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Medicinal Importance of Nitrogen and Sulphur Containing Heterocycles in the Development of Anticancer Medicine: A Review

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ABSTRACT

Breast and cervical cancers remain one of those significant global health challenges and are among the leading causes of mortality in women. Chalcone derivatives have attracted considerable attention owing to their diverse pharmacological properties, particularly their potential anticancer activity. In addition, the cytotoxicity evaluation against normal human cells indicated relatively low toxicity, highlighting the therapeutic potential and selectivity of these compounds. Collectively, in previous study [1] the results suggest that Chalcone represent promising lead candidates for the development of anticancer agents, while the MAOS methodology offers an efficient, high-yielding, and environmentally benign synthetic strategy consistent with green chemistry principles.

Keywords: Antidermal, Anticancer, Antimicrobial Screening, Heterocyclic compound

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INTRODUCTION

Cancer remains one of the three leading causes of mortality worldwide and therefore demands significant attention in the development of effective therapeutic strategies. Recent reports indicate that the number of global deaths caused by breast cancer reached approximately 700,660 cases in 2019, representing a substantial increase compared to 380,910 cases reported in 1990, and the incidence is expected to continue rising in the coming years [2]. The number of breast and cervical cancer cases continues to rise annually, and the limited availability of effective therapies has driven researchers to explore alternative approaches for cancer treatment [3–4]. Various innovative synthetic strategies have been developed in the search for new anticancer agents that exhibit high efficiency along with improved selectivity in their biological applications [5-6]. Chalcone, a subclass of flavonoids containing α, β-unsaturated carbonyl moiety, have gained considerable importance in medicinal chemistry due to their simple structure, straightforward synthesis, and diverse pharmacological properties. These naturally occurring compounds are widely distributed in nature and have been reported to possess antioxidant, anti-inflammatory, antimicrobial, and notably anticancer activities, which make them promising candidates for therapeutic applications. This review primarily emphasizes recent developments in Chalcone based anticancer research, particularly focusing on the structural characteristics associated with improved cytotoxic activity [7].

