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Review Article

Exploring the role of furan-pyrazole in the treatment of breast cancer: a comprehensive review

Akhila P Ratheesh* **and Seena Haridas**

Department of Pharmaceutical Chemistry, The Dale View College of Pharmacy and Research Centre, Punalal, Thiruvananthapuram, Kerala, India.

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***Corresponding Author:**
Akhila P Ratheesh
Email :akhila.ratheesh75@gmail.com
Phone : +918076418391

ABSTRACT

Breast cancer is one of the most prevalent malignancies among women worldwide, which is one of the major factors leading to morbidity and mortality. These compounds exhibit a range of biological activities, including anti-proliferative, pro-apoptotic, and anti-metastatic properties, making them potential candidates for therapeutic development. Moreover, their structural flexibility enables the development of more effective and selective inhibitors. The mechanism of action and therapeutic potential of furan-pyrazole derivatives may aid in designing breast cancer medicines with higher efficacy and fewer adverse effects. This review examines the role of furan-pyrazole derivatives in breast cancer therapy, focusing on their molecular mechanisms, pharmacological significance, and potential as targeted agents. This review aims to consolidate existing knowledge while highlighting recent advancements in breast cancer research and management with a focus on furan pyrazole compounds.

1. INTRODUCTION

Breast cancer is one of the most commonly occurring heterogeneous conditions. In the year 2022, approximately 2,296,840 new cases of breast cancer were reported globally among women. Moreover, 11.5% of new cases were accounted for worldwide yearly. It is still one of the top causes of cancer-related mortality in women, and this reflects a significant global burden even with improvements in early identification and treatment. Novel small compounds, such as furan pyrazole derivatives, have the potential to alter carcinogenic pathways. Pyrazole-containing compounds exhibit various biological actions, including anti-inflammatory, anti-cancer, antibacterial, and antiviral properties. To improve the biological efficacy, the combination of furan and

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pyrazole rings into a single molecular structure has been studied. By combining the advantageous qualities of both moieties, this combination may yield molecules with improved pharmacological profiles [1]. Breast cancer accounts for a significant proportion of cancer diagnoses worldwide, affecting millions of individuals annually, with a varying range of incidence rates by geographic region, socioeconomic status, and genetic predisposition. The major factors, including age, family history, lifestyle, and reproductive history, contribute to its development [2]. The leading types are triple-negative breast cancer (TNBC), invasive ductal carcinoma (IDC), ductal carcinoma in situ (DCIS), invasive lobular carcinoma (ILC) [3], while less commonly occurring are medullary carcinoma, mucinous, and tubular carcinoma [4]. Treatment includes several obstacles despite advancements in hormone therapy, immunotherapy, chemotherapy, radiation, and surgery. While resistance to medicines, especially in TNBC and metastatic instances, limits long-term efficacy, tumour heterogeneity results in a range of responses. Although accessibility, high costs and the requirement for predictive biomarkers remain barriers in the development of precision medicine and immunotherapy. To enhance outcomes and survivability in breast cancer care, a multidisciplinary, individualised strategy is needed to address these issues.

The primary purpose of this review is to comparatively explore the therapeutic potential of furan pyrazole derivatives in the treatment of breast cancer, which is one of the most prevalent and life-threatening malignancies affecting women globally. To provide insight into furan pyrazole compounds, their molecular processes, pharmacological importance, and potential as targeted anti-cancer medicines, this study aims to compile the extensive research currently available on the subject [5]. The primary objective of this study is to thoroughly examine the biological activities and structural adaptability of furan pyrazole derivatives, with a focus on how they interfere with key pathways that contribute to breast cancer development [6]. The major goal of this study is to give a comprehensive and comparative examination of the therapeutic potential of furan-pyrazole derivatives in the context of breast cancer. This aims to elucidate the molecular mechanisms of action, pharmacological significance, and potential as targeted anticancer therapies by integrating current experimental and computational data.

