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# SYNTHESIS AND BIOLOGICAL ACTIVITIES OF BENZOFURAN DERIVATIVES IN THE NEW MILLENNIUM

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**ABSTRACT**

Benzofuran and its derivatives represent a vital category of heterocyclic organic compounds with significant roles in traditional medicine, primarily recognized for their antimicrobial and hormone-regulating properties. Recently, there has been a resurgence of interest in these compounds due to their wide array of biological activities and their potential to tackle contemporary medical issues. Specifically, benzofuran derivatives have shown encouraging effectiveness against multidrug-resistant pathogens and are emerging as promising agents in targeted cancer therapies, where they selectively inhibit tumor growth while minimizing adverse effects. Their antioxidant capabilities have also been investigated for neuroprotective applications in diseases like Alzheimer's and Parkinson's. Moreover, the inherent structural versatility of benzofuran compounds facilitates the creation of powerful agents for conditions such as tuberculosis, seizures, and hyperlipidemia. Recent developments underscore their potential to improve the efficacy of current treatments while paving the way for innovative therapeutic strategies. A notable illustration is the dihydrobenzofuran framework found in morphine, wherein the furan moiety is essential for its analgesic action. The extensive structural variation and therapeutic promise of these compounds emphasize their increasing significance in drug discovery and the advancement of therapeutic solutions. Ongoing research into benzofuran derivatives is anticipated to greatly enhance the development of more effective and safer pharmaceuticals for a variety of health conditions.

**Keywords: Benzofuran Derivatives; Antimicrobial, Anticancer; Antioxidant; Anti-inflammatory; Anticonvulsant; Antitubercular and Antihyperlipidemic Agents**

## 1. INTRODUCTION:

Benzofuran compounds, composed of a fused benzene and furan ring system, are of significant interest due to their wide-ranging biological properties. Known for their antibacterial, antifungal, and anticancer applications in pharmaceuticals, these compounds are also essential in industrial areas such as agriculture and photography **[1, 4]**. Benzofuran derivatives can be sourced naturally or synthesized, showing antimicrobial, antioxidant, anticancer, and anti-inflammatory effects **[2, 3]**.

Recent studies underscore their importance in combating multidrug-resistant (MDR) pathogens; for instance, a 2022 study revealed novel benzofuran-based antimicrobials effective against MRSA and Pseudomonas aeruginosa, surpassing traditional antibiotics **[5]**. In oncology, benzofuran-based BRD4 inhibitors were shown in a 2023 study to target triple-negative breast cancer, presenting a lower-toxicity alternative to standard chemotherapy **[6]**. Research has also highlighted benzofuran derivatives' antioxidant potential; a 2023 study demonstrated their ability to boost key antioxidant enzymes, suggesting neuroprotective applications for Alzheimer's and Parkinson's disease **[7]**. In tuberculosis treatment, novel benzofuran analogs showed promising effects against MDR-TB strains **[8]**.

These findings showcase benzofuran derivatives' versatile biological roles, supported by computational advancements, in drug discovery across diverse therapeutic fields, as shown in **Figure 1 [9]**.

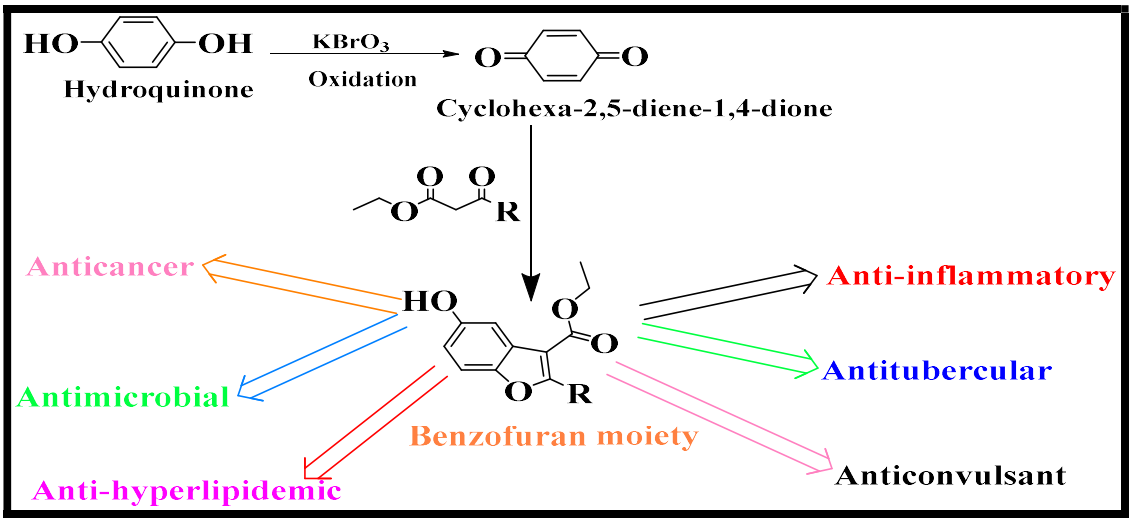



**Figure 1: Benzofuran Derivatives: Chemical Transformations and Associated Biological Functions**

## 2. Biological activity of benzofuran derivatives in the new millennium

### 2.1 Benzofuran derivative as antimicrobial agents

Despite the availability of numerous antimicrobial drugs, the ongoing search for agents with improved pharmacokinetics, pharmacodynamics, and fewer side effects remains crucial due to rising microbial resistance **[10]**. A novel benzofuran derivative has shown significant efficacy against multidrug-resistant pathogens such as MRSA and Pseudomonas aeruginosa, which are often linked to severe healthcare-associated infection **[5]**. A new series of benzo[b]furan derivatives was synthesized (as detailed in **Table 1**), beginning with iodination of 4-methyl-2-nitrophenol and followed by reactions that yielded benzo[b]furan sulfonyl derivatives with promising antibacterial properties. Compounds 6e, 6g, 6h, 6i, and 6j demonstrated excellent antibacterial activity against both Gram-positive and Gram-negative strains, with ciprofloxacin used as a reference standard (results summarized in **Table 1 [11, 12]**.

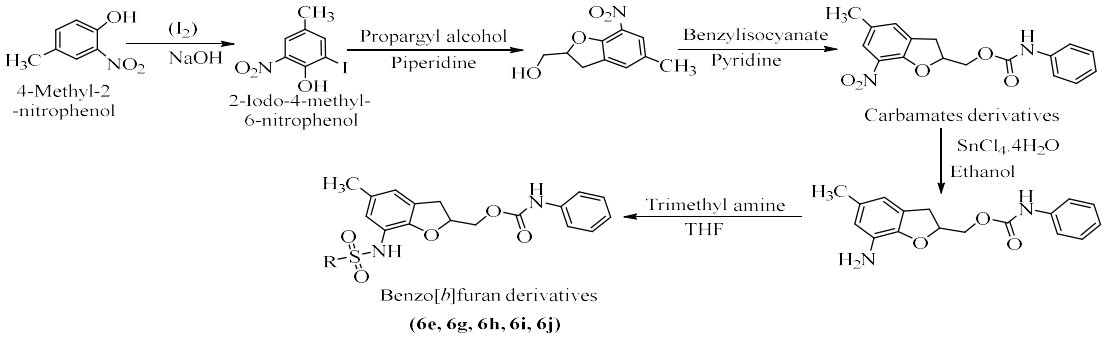



**Table 1: Evaluation of Antibacterial Efficacy of Benzofuran Derivatives against Gram-Positive and Gram-Negative Bacteria**

| Compound name | R | Gram +ve bacteria | | Gram -ve bacteria | |
|---|---|---|---|---|---|
| | | *S. aureus* | *S.poygenes* | *E. coli* | *P. aeruginosa* |
| 6e | $C_6H_5$, -4-$CH_3$ | 20 | 19 | 23 | 23 |
| 6g | -$CH_2C_6H_5$ | 20 | 21 | 23 | 24 |
| 6h | Thiophene | 19 | 19 | 24 | 22 |
| 6i | Thiophene, 4-Cl | 20 | 18 | 26 | 25 |
| 6j | Thiophene, 4-Br | 19 | 18 | 25 | 24 |
| Ciprofloxacin | ---- | 21 | 22 | 28 | 26 |

Novel benzofuran chalcone derivatives were synthesized, as summarized in **Table 2**. These derivatives underwent cyclization using hydrazine hydrate, forming the desired 2-(5-aryl-4,5-dihydropyrazol-3-yl)-3-methoxybenzofurans. The antifungal activity of all synthesized compounds was evaluated against *Candida albicans* and *Aspergillus niger*. Notably, several compounds demonstrated superior antifungal efficacy compared to the reference standard, griseofulvin. Detailed activity results are provided in **Table 2 [13]**.

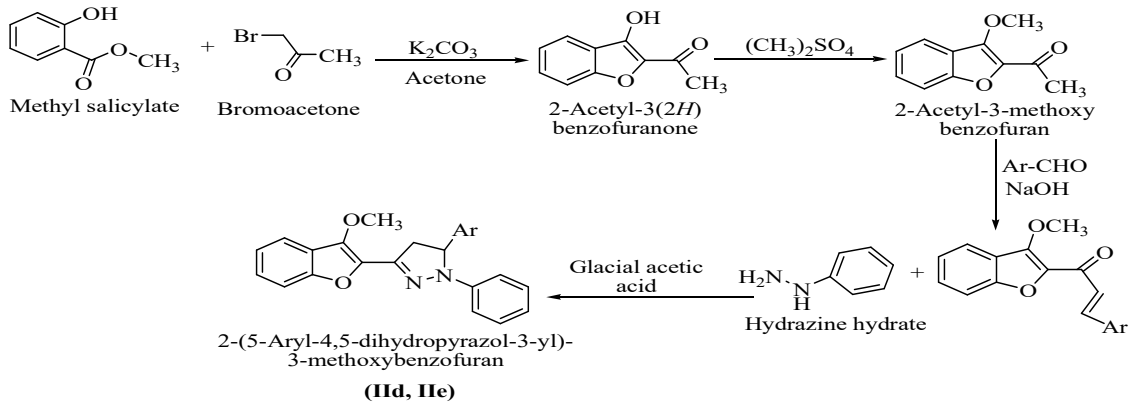



**Table 2: Assessment of Antifungal Efficacy of Benzofuran Derivatives against *Candida albicans* and *Aspergillus niger***

| Compound name | Ar | Zone of inhibition (in mm) | | | |
|---|---|---|---|---|---|
| | | *Candida albicans* | | *Asperigillus niger* | |
| | | 50 µg/ml | 100 µg/ml | 150 µg/ml | 200 µg/ml |
| IId | 3-$NO_2$-$C_6H_5$ | 20 | 24 | 19 | 25 |
| IIe | 4-Cl-$C_6H_5$ | 19 | 23 | 19 | 24 |
| Griseofulvin | --- | 21 | 25 | 20 | 26 |

A novel bisbenzofuran-2-yl-methanone was synthesized using two distinct methods, as detailed in **Table 3**. The synthesized compound was tested for antimicrobial activity against various strains, including *Bacillus megaterium, Staphylococcus aureus* (Gram-positive), *Escherichia coli, Klebsiella pneumoniae* (Gram-negative), and *Candida albicans* (fungal). Bisbenzofuran-2-yl-methanone (1) showed the highest antimicrobial activity compared to the standards streptomycin and nystatin, with results summarized in **Table 3 [14]**.

