Chalcone: A multiclass molecule as a pool for pharmaceutical agents

Bhawna[1] and Naveen Chandra[1]*

[1]Department of Chemistry, Lovely Professional University, Phagwara, 144411, India

Abstract: Chalcone and its heterocyclic compounds are known to have wide range of pharmacological activities which makes this as special in organic compounds. Further, the moiety – CO-CH=CH- is very reactive which is present between two aromatic rings and therefore it acts as an important synthon for making 5, or 6 or 7- seven membered heterocyclic scaffolds containing N, O and S atoms.

Keywords: antibacterials, anticancer, anti HIV, heterocyclic compounds

INTRODUCTION

Chalcones are having a place within the auxiliary metabolites of plants which are generally pigments and act as forerunners to synthesise isoflavonoids also flavonoids biologically which are bounteously present in palatable plants. The chalcones possess smaller size and are lyophobic in nature. The chalcones are hence referred to as Natural products because of nearby close and biogenetic connection somewhere in the range of flavanones and chalcone moieties. Chalconoid moiety exist as both cis and Trans isomeric structures out of which the Trans structure is thermodynamically increasingly stable [1]. These are open-chain flavonoids in which unsaturated carbonyl framework is utilized as a link between two *arene* rings A and B.

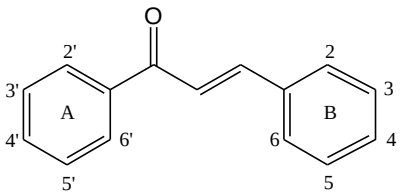


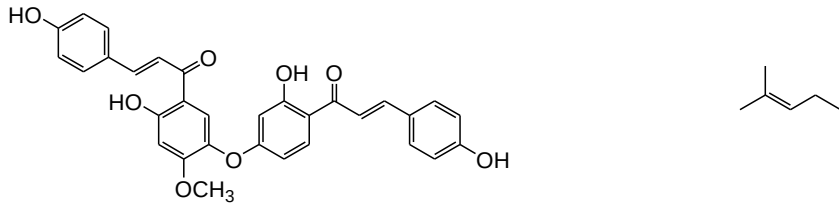
Fig. 1: Structure of chalcone

Larger part of normally happening chalcones is polyhydroxylated in the aryl rings. Primordial restorative purposes and uses of chalcones can be related to the plants and herbs utilization in ancient times for curing diverse therapeutic issues. Chalcones whether synthetic or obtained from nature shows wide range of activities, including antimalarial, cytotoxic, anticancer and anti-inflammatory. The basic skeleton present in chalcone is nonetheless but α-β unsaturated keto moieties which have been reported as main attraction for the scientific research. In addition to it, the introduction of halogens to the benzenoid part of chalcones and derivatives involving heterocyclic compounds the so called moiety – CO-CH=CH- present in chalcone as mentioned above enhances their pharmaceutical value and potential as well [2]. Chalcone bears an awesome synthon group whose assortment lead to patentable pharmaceutical products formation with hetero atoms in

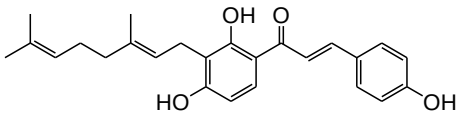
thearomatic ring ultimately leading to enhanced biological Activities. Chalcones possess three carbon moiety –CO-CH=CH- which is utilized to incorporate a few subordinates for instance cyanopyridines, pyrazolines and pyrimidines like unique Heterosystem analogs [3]**.** The chalcones have been characterized by specific aroma fixings. Cyclohexenyl subordinates of chalcones are called damascones. The majority of the structural analogue possesses but-2-en-1-one structure. Such a structural analogue could be represented by two structures exhibiting cis–trans isomerism about twofold bond present in conjugation with the C=O moiety in chalcone. A few Ionones reported to be assessed for use as flavor fixings in groceries [4]. The science of chalcones stayed an interest among scientists because of its straightforward science, simplicity of its pharmacophore, enormous number of replaceable hydrogen to yield huge number of compounds with wide number of activities. Dissolvable free conditions have additionally been applied for chalcone formation, for example, pounding or microwave irradiation like techniques. The novel base impetus $KF-Al_2O_3$ has been used in microwave illumination has likewise been applied in non-solvent Microwave illumination has likewise been applied in non-solvent frameworks to build the chalcone core [5].

Natural Chalcones

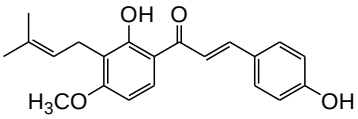
Chalcones are the core nuclei of biologically active compounds, available from natural sources. These are basically present in plants as flavonoids. Chalcones extracted from plants have many uses in medicines and so it has been studied and reported to have many biologically potent activities. Bichalcones, for example, rhuschalcone from Rhus pyroides. Ashitaba, *an asian herb*, found in Japan is having a place of indistinguishable sort from *Angelica Sinensis*. "Angelica" was given to this herb in view of its faithful impacts, to be specific its additional conventional capacity for gradually lowering the maturing course due to what Ashitaba is currently drawing in additional furthermore, more consideration from established researchers. AKK plant belongs to celery plant kingdom. The yellowish viscous fluid obtained from the stems possesses chalcone called Xanthoangelol. Delegate traditional chalcones, bis-chalcones, dihydrochalcones, chalcone copies, and melded chalcones secluded from normal sources as of late and their potential organic activities like anti-inflammatory, anti-microbial, anti-fungal, anti-malarial, anti-oxidant, anti-viral and anti- protozoal.



