Contemporary Insights into the Pharmacological Effects of Chalcones

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Abstract

The chalcones constitute a group of α, β-unsaturated ketones that have attracted considerable attention within the field of medicinal chemistry because of the multiplicity of their pharmacological effects. These substances contain the structure of 1,3-diphenyl-2-propen-1-one, with α,β-unsaturated ketone moiety being responsible for their biological activity. The chalcones occur in nature as natural components of fruits, vegetables, tea, and soy foods; they are considered precursors of flavonoids and isoflavonoids. The derivatives of chalcones are known for exhibiting numerous pharmacological effects such as anticancer, anti-inflammatory, antimalarial, antidiabetic, antiviral, and anti-Alzheimer agents. Many natural chalcones and chalconoid preparations have also been used in traditional medicine.

Key Words: Chalcones, Anticancer, Anti-inflammatory, Antimalarial, Antidiabetic, Antiviral, Anti-Alzheimer

INTRODUCTION

The chalcones refer to naturally occurring and synthetic α,β-unsaturated carbonyls with a huge range of pharmacological actions which have generated a lot of interest in medicinal chemistry. The word ‘chalcone’ comes from Chalcos, a Greek word that means bronze, based on the golden color associated with many chalcone derivatives. In terms of their chemical structure, chalcones belong to the class of 1,3-diphenyl-2-propen-1-one with two phenyl rings attached to a β-carbonyl by three carbon atoms [1]. Delocalization of electrons exists in this molecule, and therefore, electron transfer reactions are feasible. Additionally, chalcones have geometrical isomerism with regard to E (trans) and Z (cis) isomers, with trans isomer being thermodynamically more stable compared to cis isomers due to less steric hindrance.

Naturally occurring chalcones are widely distributed in fruits, vegetables, tea, soya products, flowers, roots, leaves, and stems of plants. They are regarded as important biogenetic precursors of flavonoids, isoflavonoids, and carotenoids. The biological activity of chalcones is largely due to the existence of the α, β-unsaturated carbonyl group, whereas removal of the carbonyl group markedly decreases their pharmacological potential. Chalcones are generally crystalline solids, commonly yellow, orange, or brown in colour, and are soluble in both inorganic and organic solvents such as alkaline solutions, chloroform, acetone, and dichloromethane.[2]

Chemically, chalcones undergo several important reactions including halogen addition, isomerization, and cyclization to form flavonoids such as flavones and flavanols. They also produce characteristic pink coloration with concentrated sulphuric acid, known as the Wilson test. Due to their structural versatility and reactive framework, chalcones are useful as pharmacophores for drug development.

Over the past two decades, various medicinal activities have been found for chalcones and their derivatives such as antibacterial, antifungal, antiviral, anti-inflammatory, anti-HIV, antimalarial, antidiabetic, anticancer, anti-Alzheimer, and antileishmanial effects. [3-7]. Numerous naturally occurring chalcones that have been extracted from plants, including Glycyrrhiza, Angelica, and Piper, have traditionally been employed in medical practices in Asia, Africa, and South America. Furthermore, drugs based on chalcones extracted from plants, including metochalcone and sofalcone, have had pharmaceutical uses, especially in treating disorders of the stomach. Chalcones are considered important scaffolds in the discovery of new medicinal compounds because of their wide range of biological activities and easy manipulation of their chemical structures.

Pharmacological Applications of Chalcone

The chalcone molecules are some of the key examples of biologically active molecules, whose diverse biological activity is due to the presence of the unsaturated α, β carbonyl group. These molecules offer potential for medicinal applications through their structural diversity and chemical reactivity**.**

Antibacterial Activity

Natural as well as artificial chalcones possess high level of antibacterial action towards Gram-positive and Gram-negative bacteria [8]. Chalcones containing heterocyclic moieties **(1-6)**

such as pyrazole, thiophene, triazole and fluorinated substituents have shown enhanced activity against *Staphylococcus aureus*, *Salmonella* species, *E. coli*, and *P. aeruginosa* [9-11]**.** Increased lipophilicity due to fluorine substitution further improves their antibacterial potential. The presence of fluorine atoms increases the lipophilicity of the molecules, which may enhance their ability to penetrate bacterial cell membranes and thereby improve antibacterial potency. In most reported cases, fluorinated chalcones contain one or more fluorine atoms on both aromatic rings of the chalcone framework.