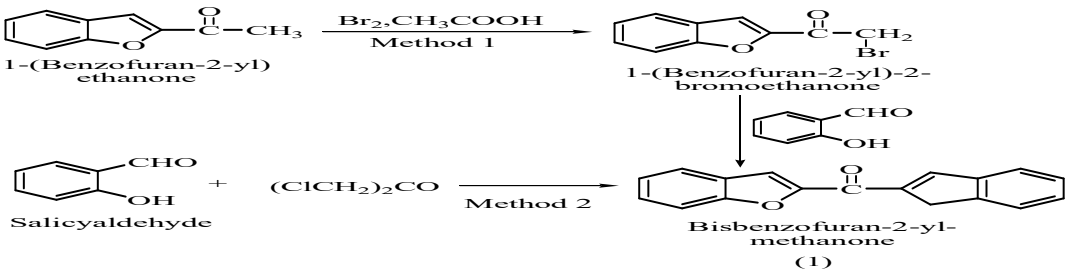



**Table 3: Assessment of Antimicrobial and antifungal activity of Benzofuran Derivatives**

| Compound name | *B. megaterium* | *S. aureus* | *E. coli* | *K. pneumonia* | *C. albicans* |
|---|---|---|---|---|---|
| 1 | 18 | 13 | 18 | 15 | 17 |
| Streptomycin | 17 | 17 | -- | 16 | -- |
| Nystatin | -- | -- | -- | -- | 18 |

A new series of aryl-5-nitrobenzofuran-2-carbamides was synthesized, as detailed in **Table 4**. All synthesized compounds were there in vitro antimicrobial activity was evaluated against *Staphylococcus aureus* and *Escherichia coli* using the cup-plate method. Notably, compounds demonstrated the highest antimicrobial activity compared to ampicillin, which served as the standard reference, as shown in **Table 4 [10]**.

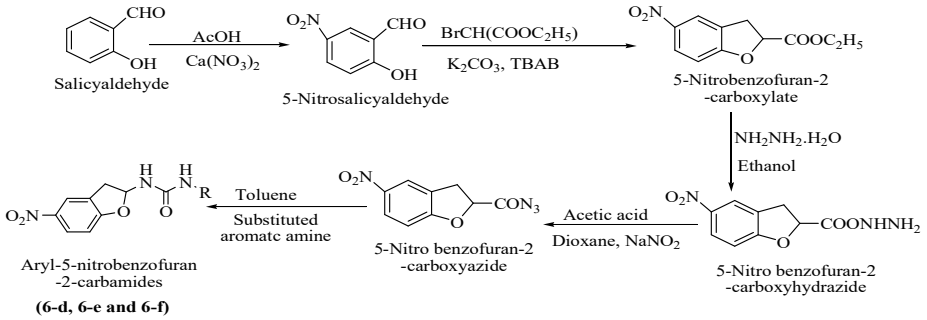



**Table 4: Evaluation of Antimicrobial Properties of Benzofuran Derivatives Against *S. aureus* and *E. coli***

| Compound name | R | *S. aureus* | *E. coli* |
|---|---|---|---|
| **6-d** | **-$C_6H_4OCH_3$(*p*)** | **19** | **09** |
| **6-e** | **-$C_6H_4OCH_3$(*o*)** | **17** | **10** |
| **6-f** | **-$C_6H_4Cl$(*m*)** | **14** | **20** |
| **Ampicillin (500µg/ml)** | **-----** | **24** | **32** |

A novel series of derivatives was synthesized, as detailed in **Tables 5 and 6**. The in vitro antimicrobial activity of these compounds was assessed using the cup-plate method against various strains, including Gram-positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*), Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*), and fungal strains (*Aspergillus fumigatus* and *Candida albicans*). Among the synthesized derivatives, several compounds exhibited significant antifungal activity against *Candida albicans* compared to the standard antifungal drug fluconazole. The results for these active compounds are summarized in **Tables 5 and 6 [15]**.

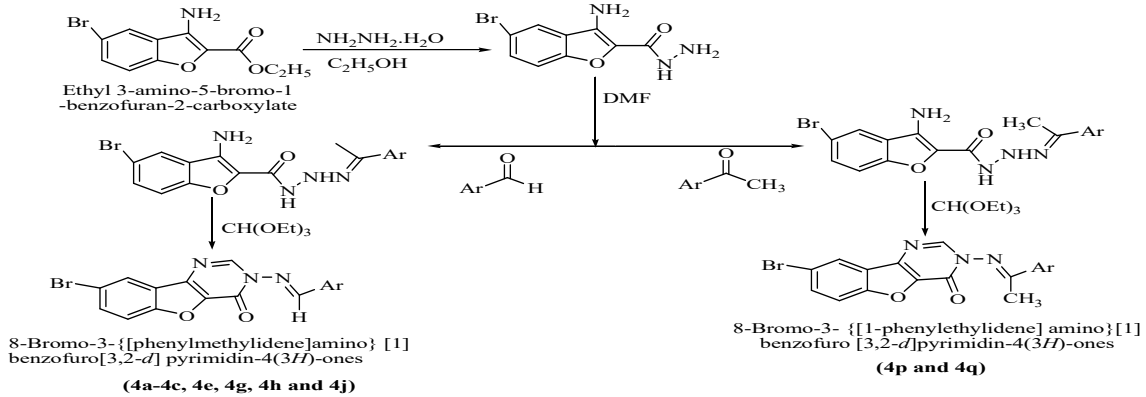


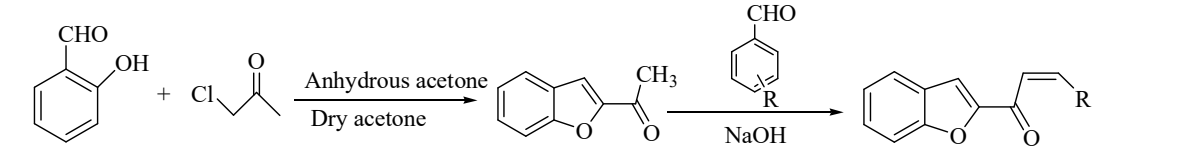

**Table 5: Evaluation of Antimicrobial Properties of Benzofuran Derivatives**

| Compound name | Ar | Zone of inhibition in mm Antibacterial activity | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | *B. subtilis* | | *S. aureus* | | *E.coli* | | *P.aeruginosa* | |
| | | 50 µg | 100 µg | 50 µg | 100 µg | 50 µg | 100 µg | 50 µg | 100 µg |
| **4c** | **$C_6H_5$** | **8** | **12** | **6** | **10** | **10** | **14** | **10** | **12** |
| **4d** | **2-Cl $C_6H_4$-** | **6** | **10** | **8** | **10** | **7** | **10** | **9** | **13** |
| **4e** | **4-Cl $C_6H_4$-** | **7** | **10** | **8** | **10** | **9** | **11** | **10** | **10** |
| **4g** | **3-$NO_2$ $C_6H_4$-** | **5** | **12** | **8** | **10** | **6** | **10** | **8** | **10** |
| **4j** | **4- $OCH_3$ $C_6H_4$-** | **8** | **12** | **6** | **10** | **7** | **10** | **5** | **12** |
| **4p** | **2-OH $C_6H_4$-** | **6** | **10** | **8** | **10** | **8** | **14** | **8** | **12** |
| **4q** | **5-Br-2-OH $C_6H_3$-** | **10** | **14** | **8** | **10** | **5** | **8** | **6** | **10** |
| **Ciprofloxacin** | **----** | **22** | **24** | **20** | **22** | **20** | **20** | **20** | **20** |
| **Ampicillin** | **----** | **15** | **15** | **10** | **10** | **15** | **14** | **11** | **10** |

**Table 6: Evaluation of Antifungal Properties of Benzofuran Derivatives**

| Compound name | Ar | Zone of inhibition in mm Antibacterial activity | |
|---|---|---|---|
| | | *C. albicans* | |
| | | 50 µg | 100 µg |
| 4a | $C_6H_5$ | 13 | 15 |
| 4b | 2-Cl $C_6H_4$- | 12 | 15 |
| 4g | 3-$NO_2$ $C_6H_4$- | 13 | 15 |
| 4h | 5-Br-2-OH $C_6H_3$- | 12 | 10 |
| 4p | 2-OH $C_6H_4$- | 12 | 14 |
| Fluconazole | ------ | 22 | 24 |

A novel series of 1-benzo[b]furan-2-yl-3-(substituted phenyl)prop-2-en-1-one derivatives was synthesized using 2-acetylbenzofuran, prepared by reacting 2-hydroxybenzaldehyde with chloroacetone and potassium carbonate. This intermediate then reacted with various aromatic aldehydes to yield chalcones. The antimicrobial activity of these compounds was tested against Gram-positive bacteria (*Enterococcus faecalis* and *Bacillus subtilis*), Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*), and fungal strains (*Candida albicans* and *Aspergillus niger*) using the cup plate method. Compounds such as B1 and B2 showed the highest activity against both bacterial and fungal strains, with amoxicillin and griseofulvin as reference standards. Results for active compounds are summarized in **Table 7 [16]**.