Furthermore, this review highlights current advances, limitations, and future research objectives to inform the rational design of next-generation furan-pyrazole-based therapies for breast cancer treatment. Furan-pyrazole hybrids offer a flexible structure that can target multiple cancer-related pathways, including VEGFR, EGFR, CDK2, and Hsp90, which helps overcome resistance, such as in triple-negative breast cancer. Despite encouraging preclinical findings, there are only a few evaluations being studied that compare them to the standard therapies, such as Tamoxifen. This study aims to provide a comprehensive analysis of furan-pyrazole derivatives, highlighting their therapeutic potential and guiding future breast cancer medication development efforts [4,5].

2. CHEMISTRY AND BIOLOGICAL SIGNIFICANCE OF FURAN-PYRAZOLE

2.1 Heterocyclic Chemistry

Heterocyclic chemistry involves a cyclic structure with two different types of atoms in a ring, containing one carbon atom or an atom other than carbon; these are known as heteroatoms. [7] These compounds have a wide range of biological and pharmacological properties and can be either aromatic or aliphatic. The aliphatic heterocyclics comprise amines, ethers, amides, etc., whereas the aromatic heterocyclics contain heteroatoms with properties similar to those of ethers, amides, etc. In contrast, aromatic heterocyclics feature heteroatoms with properties similar to those of benzene [8].

2.2 Furan

Furan is a heterocyclic ring molecule with five members, mainly consisting of an oxygen, and an unsaturated structure. The basic ring structure is found in a wide range of industrially significant products. The furan nucleus is also found in a variety of physiologically active substances. The furan ring consists of furan and tetrahydrofuran rings. Furfural, on the other hand, serves as the foundation for all commercial furan derivatives because it is the easiest and least expensive. Furan is produced from furfural by decarbonylation. Tetrahydrofuran is a saturated chemical that contains no double bonds [9]. Furan derivatives have a wide spectrum of biological relevance due to their structural flexibility, which allows for a variety of alterations that exhibit antioxidant, anticancer, and antibacterial properties. Its compounds are also being researched for antidepressants, anxiolytics, and a variety of other applications. Furan derivatives are known to have a significant cytotoxic effect against a number of cancer cell lines by causing apoptosis, disrupting mitochondrial pathways, and blocking angiogenesis. Furan hybrids, when combined with other pharmacologically active heterocycles such as pyrazoles, have shown increased potency and selectivity. For example, these compounds have been shown to inhibit tubulin polymerization, resulting in cell cycle arrest at the G2/M phase. Some furan-containing natural compounds, such as furanocoumarins, exhibit anticancer properties by generating reactive oxygen species (ROS) and inducing apoptosis in malignant cells [9].

2.3 General reactions of Furan

2.3.1 Electrophilic reactions

a) Nitration

Nitration of furan with acetyl nitrate yields an addition product, which may be removed with a mild base like pyridine to obtain 2-nitrofuran. Heating in a water bath with 70% nitric acid yielded 2,5-dintrofuran (Figure 1). Figure 1 illustrates the nitration process through electrophilic substitution, where a nitro group ($–NO_2$) is introduced into the aromatic ring. These nitro derivatives can be metabolically activated in the body, leading to the formation of DNA adducts and mutations that may contribute to the development of breast cancer [10].

b) Sulfonation

A pyridine sulphur trioxide combination is used as a sulfonating agent since sulphuric acid decomposes under acidic circumstances and cannot be used to sulfonate furan. Furan-2-sulfonic acid was formed by reacting with a pyridine sulfur trioxide complex, which was subsequently hydrolysed with acid (Figure 2). Figure 2 shows the process of sulfonation, achieved through an electrophilic substitution reaction, which incorporates a sulphonic group ($-SO_3H$) onto the furan ring. The introduction of the $-SO_3H$ group enhances the compound's polarity and solubility, thereby improving its biological activity. Notably, this modification aids in detoxification processes and lowers the risk of breast cancer growth induced by environmental toxins, making furan-2-sulfonic acid a promising candidate for further anticancer research and therapeutic development [10].

