Chalcone is an aromatic ketone that forms a central core for a variety of important biological compounds, which are collectively known as chalcones. They possess different activities like antibacterial, antifungal, anti-inflammatory and anti-tumor etc depending on the substitution made on them.

Chalcones are 1,3-diphenyl-2-propene-1-one, in which two aromatic rings are linked by a three carbon α,β-unsaturated carbonyl system. These are abundant in edible plants and are considered to be precursors of flavonoids and isoflavonoids. Chalcones possess conjugated double bonds and a completely delocalized Π-electron system on both benzene rings. Molecules possessing such system have relatively low redox potentials and have a greater probability of undergoing electron transfer reactions. The compounds with the backbone of chalcones have been reported to possess various biological activities such as antimicrobial, anti-inflammatory, analgesic, anti-platelet, anti- ulcerative, anti-malarial, antitumor and anti-inflammatory activities.

In this paper through reviewing different biological significance of chalcones and their derivatives have been reported along with their chemistry and of synthesis.

Synthetically or chemically chalcones are synthesized by two reactions:
a) Aldol condensation and
b) Claisen Schmidt condensation.

But here is a focus on chalcones synthesized by Claisen Schmidt condensation which involves the condensation between an aromatic aldehyde or ketone with an aliphatic ketone or aldehyde catalysed by the presence of dilute alkali or acid to form alpha beta unsaturated compound.

Keywords: Chalcone, Synthesis, Aldol condensation, Claisen Schmidt condensation, Biological activity.
Natural chalcone from Ashitaba angel of herb\textsuperscript{4,5,6}: To their molecular structure, and these structural characteristics of certain flavonoids found in ashitaba confer - antioxidative activity on the whole plant. This differentiates ashitaba from all other strains of flavonoids and they give the plant its characteristic yellow sap. This thick, sticky-yellow juice containing chalcones which is unique to this strain of angelica (Angelica Keiskei Koidzmi).

Chalcone are rarely found anywhere in the natural world but are the key factor in ashitaba (Angelica Keiskei Koidzmi). Research has shown that the unique properties of ashitaba are at least partly due to these remarkable compounds. The chalcones that are in ashitaba are known as Xanthoangelol, Xanthoangelol-E and 4-Hydroxyderricin and were discovered by Dr. Kimie Baba (MD, Osaka University). These organic compounds are antioxidant and some of these are explained as follows:

1. **Antiviral Activity of Substituted Chalcones and their respective Cu(ii), Ni(ii) and Zn(ii) Complexes\textsuperscript{11,12}**: Complexes of Cu(II), Ni(II) and Zn(II) with 3-(phenyl)-1-(2' -hydroxynaphthyl)-2 -propen – 1 – one (CPHPO), 3 - (4-methoxyphenyl) -1-(2' -hydroxynaphthyl)-2-propen – 1 – one (DMPHPO) have been found to be having antiviral action.

2. **Anti-Inflammatory Activity of Chalcones and Related Mannich bases\textsuperscript{3,13,14,15}**: Published results have revealed that conversion of various acyclic conjugated styryl ketones e.g. chalcones, into the corresponding Mannich bases was often accompanied by increased bioactivity both in vitro and in vivo\textsuperscript{20} Won et al.,\textsuperscript{21,22} synthesized (E)-1(2-hydroxyphenyl)-3(thiophen-
2-yl)prop-2-en-1-one, a chalcone derivative (Fig. 6) which was tested in vitro for its inhibitory activity on chemical mediators released from mast cells, neutrophils, macrophages and microglial cells with satisfactory results.

![Fig 6: 1-(2-Hydroxyphenyl)-3-(thiophen-2-yl)prop-2-en-1-one.](image)

3. Study of the Anti-inflammatory and analgesic effects of novel rigid benzofuran-3, 4- dihydroxy chalcone\textsuperscript{16,17,18}: It is reported that dihydroxy chalcones have analgesic and anti-inflammatory effects. Study of the structure activity relationship (SAR) shows that benzofuran-3-one derivatives may be more effective in this respect.

In this study, (Z)-2-(3,4-dihydroxybenzylidene)-5-methoxybenzofuran-3(2\textsubscript{H})-one (compound 5) synthesized and its analgesic and anti-inflammatory effects were evaluated by formalin, carrageenan and hot-Plate methods in mice.