2-Hydroxy benzaldehyde — Chloroacetone — 2-Acetyl benzofuran — 1-Benzo[b]furan-2-yl-3-(substituted phenyl)prop-2-en-1-one

**($B_1$, $B_2$, $B_3$, $B_4$, $B_7$ and B9)**

**Table 7: Evaluation of Antimicrobial activity of Benzofuran Derivatives**

| Compound name | R | Diameter of zone inhibition (mm) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Antibacterial activity | | | | | | | | Antifungal activity | | | |
| | | *B. subtilis* | | *E. fecalis* | | *E. coli* | | *P.aeruginosa* | | *C. albicans* | | *A. niger* | |
| | | 50 µg/ml | 100 µg/ml | 50 µg/ml | 100 µg/ml | 50 µg/ml | 100 µg/ml | 50 µg/ml | 100 µg/ml | 50 µg/ml | 100 µg/ml | 50 µg/ml | 100 µg/ml |
| $B_1$ | *p*-Nitrophenyl | 16 | 19 | 15 | 20 | 10 | 18 | 15 | 19 | 18 | 19 | 15 | 21 |
| $B_2$ | *o*-Chlorophenyl | 15 | 20 | 13 | 19 | 12 | 19 | 16 | 20 | 18 | 18 | 16 | 23 |
| $B_3$ | *P*-Chlorophenyl | 16 | 22 | 14 | 18 | 13 | 18 | 15 | 21 | 20 | 21 | 15 | 24 |
| $B_4$ | *m*-Chlorophenyl | 14 | 22 | 15 | 20 | 15 | 20 | 14 | 15 | 15 | 23 | 17 | 20 |
| $B_7$ | *p*-Bromophenyl | 18 | 21 | 15 | 18 | 15 | 16 | 10 | 18 | 17 | 26 | 08 | 20 |
| $B_9$ | *m*-Nitrophenyl | 11 | 18 | 10 | 15 | 13 | 15 | 11 | 16 | 16 | 15 | 10 | 18 |

A novel series of 3-(7-methoxy-benzofuran-2-yl)-5-aryl-4H-[1,2,4]triazole derivatives was synthesized, as shown in **Tables 8 and 9**. The synthesis began with 7-methoxybenzofuran-2-carboxylic acid ethyl ester, prepared from the reaction of *o*-

vanillin with diethyl bromomalonate. This ester was then converted to 7-methoxy-benzofuran-2-carboxylic acid hydrazide using hydrazine hydrate in ethanol, followed by a reaction with various substituted benzaldehydes and ammonium acetate to yield the desired triazole derivatives.

The antimicrobial activity of these compounds was evaluated using the broth microdilution method against several strains of Gram-positive and Gram-negative bacteria, as well as various fungal strains. Notably, compound 3d (3-(7-methoxybenzofuran-2-yl)-5-(4-nitrophenyl)-4H-1,2,4-triazole) demonstrated the highest antimicrobial activity, surpassing the standard drugs ciprofloxacin and fluconazole. The detailed results are provided in **Tables 8 and 9 [17]**.

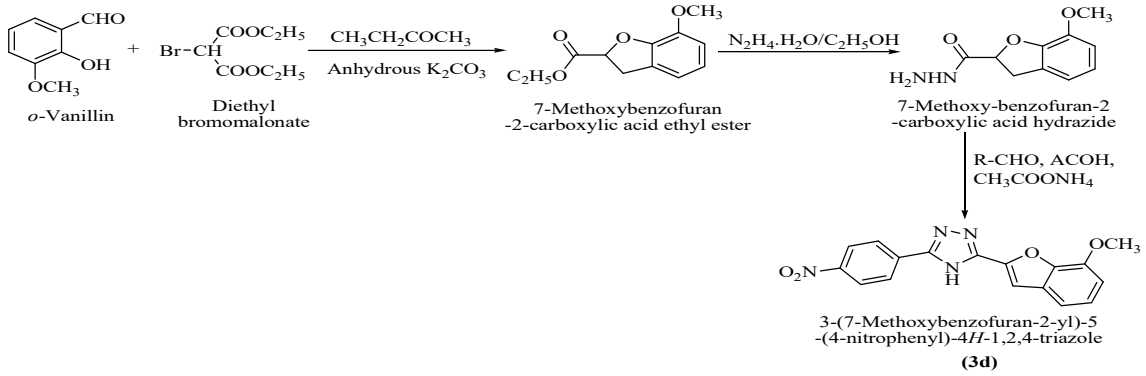



**Table 8: Evaluation of Antimicrobial activity of Benzofuran Derivative**

| Compound name | MICs (µg/ml) | | | | | |
|---|---|---|---|---|---|---|
| | Gram +ve bacteria | | | Gram -ve bacteria | | |
| | *S. faecalis* | *S. aureus* | *B. subtilis* | *P. aeruginosa* | *K. pneumoniae* | *E. coli* |
| **3d** | **1** | **1** | **1** | **2** | **2** | **2** |
| **Ciprofloxacin** | **1** | **1** | **1** | **1** | **1** | **1** |

**Table 9: Evaluation of Antifungal activity of Benzofuran Derivative**

| Compound name | MICs (µg/ml) | | | | | |
|---|---|---|---|---|---|---|
| | *C. albicans* | *A. fumigatus* | *A. niger* | *P.chrysogenum* | *M. fuscus* | *F. oxysporum* |
| **3d** | **4** | **2** | **4** | **2** | **2** | **4** |
| **Fluconazole** | **8** | **8** | **8** | **8** | **8** | **8** |

A novel series of 1-(1-benzofuran-2-yl)-2-mesitylethanone derivatives was synthesized starting from 1-chloro-3-mesitylpropane-2-ol, obtained by reacting mesitylene with epichlorohydrin using $AlCl_3$ as a catalyst. This compound was oxidized to form 1-chloro-3-mesitylacetone, which reacted with salicylaldehyde and potassium carbonate to yield 1-(1-benzofuran-2-yl)-2-mesitylethanone.

The oxime derivative was then generated through a reaction with hydroxylamine, followed by treatment with various substituted acyl chlorides to produce the final derivatives. The antimicrobial activity of these compounds was tested against

Escherichia coli ATCC 25922, Staphylococcus aureus ATCC 6538, and Candida albicans ATCC 10231. Notably, compound 9b (1-(1-benzofuran-2-yl)-2-mesitylethanone-o-benzoyloxime) demonstrated superior activity against *S. aureus* ATCC 6538 and *E. coli* ATCC 25922 compared to the standard drugs meropenem and fluconazole, as summarized in **Table 10 [18]**.

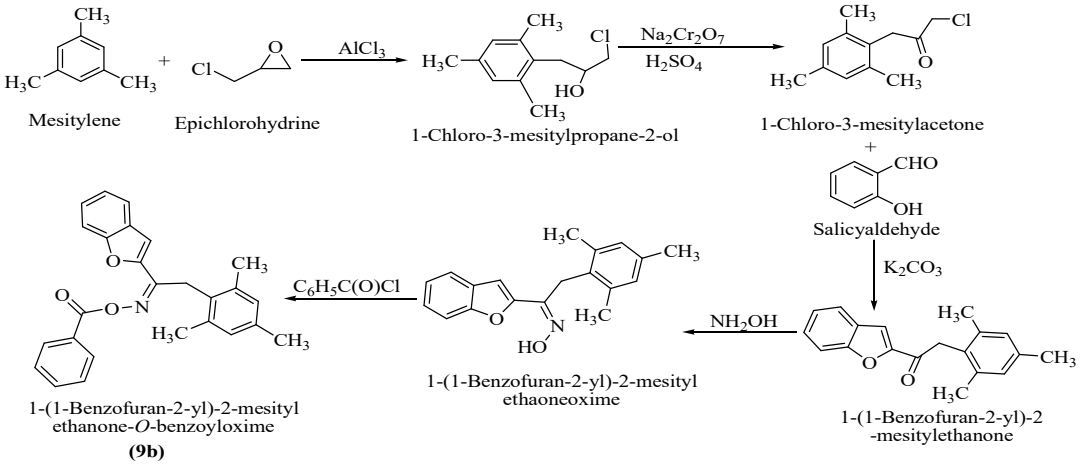



**Table 10: Evaluation of Antimicrobial activity and antifungal of Benzofuran Derivative**

| Compound name | MIC value (µg/ml) | | |
|---|---|---|---|
| | *Escherichia coli* | *Staphylococcus aureus* | *Candida albicans* |
| **(9b)** | **32** | **4** | **64** |
| **Meropenem** | **0.125** | **1** | **--** |
| **Fluconazole** | **--** | **--** | **0.25** |

A new series of 3-(benzofuran-2-yl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazole scaffolds was synthesized starting from salicylaldehyde and 1-chloropropan-2-one, using potassium tert-butoxide (t-BuOK) in the presence of molecular sieves to yield 2-acetylbenzofuran. This compound was further reacted with 4-methoxybenzaldehyde and then treated with hydrazine hydrate to produce the target pyrazole derivatives.

The synthesized compounds were evaluated for antimicrobial activity against *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa*, and several fungal strains, including *Aspergillus flavus* and *Candida albicans*. Notably, compounds 4h and 4j showed superior antimicrobial activity compared to standard drugs streptomycin and fluconazole, while compounds 4g and 4q exhibited enhanced antioxidant activity compared to butylated hydroxyanisole (BHA). The results are summarized in **Tables 11, 12, and 13 [19]**.