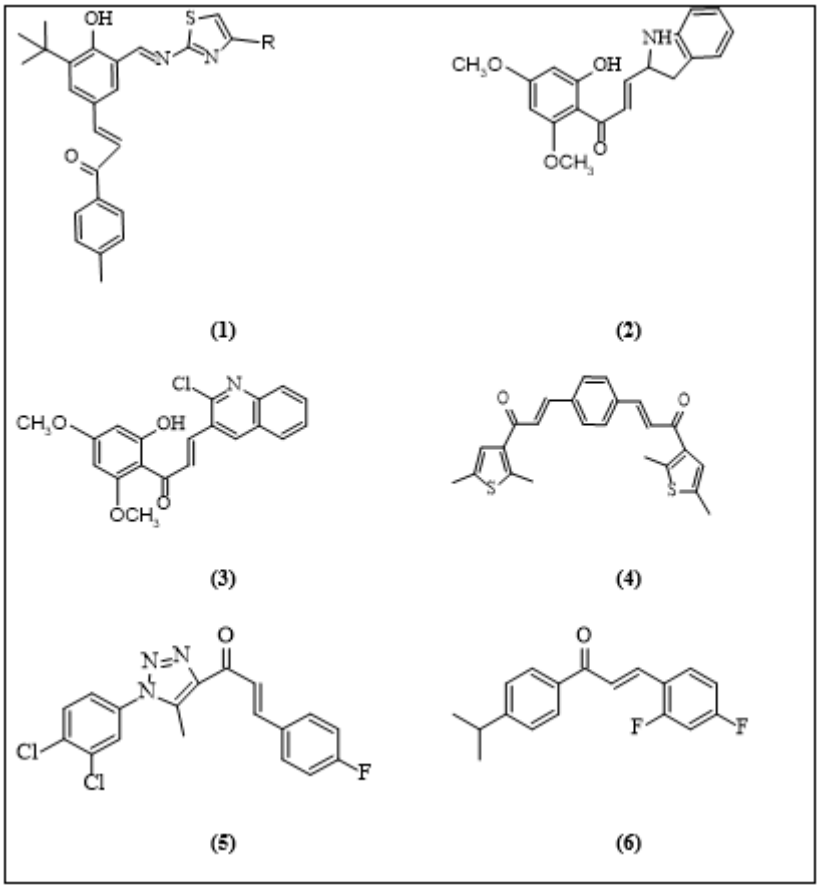

Figure 1. Chalcones with Antibacterial activity

In general, it may be concluded that chalcone derivatives have become important biological molecules due to their significant antimicrobial activity.The antibacterial activity of chalcones can be markedly improved through structural modifications, particularly by introducing heterocyclic moieties and electron-attracting substituents like fluorine. These findings emphasize the potential of chalcone-like derivatives as promising leads for the design and development of new antibacterial agents.

Anticancer Activity

Chalcones have become strong antineoplastic drugs due to their property to act on several molecular targets in the body. Homocyclic chalcones **(7-12),** shown **in Fig.2**, and heterocyclic chalcones (13-16) are active against different cell lines like those of breast, lung, liver, colon, cervical, prostrate, and leukemia cancers. Methoxy, hydroxy, nitrogen, and sulfide functionalities increase their cytotoxicity [12]. Furthermore, it was observed that N and S containing heterocyclic chalcones with methoxy functionalities were active against leukemia, prostate, and colon cancers [13-14].

