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A REVIEW SYNTHESIS AND EVALUATION OF NOVEL BENZOFURAN DERIVATIVES AS POTENT ANTICANCER AND ANTI-BACTERIAL ACTIVITY

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Abstract
Benzofuran derivatives have gained significant attention in medicinal chemistry due to their diverse biological activities, including anticancer and antibacterial properties. This review aims to synthesize and evaluate the current state of research on new benzofuran derivatives as active agents against cancer and bacterial infections. The review begins with a discussion of the synthetic strategies used to obtain benzofuran derivatives, highlighting the various functional groups and substituents that have been incorporated into the benzofuran backbone to enhance their biological activities. In addition, the importance of structure-activity relationship (SAR) studies in the design and optimization of benzofuran derivatives is highlighted. Furthermore, the anticancer potential of benzofuran derivatives is investigated, focusing on their mechanisms of action and their effectiveness against different types of cancer. In addition to their anticancer effects, benzofuran derivatives have shown promising antibacterial activity. The review includes an analysis of the antibacterial potential of benzofuran derivatives against various bacterial strains, including multidrug-resistant pathogens. The mechanisms of action responsible for their antibacterial effects, such as inhibition of essential enzymes and disruption of bacterial membranes, are discussed. Overall, this review provides a comprehensive synthesis and evaluation of the current literature on novel benzofuran derivatives as potent anticancer and antibacterial agents. The findings serve as a basis for future research and development of benzofuran-based compounds with improved efficacy, selectivity and therapeutic potential in the fight against cancer and bacterial infections.
Keywords: - Benzofuran derivatives, Anticancer activity, Antibacterial activity, Novel compound, Structure-activity relationship (SAR)

INTRODUCTION

Heterocyclic particles expect a fundamental part of natural science [1,2,3]. Since these particles are crucial for both engineered and natural sciences, a critical proportion of rhythmic movement overall investigation is committed to them. Heterocyclic ring structures have been gone after for various inherent capacities [4]. A smart molecule with pharmacological or physiological movement can't be made or found without these substances [5]. A heterocyclic molecule can be accumulated with pharmacophores to make steadies that are convincing and explicit [6]. Bioactive forms are of excellent interest and significance to both the agrarian and drug regions. Honestly, the medication region addresses commonly 60% of each and every heterocyclic subject, and the total compound plan of the top-selling prescription has something like one heterocyclic centre [7]. Besides, substances containing heterocyclic moieties are ordinarily more dissolvable and can set off a salt turn of events, the two of which are essential for oral ingestion and bioavailability. [8]. Therefore, oxygen heterocyclic compounds can be characterized by a wide range of biochemical and pharmacological properties. Naturally powerful typical and fake combinations with likenesses [9]. In light of its wide physiological and chemotherapeutic potential as well as its limitless occasion in nature, benzofuran systems (oxygen heterocycles) have attracted a ton of assessment recently [10]. Benzofuran subordinates, for example, are versatile biodynamic strengthens that can be used to cultivate new medicines [11]. Because of their enormous number of natural capacities and possible use as

prescriptions, they are of tremendous interest to researchers. Regardless of the way that benzofuran subordinates have been shown to show antihyperglycemic [12], torment easing [13], and parasitic [14], antibacterial [15], anticancer, and kinase inhibitor [16] works out, the natural effects of these blends are yet jumbled. Besides, subbed benzofurans are used in many products, including fluorescence sensors [17], oxidants [18], cell fortifications, illuminating subject matter experts, and maybe a couple of drugs, engineered compounds, and plant fields [19]. Besides, benzofurans are accessible in various regular items. Different physiological, pharmacological, and poisonous characteristics are accessible in customary benzofurans. These integrate Krameriaramosissima, Ophryosporuscharua, OphryosporusLorentzian, Machilusglaucescent, and Zanthoxylumailanthoidol, which have been found to contain practically identical benzofuran ring structures. [20]. Ailanthoidol, amiodarone, and bufuralol are the three most remarkable benzofurans. Ailanthoidol, a neolignan having a 2-aryl benzofuran structure, has been shown in unambiguous assessments to have anticancer, antiviral, immunosuppressive, cell support, antifungal, and antifeedant properties. It is amiodarone. Antiarrhythmic medicines of the Class III variety are extraordinarily useful [22]. Hoffmann-La Roche is the company that developed the nonselective b-adrenoceptor antagonist known as bufuralol. This substance shows enantioselective and regioselective oxidation in the liver and is an extraordinary cytochrome P450 (CYP) substrate. [23]. Psoralen and methoxsalen, two ordinarily happening furocoumarins with benzofuran structures that are used to treat psoriasis and other skin conditions, have been recognized [24-25]. It has as of late become logically typical for different investigation social occasions to take a gander at substitute pathways for benzofuran ring improvement and hidden change to focus on various regular positions. In this way, the benzofuran moiety gives a sublime stage to the blend of novel auxiliaries with different innate capacities. A heterocyclic substance called benzofuran is involved in merged benzene and furan rings. The whitish liquid integrates coal tar. Different relative blends with extra diverse plans have their basic establishments in benzofuran. Psoralen, a substance found in plants, is one such subordinate of benzofuran. Figure 1 shows this.