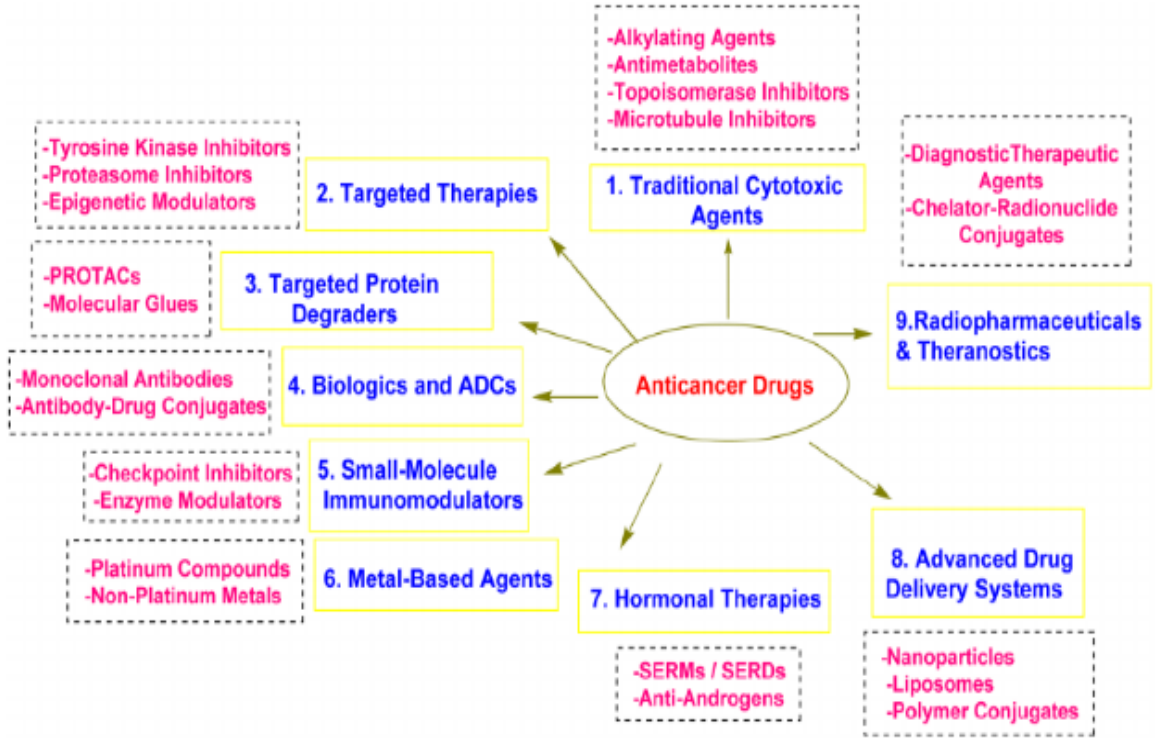


Figure 1: Classifications of anticancer drug

The field of anticancer agents has evolved remarkably over the past decades, directed by advances in medicinal chemistry that have enabled the design of increasingly selective and effective therapeutic modalities [8-9]. These agents can be broadly categorized based on their mechanism of action, molecular targets, and chemical structures, each reflecting different phases in the history and innovation of cancer therapy (As seen in Figure 1) [10]. Cancer remains one of the most challenging diseases to treat because of its biological complexity, genetic heterogeneity, and ability to evade conventional therapies [11].

Antimicrobial peptides (AMPs) are small molecules vital to the immune defense of most organisms, from bacteria to animals. With strong antibacterial, antifungal, and antiviral properties, AMPs are essential components of host defense peptides (HDPs), offering broad-spectrum protection against pathogens [12-13] Heterocyclic compounds are an important class among different types of organic compounds. They found applications not only in medicinal chemistry but also in material science and agrochemicals [14]. Various pharmacological activities reported like analgesic activity, antipyretic activity, pregnancy interceptive activity, anti-inflammatory activity, antifungal activity, antidermal activity. Calotropis Gigantea Linn is well-known Healthful herb, it also known as Milkweed; it has been used in Unani, Ayurvedic and Siddha system of medicines for many years [15].

Heterocyclic compounds are extremely useful for medicinal chemistry applications due to their unique physical properties and adaptable chemistry. Each heteroatom in the ring produces a distinct electronic impact that affects reactivity and gives the molecules special ways to interact with biological target [16].

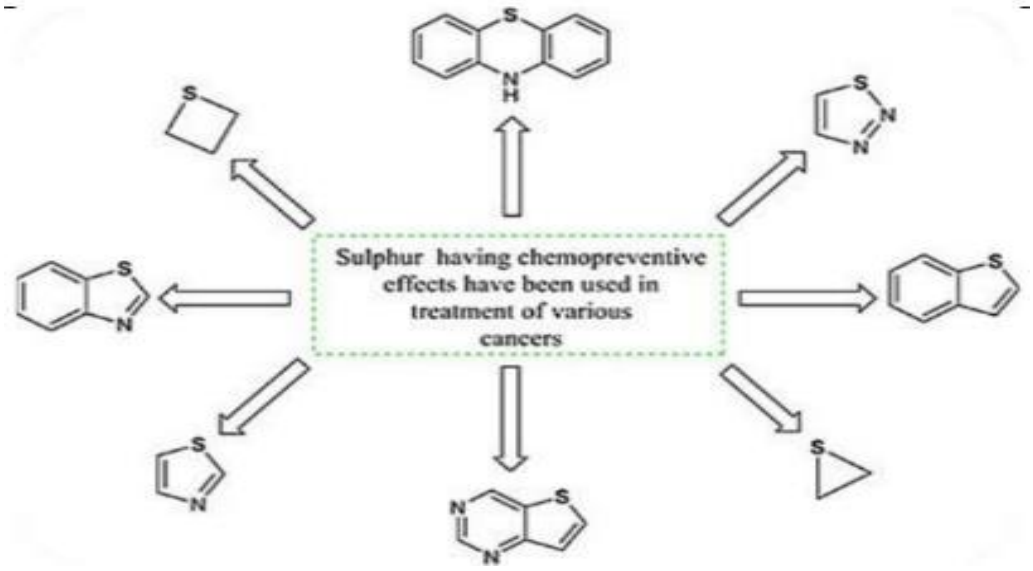
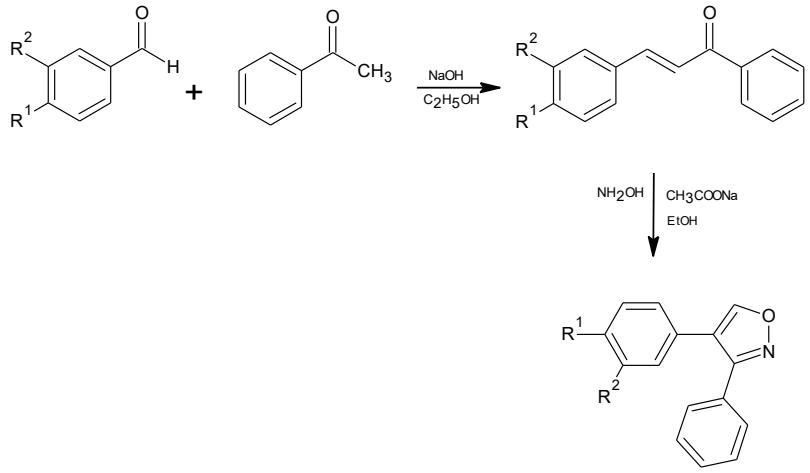