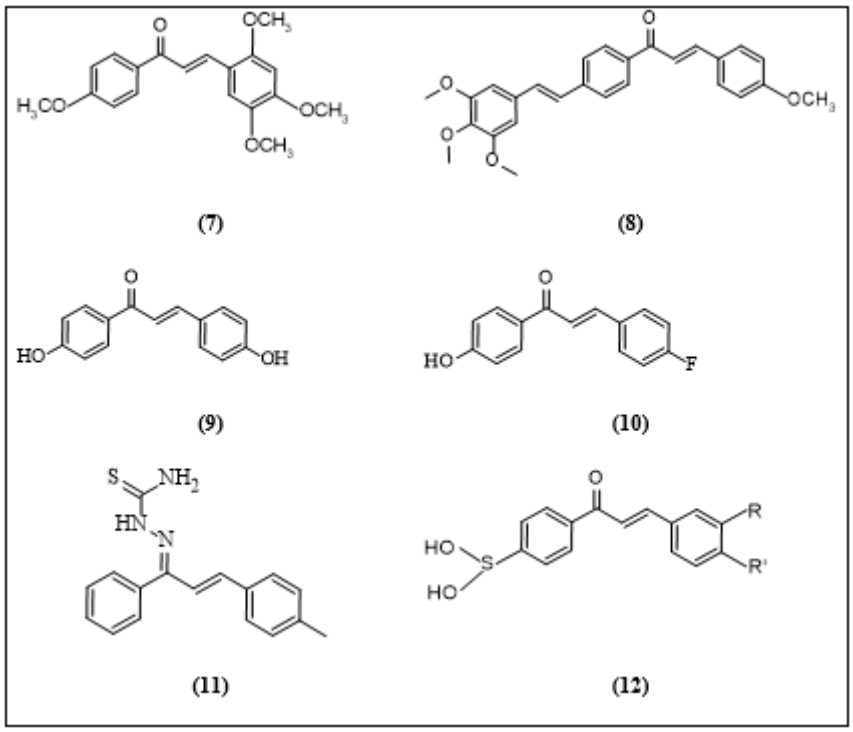

Figure 2. Homocyclic Chalcones active against Cancer

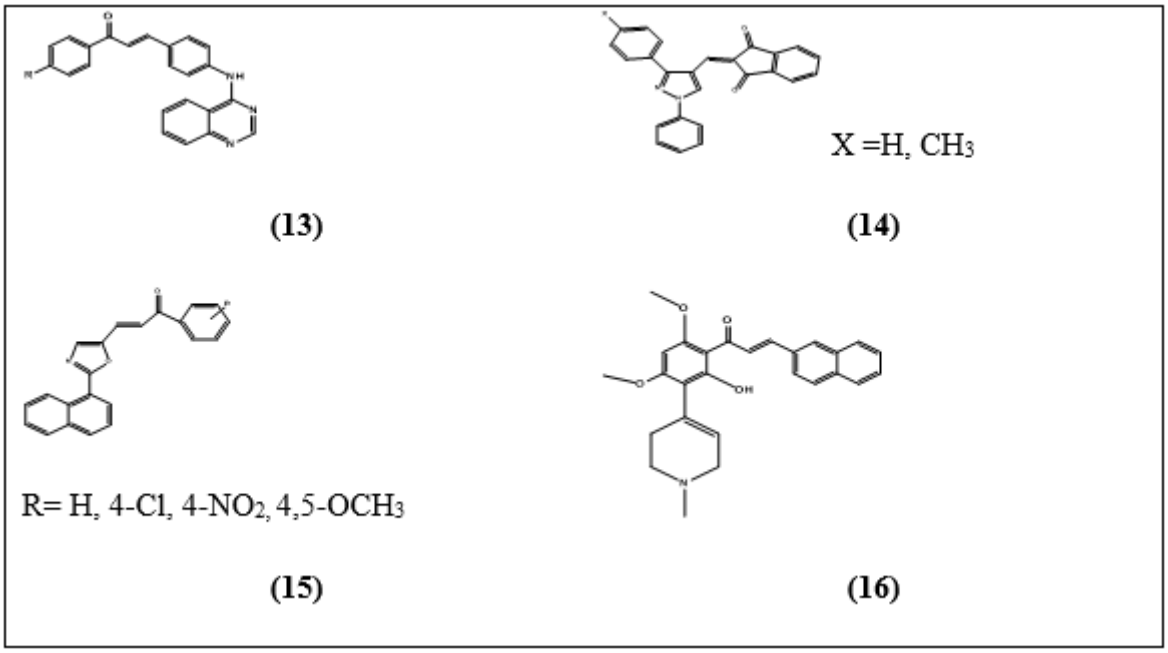

Figure 3. Heterocyclic Chalcones wth Anticancer Activity

Overall , chalcone and its derivatives have shown excellent anticancer properties against different types of cancer cell lines. The main mechanism of anticancer activity in chalcones and its derivatives is based on cell proliferation inhibition, induction of apoptosis, and interference with different cellular processes. Modifications in the chalcone structure, like the addition of heterocyclic units and methoxy or hydroxy groups, improve the cytotoxic properties of chalcones.

Antioxidant Activity

The antioxidant properties of chalcones include their ability to scavenge free radicals and reactive oxygen species (ROS), thus preventing cellular damage to macromolecules through oxidative stress. Chalcone pentoxide **(17)** isolated from licorice (*Leguminosae*) exhibited strong radical-scavenging activity in the DPPH test & has been recommended for medicinal use in China [15]. Naturally occurring chalcones such as licochalcone and glycyglabrone isolated from *Glycyrrhiza glabra* have demonstrated remarkable antioxidant activity [16]. The compounds (18-20) have demonstrated potent antioxidant activity, highlighting the significance of chalcone derivatives as promising natural antioxidant agents.