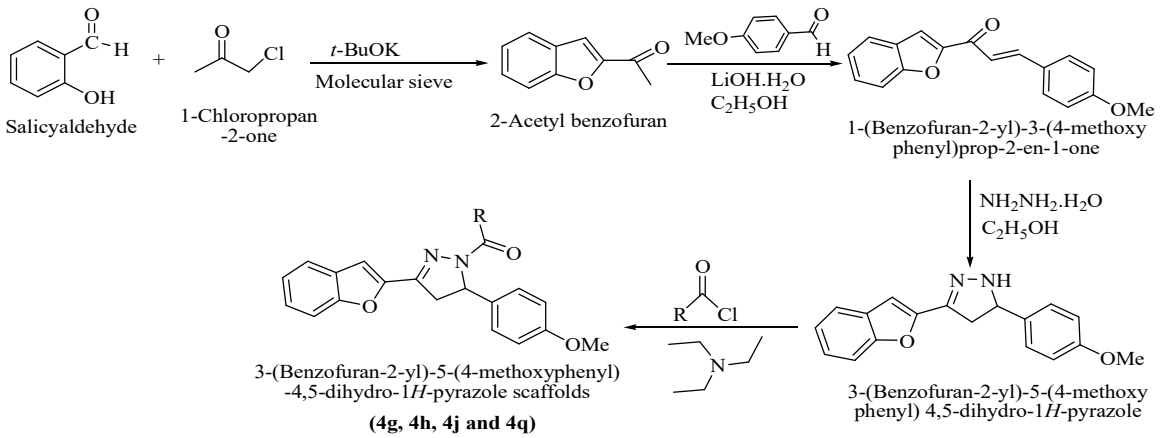



**Table 11: Evaluation of Antimicrobial activity of Benzofuran Derivatives**

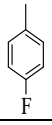
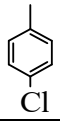
| Compound name | R | Inhibitory zone (Diameter) in mm | | | | | |
|---|---|---|---|---|---|---|---|
| | | *E. coli* | | *S. aureus* | | *P. aeruginosa* | |
| | | 1.0 | 0.5 | 1.0 | 0.5 | 1.0 | 0.5 |
| **4h** |  | **19±0.03** | **13±0.02** | **15±0.01** | **10± 0.02** | **16 ±0.02** | **13 ±0.02** |
| **4j** |  | **17±0.02** | **11±0.01** | **13±0.01** | **9± 0.01** | **15 ±0.01** | **12 ±0.02** |
| **Streptomycin** | **----** | **1 8±0.01** | **12±0.01** | **15±0.02** | **12± 0.01** | **17 ±0.01** | **13 ±0.01** |

**Table 12: Evaluation of antifungal activity and of Benzofuran Derivative**

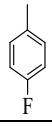
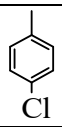
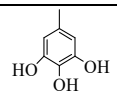
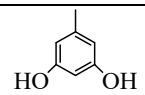
| Compound name | R | Inhibitory zone (Diameter) in mm | | | | | |
|---|---|---|---|---|---|---|---|
| | | *A. flavus* | | *C. keratinophilum* | | *C. albicans* | |
| | | 1.0 | 0.5 | 1.0 | 0.5 | 1.0 | 0.5 |
| **4h** |  | **9 ± 0.02** | **6 ± 0.01** | **9 ± 0.01** | **8 ± 0.01** | **11± 0.01** | **10 ± 0.02** |
| **4j** |  | **12 ± 0.03** | **10 ± 0.02** | **17 ± 0.01** | **15 ± 0.02** | **21± 0.02** | **19 ± 0.02** |
| **Fluconazole** | **----** | **14± 0.01** | **12±0.02** | **17± 0.02** | **16 ±0.01** | **20±0.02** | **18 ±0.02** |

**Table 13: Evaluation of Antioxidant activity of Benzofuran Derivatives**

| Compound name | R | Scavenging activity ($IC_{50}$) in µM | | |
|---|---|---|---|---|
| | | DPPH | LPO | ABTS |
| **4g** |  | **9 ±0.58** | **4.3± 0.21** | **18.9 ±0.11** |
| **4q** |  | **10 ±0.62** | **5.2± 0.21** | **19.7 ±0.14** |
| **BHA** | **---** | **12.5 ±0.12** | **6.4± 0.12** | **20.9 ±0.12** |

A novel series of (benzofuran-2-yl)(3-phenyl-3-methylcyclobutyl) ketoxime derivatives was synthesized from salicylaldehyde and 1-phenyl-1-methyl-3-(2-chloro-1-oxoethyl)cyclobutane using potassium carbonate, yielding (benzofuran-

2-yl)(3-methyl-3-phenylcyclobutyl) methanone. This intermediate was converted into ketoximes with hydroxylamine and subsequently reacted with epichlorohydrin and various substituted halogens to produce (benzofuran-2-yl)(3-phenyl-3-methylcyclobutyl)-o-glycidyl ketoxime and substituted N-oxime ethers.

The antimicrobial activity of these derivatives was assessed against *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Candida albicans*. Notably, (benzofuran-2-yl)(3-phenyl-3-methylcyclobutyl)-o-benzyl ketoxime (6a) exhibited strong activity against *C. albicans*, while (benzofuran-2-yl)(3-phenyl-3-methylcyclobutyl)-o-[2-hydroxy-3-(N-methylpiperazino)propyl] ketoxime (7d) showed enhanced activity against *S. aureus*. The results are summarized in **Table 14 [20]**.

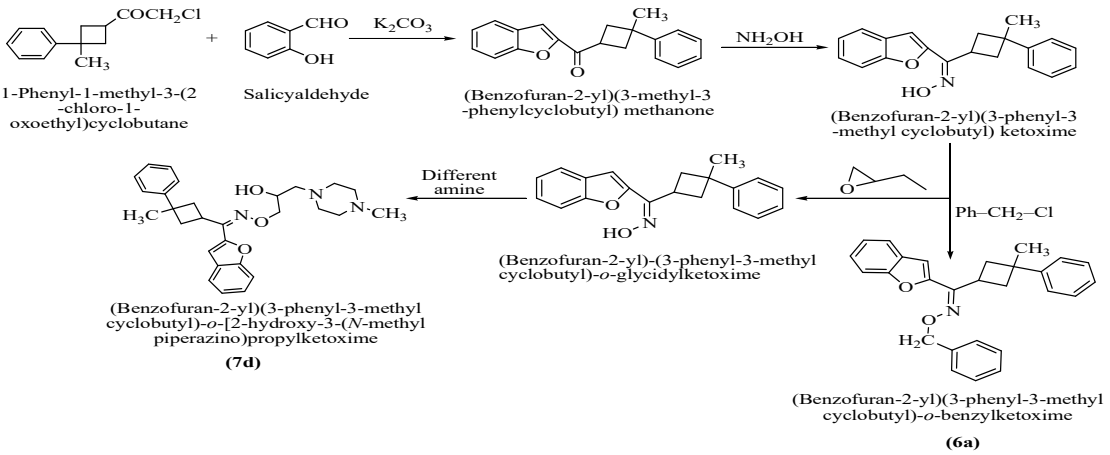



**Table 14: Evaluation Antimicrobial activity of Benzofuran Derivative**

| Compound name | *S. aureus* | *C. albicans* |
|---|---|---|
| 6a | -- | 2.5 |
| 7d | 0.039 | -- |

A series of benzofuran-based imidazothiazole derivatives was synthesized using 1-(1-benzofuran-2-yl)-2-bromoethanones as the starting material **(Tables 15 and 16)**. The bromoethanones were reacted with thiazol-2-amines, producing imidazothiazole derivatives that were tested for antimicrobial activity against various strains. Compounds 5b and 6b showed strong antibacterial effects against S. aureus and P. aeruginosa, while 5e and 5f were effective against *S. aureus* and *E. coli*. Additionally, compounds 5b, 5c, and 6d demonstrated notable antifungal activity against *A. niger* and *T. viride*, with ampicillin and fluconazole used as standards for comparison **[21]**.

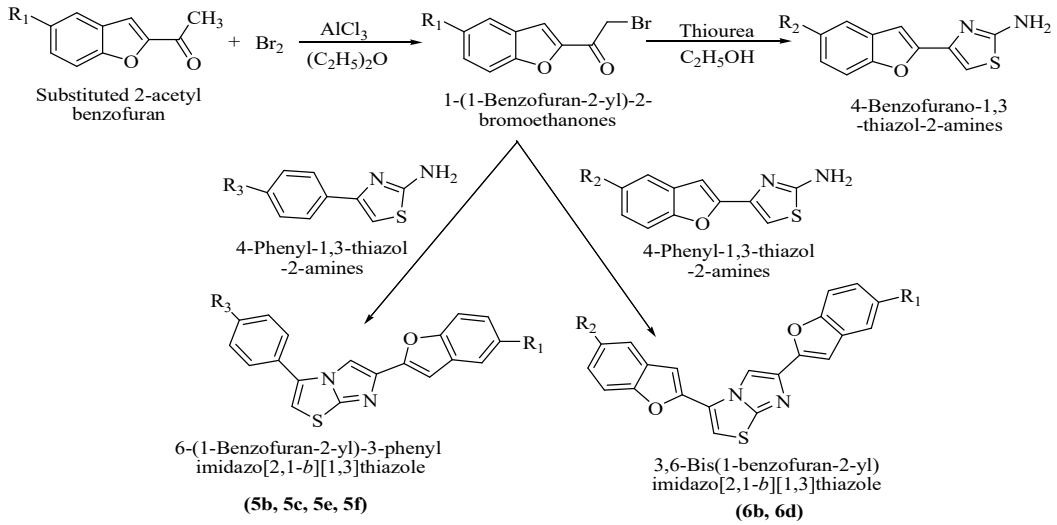



**Table 15: Evaluation Antibacterial activity of Benzofuran Derivatives**

| Compound name | $R_1$ | $R_2$ | $R_3$ | *S. aureus* | | *K. pneumona* | | *P. aeruginosa* | | *E. coli* | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 50µL | 100µL | 50µL | 100µL | 50µL | 100µL | 50µL | 100µL |
| 5b | Br | - | H | 20 | 27 | 16 | 22 | 18 | 25 | 15 | 18 |
| 5e | H | -- | F | 14 | 17 | 06 | 16 | 12 | 14 | 18 | 20 |
| 5f | Br | -- | F | 18 | 22 | -- | 10 | 14 | 18 | 16 | 20 |
| 6b | H | Br | -- | 23 | 28 | 13 | 18 | 18 | 24 | 12 | 16 |
| Ampicillin | ----- | | | 24 | 30 | 28 | 32 | 20 | 28 | 28 | 31 |

**Table 16: Evaluation Antifungal activity of Benzofuran Derivatives**

| Compound name | $R_1$ | $R_2$ | $R_3$ | *A. niger* | | *T. virdae* | |
|---|---|---|---|---|---|---|---|
| | | | | 50µL | 100µL | 50µL | 100µL |
| 5b | Br | - | H | 19 | 22 | 15 | 19 |
| 5c | H | -- | $CH_3$ | 22 | 26 | 24 | 26 |
| 6d | Br | Br | -- | 23 | 26 | 21 | 25 |
| Fluconazole | ------- | | | 28 | 34 | 28 | 30 |

A series of 4-(1-benzofuran-2-yl)-1,3-thiazole-2-amine derivatives was synthesized **(Tables 17, 18, 19)** from 2-acetylbenzofuran, obtained by reacting salicylaldehyde with bromoacetone. The intermediate was brominated, then refluxed with thiourea to yield 4-(1-benzofuran-2-yl)-1,3-thiazole-2-amine, which was further reacted with various aromatic aldehydes.