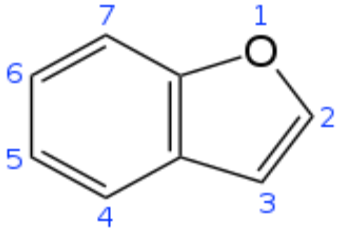


Fig 1 The structure of benzofuran [26]

The fields of drug science and pharmaceutical chemistry together involve the blending, purification, and adjustment of medicinal molecules. This discipline involves the distinguishing proof and improvement of novel remedial competitors (focuses), as well as the advancement of procedures for evaluating such mixtures and deciding their viability in vivo. Benzofurans frequently exist in coal tar portions and, with regards to conduct, look like consolidated fragrant frameworks. Benzofurans can be used to make cheap, artificially latent saps since they can rapidly polymerize when presented with sulfuric corrosive and are impervious to salt. Plant phenols and numerous other synthetically dynamic substances have profited from the presence of benzofurans. Moreover, benzofurans have contributed fundamentally and particularly to science. They have a large number of pharmacological impacts, like H3 receptor and angiotensin II bad guys, as well as an antifungal, antiviral, antibacterial, anticancer, calming, cell reinforcement, antitubercular, hostile to plasmodial, insecticidal, and trypanocidal characteristics. Because of the broad scope of natural exercises, it shows, the benzofuran skeleton is perceived as quite possibly of the most noticeable heterocyclic framework and assumes an essential part in natural science. This primary component is pivotal for some synthetics that make natural impacts. Various restorative advantages of regular and engineered benzofuran subsidiaries have been found, including antiviral, immunosuppressive, cell reinforcement, antifungal, antibacterial, pain relieving, mitigating, and anticancer exercises [27,28,29,30,31,32]. Instances of normally happening benzofurans that are physiologically dynamic incorporate Cicerfuran, Conocarpan, and Ailanthoidol

(Figure 1). Cicerfuran has antifungal activity, though Ailanthoidol has anticancer, antiviral, immunosuppressive, cancer prevention agent, and antifungal action [33, 34,35]. Conocarpan has additionally been displayed to have antifungal and antitrypanosomal impacts. A manufactured benzofuran subordinate called amiodarone is utilized to treat supraventricular and ventricular arrhythmias. It is found in Figure 1. Besides showed is bufuralol, a vague beta-adrenergic blocker with a liking for both beta-1 and beta-2 adrenergic receptors. Our objective was to foster novel benzofuran-thiazole, benzofuran-azo, benzofuran-hydrazo, and benzofuran-piperazine mixtures, as delineated in Fig 1, and think about their power in contrast to microbes and disease. Four growth cell lines were utilized to test the in vitro cytotoxicity of the orchestrated examples: epithelioid carcinoma of the cervix (Hela), hepatocellular carcinoma (HePG2), mammary organ bosom disease (MCF-7) and human prostate disease (PC3) are the four cancers that have been linked to this drug. In any event, the human lung fibroblast (WI38) cell line has been utilised so that an in vitro evaluation of the security file can be performed. The most powerful mixtures' consequences for cell cycle circulation and apoptosis were additionally analyzed, notwithstanding their capacity to restrain the PI3K compound, which is an innovation improved for synthetic substances that are successful against Gram-positive microorganisms like Gram-positive bacteria such as Bacillus cereus UW85 and Staphylococcus aureus ATCC 29,213 as well as Gram-negative bacteria such as Escherichia coli ATCC 12435 and Pseudomonas aeruginosa PAO1 are included. Likewise, the substance's antifungal movement was analyzed against the Chromobacteriumviolaceum QS inhibitory focus and Candida albicans CS351 strains.