![Fig 7: Synthesis of (Z)-2-(3,4-dihydroxybenzylidene)-5-methoxybenzofuran-3(2H)-one-(compound 5)](image)

4. Antimicrobial Activity of Some Novel Chalcones of 2-Hydroxy -1-Acetonaphthone and 3-Acetyl Coumarin\textsuperscript{19,20,21}: Chalcones either natural or synthetic are known to exhibit various biological activities. They have been reported to possess antioxidant\textsuperscript{27-30}, antimalarial\textsuperscript{31}, antileishmanial\textsuperscript{32}, antiinflammatory\textsuperscript{33}, antitumor\textsuperscript{34} and antibacterial activity\textsuperscript{35}. The presence of a reactive alpha, beta unsaturated keto function in chalcones is found to be responsible for their antimicrobial activity, which may be altered depending on the type and position of substituent on the aromatic rings. In the present communication we report the reaction of 2-hydroxy-1- acetonaphthone as well as 3-acetyl coumarin with different aromatic and heterocyclic aldehydes to form Chalcones.

![Fig 8: 3-acetyl coumarin](image) ![Fig 9: 2-hydroxy aceto napthone](image)

5. Antimicrobial Activity of Some Chalcone Derivatives\textsuperscript{22,23}: In an effort to develop antimicrobial agents, a series of chalcones prepared by Claisen-Schmidt condensation of appropriate acetophenones with appropriate aromatic aldehydes in the presence of aqueous solution of potassium hydroxide and ethanol at room temperature were found to be having antibacterial and antifungal activities.

![Fig 10: Reaction of 2-hydroxy-1-aceto napthone with aryl aldehyde](image)

6. Some new Chalcones and Flavanones having 2-chloro-8-methoxyquinolinyl moiety\textsuperscript{24,25,26}: Chalcones, analogs of 1,3-diarylprop-2-en-1- one, form a wide class of compounds containing two aromatic rings bound with vinyl ketone fragment. They are useful in synthesis of various heterocyclic compounds.

Chalcones present great interest as compounds exhibiting antimalarial, antibacterial, antifibrogenic, anticancer, antitraumatic, antiinflammatory, antileishmanial, cytotoxic and antitrypanosoma cruzi activities. While the flavonoid compounds are a group of natural products found in fruits, vegetables, nuts, seeds and flowers as well as in teas and are important constituent of human diet. They have been demonstrated to possess antioxidant, antihypertensive, antiallergic, antinocicepative, trypsin inhibitors, plant growth regulator, antibacterial and antifungal activities.

![Fig 11: Reaction of 3-acetyl coumarin with aryl aldehyde](image)

7. Novel quinolinyl chalcones as antibacterial agents\textsuperscript{27,28,29}: Biological activity of some quinolinyl chalcones and pyrimidines chalcones are a class of privileged structures that have a wide range of biological properties. Chalcones are also reported as anticancer agents, and antimalarial agents. Quinoline-based fused heterocyclic systems are found as potential anticancer agents and have antimalarial activities. Pyrimidine derivatives form a component in a number of useful drugs and are associated with many biological pharmaceutical and therapeutic activities. Condensed pyrimidine derivatives have been reported as analgesics, antiviral...
and as anti-inflammatory agents, antibacterial and anti-
tuberculostatic agent, diaryl pyrimidine (DAPY’S) appears to
be the more effective against wild type and various mutant
strains of HIV-1.

**Fig. 14: Synthesis of quinoline carbaldehydes**

**Fig 15 : Synthesis of Novel Quinolinyl Chalcone derivatives**

8. Chalcone with antihepatotoxic activity\(^4,30,31\):
Some of the compounds namely 2-hydroxy- 4-methoxy-3',4'- (2''- hydroxy methyl-1'' , 4''- dioxano) chalcone and 2-hydroxy- 4, 6 - dimethoxy-3',4'- (2''- hydroxy methyl-
yl-1'' , 4''- dioxano) chalcone showed a potent antihepatotox-
ic activity, whereas other compounds exhibited moderate activity with respect to standard drug silybon-70.