Figure 2: Efficiency profile of sulphur based nucleus present in anticancer drug [17]

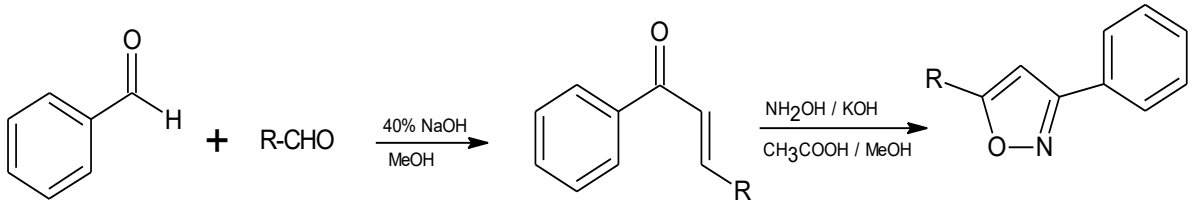
The addition of sulphur atoms to heterocyclic structures significantly modified the compounds' chemical, biological, and physical characteristics [18].

Literature survey reveals that nitrogen and sulphur containing heterocyclic compounds have significance in the field of pharmaceutical and medical sciences. They exhibit anticancer [19, 20] , antioxidant [21], antitubercular [22], anti-inflammatory [23], anthelmintic [24], antimicrobial [25], therapeutic [26], anti-invasive [27], insect-antifeedant [28] and many more diverse biological properties. In this context, researchers have implemented their hypothesis towards the development of potent and novel 1,2-azoles with versatile approaches. More emphasis was given to their synthetic strategy considering their medicinal utility.

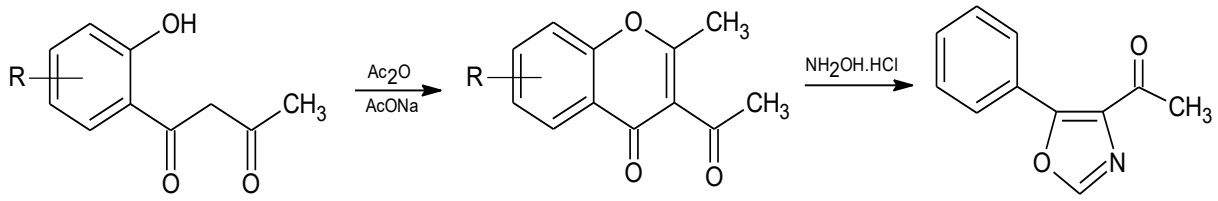
Synthesis of biologically active isoxazole derivatives is reported [29] from the reaction of Chalcone with hydroxylaminehydrochloride, catalyzed by sodium acetate in alcoholic solvent.