2.3.2 Metalation Reaction

Furan is readily metalated using butylithium and mercuric chloride or acetate to produce 2-metalated furan. Furan can be lithiated with alkylithium in dry ether at reflux temperature to generate 2-lithiofuran.In contrast, lithiation in the presence of TMEDA produced 2,5-dilithiofuran (Figure 3). In Figure 3, it can be observed that the metalation reaction is being carried out using butyl lithium and mercuric chloride or acetate. This process not only facilitates the introduction of reactive functional groups but also forms furan metal complexes that have demonstrated enhanced cytotoxic activity, primarily through mechanisms involving DNA cleavage and mitochondrial apoptosis. Such reactivity underscores the potential of metalated furan derivatives as powerful agents in anticancer strategies, warranting further investigation into their therapeutic applications [10].

2.3.3 Coupling Reactions

At pH 8-9, arenediazonium salts react with furan to produce aryl-substituted furans. It is mostly applicable regarding the parent furans. When combined with copper(II) ions, the substituted furans undergo arylation at pH 4-6. Electron withdrawing groups need a pH of 1-2 (Figure 4). As illustrated in Figure 4, this coupling reaction of the furan ring yields aryl-substituted furans, which are biologically significant because they inhibit tubulin polymerization and induce G2/M cell cycle arrest in breast cancer cells [10].

2.4 Pyrazole

Pyrazole is a five-membered heterocyclic ring that serves as an appropriate chemical compound for the development of potent bioactive compounds. They mostly have a five-membered ring structure with three carbon and two nitrogen atoms in adjacent places, as well as an unsaturated parent moiety. These chemicals are classified as alkaloids due to their chemical constituents and pharmacological effects on humans [11]. Pyrazoles have a wide range of biological actions, including anti-inflammatory, antiviral, anticancer, and antibacterial properties.

2.5 General reactions of pyrazole

2.5.1 Oxidation reaction

The pyrazole ring is highly resistant to oxidation, with oxidizing agents often targeting the side chains primarily. Potassium permanganate has been the most extensively used agent for side-chain oxidation, generally in a neutral or alkaline medium, but occasionally with sulfuric acid. This oxidizing agent transforms side chains at any location of the

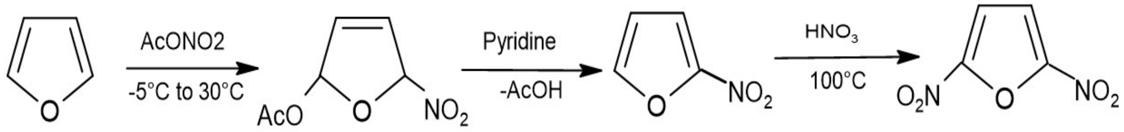

Figure 1: Nitration of the furan ring through electrophilic substitution.

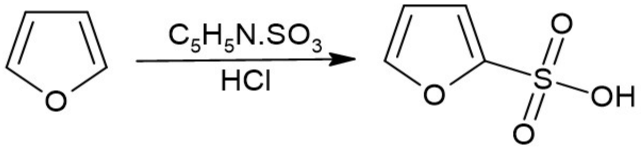

Figure 2: Sulphonation of the furan ring via electrophilic substitution.

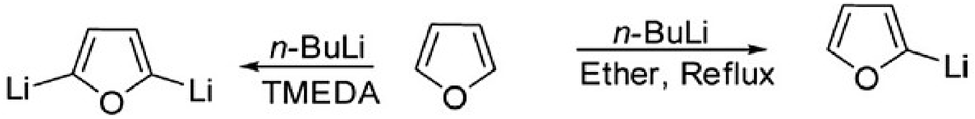

Figure 3: Metalation of the furan ring using n-butyllithium to generate reactive furan-metal intermediates.

