Unlocking the potential of aromatase inhibitors: recent advances in drug design, synthesis, docking activity, and in vitro bioactivity evaluations

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ABSTRACT

Breast cancer, a global health concern claiming approximately 685,000 lives in 2020, necessitates continual advancements in therapeutic strategies. Estrogen and aromatase play pivotal roles in hormone-responsive breast cancer, with 80% of patients exhibiting estrogen receptor-positive tumors. Aromatase inhibitors (AIs), notably non-steroidal inhibitors like anastrozole and letrozole, have significantly improved outcomes, yet challenges persist, including side effects. This review focuses on recent developments in AIs, exploring xanthone derivatives, imidazole derivatives, and curcumin derivatives as potential inhibitors of aromatase. Molecular docking studies, employing Auto Dock and other tools, reveal the binding affinities and interactions of these compounds with the aromatase enzyme. Among xanthones, Erythrommone emerges as a potent inhibitor, holding promise for clinical trials. Imidazole derivatives, synthesized through the Debus-Radziszewski reaction, demonstrate anticancer potential, with compounds like 1a exhibiting superior efficacy against MCF7 cells. ADME-Tox analyses indicate promising drug-likeness but reveal potential mutagenic effects and environmental impacts. Curcumin derivatives, particularly 1,5-diaryl-1,4-pentadien-3-ones, present alternatives to address curcumin’s bioavailability challenges. A study of 25 compounds (DKC) identifies DKC-10 as a potent inhibitor, outperforming established breast cancer drugs in terms of binding affinity and interactions with aromatase and ERα receptors. These findings underscore the importance of exploring diverse chemical structures in developing AIs, paving the way for more effective and well-tolerated therapeutics. The integration of computational techniques, such as molecular docking studies, accelerates drug discovery by predicting interactions at the molecular level. Overall, this comprehensive review provides valuable insights into the evolving landscape of aromatase inhibitors, offering a roadmap for future research and the development of advanced breast cancer therapeutics.

1. Introduction

According to the World Health Organization (WHO) website, breast cancer claimed the lives of approximately 685,000 people worldwide in 2020. Strikingly, roughly half of all breast cancer cases occur in women who have no specific risk factors apart from their gender and age [1]. It is a disease that knows no geographical boundaries, affecting...
women in every country across the globe. Moreover, breast cancer, while predominantly associated with women, also affects a smaller, but still significant, portion of men, with approximately 0.5–1% of all breast cancer cases being diagnosed in males. This information highlights the global prevalence and impact of breast cancer as a public health concern [2].

The role of estrogen and the enzyme aromatase in breast cancer is pivotal and well-established. In breast cancer, approximately 80% of patients have hormone-responsive breast cancer, meaning that estrogen receptors play a critical role [3, 4]. Estrogen production varies in premenopausal and postmenopausal women, with the ovaries being the primary source of estrogen in premenopausal women, while peripheral tissues contribute significantly in postmenopausal women [5]. In patients with estrogen receptor-positive breast cancer, estrogen assumes a central role in promoting the growth of neoplastic breast epithelial cells by activating estrogen receptor-mediated pathways. This connection between estrogen and breast cancer is particularly important in hormone-dependent breast cancer types [6].

Estrogens, including estradiol and estrone, are biosynthesized from androgens such as androstenedione and testosterone. This transformation is facilitated by a rate-limiting enzyme called aromatase, which is also known as CYP19. Aromatase catalyzes the process of demethylation and aromatization, converting androgens into estrogens [7]. The overproduction of estrogen due to increased aromatase activity has been associated with a higher risk of breast cancer recurrence and metastasis in hormone-dependent breast cancer patients. This link underscores the critical role of estrogen and aromatase in the development and progression of hormone-responsive breast cancer, making them important targets for therapeutic interventions and prevention strategies [8].

The final stage in the biosynthesis of estrogen is the aromatase reaction. The biosynthesis of additional steroid classes is protected from disruption by inhibiting this last step [9]. Aromatase activity in the breast, bone, vascular endothelium, and central nervous system is the main source of estrogen in postmenopausal women. Additionally, gonadotropin regulation is unable to control the amount of aromatase in women who have gone through menopause, preventing the difficulties brought on by the feedback regulatory mechanism that raises FSH and LH following aromatase suppression. Consequently, artificial intelligence is used in breast cancer therapy [10].