The biological activities were evaluated for antibacterial effects against *Staphylococcus aureus* and *Escherichia coli,* as well as analgesic and anti-inflammatory activities. Compounds VIa and VIb showed good antibacterial activity, while VIc, VIf, and VIj exhibited significant anti-inflammatory effects. Compounds VIa, VIe, VIf, and VIj also demonstrated superior analgesic activity compared to standard drugs amoxicillin, ibuprofen, and pentazocine. Results are summarized in **Tables 17, 18, and 19 [1]**.

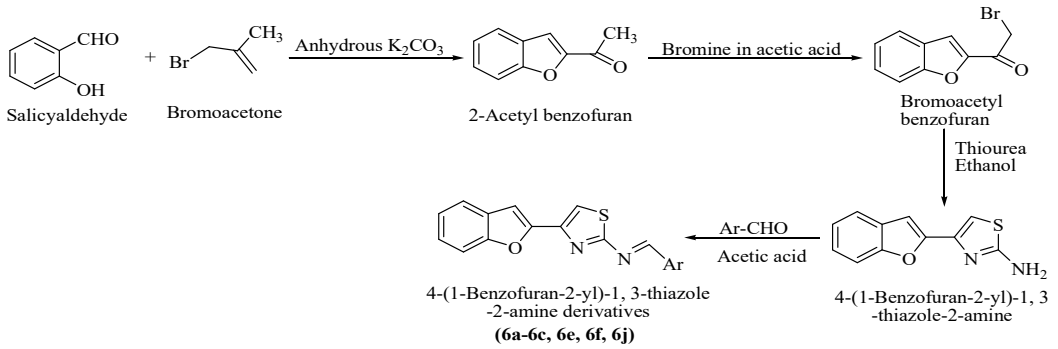



**Table 17: Evaluation Antibacterial activity of Benzofuran Derivatives**

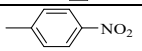
| Compound name | Ar | Zone of inhibition (mm) | |
|---|---|---|---|
| | | *E. coli* | *S. aureus* |
| VIa |  | 16 | 17 |
| VIb |  | 17 | 16 |
| Amoxicillin | ---- | 23 | 21 |

**Table 18: Evaluation Anti-inflammatory activity of Benzofuran Derivatives**

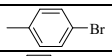
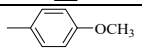
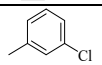
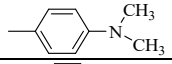
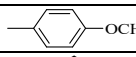
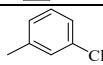
| Compound name | Ar | Dose | Increase in paw volume (ml) | % Inhibition |
|---|---|---|---|---|
| VIc |  | 20mg/kg | 0.25±0.01 | 59.01 |
| VIf |  | 20mg/kg | 0.29±0.01 | 52.45 |
| VIj |  | 20mg/kg | 0.24±0.02 | 60.65 |
| Ibuprofen | --- | 5mg/kg | 0.14±0.01 | 75.90 |

**Table 19: Evaluation Analgesic activity of Benzofuran Derivatives**

| Compound name | Ar | Dose | Number of writhings in 10 minutes (mean ± SEM) | % Inhibition |
|---|---|---|---|---|
| VIa |  | 20mg/kg | 32.33 ± 2.30 | 59.68 |
| VIe |  | 20mg/kg | 38.33 ± 2.30 | 51.84 |
| VIf |  | 20mg/kg | 35.5 ± 1.88 | 55.40 |
| VIj |  | 20mg/kg | 40.51 ± 2.57 | 49.10 |
| Pentazocine | ----- | 5mg/kg | 21.66 ± 1.06 | 72.78 |

## 2.2 Benzofuran derivative as antitumor agents:

Cancer is the leading cause of death worldwide, necessitating new effective treatments. A primary challenge is developing agents that selectively target tumor cells without general toxicity, limiting traditional chemotherapy's efficacy. Cytotoxic drugs are essential in cancer treatment, often combined with innovative therapies like signal inhibitors. Recent advancements have focused on triple-negative breast cancer (TNBC), known for its aggressiveness and limited options. Benzofuran hybrids are promising due to their ability to inhibit bromodomain-

containing protein 4 (BRD4), a key regulator in TNBC.

A novel series of benzofuran-2-carboxamide derivatives was synthesized by reacting benzofuran-2-carbonyl chloride with substituted anilines and amino-pyridines in dry toluene, as well as with benzimidazole derivatives. These compounds were evaluated for anticancer activity against various cell lines, including MCF-7, SK-BR-3, SW620, MiaPaCa-2, WI38, and HeLa. Among them, N-(2-acetamidopyridin-3-yl)benzofuran-2-carboxamide (3h) and N-[4-(2-imidazolyl)phenyl]benzofuran-2-carboxamide hydrochloride (3i) showed the highest activity against SW620. Additionally, N-[6-(2-imidazolyl)benzimidazol-2-yl]benzofuran-2-carboxamide hydrochloride (6f) exhibited superior activity against SK-BR-3. Significant results are summarized in **Table 20 [23]**.

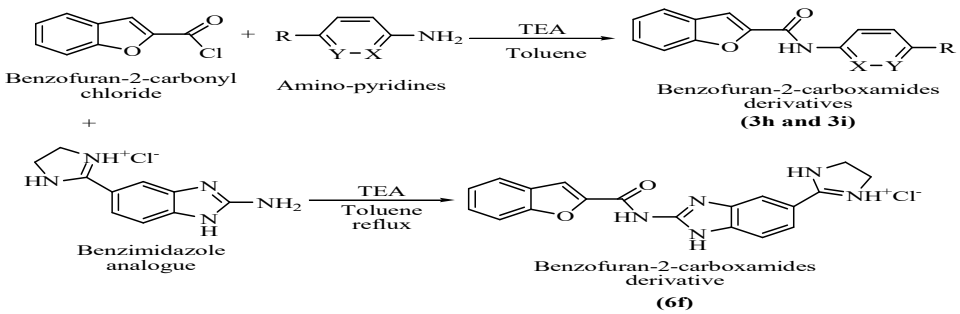



**Table 20: Evaluation Antitumor activity of Benzofuran Derivatives**

| Compound name | X | Y | R | $IC_{50}$(μM) | |
|---|---|---|---|---|---|
| | | | | Cell lines | |
| | | | | SW620 | SK-BR-3 |
| 3h | CH | N | $NHCOCH_3$ | 1.1 | -- |
| 3i | CH | CH |  | 67.1 | -- |
| 6f | ------ | | | -- | 3.83 |

A novel series of 2-alkylbenzofuran-imidazole hybrids was synthesized from benzofuran-2-carbaldehyde, prepared via Vilsmeier–Haack conditions. This derivative was reduced with sodium borohydride ($NaBH_4$) to obtain benzofuran-2-methanol, which was then mesylated to form the respective hybrids. The final step involved refluxing the intermediates with substituted imidazoles.

The anticancer activity of the compounds was evaluated against various cancer cell lines, including leukemia (HL-60), colon carcinoma (SW480), lung carcinoma (A549), breast carcinoma (MCF-7), and myeloid liver carcinoma (SMMC-7721). Notably, compound 1-((benzofuran-2-yl)methyl)-3-(2-(2-(naphthalen-2-yl)-2-oxoethyl)-2-methyl-1H-imidazol-3-ium bromide (29) exhibited excellent activity

against all tested cell lines. Additionally, compound 1-((benzofuran-2-yl)methyl)-3-(2-(4-methoxyphenyl)-2-oxoethyl)-2-methyl-1H-imidazol-3-ium bromide (26) showed significant activity against SW480 and MCF-7. The efficacy of these compounds was compared to cisplatin (DDP), with superior results presented in **Table 21** [**6], [23]**.

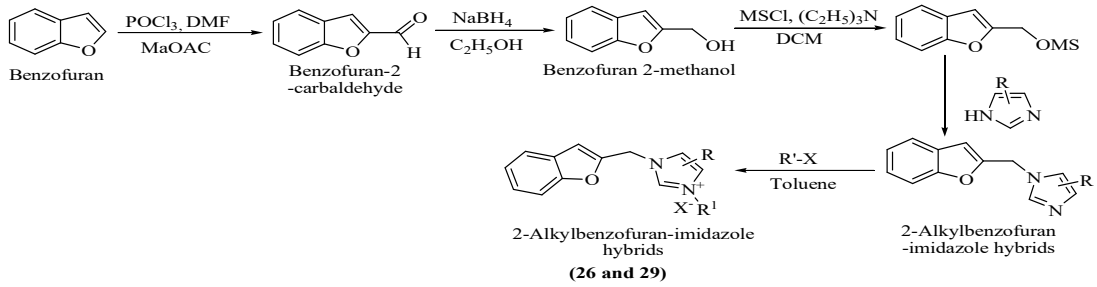



**Table 21: Evaluation Antitumor activity of Benzofuran Derivatives**

| Compound name | R | $R^1$ | X | $IC_{50}$(μM) | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | HL-60 | SW480 | A549 | MCF-7 | SMMC-7721 |
| 26 | 2-Methyl | 4-methoxyphenacyl | Br | 0.78 | 0.28 | 0.37 | 1.44 | 11.59 |
| 29 | 2-Ethyl | Naphthyacyl | Br | 1.04 | 1.03 | 4.97 | 1.09 | 3.50 |
| Cisplatin | ----- | | | 3.10 | 12.32 | 13.61 | 10.64 | 14.75 |

## 2.3 Benzofuran Derivatives as Anti-Inflammatory Agents

Nonsteroidal anti-inflammatory drugs (NSAIDs) like mefenamic, meclofenamic, and flufenamic acids are widely employed to alleviate pain and inflammation by inhibiting prostaglandin synthesis through the enzyme cyclooxygenase (COX). They are often first-line treatments for inflammatory conditions, including rheumatoid arthritis, soft tissue injuries, fever, and respiratory infections **[28]**. Recent research has focused on benzofuran compounds that target key inflammatory pathways, such as NF-kB and MAPK, which are implicated in autoimmune and inflammatory diseases. By influencing these pathways, benzofuran derivatives present promising therapeutic potential for managing inflammation **[24]**.