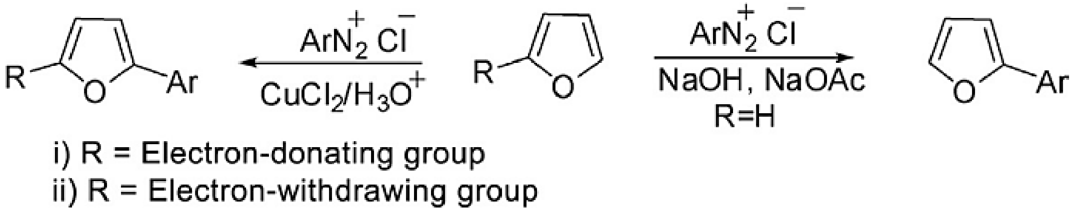

Figure 4: Aryl coupling of the furan ring to yield aryl-substituted furan derivatives.

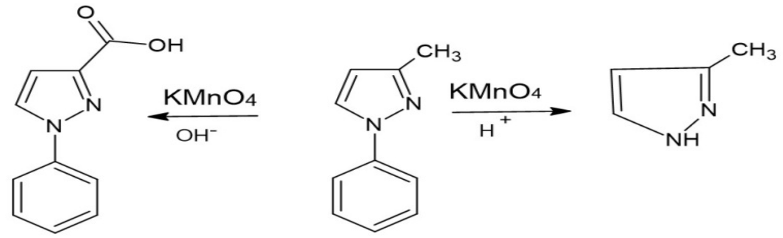

Figure 5: Oxidation of the pyrazole ring employing potassium permanganate ($KMnO_4$) as oxidant.

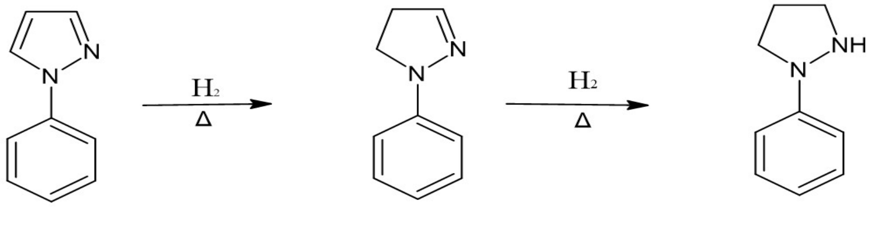

Figure 6: Reduction of the pyrazole ring under catalytic hydrogenation conditions.

pyrazole ring to carboxylic groups (Figure 5). As shown in Figure 5, the oxidation of the pyrazole ring by potassium permanganate is significant, since combining such oxidative stress inducers with inhibitors of antioxidant defense mechanisms has been shown to overcome resistance in breast cancer [10].

2.5.2 Reduction of the pyrazole ring

Reduction processes begin with the pyrazole ring, resulting in the synthesis of pyrazolines and pyrazolidines or the removal of specific substituents. The most widely used reagents for reducing pyrazole compounds include sodium and alcohols, amalgamated sodium and hydrogen with catalysts (mostly palladium supported on barium sulfate), and, in rare cases, zinc and acetic acid (Figure 6). As depicted in Figure 6, the reduction of the pyrazole ring not only produces pyrazolines and pyrazolidines but also induces enzymatic reduction in breast cancer cells, ultimately leading to cell death [10].

2.6 FURAN-PYRAZOLE HYBRIDS

Furan-containing pyrazoles and furan-substituted pyrazoline hybrids broaden chemical space and improve target affinity. Chalcone-bridged furan-pyrazolyl complexes have shown activity across MCF-7, with SAR pointing to the significance of electron-drawing aryl substitutions and the arrangement of the enone linker [11]. A broader overview of furan–pyrazole and related pyrazole derivatives evaluated in breast cancer models is presented in Table 1, highlighting their chemotypes, putative targets, model systems, and key biological outcomes such as apoptosis, cell cycle arrest, and DNA damage.