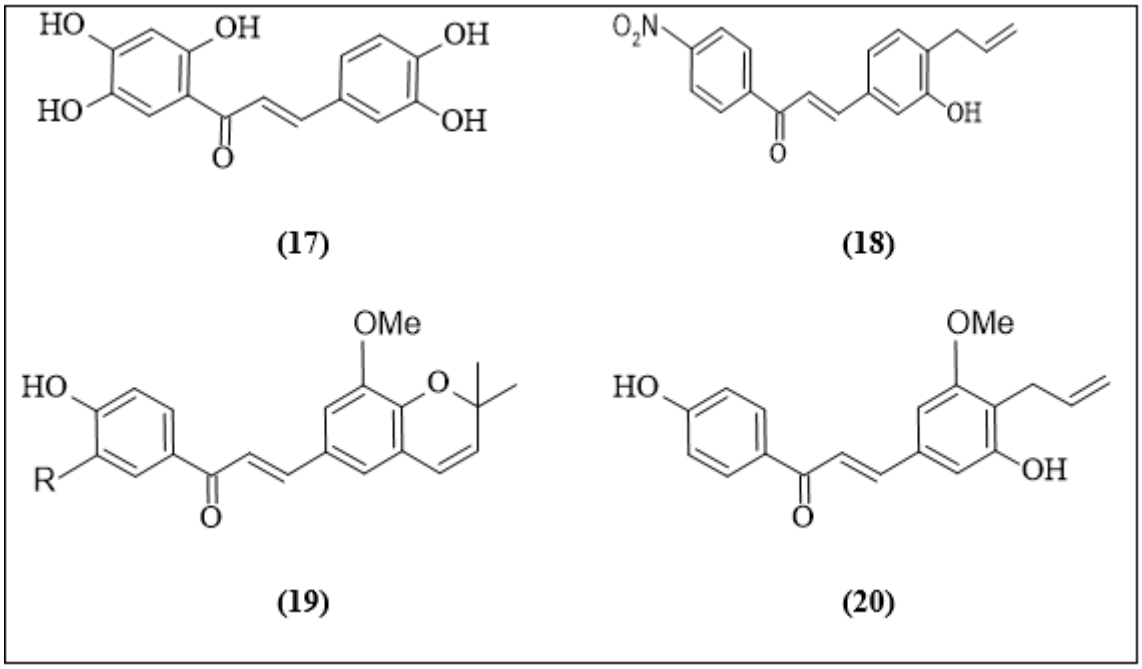

Figure 4. Chalcones with Antioxidant activity

Antidiabetic Activity

Several chalcone derivatives have shown promising antidiabetic activity through inhibition of enzymes such as protein tyrosine phosphatase (PTP1B) (21), AMP-kinase (22) and α-glucosidase (23) [17-18]. Halogenated (24-25) and heterocyclic chalcones (26) were reported to exhibit better antidiabetic efficacy than some standard drugs. (Fig. 5).

Overall, these studies indicate that chalcone derivatives are a promising class of compounds for the development of novel antidiabetic drugs. Their capability to regulate various enzymatic and molecular targets associated with glucose metabolism highlights their therapeutic potential in the treatment and management of diabetes mellitus.