Aromatase inhibitors may be divided into two subtypes, steroidal and nonsteroidal [4, 11]. Non-Steroidal Aromatase Inhibitors (NSAIs), such as anastrozole and letrozole, block the action of the aromatase enzyme to reduce estrogen levels in postmenopausal women, while Steroidal Aromatase Inhibitors, exemplified by exemestane, irreversibly bind to the aromatase enzyme to inhibit its activity and lower estrogen production in postmenopausal women with hormone receptor-positive breast cancer [4, 12, 13].

There is another classification for aromatase inhibitors: first, second and third generation [14]. Aminoglutethimide, first generation of AIs, originally was an anti-epileptic drug, was explored in the late 1970s as a treatment for breast cancer by inhibiting adrenal steroid production, but its use was limited due to the need for cortisol replacement and significant side effects, despite its effectiveness in reducing estrogen levels through aromatase inhibition[15,16].

The second generation of aromatase inhibitors consists of selective inhibitors that were previously developed but are no longer in clinical use [17]. In the 1980s, 4-OH-A, later named formestane, became the first effective “selective” aromatase inhibitor for breast cancer [4]. Major systemic side effects include hot flushes and vaginal spotting, lethargy, rash, nausea, and dizziness. Formestane is not FDA approved for breast cancer treatment [10].

Imidazole derivatives are the other second-generation AIs, which are not using now. They are Fadrozole, Rogletimide and Vorozole [18]. And the third generation of these drugs are: Exemestane (Aromasin®) Letrozole (Femara®) Anastrozole (Arimidex®) [15]. Three aromatase inhibitors are currently approved by the Food and Drug Administration (FDA). anastrozole, letrozole and exemestane [19].

The development of novel selective aromatase inhibitors with fewer side effects is of paramount importance in the field of breast cancer treatment [20]. Aromatase inhibitors have revolutionized hormone therapy for hormone receptor-positive breast cancer, significantly improving patient outcomes. However, the existing aromatase inhibitors can be associated with certain side effects, such as musculoskeletal issues and bone density loss. As a result, there is a growing need for more effective and well-tolerated inhibitors. Achieving this objective is crucial as it can lead to improved patient compliance and overall quality of life for breast cancer survivors [21].

Molecular docking studies have emerged as a powerful tool in addressing this challenge. This computational technique allows researchers to predict how potential drug candidates or molecules interact with specific biological targets, such as the aromatase enzyme [22]. By simulating these interactions at the molecular level, researchers can identify new compounds or modifications to existing inhibitors that could enhance their selectivity and reduce side effects. In essence, molecular docking studies help streamline the drug discovery process by narrowing down the pool of potential candidates, ultimately leading to the development of more effective and safer aromatase inhibitors [23]. As we continue to advance in the field of cancer research, molecular docking studies play a pivotal role in accelerating the discovery of improved therapeutics and addressing the pressing need for better breast cancer treatment options [24].

In this article, our primary focus is on reviewing a series of newly designed drugs and their bioactivity evaluations. The rapid advances in medicinal chemistry and drug development have led to the creation of a wide array of innovative pharmaceutical compounds. These novel drug candidates hold tremendous promise in addressing a variety of health challenges, from complex diseases to unmet medical needs. As such, it is crucial to assess their bioactivity comprehensively, as this step is fundamental to determining their efficacy and potential clinical applications.

Through this review, we aim to provide an in-depth analysis of the chemical structures, mechanisms of action, and therapeutic potentials of these recently developed drugs. Bioactivity evaluation is a critical phase in drug discovery, involving a range of studies to examine how these compounds interact with specific biological targets and their effects on living systems. By consolidating the latest research and findings, we hope to shed light on the effectiveness and safety profiles of these new drugs, facilitating the identification of promising candidates for further clinical development. In an era of rapid pharmaceutical innovation, this article serves as a valuable resource for researchers, clinicians, and pharmaceutical professionals seeking to stay updated on cutting-edge drug design and bioactivity assessment [25].
2. Review of three types of studied derivatives, xanthones, benzimidazoles and decetene curcumin derivatives