3. STRUCTURE ACTIVITY RELATIONSHIP (SAR)

- Hybridization with chalcone or thiazole fragments can bias action toward inhibiting tubulin polymerization.
- Substituting the furan at the para or meta position can lead to increased binding in the hydrophobic pockets and result in kinase inhibition.
- The ferrocenyl-pyrazole-platinum (II) complexes demonstrate a DNA intercalating mechanism that correlates with the kinase/tubulin effects.
- The substituent at the N1/N2 atoms and the 4th position of the pyrazole represent the target selectivity [13].

4. MECHANISM OF ACTION OF FURAN-PYRAZOLE IN BREAST CANCER

4.1 Molecular targets in breast cancer

Breast Cancer is a complex and varied disorder with several molecular subtypes, each with its own therapeutic targets that influence clinical care and treatment outcomes. Hormone receptors, such as estrogen receptors (ER) and progesterone receptors (PR), are frequently targeted in luminal breast cancers and are treated with hormonal agents, including tamoxifen and aromatase inhibitors. Another common target is the human epidermal growth factor receptor 2 (HER2), which is overexpressed in 15-20% of breast cancer patients and has been targeted with drugs like trastuzumab, pertuzumab, and lapatinib. In contrast,triple-negative breast cancer(TNBC), which lacks ER, PR, and HER2, presents a therapeutic challenge owing to the lack of typical targets, prompting research into alternatives such as androgen receptors and immunological checkpoints(e.g., PD-1/PD-L1). The identification and execution of these molecular targets have hastened the evolution of individualized therapy in breast cancer, enabling more precise and effective therapeutic regimens. The PI3K pathway controls cell development, division, and metabolism. Growth hormones bind to the tyrosine kinase, which activates the phosphatidylinositol 3-kinase (PI3K).PI3K produces PIP3 and activates AKT and other targets, such as mTOR (mammalian target of rapamycin), which regulates protein synthesis and cell proliferation [14]. The tumor suppressor protein, p53, induces cell cycle arrest and apoptosis. It maintains genomic stability by activating genes involved in DNA-dependent cell death. TP53 mutations occur in a large number of breast cancer cases, which impairs the protective function by allowing the cells with damaged DNA to proliferate and contribute to tumor formation and therapeutic resistance. The intrinsic apoptotic pathway is strictly regulated by the Bcl-2 protein family, which comprises both pro-apoptotic and anti-apoptotic members, including Bax and Bak, as well as Bcl-2 and Bcl-xL. Overexpression of anti-apoptotic Bcl-2 in breast cancers stabilizes the mitochondrial membrane, limits cytochrome C release, and suppresses apoptosis, leading to chemotherapy resistance and poor prognosis. Finally, caspase cascades act as apoptosis executors, with initiator caspases (e.g., caspase-9) activated by mitochondrial signals such as

Table 1: Furan-Pyrazole Exemplars [12]

Chemotype / Example	Putative Target	Breast Model	Key Effect
Pyrazole (TNBC active)	Tubulin polymerization	TNBC cells	G2/M arrest; apoptosis
Pyrazole derivative PCW-1001	Radio sensitization; apoptosis	Breast cancer (*in vitro*/*in vivo*)	Enhanced RT response; tumour growth delay
Furan-pyrazolyl chalcones	Multi-target (tubulin/ROS)	MCF-7 (ER+)	Antiproliferative; DNA damage
Aurora-A-oriented pyrazolyl-thiazolidinones	Aurora-A kinase	Breast lines	Cell-cycle arrest; growth inhibition

Table 2: Comparative analysis of furan–pyrazole derivatives with the established breast cancer drug Tamoxifen [17,18].

