 5.35 (s, 2H), 5.28 (s, 2H), 2.43 (s,3H),2.40(s,3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 158.9, 144.5, 139.0, 138.0, 134.6, 134.4, 131.2, 131.0, 130.2, 129.1, 128,8,128.1, 126.9, 126.4, 121.0, 120.5, 120.1, 115.0, 62.1, 40.5, 21.1;

LC-MS m/z: 655 [M+H]+; Anal. Calcd for $C_{41}H_{34}N_8O$: C, 75.21; H, 5.23; N, 17.11;Found: C, 75.18; H, 5.17; N, 17.06.

**1-(2-methoxyphenyl)-4-((2-(4-((1-(2-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methoxy)phenyl)-4,5-diphenyl-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazole(9d)**

Yield 86%, mp: 108-110 $^oC$; Rf = 0.4 (EtOAc:n-Hexane 2:3); IR (KBr): 1604, 1502, 1244, 1020, 839 cm–1;$^1H$ NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.75(m,4H), 7.53-7.37 (m, 9H), 7.19-7.03 (m, 10H), 5.34 (s, 2H), 5.27 (s, 2H), 3.88(s, 3H), 3.81 (s, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 157.1, 149.2, 149.1, 145.9, 142.9, 142.2, 136.0, 132.5 1293, 128.9,128.3,127.1, 126.2, 125.0, 123.6, 123.4, 122.3, 119.3, 118.4, 113.3,110.3,60.2, 54.0, 38.9, LC-MS m/z: 687[M+H]+; Anal. Calcd for $C_{41}H_{34}N_8O_3$ :C, 71.70; H, 4.99; N, 16.32; Found: C, 71.62; H, 4.87; N, 16.28.

**1-(2-methoxy-4-nitrophenyl)-4-((2-(4-((1-(2-methoxy-4-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)phenyl)-4,5-diphenyl-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazole(9e)**

Yield 90%, mp: 96-98 $^oC$; Rf = 0.37 (EtOAc:n-Hexane 2:3); IR (KBr):1610, 1531, 1344, 1242, 1020 cm–1;$^1H$ NMR H NMR (500 MHz, $CDCl_3$) δ 8.40 (s ,1H), 8.14 (m, 1H), 8.03 – 7.97 (m, 4H), 7.93 – 7.88 (J=7.2HZ, 2H), 7.79 (d, *J* = 6.6 Hz, 2H), 7.52 – 7.37 (m, 10H), 7.20 – 7.14 (m, 3H), 5.37 (S, 2H), 5.32 (S, 2H), 4.06 (S, 3H), 4.00 (S, 3H).$^{13}C$ NMR (101 MHz, $CDCl_3$) δ 157.1,, 148.8, 148.6, 146.3 142.4, 142.0, 136.2, 135.9, 132.4, 129.3,128.7, 126.3, , 125.1, 124.7, 124.7, 123.4, 123.2, 122.2, 114.9, 1133 106.0, 71.9, 60.1, 55.1; LC-MS m/z: 777 [M+H]+; Anal. Calcd for $C_{41}H_{32}N_{10}O_7$: C, 63.40; H, 4.15; N, 18.03; Found: C, 63.38; H, 4.11; N, 17.09.

**1-(4-methoxy-2-nitrophenyl)-4-((2-(4-((1-(4-methoxy-2-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)phenyl)-4,5-diphenyl-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazole(9f)**

Yield 85%, mp: 79-82 $^oC$; Rf = 0.36 (EtOAc:n-Hexane 2:3); IR (KBr): 1608, 1535, 1352, 1240, 1041 cm–1; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.77 (d, *J* = 8.6 Hz, 2H), 7.58 (s, 1H), 7.53 (m, 4H), 7.45 – 7.39 (m, 5H), 7.30 (s,1H), 7.22 – 7.12 (m, 7H), 6.95 (s, 1H), 5.38 (s, 2H), 5.26(s,2H), 3.96(s,3H), 3.94(s,3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ158.8, 156.7, ,145.6,143.0, 142.1,142.0,135.6,129.1,128.8,127.3,127.05,126.9,125.9,124.8,124.4122.9,121.9,120.7,117.1,113.1,10 8.5,59.8,54.2,; LC-MS m/z: 462 [M+H]+; Anal. Calcd for$C_{41}H_{32}N_{10}O_7$: C, 63.40; H, 4.15; N, 18.03; Found: C, 63.38; H, 4.11; N, 17.09

**1-(2-nitrophenyl)-4-((2-(4-((1-(2-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)phenyl)-4,5-diphenyl-1*H*-imidazol-1-yl)methyl)-1H-1,2,3-triazole(9g)**

Yield 86%, mp: 218-220 $^{o}$C; Rf = 0.5 (EtOAc:n-Hexane 2:3); IR (KBr): 1608, 1531, 1344, 1240, 1020 cm–1; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.03 (m, 2H), 7.96 (s, 1H), 7.81 – 7.64 (m, 7H), 7.53 (d, *J* = 7.1 Hz, 2H), 7.46 – 7.38 (m, 6H), 7.22 – 7.12 (m, 5H), 7.00 (s, 1H), 5.40 (s, 2H), 5.28 (s, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 158.9 , 144.3,133.9, 133.8, 131.2,130.9,130.1,129.8.129.1, 128.1,128.0,127.7,127.0,125.5,124.6,123.6,115.3,61.9,40.5; LC-MS m/z: 717 [M+H]+; Anal. Calcd for $C_{39}H_{28}N_{10}O_5$: C, 65.36; H, 3.94; N, 19.54; Found: C, 65.25; H, 3.88; N, 19.46.

**1-(4-nitrophenyl)-4-((2-(4-((1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)phenyl)-4,5-diphenyl-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazole(9h)**

Yield 89%, mp: 207-210$^{o}$C; Rf = 0.5 (EtOAc:n-Hexane 2:3); IR (KBr): 1608, 1534, 1342, 1240, 1020 cm–1;$^{1}$H NMR (400 MHz, DMSO) δ 9.22 (s, 1H), 8.44 (m, 4H), 8.33 (s, 1H), 8.25 (d, *J* = 9.1 Hz, 2H), 8.07 (d, *J* = 9.1 Hz, 2H), 7.78 (d, *J* = 8.7 Hz, 2H), 7.48-7.35 (m, 7H), 7.21 (m, 4H), 7.13 (m 1H), 5.35 (s, 2H), 5.25 (s, 2H); $^{13}$C NMR (101 MHz, DMSO) δ 158.3, 146.8,146.7, 144.8, 144.3, 140.7, 140.4, 136.3, 134.5, 130.8, 130.3, 129.4, 128.9, 128.0,126.1, 125.9, 125.5, 123.4, 121.4, 120.7,120.5, 114.8, 60.9; LC-MS m/z: 717 [M+H]+; Anal. Calcd for $C_{39}H_{28}N_{10}O_5$: C, 65.36; H, 3.94; N, 19.54;; Found: C, 65.31; H, 3.83; N, 19.

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**Highlights**

- A series of new imidazolo-1,2,3-triazoles was synthesized by microwave method.
- The newly synthesized imidazolo-1,2,3-triazoles are screened for antioxidant, antimicrobial activities shows excellent activities.
- *In-silico* molecular docking studies were performed using Schrodinger software. (PDB: 3HUN and PDB: 3ITA) compounds 6c, 6h, 9d and 9e showed maximum dock score and found to exhibit Promising activity.