2.1. Xanthone Derivatives

In a study conducted by Singh and colleagues in 2023 [7], a computational approach was employed to explore the potential of xanthones, natural phytochemicals, as inhibitors of CYP19A1, an enzyme integral to steroid production. The crystal structure of human placental aromatase complexed with the breast cancer medication Exemestane (PDB ID: 3S7S) served as the foundation for the CYP19A1 structure. AutoDock 4.2.6 was used for molecular docking simulations. The receptor molecule was prepared by eliminating heteroatoms, introducing explicit hydrogen molecules, and assigning Kollman charges. Nine common xanthones, including Demethylchodatin, Erythrommone, Lichexanthone, Norlichexanthone, Griseoxanthone, and Thiophaninic Acid, along with three other compounds (Gentisine, Norathyriol, and Mangiferin), were subjected to docking studies, with Exemestane used as a positive control. Three-dimensional structures of the xanthones were generated with Gauss View 5.0, and ligands were configured with hydrogen atoms and Gasteiger charges. The docking process incorporated ligand flexibility and utilized the Lamarckian genetic algorithm and grid-supported energy evaluation. The outcomes were assessed based on the highest binding affinity scores, and the resulting molecular poses and interactions with CYP19A1 were visually examined and analyzed using LigPlot. This comprehensive investigation provided insights into the potential of xanthones as aromatase inhibitors and facilitated comparison with the known inhibitor Exemestane, contributing to our understanding of their therapeutic potential in diseases such as breast cancer [7].

Molecular docking is a computer method that helps us understand how certain substances interact with proteins in our bodies. In this study, they found that Xanthones, which are in some plants, can bind to a protein called CYP19A1, just like a known inhibitor called Exemestane. These Xanthones have similar binding strengths, and they attach to the same places on the protein. They also form special bonds with the protein. Among the Xanthones, Erythrommone stood out as a strong inhibitor. It turns out that the oxygen in Xanthones, as seen in computer simulations, helps form important bonds with the protein. Erythrommone's specific electronic properties and low energy gap make it a potent inhibitor, and experiments confirmed that it binds the most tightly to the protein. All of these factors play a role in how well these Xanthones can block the protein's action. While the binding energy of Exemestane as a controlled drug was -8.13 kcal/mol, Erythrommone as a xanthine derivative has a binding energy of -7.43 kcal/mol, followed by Griseoxanthone with energy of -6.42 kcal/mol as recommended drugs for future clinical trials [7].

2.2. Imidazole derivatives

Some researchers delve into various aspects of these compounds, from the initial design and synthesis of the imidazole derivatives to their biological activity assessment, molecular docking simulations, and computational studies on absorption, distribution, metabolism, excretion, and toxicity (ADME-Tox).

Imidazoles may be easily synthesized from 1,2-diketones, aldehydes, and a source of ammonia (usually ammonium acetate) via the Debus-Radziszewski reaction. This one-pot synthesis method offers substantial time savings. This is accomplished by heating a combination of ammonium acetate, an aldehyde derivative, and a benzyl derivative in acetic acid under reflux conditions while stirring for three hours to get the final chemicals. An aldehyde and a dicarbonyl molecule condense to make a diimine, which then interacts with the aldehyde to produce the imidazole ring. This is the first stage of the synthesis mechanism [24].

Table 1. Binding affinity of well performed studied xanthone derivatives and known AI exemestane.

<table>
<thead>
<tr>
<th>Ligands</th>
<th>R_1</th>
<th>R_2</th>
<th>R_3</th>
<th>R_4</th>
<th>R_5</th>
<th>R_6</th>
<th>R_7</th>
<th>Binding Energy (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exemestane</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-8.13</td>
</tr>
<tr>
<td>Erythrommone</td>
<td>Cl</td>
<td>OAc</td>
<td>Cl</td>
<td>Cl</td>
<td>OAc</td>
<td>H</td>
<td>CH_3</td>
<td>-7.43</td>
</tr>
<tr>
<td>Griseoxanthone</td>
<td>H</td>
<td>OMe</td>
<td>H</td>
<td>H</td>
<td>OH</td>
<td>H</td>
<td>CH_3</td>
<td>-6.42</td>
</tr>
<tr>
<td>Lichexanthone</td>
<td>H</td>
<td>OMe</td>
<td>H</td>
<td>H</td>
<td>OMe</td>
<td>H</td>
<td>CH_3</td>
<td>-6.27</td>
</tr>
</tbody>
</table>

Fig. 1. 2D Xanthone derivatives structure and exemestane as a control AI. (by ChemDraw Pro 8.0)
Table 2. Binding affinity of well performed studied imidazole derivatives and known AI letrozole.