Parameter	Furan–Pyrazole-Based Compounds	Tamoxifen
Chemical Nature	Synthetic heterocyclic structures that often combine pyrazole with other bioactive fragments like benzofuran or pyrimidine.	Non-steroidal compound classified as a selective estrogen receptor modulator (SERM).
Mechanism of Action	Acts on multiple cancer pathways, including the inhibition of VEGFR-2, EGFR, CDK2, and Hsp90; it can induce apoptosis and generate oxidative stress, while also arresting cell cycle progression.	Competes with estrogen for binding to estrogen receptors, thereby blocking estrogen-driven tumor growth (effective in ER-positive cancers).
Cancer Type Targeted	Shows effectiveness against a broad spectrum of breast cancer types, including hormone receptor-negative and triple-negative subtypes.	Mainly effective against hormone-sensitive (ER-positive) breast cancer.
Cytotoxic Activity (*in vitro*)	Some molecules demonstrate very strong potency, with IC_{50} values in the nanomolar range.	Typically exhibits micromolar-level cytotoxicity in ER-positive cells.
Selectivity for Cancer Cells	Generally, demonstrates high selectivity for tumor cells over normal cells; low toxicity is observed in preclinical models.	Effective but may cause side effects like hot flashes, blood clots, and increased endometrial cancer risk.
Drug Resistance	Still under investigation, but the multitarget design suggests potential to avoid or delay resistance development.	Resistance is a common limitation, especially in advanced or long-term therapy cases.
Combination Therapy Possibility	Strong potential to be used alongside chemotherapy, targeted therapy, or even immunotherapy due to its diverse mechanisms.	Commonly used with other hormone therapies or after chemotherapy in ER-positive cancers.
Stage of Development	Currently under laboratory and animal testing; not yet tested in clinical settings.	Widely used and approved; standard treatment in hormone receptor-positive breast cancer.
Mode of Administration	Being studied for oral and nano-formulated injectable routes.	Used orally as a daily tablet.
Clinical Application	Potential candidate for treating various types of breast cancer, including those that don't respond to hormonal treatment.	Primary choice for managing ER-positive breast cancer, especially in early or postsurgical stages.

Table 3: Docking-based interaction profiles of furan–pyrazole derivatives with key breast cancer targets [19].

Target Protein	Docking Platform	Key Molecular Interactions	Insights
EGFR	AutoDock, Schrödinger (Glide)	The furan ring occupies a hydrophobic pocket, creating π-π and van der Waals interactions; the pyrazole contacts the hinge area via H-bonds.	Hydrophobic changes on furan increase binding, whereas tiny polar groups on pyrazole boost hydrogen bonding and total docking score.
VEGFR-2	Schrödinger (Glide), MOE	Furan participates in π-π stacking within the hydrophobic pocket, whereas pyrazole creates H-bonds in the ATP-binding site.	Lipophilic furan substitutions boost affinity, but hydrogen bonding from pyrazole is necessary for target selectivity.
PI3K	AutoDock, MOE	Pyrazole forms hydrogen bonds with hinge residues, whereas furan adds van der Waals interactions.	Polar groups on pyrazole enhance binding energy, while the orientation of furan influences pocket attachment.

cytochrome c release, which then activate executioner caspases (e.g., caspase-3 and -7) to cleave cellular substrates and induce programmed cell death. Dysregulation at any level of these interrelated networks enables cancer cells to dodge apoptosis, proliferate uncontrollably, and acquire resistance to therapies, emphasizing their importance as targets for new breast cancer treatments [11].

Furan-pyrazole compounds have emerged as effective drugs with strong cytotoxic and apoptosis-inducing capabilities, making them intriguing leads in anticancer treatment research. These chemicals have a considerable inhibitory effect on cancer cell growth by interfering with key biological processes. According to research,furan-pyrazole hybrids cause programmed cell death through both intrinsic and extrinsic mechanisms, including alterations in mitochondrial membrane potential, caspase activation, and modulation of apoptosis-related proteins, including the Bcl-2 family. Interestingly, they tend to exhibit selective toxicity against malignant cells while causing minimal injury to normal tissues, which adds to their therapeutic value. Modifications to the furan and pyrazole frameworks have a considerable influence on their biological activities, highlighting the importance of structure-activity relationship (SAR) investigations in optimizing their anticancer potential. Thus, furan-pyrazole shows tremendous potential in the creation of novel chemotherapy medicines [11].