In a novel study, a series of benzofuran-based fenamate derivatives were synthesized by refluxing 3-arylaminobenzofuran-2-carbohydrazides with carbon disulfide and potassium hydroxide in ethanol. Screening of these compounds for anti-inflammatory effects in carrageenan-induced rat paw edema models showed that compounds 2a, 2c, 2e, and 2f demonstrated substantial activity, outperforming diclofenac sodium, which served as the standard reference compound. The results for these active compounds are summarized in **Table 22 [24], [26]**.

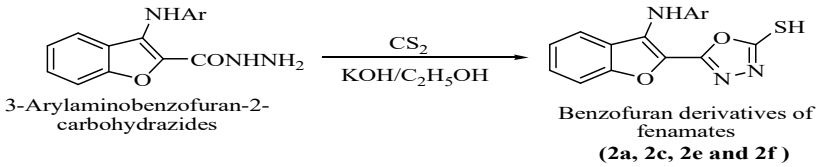



**Table 22: Evaluation Anti-inflammatory activity of Benzofuran Derivatives**

| Compound name | R | Dose (mg/kg) | Mean difference in paw volume + S.E after 3 hrs (ml) | % Inhibition |
|---|---|---|---|---|
| 2a | $C_6H_5$ | 100 | 0.36 ± 0.02 | 60 |
| 2c | $C_6H_5Cl$ (*p*) | 100 | 0.32 ± 0.01 | 64 |
| 2e | $C_6H_5Cl$, F (*m*, *p*) | 100 | 0.29 ± 0.02 | 68 |
| 2f | $C_6H_5Cl$ (*o*) | 100 | 0.34 ± 0.01 | 62 |
| Diclofenac sodium | ------ | 100 | 0.14 ± 0.01 | 84 |

A new aryl-5-nitrobenzofuran-2-carbamide series was synthesized through a series of reactions, starting from salicylaldehyde and yielding the final carbamides after treatment with substituted amines. Anti-inflammatory effects were measured using the carrageenan-induced rat paw edema model, while antimicrobial activity was tested against *S. aureus* and *E. coli*. Compounds 6-d and 6-f exhibited the highest anti-inflammatory efficacy, and 6-d, 6-e, and 6-f showed superior antimicrobial activity compared to ibuprofen and ampicillin. The activities of the active compounds are summarized in **Table 23** and **24 [10]**.

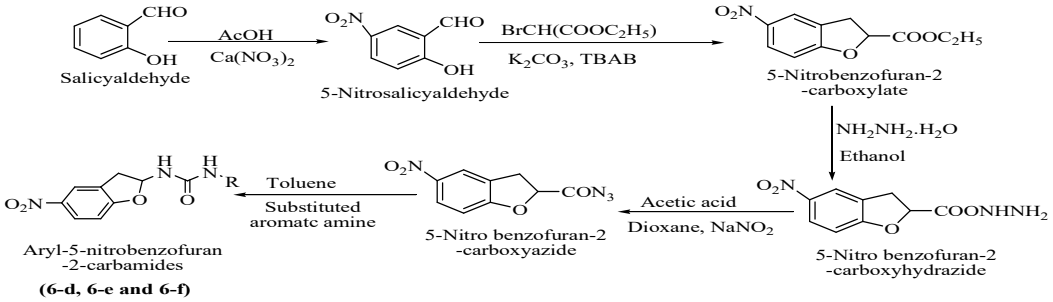



**Table 23: Evaluation Anti-inflammatory activity of Benzofuran Derivatives**

| Compound name | R | Mean increase in paw volume ± Standard deviation and % inhibition | | |
|---|---|---|---|---|
| | | 1hr. | 2 hr. | 3 hr. |
| 6-d | -$C_6H_4OCH_3$(*p*) | 0.77± 0.074<br>52.17% | 0.73±0.09<br>60.10% | 0.71 ± 0.05<br>64.14% |
| 6-f | -$C_6H_4Cl$(*m*) | 0.75 ± 0.03<br>53.41% | 0.74 ± 0.009<br>59.56% | 0.72 ± 0.01<br>63.63% |
| Ibuprofen (20µg/ml) | ----- | 0.74 ± 0.070<br>54.03% | 0.70 ± 0.008<br>61.74% | 0.76 ± 0.02<br>61.6% |

**Table 24: Evaluation Antimicrobial activity of Benzofuran Derivatives**

| Compound name | R | Zone of inhibition (mm) | |
|---|---|---|---|
| | | *S. aureus* | *E. coli* |
| 6-d | -$C_6H_4OCH_3$(*p*) | 19 | 09 |
| 6-e | -$C_6H_4OCH_3$(*o*) | 17 | 10 |
| 6-f | -$C_6H_4Cl$(*m*) | 14 | 20 |
| Ampicillin (500µg/ml) | ----- | 24 | 32 |

A novel series of benzofuranyl ethers of coumarins was synthesized, starting from 4-(4'-acetyl-3'-hydroxy-phenoxy methyl)-coumarin, derived by reacting 4-(bromomethyl)-6-chlorocoumarin with 2,4-dihydroxyacetophenone in acetone. This intermediate was then refluxed with phenacyl bromide and potassium carbonate. Anti-inflammatory and analgesic activities were assessed using the carrageenan-induced rat paw edema and abdominal constriction tests. Among the compounds, (5-((6-chloro-2H-chromen-4-yl)methoxy)-3-methyl benzofuran-2-yl)(phenyl)methanone (5d) showed the highest activity compared to the standard, indomethacin. The activities of the active compounds are summarized in **Table 25 [27]**.

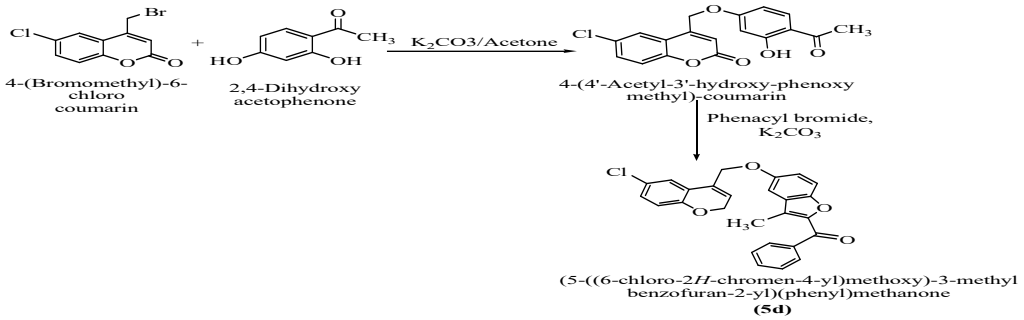



**Table 25: Evaluation Anti-inflammatory and analgesic activity of Benzofuran Derivative**

| Compound name | Anti-inflammatory activity | Analgesic activity | |
|---|---|---|---|
| | % Inhibition | % Protection | |
| | 100mg/kg | 1mg/kg | 10mg/kg |
| 5d | 62 | 32 | 60 |
| Indomethacin | 62 | 55 | -- |

A series of benzofuran-based prodrugs was synthesized starting with hydroquinone oxidation to cyclohexa-2,5-diene-1,4-dione, which was then converted to ethyl 2,3-dihydro-5-hydroxy-2-methylbenzofuran-3-carboxylate. Anti-inflammatory effects were tested in a carrageenan rat model, with ethyl 5-(p-tolyloxy)-2-methylbenzofuran-3-carboxylate (3c) showing superior activity compared to the standard, nimesulide. Best result of the active compounds is showing in **Table 26 [28]**.

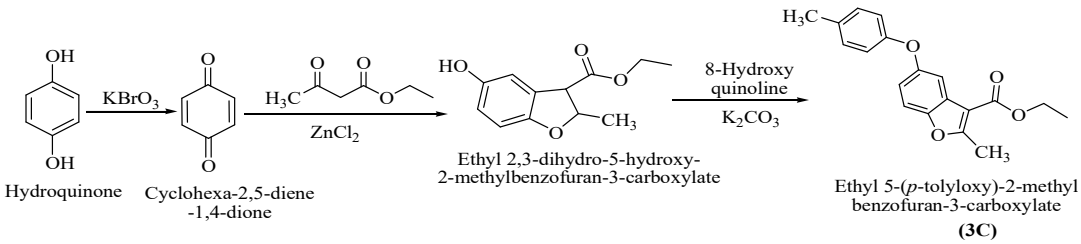


**Table 26: Evaluation Anti-inflammatory and analgesic activity of Benzofuran Derivative**

| Compound name | 0 min | 30 min | 90 min |
|---|---|---|---|
| 3c | 0.98 ± 0.031 | 1.06 ± 0.038 | 1.11 ± 0.045 |
| Nimesulide | 1.02 ± 0.054 | 1.16 ± 0.065 | 1.26 ± 0.038 |

## 2.4 Benzofuran derivative as antitubercular agents:

Studies have shown that novel benzofuran compounds exhibit strong antitubercular effects against both Mycobacterium tuberculosis (MTB) and multidrug-resistant strains (MDR-TB), addressing urgent treatment needs as resistance to current drugs grows. A new series of N'-benzylidene benzofuran-3-carbohydrazide derivatives was synthesized and demonstrated strong antitubercular and antifungal activity. Compounds 8a and 8k outperformed standard drugs like isoniazid and clotrimazole against MTB and Candida albicans, respectively. The significant results of these active compounds are summarized in **Table 27 [8], [25], [36]**.