<table>
<thead>
<tr>
<th>Ligand</th>
<th>X</th>
<th>R</th>
<th>R₂</th>
<th>Binding Energy (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Letrozole</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-6.876</td>
</tr>
<tr>
<td>1a</td>
<td>-O</td>
<td>4-Methylphenyl</td>
<td>-CH₃</td>
<td>-8.224</td>
</tr>
<tr>
<td>1b</td>
<td>-O</td>
<td>4-Methylphenyl</td>
<td>-NO₂</td>
<td>-8.059</td>
</tr>
<tr>
<td>1d</td>
<td>-NCH₃</td>
<td>4-Methylphenyl</td>
<td>-H</td>
<td>-6.676</td>
</tr>
<tr>
<td>1k</td>
<td>-S</td>
<td>Furan-2-yl</td>
<td>-CH₃</td>
<td>-6.054</td>
</tr>
</tbody>
</table>

The study examined the anticancer potential of compounds that derivated from imidazole, against MCF7 and L929 cells. In addition, the effectiveness of compounds, and cisplatin was illustrated in a concentration-dependent cell inhibition plot. Some compounds exhibited promising results in the MCF7 cell line. Compound 1a, in particular, displayed an IC50 value of 7.9 µM, surpassing that of cisplatin (9.75 µM). Compounds 1b and 1d also demonstrated superior efficacy with IC50 values of 8.2 µM and 8.7 µM, respectively. The synthesis of these compounds involved three different diketone derivatives: 4,4'-dimethylbenzyl, α-furyl, and 4,4'-difluorobenzyl. Notably, compounds featuring the 4,4'-dimethylbenzyl derivative exhibited remarkable activity, with compound 1a, bearing a 5-methylfuran ring in the 2nd position of the imidazole ring, showing the highest activity in the series. Compound 1b, with a 5-nitrofuran ring, displayed activity close to that of 1a. The introduction of methyl or nitro groups at the 5th position of the furan ring did not significantly alter the activity. To evaluate the selectivity of the compounds, the L929 healthy mouse fibroblast cell line was used. The cytotoxic effect of the synthesized compounds on healthy cells was found to be comparable to that of the reference drug cisplatin, which is quite promising. Therefore, compounds 1a, 1b, 1d, and 1k identified as effective against the MCF-7 cancer cell line, were selected for further investigation of in vitro aromatase activity (Fig. 2) [24].

In assessing the potential of newly developed compounds for drug candidacy, scientists performed an ADME-Tox analysis on the compounds mentioned. Using SwissADME, they confirmed that the compounds adhered to essential drug-likeness rules [23]. Subsequently, employing pkCSM, they predicted various aspects of the compounds' behavior in the body. Notably, the compounds displayed low water solubility but were skin-permeable, and they generally complied with parameters related to distribution, metabolism, and excretion. However, some compounds showed potential mutagenic effects and low tolerance, and one exhibited cardiac impact [24]. Additionally, environmental assessments revealed a potential toxic impact on bacteria. This comprehensive analysis provides insights into how these compounds might function as drugs and their potential effects on the human body and the environment.

2.3. Curcumin derivatives

One of the polyphenolic compounds found in South Asian Curcuma domestica plants is curcumin; it is a member of the curcuminoid group, which also contains demethoxycurcumin and bisdemethoxycurcumin. Curcumin is a well-known herb with a wide range of therapeutic uses that was used in Ayurveda for its anti-inflammatory, analgesic, antioxidant, and antibacterial qualities [26]. It works well to prevent a variety of human carcinomas, including those that affect the head, neck, breast, colon, pancreas, prostate, and gonads, as well as malignant melanoma. Additionally, curcumin compounds show biological efficacy against the powerful COVID-19 virus [27]. The curcumin compounds exert their inhibitory influence on human malignancies primarily by regulating biochemical cascades, a variety of transcription factors, growth factors, pro-inflammatory cytokines, supramolecular kinases, and diverse enzymes [26].