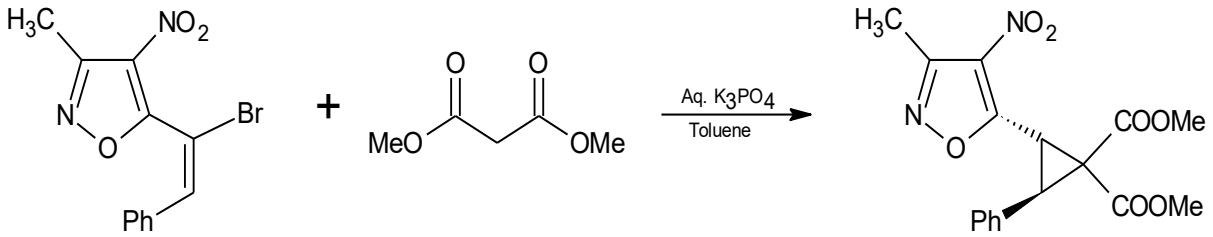
Kumara *et al*. [30] prepared some derivatives of isoxazole started with acylation of resorcinol followed by the action of isoprene afforded corresponding chromons. This, on treatment with p-substituted benzaldehyde, yield substituted Chalcone which undergo into cyclization with hydroxylaminehydrochloride to form isoxazole derivatives. In continuation with the same principle, Murthy *et al.* [31] also reported some substituted chromanoisoxazoles having optical power limiting properties. Yazdan *et al.* [32] studied condensation Chalcone of with hydroxylamine-hydrochloride in basic medium to obtain isoxazole analogues by Claisen-Schmidt reaction.



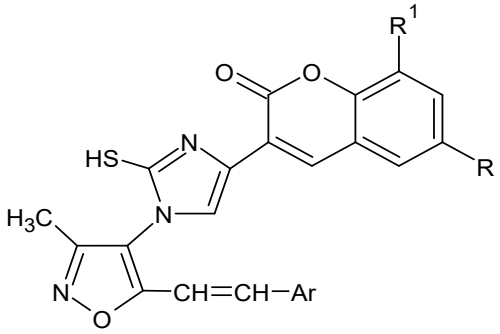
Acid catalyzed cyclization of 2-hydroxyaroylacetone analogues yields 3-acyl-2-methylchromones, which on further treatment with hydroxylaminehydrochloride followed by subsequent cyclization afford methyl substituted acetyl derivatives of isoxazole reported by Lacova *et al.* [33]



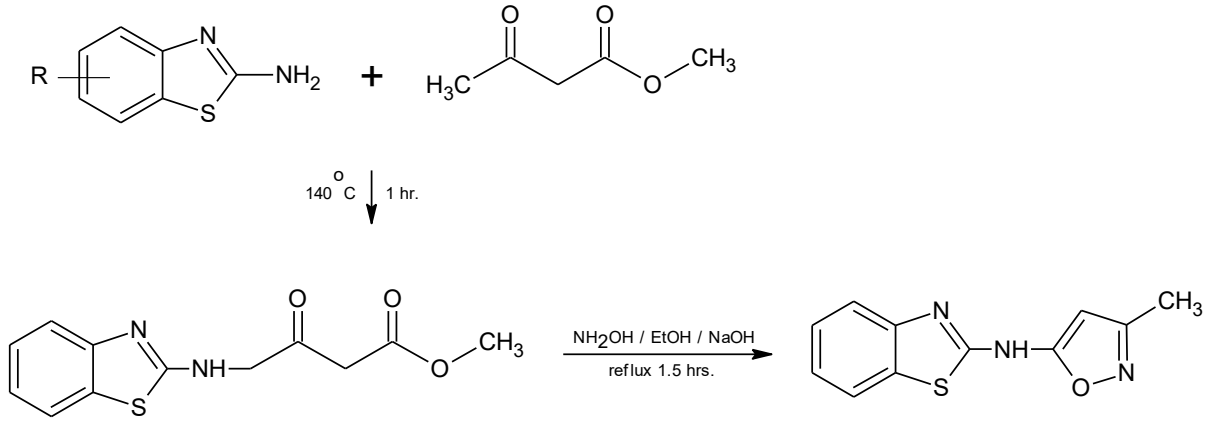
A series of substituted isoxazoles was reported [34] from the reaction of 1,5-diarylpent-1-yne-3,5-diones with hydroxylaminehydrochloride in ethanolic solvent. Piras *et al.* [35] reported cyclopropanation of 5-(1-bromo-2-phenyl-vinyl)-3-methyl-4-nitroisoxazoles with dimethyl malonate in toluene by phase transfer catalysis to yield 2-(3-methyl-4-nitroisoxazol-5-yl)-3-phenyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester.