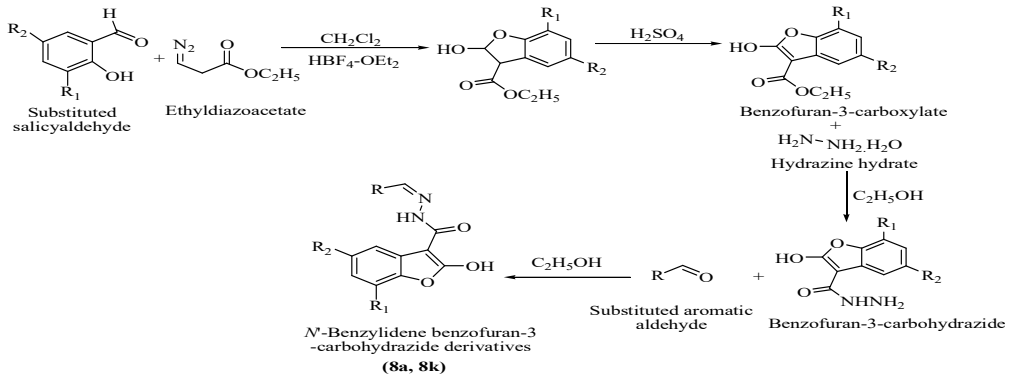



**Table 27: Evaluation Antitubercular and antifungal activity of Benzofuran Derivatives**

| Compound name | $R_1$ | $R_2$ | R | Antitubercular MIC (µg/ml) | Antifungal MIC (µg/ml) |
|---|---|---|---|---|---|
| 8a | H | H | Phenyl | 2.0 | >250 |
| 8k | Cl | Cl | Phenyl | 2.0 | >250 |
| Isoniazid | ------ | | | 0.25 | -- |
| clotrimazole | ------ | | | -- | 0.50 |

A series of hybrid molecules, 1-(2,3-dihydronaphtho(benzo)furan-2-yl-methyl) 4-alkyl/aryl-1,2,3-triazoles, were synthesized through [3+2] cycloaddition of 2-(azidomethyl)-dihydronaphtho(benzo)furans with various alkynes. These compounds were evaluated for antitubercular activity against Mycobacterium tuberculosis H37Rv, with compounds 2a, 7, 9, and 12 exhibiting superior efficacy compared to the standard drugs isoniazid and ethambutol. The enhanced efficacy of the most active compound is presented in **Table 28 [37]**.

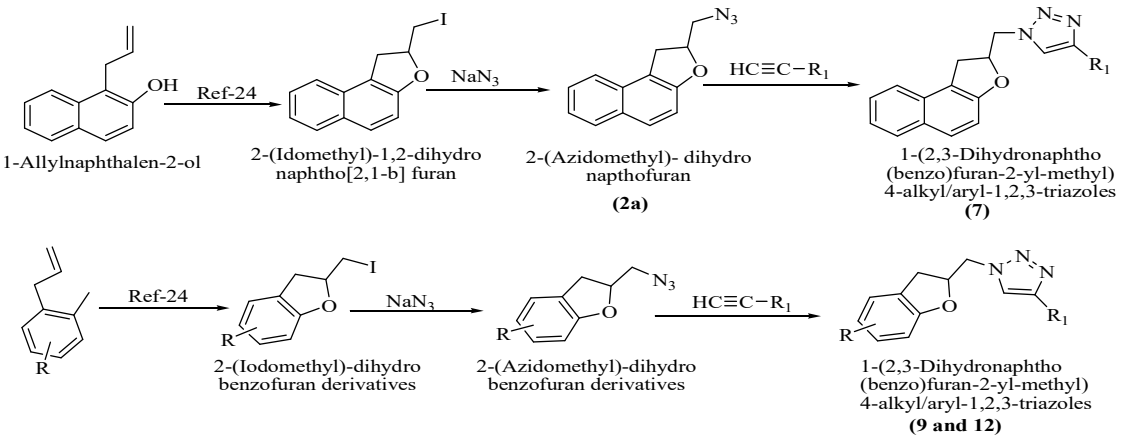



**Table 28: Evaluation Antitubercular of Benzofuran Derivatives**

| Compound name | R | $R_1$ | MIC (µg/ml) |
|---|---|---|---|
| **2a** | ------ | | **3.12** |
| **7** | -- | $-CH_2CH_2OH$ | **12.5** |
| **9** | $-2,5-(CH_3)_2$ | $-CH_2OH$ | **12.5** |
| **12** | $-2,5-(CH_3)_2$ | $-C_6H_5$ | **6.25** |
| **Isoniazid** | ----- | | **0.75** |
| **Ethambutol** | ----- | | **3.25** |

A series of compounds, 1-[3-(5-hydroxybenzo[b]furan-2-yl)-5-substituted phenyl-4,5-dihydro-1H-1-pyrazolyl]-2-(5H-indolo[2,3-b]quinoxalin-5-yl)-1-ethanone, was synthesized from 2,4-dihydroxybenzaldehyde and chloroacetone to yield 5-hydroxy-2-acetylbenzofuran, which reacted with various aromatic aldehydes to form derivatives. These derivatives were then reacted with 2-(5,8-dihydroquinoxalino[2,3-b]indol-5-yl)acetohydrazide to produce the final products. The compounds were tested for antitubercular activity against Mycobacterium tuberculosis H37Rv and multidrug-resistant strains, with compounds 5e, 5h, 5i, 5j, and 5m showing superior efficacy to rifampicin and gatifloxacin, as shown in **Table 29 [29]**.

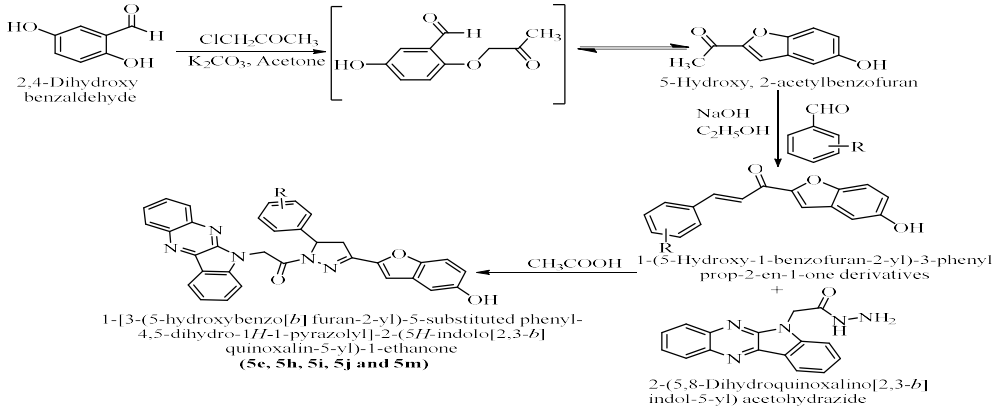


**Table 29: Evaluation Antimicrobial and Antitubercular of Benzofuran Derivatives**

| Compound name | R | Result against MTB | | Result against MDR-TB | | $IC_{50}$(µM) |
|---|---|---|---|---|---|---|
| | | $MIC_{50}$(µg/ml) | $MIC_{90}$(µg/ml) | $MIC_{50}$(µg/ml) | $MIC_{90}$(µg/ml) | |
| 5e | -$NO_2$ (*m*) | 0.62 | 1.24 | 1.20 | 2.00 | >180.2 |
| 5h | -Cl (*p*) | 2.45 | 4.20 | 5.23 | 8.66 | >205.4 |
| 5i | -Cl (*o*) | 1.75 | 2.56 | 4.68 | 8.61 | >195.6 |
| 5j | -$NO_2$ (*o*) | 0.16 | 0.42 | 3.24 | 7.2 | >144.3 |
| 5m | Furan ring | 1.1 | 3.12 | 6.40 | 9.78 | >198.2 |
| Rifampicin | --- | 0.5 | 2.0 | 4.21 | 7.37 | >77.4 |
| Gatifloxacin | --- | 0.12 | 0.5 | 14.7 3 | 28.46 | >159.5 |

## 2.5 Benzofuran Derivatives as Antioxidant Agents:

The antioxidant activity of benzofuran derivatives was assessed using DPPH and hydroxyl radical scavenging assays, with results compared to standard drugs. The DPPH assay measures hydrogen atom acceptance from antioxidants, while hydroxyl radicals attack deoxyribose substrates. The DPPH radical, with maximum absorption at 517 nm, allows for IC50 calculations based on triplicate readings. Findings indicate that benzofuran derivatives enhance antioxidant enzyme activity, relevant for neurodegenerative diseases **[30, 31]**.

A series of benzofuran-1,3-thiazolidin-4-one derivatives was synthesized from 5-((E)-1-(substituted imino)ethyl)-4,7-dimethoxybenzofuran-6-ol, derived from khellinone and an aliphatic amine. After refluxing with thioglycolic acid, the antioxidant activity was evaluated using DPPH and hydroxyl radical assays. Compounds 3c, 3d, 3f, and 4d demonstrated superior antioxidant activity compared to the standard drug trolox, as shown in **Table 30 [7, 30, 31]**.

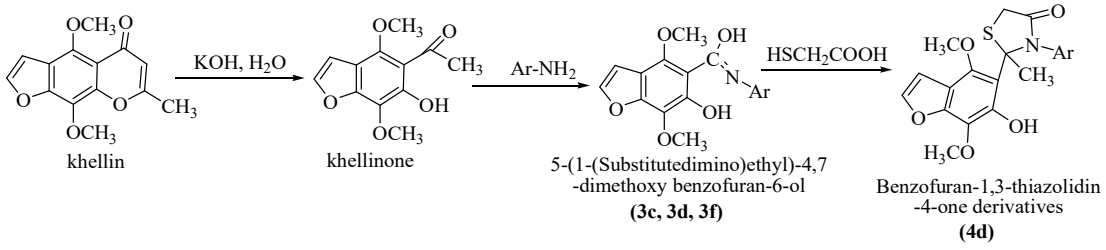



**Table 30: Evaluation Antioxidant activity of Benzofuran Derivatives**

| Compound name | Ar | $IC_{50}$(µM) |
|---|---|---|
| 3c | 2-Nitrophenyl | 8.57 |
| 3d | 4-Methylphenyl | 9.72 |
| 3f | 4-Methoxyphenyl | 8.27 |
| 4d | 4-Methylphenyl | 10.59 |
| Trolox | ---- | 5.42 |

A series of 5-phenyl-1-benzofuran-2-yl derivatives was synthesized from 2-bromo-1-(4-bromophenyl)ethanone and 5-bromo-2-hydroxybenzaldehyde using

DMAP and sodium carbonate, resulting in 5-bromo-1-benzofuran-2-yl (4-bromophenyl) methanone. This intermediate reacted with sodium carbonate and $Pd(PPh_3)_4$ in toluene to yield biphenyl methanones, which were reduced with sodium borohydride in anhydrous 1,4-dioxane. The compounds were assessed for antioxidant activity using the DPPH method and antimicrobial activity against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli,* and *Candida albicans*. Biphenyl-4-yl-(5-phenyl-benzofuran-2-yl)methanol (4a) exhibited superior antioxidant activity compared to BHT, while compounds 1, 2a, 2f, and 2g showed enhanced antimicrobial activity against ampicillin and nystatin, as shown in **Tables 31 and 32 [33]**.