**Fig 16: Reacetophenone synthesis**

9. Chalcone with hypoglycemic activity\(^3, 32,33\):
The aryloxypropanolamines were first described as β3-AR agonists. Chalcones with proper substitution have recently
been isolated from *Broussonetia papyrifera* known to selectively inhibit enzymes like protein tyrosine phosphatase 1B (PTP1B) and aldose reductase. Their antioxidant property
attracted to explore hybrid structures as antihyperglycemic
agents, because oxidative stress also plays an important
role in diabetic patients leading to vascular complications.
3, 4-Dimethoxy compound displayed significant antihyper-
glycemic effect. Mono methoxy series showed bloodgly-
ucose lowering activity. Compounds vicinally deoxygenat-
ed as dimethoxy and methylenedioxy substitution showed
the best antihyperglycemic activity when compared to the
 corresponding monomethoxy compounds.

Compounds containing propanolamine chain at para po-
sition showed significant activity as compared to meta and
ortho substituted compounds.

10. Chalcone with Antioxidants activity\(^1,34,35\):
Antioxidants are the agents, which can inhibit or delay the
oxidation of an oxidisable substrate in a chain reaction.
Chalcones belongs to the largest class of plant secondary
metabolites. Which, in many cases, serve in plant defense
mechanisms to counteract reactive oxygen species (ROS)
in order to survive and prevent molecular damage and
damage by microorganisms, insects, and herbivores. They
are known to possess antioxidant character at various ex-
tents. The antioxidant activity of natural compounds like
chalconoids is related to a number of different mechanisms
such as free radical scavenging, hydrogen donation singlet
oxygen quenching, metal ion chelation and acting as a sub-
strate for free radicals such as superoxide and hydroxide.
11. Chalcone with potent antiplatelet activity\textsuperscript{36}:

In an effort to continually develop potent antiplatelet agents with vasorelaxing and antiinflammatory actions, a novel series of antiinflammatory chalcones was continually screened to evaluate their antiplatelet and vasorelaxing effects. Their structure–activity relationships and mode of action were discussed and characterized. A novel series of antiinflammatory chalcones was studied on antiplatelet effect in rabbit washed platelets and human platelet-rich plasma (PRP) and vasorelaxing effect in rat thoracic aorta. Arachidonic acid–induced platelet aggregation was potently inhibited by almost all the chalcone derivatives and also had a potent inhibitory effect on cyclooxygenase. Lyphoid-induced platelet aggregation was potentiated by almost all the chalcone derivatives and also had a potent inhibitory effect on cyclooxygenase.

The selective chalcones tested in human PRP significantly inhibited secondary aggregation induced by adrenaline. In rat thoracic aorta, most of chalcones at high concentration inhibited secondary aggregation induced by adrenaline. In rat thoracic aorta, the phenylephrine- and high K+-induced contractions caused by norepinephrine (3 μM). In the rat thoracic aorta, the phenylephrine- and high K⁺-induced 

12. The antileishmanial activity of novel oxygenated chalcones\textsuperscript{37}:

Licochalcone A, an oxygenated chalcone, has antileishmanial and antimalarial activities, and alters the ultrastructure and function of the mitochondria of Leishmania spp. parasites. The study investigates the antileishmanial activity and the mechanism of action of a group of new oxygenated chalcones. The tested oxygenated chalcones inhibited the in-vitro growth of Leishmania major promastigotes and Leishmania donovani amastigotes. Treatment of hamsters infected with L. donovani with intraperitoneal administration of two oxygenated chalcones resulted in a significant reduction of parasite load in the liver and the spleen compared with untreated control animals. The oxygenated chalcones also inhibited the respiration of the parasite and the activity of mitochondrial dehydrogenases. Electron microscopic studies illustrated that they altered the ultrastructure of the mitochondria of L. major promastigote. The data clearly indicate that this group of oxygenated chalcones has a strong antileishmanial activity and might be developed into a new antileishmanial drug. The antileishmanial activity of oxygenated chalcones might be the result of interference with function of the parasite mitochondria.

13. Chalcone with Immunosuppressive activity\textsuperscript{38,39}:

The immunosuppressive activity of licochalcone A was noted during investigations of its antileishmanial activity, when low concentrations of licochalcone A were found to inhibit proliferation of phytohemmagglutinin A-stimulated lymphocytes. It was subsequently shown that the structural requirements for antileishmanial and lymphocyte-suppressing activities were different and it would be possible to design chalcones with selective activity. The immune suppressing potential of chalcones is not altogether an undesirable feature. Immunosuppression reduces graft-related symptoms and is beneficial for certain autoimmune diseases. Licochalcone A and some synthetic analogues have been reported to inhibit generalized lymphocyte proliferation that was not restricted to any particular T lymphocyte subset. The same study reported the chalcones to cause down regulation of pro- and anti-inflammatory cytokine production from monocytes as well as to interfere with the production but not release of tumor necrosis factor – α (TNF-α). The substitution pattern on the chalcone skeleton is important to this end but no details were revealed in the report.