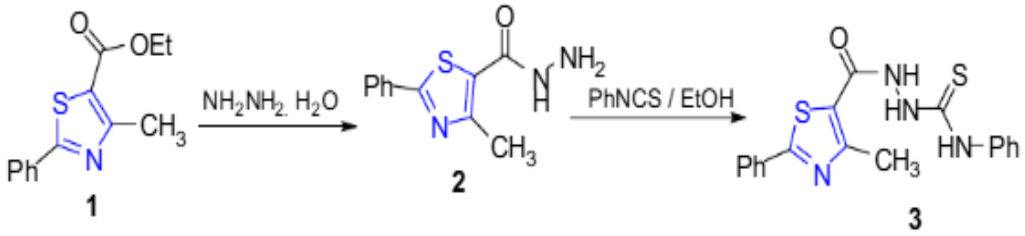
Rajanarendar *et al.* [36] reported the reaction of substituted 4-amino-3-methyl-5-styrylisoxazoles with 3-(2-bromoacetyl)coumarin in alcoholic solvent to form of 3-[2-(3-methyl-5-styryl-4-ylamino)acetyl]chromen-2-ones which on treatment with KSCN, undergoes cyclisation to form 3-[1-(3-methyl-5-styrylisoxazol-yl)-2-mercapto-1*H*-imidazol-4-yl]-1-benzopyran-2*H*-ones.



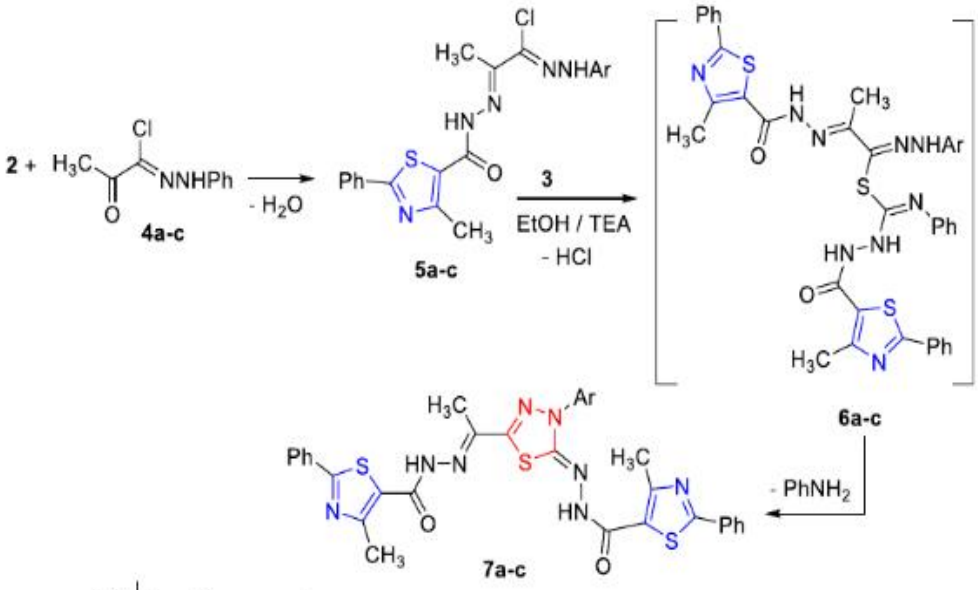
Magar *et al.* [37] used 3-carboxamideo-(benzothizazole-2yl)-propane-2-ones prepared from reaction of various substituted amines with substituted phenylthiourea and treated with hydroxylaminehydrochloride in ethanolic alkaline medium for about 1.5 hrs. to obtain 5-(substituted-benzothizazole-2-yl)-amino-3-methylisoxazole derivatives. Further, these were screened for their antimicrobial properties.