Curcumin faces challenges in terms of low bioavailability attributed to inadequate stomach absorption, limited tissue distribution, rapid metabolism, and subsequent elimination from the body. To tackle this issue, we turned to derivatives of deketene curcumin, opting for modifications that could potentially enhance metabolic stability by eliminating the b-diketone moiety. Despite debates about the necessity of the b-diketone moiety for curcumin's therapeutic properties, recent research has revealed that certain analogues without the b-diketone but...
with a 5-carbon-eneone spacer maintained or even improved growth-suppressive activity against various cancer cells. Some mono-carbonyl analogues lacking the b-diketone displayed superior anti-bacterial and anti-inflammatory activity compared to curcumin. Compounds with the chemical formula 1, 5-diaryl-1, 4-pentadien-3-ones, derived from deketene curcumin or mono-carbonyl analogues, share structural similarities with curcumin and exhibit greater biological activity than pure curcumin. This underscores the potential of these derivatives in overcoming the bioavailability limitations associated with curcumin [26].

In this study, they successfully examined 25 compounds known as DKC in relation to two important components in the human body: the placental aromatase cytochrome p450 and the Erα+ receptor. These were identified using specific codes (PDB ID: 3S79 for aromatase and 3ERT for Erα). To gain a better understanding, they also compared the docking of these DKC compounds with four commonly used drugs (tamoxifen, anastrozole, exemestane, and letrozole), which are used for treating breast cancer.

It's important to note that tamoxifen functions as an antagonist, specifically targeting Erα+ receptors, while the other three drugs (anastrozole, exemestane, and letrozole) operate as aromatase inhibitors. Due to this difference in function, distinct PDBs were utilized for the comparative study. To evaluate the effectiveness of these compounds, they selected the best poses and calculated MolDock scores, H-bonding, re-rank scores, and steric scores between the breast cancer proteins and the ligands (DKC derivatives and the four drugs) [28].

As mentioned in existing literature, it has been established that ligands (specifically DKC-10, DKC-20, and DKC-21 for Erα+) with binding affinities lower than −150 kcal/mol are considered more effective inhibitors. In that study, they focused on three DKC derivatives (DKC-10, DKC-20, and DKC-21) out of the 25, as these demonstrated superior binding energies (−204.461 kcal/mol, −177.278 kcal/mol, and −161.958 kcal/mol, respectively, for Erα+; −201.613 kcal/mol, −131.397 kcal/mol, and −123.724 kcal/mol, respectively, for aromatase), re-rank scores, and H-bonding [29].

Comparing the MolDock scores of these DKC derivatives with the core DKC-1, which was chosen as a reference among the three ligands, revealed that the selected three ligands had notably better energy profiles. Interestingly, among the 25 DKC derivatives, including the core DKC-1, the other 21 ligands demonstrated optimal binding affinity compared to DKC-1. However, it's noteworthy that the three DKC derivatives showed lower activity in terms of binding affinity for aromatase when compared to the estrogen receptor [29].

<table>
<thead>
<tr>
<th>Ligand</th>
<th>Binding Energy kcal/mol 3S79 or MolDock score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole</td>
<td>-107.965</td>
</tr>
<tr>
<td>Exemestane</td>
<td>-92.794</td>
</tr>
<tr>
<td>Letrozole</td>
<td>-108.904</td>
</tr>
<tr>
<td>DKC-10</td>
<td>-201.613</td>
</tr>
</tbody>
</table>

Fig. 3. 2D Structure of DKC10 (by ChemDraw Pro 8.0).
The detailed analysis of the interactions between DKC ligands (DKC-1, DKC-10, DKC-20, and DKC-21) and crucial proteins (Erα + and aromatase) sheds light on the molecular mechanisms underlying their potential as therapeutic agents for breast cancer. DKC-1 forms hydrogen bonds with specific amino acids in both Erα + and aromatase, engaging in interactions with His 524, Gly 521, Gly 420, Thr 347, Leu 387, Arg 394, Arg 403, Tyr 366, Gln 367, Met 68, Ser 72, and His 475. Steric interactions involve various amino acids, with Erα + incurring more residues than aromatase. Similar trends are observed for DKC-10, with additional hydrogen bonding interactions and steric interactions with Ser 341, Cys 530, Leu 536, Tyr 526 for Erα +, and Arg 400, Arg 79, Leu 479, His 475, Lys 473, Met 68, Trp 67, and Ser 72 for aromatase. DKC-20 engages in hydrogen bonding with Leu 346, Glu 353, Thr 347 for Erα +, and Pro 481, His 480, Glu 483, Arg 192, Lys 243, and Tyr 249 for aromatase, while steric interactions involve numerous amino acids. DKC-21, exhibiting H-bonding with Erα + and aromatase, reveals intricate interactions with Asp 351, Gly 420, Leu 525, Met 421, Met 343, Ala 350 for Erα +, and Glu 218, Glu 483, Asp 222, Ile 474, Glu 225, Ala 226, and Met 68 for aromatase [29].