14. A Boronic-Chalcone Derivative Exhibits Potent Anticancer Activity\textsuperscript{40}:

Chalcones and their derivatives have been shown to have potent anticancer activity. However, the exact mechanisms of cytotoxic activity remain to be established. In this study a series of boronic chalcones were evaluated for anticancer activity and mechanisms of action. Among them 3,5-bis-(4-boronic acid-benzylidene)-1-methyl-piperidin-4-one (AM114) exhibited most potent growth inhibitory activity with IC\textsubscript{50} values of 1.5 and 0.6 μM in 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay and colony formation assay, respectively. The cytotoxic activity of AM114 was shown to be associated with the accumulation of p53 and p21 proteins and induction of apoptosis. Mechanistic studies showed that AM114 treatment inhibited the chymotrypsin-like activity of the 20S proteasome in vitro, leading to a significant accumulation of ubiquitinated p53 and other cellular proteins in whole cells.
15. Antimalarial chalcones:
Gan Cao as a plant is a perennial herb used in traditional Chinese medicine as a sweetening agent and as a tonic to improve the immune response of the body. The isolate from the Gan Cao root (licochalcone A) was found to inhibit the *in vitro* growth of chloroquine resistant and chloroquine sensitive *P. falciparum* and protected mice from lethal infections of *P. yoelii*. However, it was also observed to inhibit phytohemagglutinin A-induced proliferation of human lymphocytes in vitro, which are indicative of immunosuppressive effects. This led to the synthesis of other oxygenated chalcones, of which 2,4-dimethoxy-4'-butoxychalcone was found to be outstanding. This compound is comparable to licochalcone A in terms of antimalarial activity but is significantly less toxic than licochalcone A against human leukocytes.

**Fig 23**: Gan cao plant

**Fig 24**: Structures of chalcone with antimalarial action

16. Biological evaluation of some heterocyclic derivatives of Chalcones:
Some novel heterocyclic derivatives such as Thazines, Oxazoles and Pyrazoles of chalcone were characterized for their Anti inflammatory, Anti Bacterial and Anti fungal activities.

Chalcones are prepared by condensing Aryl ketones with aromatic aldehydes in presence of suitable condensing agents. They undergo a variety of chemical reactions and are found useful in synthesis of variety of heterocyclic compounds. Chalcones have been used as intermediate for the preparations of compounds having therapeutic value. Literature review reveals that chalcone derivatives exhibit diverse pharmacological activities such as potential cytotoxic agents, antimicrobial agents, antiviral, antiinflammatory, anesthetics, mydriatics etc. Based on the above observation it is worthwhile to prepare newer compounds for their antimicrobial and antiinflammatory activities.

**CONCLUSION:**
There is a continuous methodology for the synthesis of variety of chalcone derivatives with increase in the number of diseases. Since the chalcone back bone is found be very effective and potent against a list of diseases. They place a wide range of medicinal activity in today’s life. They are the precursors in flavanoid synthesis found in every edible plant but difficult to isolate. Initially they were found in natural source like ashitaba herb also know as angel of herb because of wide range of biological significance like purifies blood, strengthens immune system, monitors cholesterol level, regulates blood pressure, suppresses acid secretion, prevents thrombus, suppresses cytophy, antibacterial, prevents cancer, and promotes metabolism etc. and from that it is thought to synthesize chalcone meant for a specific disease. Chalcone are rarely found anywhere in the natural world but are the key factor in ashitaba. This has created the need for synthesizing chalcones synthetically i.e from aromatic aldehyde and aliphatic ketone by claisen Schmidt condensation. The various activities of chalcone includes antimicrobial, anti-inflammatory, analgesic, antiplatelet, antiulcerative, antimalarial, anticancer, antiviral, antileishmanial, antioxidant, antitubercular, antihyperglycemic, immunomodulatory, inhibition of chemical mediators release, inhibition of leukotriene B4, inhibition of tyrosinase and inhibition of aldose reductase activities.

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