Pyrazole-based compounds, particularly those containing furan moieties, have emerged as promising candidates for inhibiting cancer cell proliferation and metastasis. These chemicals are known to disrupt critical biological pathways, such as cell proliferation, programmed cell death, angiogenesis, and cellular motility. According to research findings, furan-containing pyrazole derivatives can arrest the cell cycle by altering critical regulators, such as cyclin-dependent kinases and tumor suppressor proteins like p53 [15]. They also cause apoptosis by inhibiting mitochondrial activity and activating caspase enzymes. Furthermore, these drugs have been found to be beneficial in preventing metastatic behavior by inhibiting matrix metalloproteinase production and modifying markers associated with epithelial-mesenchymal transition. Being able to target various systems, along with their diverse chemical structures, supports their potential as useful leads in the development of anticancer medicines that target both suppressing tumor progression and stopping metastasis [5].

4.2 *In vitro* and *in vivo* pharmacology

The most commonly used models in the series are MCF-7 (ER+), T4TD (ER+), and MDA-MB-231 (TNBC). The pyrazoles have shown IC_{50} values ranging from low micromolar to sub-micromolar in MCF-7 cells.TNBC is less susceptible unless the mechanism is antimitotic. The *in vivo* studies of the pyrazole reduce the tumor burden. However, future studies are necessary to determine the dose-limiting toxicity and therapeutic index [16].

5. RECENT ADVANCES IN FURAN-PYRAZOLE DERIVATIVES FOR BREAST CANCER THERAPY

Table 2 presents a comparative analysis of furan–pyrazole derivatives and Tamoxifen in breast cancer treatment, highlighting differences in chemical structure, mechanism of action, target cancer subtypes, cytotoxic potency, selectivity, resistance potential, suitability for combination therapy, development stage, administration mode, and clinical applications. It demonstrates that furan–pyrazoles offer promising activity across multiple breast cancer subtypes, whereas Tamoxifen remains a proven therapy specifically for ER-positive tumors.

5.1 Computational Design And Docking

Prioritization against EGFR, VEGFR-2, PI3K, CDKs, and tubulin was based on docking and molecular dynamics, with the help of 3D-QSAR for SAR rationalization [19]. Fragment to lead case studies, show how high ligand efficiency fragments may become effective multi-target medicines. Docking indicates that the furan ring occupies a hydrophobic sub-pocket, contributing to π-π and van der Waals interactions. In contrast, the pyrazole core offers directional H-bonding and hinge binding in kinase [20]. Table 3 outlines the docking platforms employed (AutoDock, Schrödinger Glide, and MOE), major ligand–protein interactions, and observed structure–activity trends.

5.2 ADME and Safety Considerations

Pyrazoles typically exhibit good metabolic stability; however, oxidation at the benzylic and furan positions can be problematic. Balancing lipophilicity and polarity is crucial for avoiding low solubility or high clearance. hERG risk is scaffold-dependent, with cationic side chains and strong lipophilicity potentially increasing risk. To enhance oral bioavailability, formulation methods such as amorphous dispersions and lipid carriers are employed [21].

6. CHALLENGES AND LIMITATIONS

Furan–pyrazole derivatives have received considerable attention as promising anticancer candidates, and several challenges have hindered their advancement towards clinical use. Whereas *in vitro* experiments show selective action against cancer cells, information about their long-term safety and organ-specific toxicities remains insufficient. Many investigations have been confined to cell-based studies and animal models, but limited clinical trials have been reported to evaluate the safety and therapeutic value in humans. An extensive preclinical research is essential to confirm their potential and ensure their safe application in breast cancer therapy. Toxicology has been a significant concern for the heteroaromatic rings because of their capability to metabolically activate the reactive intermediates, which cause liver injury and DNA damage. The poor water solubility and limited oral bioavailability limit the use of *in vivo* studies when there is significant cytotoxicity for pyrazole, which is prone to N-dealkylation or hydroxylation. However, promising preclinical studies have led to few derivatives progressing to clinical trials. This highlights the need for more systematic studies of pharmacokinetics, safety, and formulation approaches. Addressing these difficulties through structural modification, drug delivery techniques, and toxicity reduction will be critical to realizing the full potential of furan and pyrazole derivatives in cancer treatment [22].