Remarkably, DKC-10 emerges as the most promising, displaying the highest MolDock score, owing to robust H-bond and steric interactions, coupled with shorter interacting distances. Comparative analysis with current breast cancer drugs—tamoxifen, exemestane, anastrozole, and letrozole—reveals the superior performance of DKC derivatives in terms of MolDock score, hydrogen bonding, and steric interactions. Notably, tamoxifen exhibits poor interactions, while the aromatase-blocking drugs (exemestane, anastrozole, letrozole) also fall short in comparison to DKC derivatives. This underscores the potential of DKC compounds as more effective therapeutic agents for breast cancer treatment. The comprehensive data on interacting distances, energies, and strengths provided in the tables further support the superior performance of DKC derivatives. Overall, these findings suggest that DKC compounds, particularly DKC-10, hold promise for further exploration as advanced breast cancer therapeutics (Fig. 3) [30].

3. Conclusions

The article delves into the critical role of aromatase inhibitors in addressing the global health concern of breast cancer, which claimed the lives of approximately 685,000 people worldwide in 2020. Given that estrogen and the enzyme aromatase play a pivotal role in hormone-responsive breast cancer, the inhibition of aromatase activity has become a cornerstone in therapeutic interventions. The paper highlights the two main types of aromatase inhibitors, steroidal and nonsteroidal, and categorizes them into three generations based on their development and clinical use.

The third generation of aromatase inhibitors, including exemestane, letrozole, and anastrozole, has received FDA approval, significantly advancing hormone therapy for breast cancer. However, the article stresses the need for continued innovation in this field to develop more effective and well-tolerated inhibitors, considering the side effects associated with existing options, such as musculoskeletal issues and bone density loss.

The emergence of molecular docking studies as a powerful tool in drug discovery is emphasized. This computational technique enables researchers to predict how potential drug candidates interact with specific biological targets, such as the aromatase enzyme. By simulating these interactions at the molecular level, researchers can identify compounds or modifications to existing inhibitors that could enhance selectivity and reduce side effects. The article underscores the pivotal role of molecular docking studies in accelerating the discovery of improved aromatase inhibitors and, consequently, better breast cancer treatment options.

The focus of this article then shifts to a detailed review of recent research on newly designed drugs, with an emphasis on xanthone derivatives, imidazole derivatives, and curcumin derivatives. In a study by Singh and colleagues, xanthones, natural phytochemicals found in certain plants, were explored as potential aromatase inhibitors. Molecular docking simulations revealed that these xanthones could bind to the aromatase enzyme, similar to the known inhibitor exemestane. Among them, Erythrommonone stood out as a strong inhibitor, with specific electronic properties and a low energy gap contributing to its potency. This study suggests the potential of xanthones, particularly Erythrommonone, as candidates for future clinical trials.

Imidazole derivatives, synthesized through the Debis-Radziszewski reaction, were evaluated for their anticancer potential. Some compounds demonstrated promising results against the MCF7 cancer cell line, with compound 1a surpassing the efficacy of cisplatin. ADME-Tox analysis provided insights into the compounds’ drug-likeness, behavior in the body, and potential effects on the environment. The study highlights the importance of selectivity, as these compounds showed comparable cytotoxic effects on healthy cells to the reference drug cisplatin.

The article also explores curcumin derivatives, addressing the challenges of low bioavailability associated with curcumin. Modifications of deketene curcumin were examined to enhance metabolic stability, with 25 compounds known as DKC undergoing evaluation. Molecular docking studies compared the binding affinities of DKC derivatives with crucial proteins involved in breast cancer, Erα + receptor, and aromatase. DKC-10 emerged as the most promising, displaying superior interactions compared to current breast cancer drugs.

In conclusion, the article underscores the significance of aromatase inhibitors in breast cancer treatment and the need for continuous advancements in drug design. The exploration of xanthone, imidazole, and curcumin derivatives demonstrates the diverse approaches to developing novel inhibitors with improved efficacy and safety profiles. Molecular docking studies serve as a crucial tool in this process, aiding in the identification of potential candidates for further clinical development. The comprehensive review contributes to our understanding of the evolving landscape of aromatase inhibitors and holds promise for the future of breast cancer therapeutics.

References