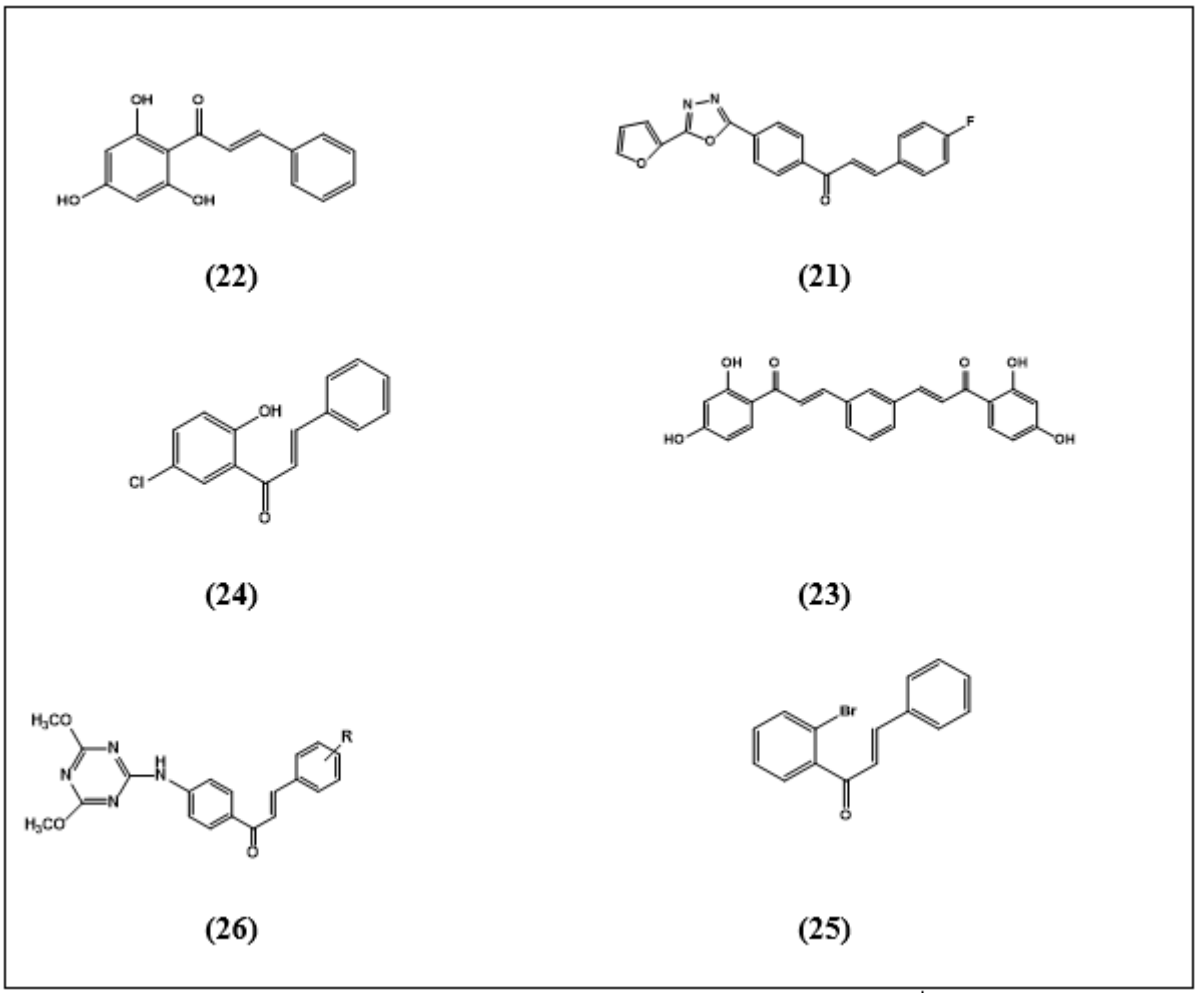

Figure 5. Chalcones with Antidiabetic activity

Anti-inflammatory Activity

Inflammation is an important immune response elicited in reaction to injuries or threats. Anti-inflammatory drugs are substances that play a role in alleviating inflammation through treatment of symptoms such as pain, swelling, and redness. Chalcones have been identified as a compound group that can inhibit inflammation through inhibition of cytokines production. Fluorinated & heterocyclic chalcones containing pyrrolidine **(27)**, nitrofuran, and apocynin moieties **(28)** have shown potent anti-inflammatory activity comparable to conventional anti-inflammatory agents [19]. A β-hydroxybenzofuran chalcone, Pongamol **(29)** isolated from *Pongamia pinnata*, known to exhibit both anti-inflammatory and antioxidant activities [20]. A Natural chalcones such as *isobacachalcone* **(30)** extracted from *Artocarpus communis* for the first time and found to have remarkable anti-inflammatory properties. **(Fig. 5)**

Overall, these findings suggest that chalcone derivatives exhibit remarkable anti-inflammatory potential. Their ability to regulate inflammatory mediators, including cytokines and COX-2 enzymes, makes them promising candidates for the development of novel therapies for inflammatory and immune-related diseases.