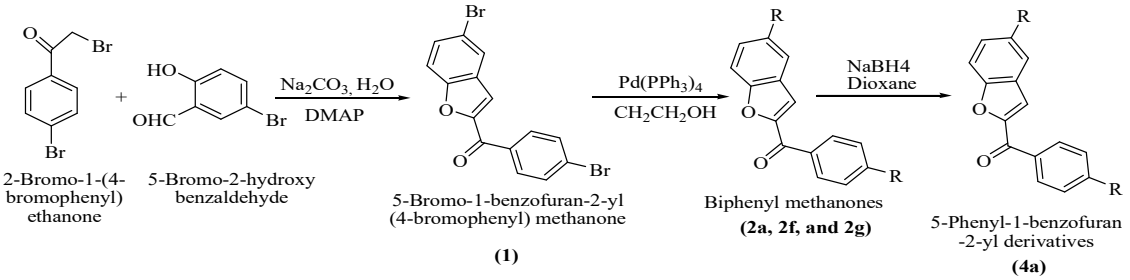
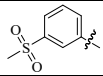



**Table 31: Evaluation Antioxidant activity of Benzofuran Derivatives**

| Compound name | R | DPPH assay in % |
|---|---|---|
| 4a |  | 79.5 |
| Butylated hydroxytoluene | ---- | 90.42 |

**Table 32: Evaluation Antimicrobial activity of Benzofuran Derivatives**

| Compound name | R | Zone of inhibition (mm) | | | | Minimum inhibitory concentration (mg/ml) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | *S. aureus* | *B. subtilis* | *E.coli* | *C. albicans* | *S. aureus* | *B. subtilis* | *E.coli* | *C. albicans* |
| 1 | --- | 23 | 24 | 17 | 15 | 0.050 | 0.050 | 0.050 | 0.050 |
| 2a |  | 15 | 22 | 0 | 10 | 0.001 | 0.010 | -- | 0.010 |
| 2f |  | 0 | 16 | 0 | 6 | -- | 0.500 | -- | 0.500 |
| 2g |  | 10 | `16 | 0 | 6 | 0.250 | 0.050 | -- | 0.500 |
| Ampicillin | --- | 16 | 15 | 20 | 0 | -- | -- | -- | -- |
| Nystatin | --- | 0 | 0 | 0 | 6 | -- | -- | -- | -- |

## 2.6 Benzofuran Derivatives as Anticonvulsant Agents:

Epilepsy, characterized by sudden and unpredictable seizures, affects approximately 50 million people globally, with 25% of patients experiencing inadequate control of seizures despite current drug therapies. Phenytoin and phenobarbital are commonly used anticonvulsants for generalized seizures.

The anticonvulsant activity of benzofuran derivatives was evaluated using two models: the maximal electroshock (MES) test and the pentylenetetrazol (scPTZ) test **[31]**. Recent studies indicate that benzofuran compounds may offer improved seizure control in genetic epilepsy models, highlighting their potential as epilepsy treatments **[32].**

A novel series of N-1',N-3'-disubstituted-2'H,3H,5H-spiro-(2-benzofuran-1,4'-imidazolidine)-2',3,5'-triones was synthesized **(Table 33)**. The synthesis began with ethanamine and 1-isocyanato-4-nitrobenzene, yielding 1-ethyl-3-(4-nitrophenyl)urea. This compound was refluxed with ninhydrin in benzene to produce indeno-[1,2-d]-imidazole intermediates, which were then treated with sodium periodate to form the target compounds. Anticonvulsant activity was assessed using the scPTZ and MES tests in mice. Among the synthesized compounds, the N-1'-p-nitrophenyl, N-3'-ethyl derivative (30) exhibited the highest activity in the scPTZ model, with phenobarbital and phenytoin as reference standards. The results for this active compound are shown in **Table 33 [31]**.

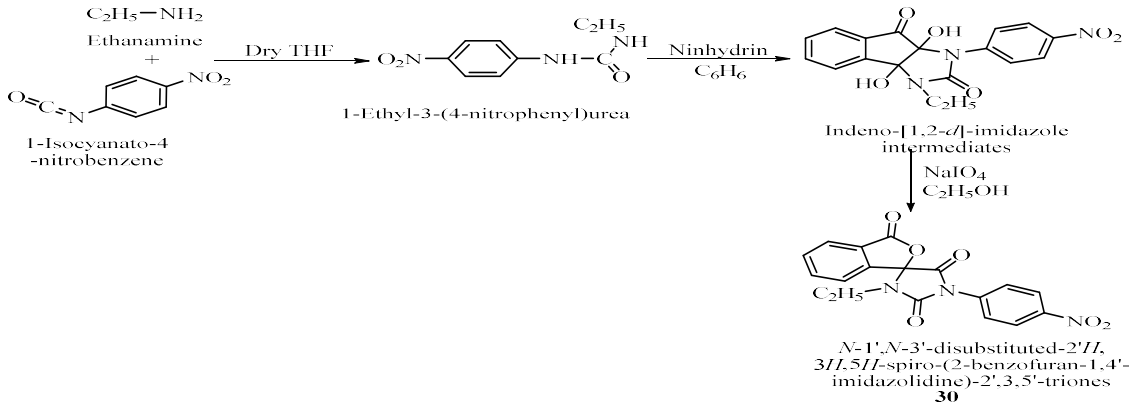



**Table 33: Evaluation Anticonvulsant activity of Benzofuran Derivatives**

| Compound name | $ED_{50}$ | |
|---|---|---|
| | scPTZ test | MES test |
| 30 | 41.8 (39.2-44.5) | -- |
| Phenobarbital | 20[a] (16)[b] | -- |
| Phenytoin | -- | 8.1[a] (9)[b] |

[a]Experimental $ED_{50}$value., [b]Literature $ED_{50}$value.

## 2.7 Benzofuran Derivatives as Anti-Hyperlipidemic Agents:

Hyperlipidemia is a major metabolic disorder linked to heart disease, stroke, and high mortality in developed countries, characterized by elevated triglycerides, low HDL-C, and high LDL-C levels. Treatments include niacin, fibrates, statins, and bile acid sequestrants, which lower cholesterol by inhibiting HMG-CoA reductase. Recent studies indicate that benzofuran derivatives could be promising cholesterol-lowering

agents. A new series of benzofuran-bisindole derivatives was synthesized through a modified Duff reaction, yielding compounds that significantly reduced triglycerides, total cholesterol, and phospholipids while enhancing lipolytic activity in hyperlipidemic rats, outperforming the standard drug gemfibrozil. The significant results of these active compounds are presented in **Table 34 [34], [35]**.

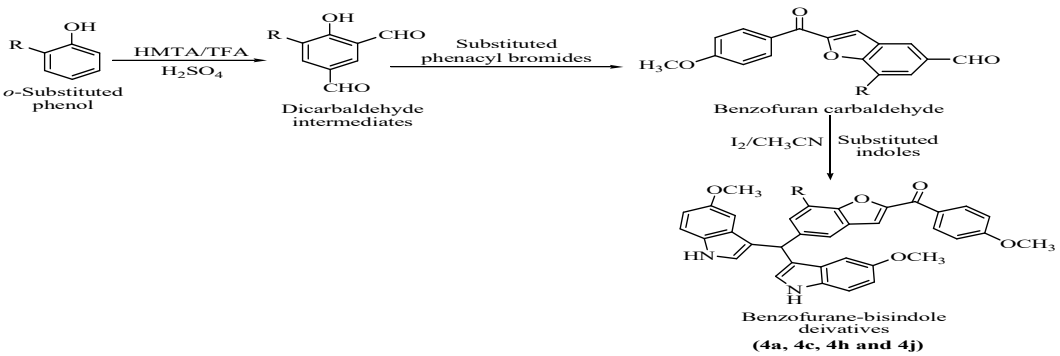



**Table 34: Anti-hyperlipidimic activity of compounds 4a, 4c, 4h and 4j**

| Compound name | R | Lipid profile | | | PHLA |
|---|---|---|---|---|---|
| | | Total cholesterol (TC) | Phospholipids (PL) | Triglycerides (TG) | |
| 4a | $CH_3$- | 141.84 ± 10.74 | 159.29 ± 15.11 | 164.24 ± 12.48 | 15.32 ± 1.11 |
| 4c | $(CH_3)_3C$- | 139.99 ± 9.63 | 159.29 ± 10.08 | 166.40 ± 10.28 | 15.45 ± 1.09 |
| 4h | $CH_3(CH_2)_2$- | 139.99 ± 12.33 | 159.29 ± 10.66 | 166.40 ± 9.64 | 15.32 ± 1.41 |
| 4j | $CH_3CH_2$- | 132.63 ± 10.76 | 146.88 ± 11.23 | 155.59 ± 11.75 | 15.58 ± 1.18 |
| Gemfibrozil | ---- | 121.57 ± 10.82 | 134.47 ± 12.81 | 142.63 ± 12.26 | 15.85 ± 1.27 |

## CONCLUSION:

Benzofuran derivatives represent a significant class of compounds with diverse biological activities, making them appealing for pharmaceutical research. This review highlights their synthesis and biological evaluations, showcasing their potential in various therapeutic areas. Their structural flexibility allows for extensive modifications, enhancing their biological activity. Notably, benzofuran derivatives have shown promise as antimicrobial agents against multidrug-resistant pathogens and possess potent anticancer activity, particularly against hard-to-treat cancers like triple-negative breast cancer through mechanisms such as BRD4 inhibition.

Additionally, these compounds exhibit significant anti-inflammatory, antioxidant, anticonvulsant, and antitubercular properties, supporting their use in chronic inflammatory conditions, neurodegenerative disorders, and tuberculosis. Their antioxidant capabilities suggest potential neuroprotective roles in Alzheimer's and Parkinson's diseases.

Overall, the pharmacological versatility of benzofuran derivatives positions them as valuable scaffolds for drug discovery, with ongoing research likely to produce novel compounds that enhance efficacy and safety, addressing global health challenges in cancer, infections, and metabolic disorders.

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