2-(4-Methyl-2-phenylthiazole-5-carbonyl)-N-phenylhy-drazinecarbothioamide (3) [38] was prepared via reaction of 4-methyl-2-phenylthiazole-5-carbohydrazide (2) with Phenyl isothiocyanate in EtOH.

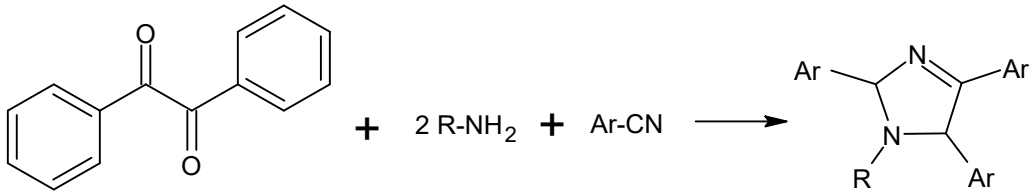


The reaction of compound 2 with the appropriate hydrazonoyl chlorides 4a–c [39] in refluxing ethanol yielded the corresponding condensation product 5. Treatment of thioamide derivative 3 with the appropriate hydrazonoyl halides of type 5a–c in refluxing EtOH containing TEA gave the corresponding thiadiazole derivatives 7a–c shown in following scheme.



4-7	a	b	c
Ar	Ph	4-MePh	4-ClPh

However, Bourissou et al. synthesized the 1-substituted, 2-aryl, 4,5-phenylimidazole with a respectable degree of efficiency by using benzyl, benzonitrile, and primary amines on the surface of silica gel under solvent-free conditions and microwave irradiation [40].



DISCUSSION:

This study investigates the antimicrobial potential of compounds containing heteroatoms and their possible role in the treatment of microbial diseases. The researchers synthesized a range of molecules incorporating heteroatoms such as nitrogen, oxygen, and sulfur, which are recognized for their contribution to biological activity. Researchers have employed various suitable experimental procedures to evaluate the effectiveness of these compounds against different bacterial and fungal species. The findings revealed that several synthesized derivatives displayed notable antimicrobial properties, emphasizing the significance of heteroatoms in improving biological effectiveness. The research is strengthened by its clearly defined objectives, well-structured experimental methodology, and thorough assessment of antimicrobial performance. Nevertheless, the study was confined to laboratory-based investigations and the exact mechanisms responsible for the observed antimicrobial effects were not comprehensively examined. Overall, the work offers important contributions to the design and development of heteroatom-containing antimicrobial agents and highlights the necessity for additional studies, including toxicity assessments and in vivo evaluations, to validate their clinical applicability.

CONCLUSION:

This study underscores the potential of nitrogen and sulphur containing heterocyclic compounds as promising anticancer agents for future therapeutic applications. The incorporation of heteroatoms, including nitrogen, oxygen, and sulfur, significantly contributes to the enhancement of antimicrobial activity against various microbial species. These findings provide valuable insights into the structure–activity relationships of such compounds and emphasize their importance in antimicrobial drug discovery. Despite these encouraging results, further research is needed to evaluate their toxicity profiles, clarify their mechanisms of action, and assess their effectiveness through in vivo studies. Overall, this work establishes a solid framework for the continued development and optimization of heteroatom-based compounds as novel antimicrobial agents.

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