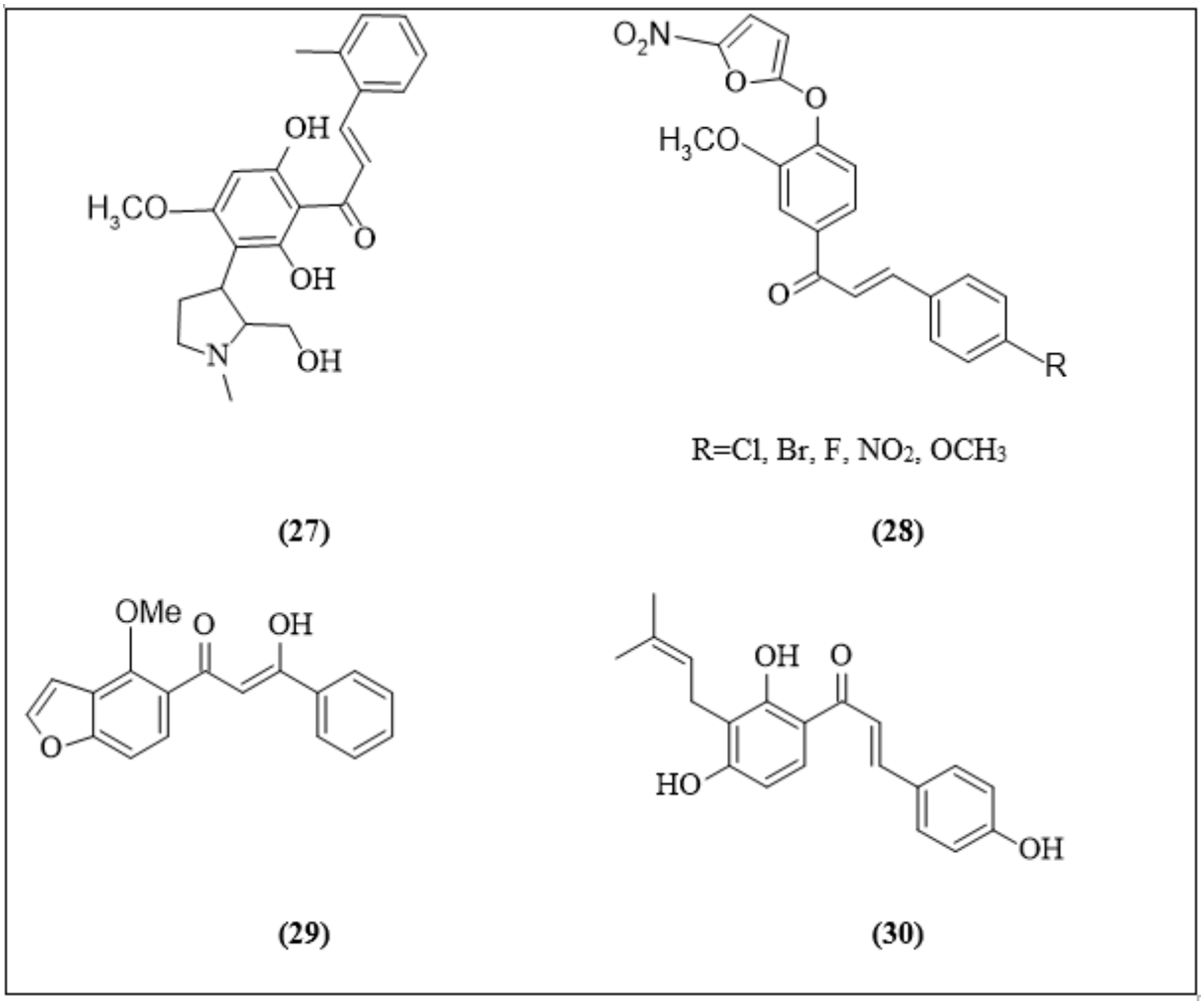

Figure 6. Chalcones against Anti-inflammatory Action

Neuroprotective Activity

Some derivatives of chalcone have neuroprotective activity and are helpful in treating neurodegenerative diseases like Alzheimer's disease and Parkinson's disease.. Chalcones acting as acetylcholinesterase inhibitors and transglutaminase inhibitors help in reducing neuronal damage and amyloid-beta aggregation. Thienylchalcone **(31)** is compound which is a powerful of transglutaminase and used in treatment of Alzheimer's [21]. A synthetic coumarin-chalcone hybrid **(32)** was potent AChE inhibitor that may be helpful in the treatment of neuro related problems [22]. **(Fig. 6)**