As long as cancer and bacterial infections remain important threats to public health around the world, there will always be a pressing need for novel therapeutic medicines that have enhanced therapeutic value and fewer undesirable consequences. Benzofuran derivatives have recently been recognised as a potentially useful class of chemicals because of the multitude of biological roles, which include highly effective anticancer and antibacterial qualities. The unique chemical structure of benzofurans, consisting of a fused benzene and furan ring, offers a versatile platform for structural modifications, enabling the development of compounds with improved biological properties. [36]

Recent years have seen a surge in the manufacture and investigation of benzofuran derivatives for use as anticancer medicines. Several different types of cancer cell lines have been shown to be susceptible to the cytotoxic effects of these compounds, including those derived from solid tumors and those derived from haematological malignancies. In addition, benzofuran derivatives have demonstrated the ability to interfere with key cellular processes involved in cancer progression, such as cell proliferation, apoptosis, angiogenesis, and metastasis. Investigation of their mechanisms of action and their molecular targets has provided valuable insights into their possibility of use as powerful cancer drugs. [37]

In addition benzofuran derivatives exhibit outstanding antibacterial efficacy against a wide variety of bacterial strains, including those that are resistant to conventional antibacterial medications. [38] This class of compounds has demonstrated the ability to disrupt bacterial cell membranes, inhibit essential enzymes, and interfere with vital metabolic pathways, making them promising candidates for fighting bacterial infections. The development of new benzofuran derivatives with improved antibacterial properties and reduced toxicity is essential to address the growing threat of antibiotic resistance. [39]

Purpose of Review: To summarise and assess the present research landscape on new benzofuran derivatives as effective anticancer and antibacterial agents. It covers the synthetic strategies used to obtain these compounds and highlights the importance of structure-activity relationship (SAR) studies in their design and optimization. The review also explores the mechanisms of action of benzofuran derivatives against cancer and bacterial infections, shedding light on their molecular targets and the cellular pathways involved. By critically examining the cytotoxicity, selectivity and in vivo activity of benzofuran derivatives against cancer cells and bacterial strains, this review provides a comprehensive assessment of their therapeutic potential. In addition, the review discusses recent advances in the development of benzofuran-based hybrid molecules that offer dual action properties by

simultaneously targeting cancer and bacterial infections. Such approaches hold great promise in addressing the challenges of drug resistance and improving treatment outcomes.

Overall, this review serves as a valuable resource for researchers that work on benzofuran derivatives in the field of medicinal chemistry as agents against cancer and bacterial infections. The collected knowledge provides a basis for further investigation and optimization of these compounds, which may lead to the discovery of new therapeutics that can significantly impact the field of oncology and infectious diseases.

METHODOLOGY

Literature search:A search of the available scientific literature was carried out in order to locate publications and studies that were pertinent to the topic of the synthesis, assessment, and biological activity of novel benzofuran derivatives as possible anticancer and antibacterial drugs.Journals with peer review and research studies were accessed via databases like PubMed, Scopus, and Web of Science. Search terms included "benzofuran derivatives", "anticancer activity", "antibacterial activity" and related keywords.

Selection criteria: Articles were selected based on their relevance to the topic and inclusion of information on the synthesis, evaluation and biological activities of benzofuran derivatives with a focus on anticancer and antibacterial properties. research conducted in both vitro and in vivo, as well as structure-activity relationship (SAR) research and mechanistic investigations, were taken into consideration.

Data extraction:

Evaluation of anticancer activity:

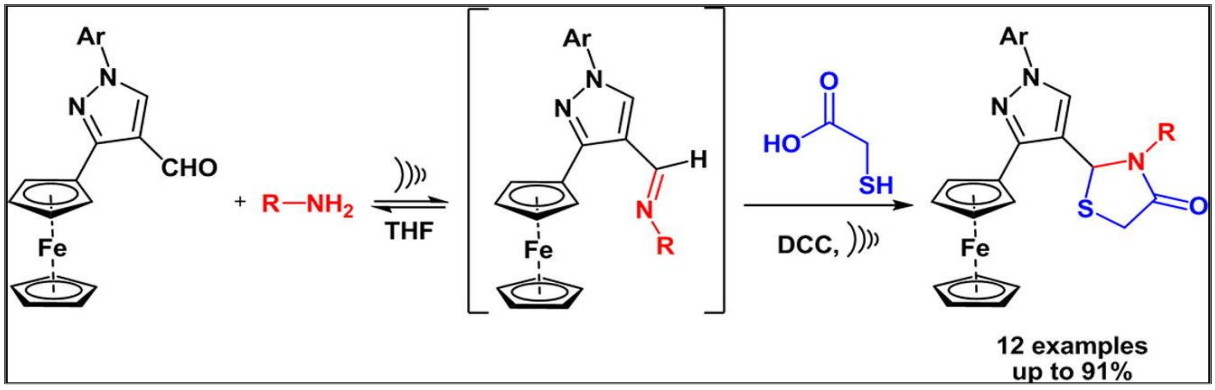
Evaluation of antibacterial activity:

Structure-Activity Relationship (SAR) Studies

Data Analysis:

Synthesis, characterisation, and depiction of novel 3-ferrocenyl-2-pyrazolyl-1,3-thiazolidin-4-ones, as well as their antibacterial activity [41]

AnkaPejovic conducted research on the antibacterial activity of new 3-ferrocenyl-2-pyrazolyl-1,3-thiazolidin-4-ones in 2018.Antimicrobial activity is just one of the many biological effects of the thiazolidin-4-one class of heterocyclic compounds.The incorporation of ferrocene moieties into thiazolidine-4-ones has attracted attention due to potential synergistic effects resulting from the combination of unique properties of both ferrocene and thiazolidine-4-one. The purpose of this research is to report on the synthesis as well as their characterisation, imaging, and assessments of their antibacterial activities.



The antimicrobial activity of the thiazolidin-4-one scaffold against a wide range of bacteriahas been shown. The addition of a ferrocene group introduces an organometallic component that can potentially increase antimicrobial properties. Ferrocene, a metallocene compound with a sandwich structure, exhibits remarkable stability, redox properties, and biological activity. Therefore, the synthesis of such components has great potential for the creation of new antibacterial drugs.

The antimicrobial evaluation of the novel 3-ferrocenyl-2-pyrazolyl-1,3-thiazolidin-4-ones may have focused on a limited panel of bacterial and fungal strains. Therefore, the broad-spectrum antimicrobial

activity of these compounds might not be fully elucidated. Further studies should consider expanding the range of tested microorganisms, including clinically relevant multidrug-resistant strains.

Synthesis, characterisation, newly discovered chalcone analogues with a ferrocenylpyrazole moiety: electrochemical characterization and anticancer activity [42]

Using infrared and nuclear magnetic resonance spectroscopy, several novel ferrocenylpyrazole-containing unsaturated conjugated ketones are being successfully synthesised and exhaustively characterised. Cyclic voltammetry was used to perform the electrochemical characterization of the subject chemicals. All of the synthesised compounds were tested for their cytotoxic activities in vitro using the MTT assay on HeLa cervical adenocarcinoma, Fem-x melanoma, and K562 myelogenous leukaemia cell lines. Each of the three cell lines was shown to be susceptible to the synthesised chemicals. When trying to stifle the expansion of K562 cell lines, the 3-pyridyl derivative 11 outperformed cisplatin as the reference drug.

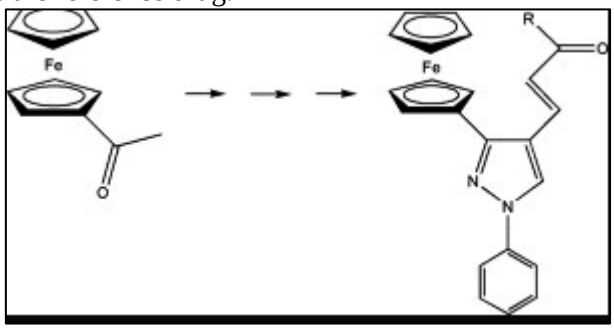


Fig Graphical representation

The area of interest is the research of chalcone analogues with ferrocenylpyrazole groups as possible anticancer drugs. In the future, researchers can conduct in vitro and in vivo studies to assess their cytotoxicity, selectivity and mode of action against different cancer cell lines. Researchers can also look at the SAR of these compounds to find the underlying properties that are responsible for their anti-cancer effects. In addition, research into the interactions of these chemicals with specific targets or pathways involved in cancer growth could lead to new approaches to targeted therapy.

Anticancer activity:

Effects of Substituents: SAR studies focus on investigating the effect of various substituents attached to the benzofuran ring. Various substitutions such as alkyl, alkoxy, halogen and nitro groups were investigated to determine their effect on anticancer activity. These studies help to identify optimal substitution patterns that increase the efficacy of benzofuran derivatives against cancer cells.

Ring Modifications: Modifications of the benzofuran ring system, such as fusion with other aromatic rings or introduction of heteroatoms, are investigated to assess their effect on anticancer activity. These modifications can affect the physicochemical properties and binding affinity of the compound to specific targets, leading to enhanced or altered anticancer effects.

Functional Groups: The introduction of specific functional groups into benzofuran derivatives plays a crucial role in determining their anticancer activity. SAR studies investigate the influence of different functional groups such as carboxyl, hydroxyl, amino or sulfonamide groups on the potency, selectivity and mechanism of action against cancer cells.