7. DEVELOPMENT GUIDANCE FOR FURAN-PYRAZOLE LEADS

- Determine target activation at an early stage (e.g., tubulin polymerization tests, kinase panels, CETSA/thermal shift).
- Use of orthogonal cell models (ER+, HER2+, TNBC) and resistance models to assess apoptosis and clonogenic survival.
- Optimize the physicochemical parameters by maintaining the potency.
- Use ADME/Tox gates for CYP inhibition/induction, hERG, mitochondrial toxicity, and (mainly for furan) [23].
- Drugs with appropriate exposure in mice (AUC/MIC-like coverage vs. i*n vitro* IC_{50}) show effectiveness in xenograft or PDX models.
- The usage of translational biomarkers (phospho-AKT, phospho-histone H3) to reduce the likelihood of clinical progression [24].

8. FUTURE PERSPECTIVES

Many strategies have been developed to improve the therapeutic efficacy of the furan - pyrazole moieties in the management of breast cancer. The use of computational drug design tools primarily includes *in silico* modeling, which aids in predicting the binding potential and interaction with cancer targets. This not only aids in the discovery process but also helps lower the cost of developing new strategies through the trial-and-error method. Another advancement in the development of targeted drug delivery systems involves nanoparticles, liposomes, and polymer-based carriers, which enhance bioavailability and tumour selectivity, thereby reducing unwanted side effects. However, there has been an increasing interest in the field of personalized medicine, which offers an opportunity to improve treatment precision and achieve patient-specific outcomes [25]. When paired with known chemotherapeutics, these substances disrupt the resistance mechanism and produce synergistic therapeutic benefits. The advancements in nanomedicine platforms enable prolonged release, encourage tumor accumulation, and enhance the pharmacokinetic behavior of furan–pyrazole drugs. This customized strategy is quite beneficial for patients with aggressive or treatment-resistant breast cancer, such as triple-negative disease. When combined, precision medicine techniques, nanotechnology-based delivery, and multidrug regimens may accelerate the conversion of furan–pyrazole candidates into treatments suitable for clinical use [22].

9. LIMITATIONS OF THE CURRENT EVIDENCE

The majority of research is still in the preclinical stage, with minimal pharmacokinetic and safety data and tiny breast cancer model populations. Assay variability impedes cross-study comparisons. Validating this chemotype will require a rigorous and systematic examination, particularly *in vivo* [26].

10. CONCLUSION

The recent development of furan-pyrazole derivatives has shown promising anticancer properties, mainly in breast cancer. These compounds exhibit cytotoxic effects and target-specific interactions; structural modification enhances their efficacy. When compared to conventional breast cancer drugs such as tamoxifen, the furan pyrazole derivatives have the potential to exhibit a unique mechanism of action, help overcome drug resistance, and lead in better treatment outcomes. Despite these findings, several challenges remain, including limited bioavailability, toxicity profiles, and a lack of *in vivo* clinical evaluations. Computational drug design and targeted drug delivery systems help enhance the development of drugs. Future research will focus on pharmacokinetics, safety, and therapeutic combinations. The furan-pyrazole holds a substantial potential for effective and innovative agents in the future landscape of breast cancer treatment. The major takeaway message is that although these heterocycles are excellent pharmacophores. Still, their full therapeutic potential can only be achieved through rational structural optimization and enhanced drug delivery techniques that increase the bioavailability and safety. Future research should prioritize *in vivo* studies, detailed pharmacokinetic and toxicity evaluations, and clinical trials to close the gap between laboratory findings and practical anticancer applications, allowing for the development of more effective and safer therapeutics based on furan and pyrazole scaffolds.

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Conflict of interest

The authors declare no conflict of interest.

Data availability statement

All data related to this manuscript have been disclosed within the article, and no additional datasets were generated or analyzed during the preparation of this review.

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