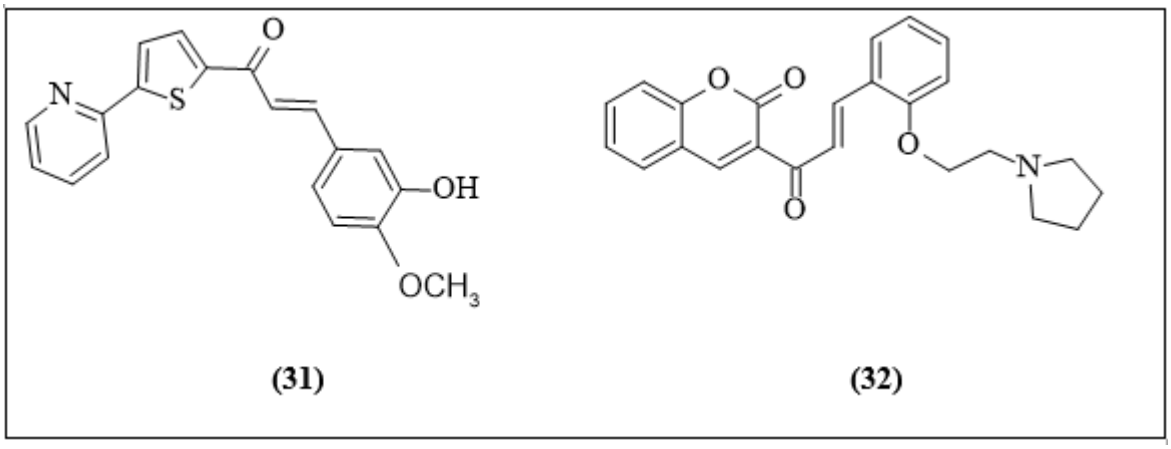

Figure 7. Chalcones with Neuroprotective Activity

Antimalarial Activity

Various chalcone derivatives exhibit potent antimalarial activity against drug-resistant strains of *Plasmodium falciparum*. Quinoline-, chromene-, imidazole-, and pyrrolidine-based chalcones have demonstrated significant efficacy and are considered promising candidates for antimalarial drug development [23-25].

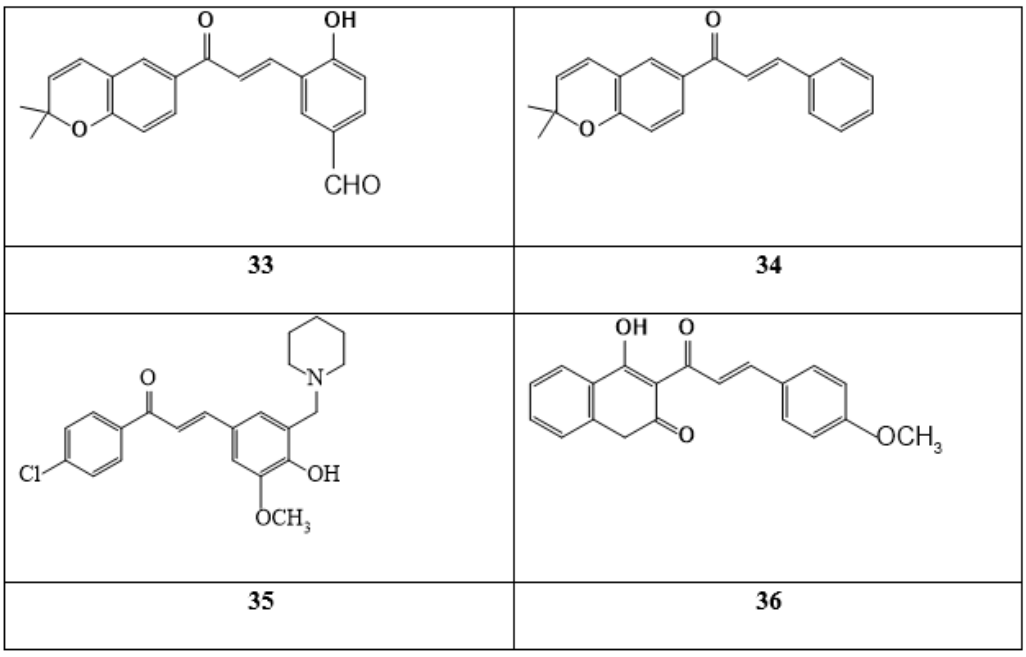

Figure 8. Chalcones with Antimalarial Activity

Overall, chalcones and their derivatives continue to attract considerable interest as multifunctional therapeutic agents owing to their diverse biological activities and pharmacological significance.

CONCLUSION

In this present study, different therapeutical actions of chalcone and its derivatives have been highlighted. Changes made in the chemical structure of these compounds will act as lead molecules for treating chronic diseases. Further investigation is needed in order to discover chalcone derivatives as an important chromophore.

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