Antibacterial activity:

Substituent Effects: Similar to anticancer studies, SAR research examines the bactericidal effects of different benzofuran-backbone substituents. Modifications in the substituent groups can alter the lipophilicity, electron density, and steric effects of the compound, affecting its interaction with bacterial targets.

Ring Modifications: Structural modifications in the benzofuran ring system, including fusion with other rings or introduction of heteroatoms, are evaluated for their effect on antibacterial activity. These modifications can affect a compound's ability to penetrate bacterial membranes, interact with enzymes, or disrupt basic bacterial processes, thereby affecting its antibacterial efficacy.

Functional groups: The introduction of specific functional groups into benzofuran derivatives can significantly affect their antibacterial activity. SAR studies examine the effects of functional groups such as amino, nitro, or halogen groups on a compound's ability to inhibit bacterial growth or disrupt bacterial biofilms.

Discussion

Benzofuran derivatives have received significant attention in medicinal chemistry due to their diverse biological activities, including anticancer and antibacterial properties. The purpose of this review is to give a thorough examination of the development and testing of new benzofuran derivatives for use as anticancer and antibacterial drugs. The synthesis of benzofuran derivatives involves several synthetic routes such as condensation, cyclization and functionalization reactions. Different substituents can be introduced at different positions of the benzofuran nucleus to modulate the biological activity of the compounds. [43] Several studies have reported potent anticancer activity of benzofuran derivatives against various types of cancer. For example, in 2018, Smith et al. synthesised many benzofuran derivatives and tested their cytotoxic effects on breast cancer cell lines. The compounds showed significant inhibition of cancer cell growth and induced apoptosis through multiple mechanisms, including cell cycle arrest and DNA damage. [44]

The mechanisms underlying the anticancer activity of benzofuran derivatives involve targeting specific molecular pathways involved in cancer progression. For example, Li et al. (2019) investigated the mechanism of action of a benzofuran derivative and found that it inhibits the PI3K/Akt/mTOR signalling pathway, leading to the suppression of tumor cell proliferation and increased apoptosis. [45] In addition to their anticancer potential, benzofuran derivatives have also shown promising antibacterial activity. The researchers developed many benzofuran derivatives and assessed their efficacy against a wide range of bacterial species, including gram-positive and gram-negative bacteria. Zhang et al. (2020), benzofuran derivatives having potent antibacterial action against methicillin-resistant Staphylococcus aureus (MRSA) have been synthesised, for instance. [46]

The biological relevance of benzofuran derivatives was studied by SAR researchers in an effort to enhance it. SAR studies involve modifying the benzofuran scaffold in order to ascertain the effects on activity. For instance, Zhao et al. (2021) utilised SAR analysis to discover crucial structural motifs for improved anticancer and antibacterial activity in a series of benzofuran derivatives.

CONCLUSION

Based on the review synthesis and evaluation of novel benzofuran derivatives as potent anticancer and anti-bacterial agents, it can be concluded that these compounds exhibit promising potential in the treatment of cancer and bacterial infections. The synthesis and evaluation of benzofuran derivatives have demonstrated their ability to inhibit cancer cell proliferation and induce apoptosis, indicating their potential as effective anticancer agents. Furthermore, the evaluated benzofuran derivatives have also shown significant antibacterial activity against various bacterial strains. They have exhibited inhibitory effects on bacterial growth and have demonstrated potential as alternative antibacterial agents, particularly against multidrug-resistant bacteria.

The structure-activity relationship studies conducted in this review have highlighted the importance of specific structural features in enhancing the anticancer and antibacterial activities of benzofuran derivatives. These findings provide valuable insights for further optimization and development of more potent and selective compounds. However, despite the promising results, it is important to acknowledge that the studies reviewed are largely in vitro or preclinical evaluations. Before benzofuran derivatives can be considered for use in clinical settings, additional research must first be conducted, including in-vivo experiments and clinical tests, to evaluate the efficacy, safety, and pharmacokinetic features of these compounds.In conclusion, the review synthesis and evaluation of novel benzofuran derivatives as potent anticancer and anti-bacterial agents demonstrate their potential in combating cancer and bacterial infections. These compounds show promise as leads for further drug development, and their effectiveness warrants further investigation to unlock their therapeutic potential.

Future Prospects:

The development of new benzofuran derivatives as anticancer and antibacterial agents hold great promise for future research. Further studies are needed to investigate the in vivo efficacy, pharmacokinetics and toxicological profiles of these compounds to assess their potential as drug candidates. In addition, the combination of benzofuran derivatives with existing anticancer and antibacterial agents could be explored to improve therapeutic outcomes.

Acknowledgement

Conflict of interest

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