Rhuschalcone



Xanthoangelol



4- Hydroxyderricin

Fig. 2: few natural chalcones

Synthetic Chalcones

These are the class of chalcones which are being synthesised in Laboratory with usage of various chemical reagents and conditions and involving named reactions like Claisen Schimdt, Aldol reaction for synthesis also various other coupling reactions are seen like heck and Suzuki coupling and many other named organometallic reactions like Stille coupling and many more [3].

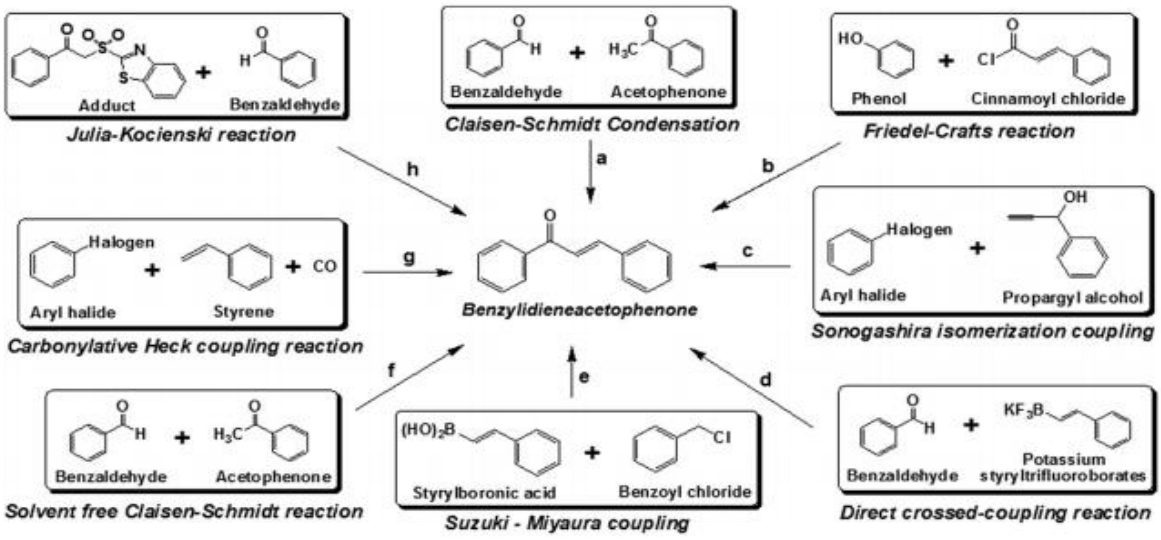


Fig.3: synthetic chalcones prepared by Suzuki couplings

Biosynthesis of Chalcones

Chalcone is formed during the flavonoid pathway of biosynthesis. It is the most demanding molecule since it can be easily obtained by synthesizing chemically in laboratories. Universal chemical in higher plants is “CHS-like” enzyme which is used to biosynthesise chalcones. “CHS-like” catalysts are used to synthesise biologically stilbene like, and flavonoid like secondary metabolite. CHS from the vegetable source gives the complete pathway to synthesise Chalcone proactively. Initially by migration of coumaroyl moiety from one 4- coumaroyl-coenzyme A (CoA) to Cys164, CHS produces chalcone. In this manner, 3 thio-ester moiety of malonyl

Coenzyme A structure by means of a polyketide response transfer of coumaroyl moiety to cysteine residue take place [6]**.** Then with regiospecific Claisen type ring closing reaction take place due to production of thioester type moiety and end up with naringenin (NC) type of chalconoid. This NC chalcone was then changed over into 6′-deoxyNC chalcone in the presence of "CHS- like and CHR" like enzymes. The relating reactant enzymes also used to form many other plant pigments which are so produced utilizing NC as the substrates. Chalcones filling in as forerunners have created a scope of plant metabolites, uncovering fascinating natural activities, which will be examined in the accompanying areas. Basic chalcones have been artificially hybridized with different formats, for example, stilbenes [5].

Chemical Synthesis of Chalcones

Earlier method includes various bases like sodium hydroxide, Barium hydroxide, potassium carbonate, potassium hydroxide and many more which employs Claisen-Schimdt reaction for chemical synthesis. Another alternative is Aldol reaction involving use of Lewis acid as catalyst like boron trichloride, anhydrous aluminium chloride and many more. Chalcones are commonly arranged by buildup responses by means of base or corrosive catalysis. Despite the fact chalconoid (α,β-unsaturated conjugated moiety) is effectively and is easily synthesizable thereby leading to development of enormous amount of systems lately and methodology is thereby found to provide reasonable justification for their fascinating natural potent activity and the advancement of different impetuses or response conditions.

Pharmaceutical Potential of Chalcones

Chalcone is a one of a pharma core nucleus that is related with a various medical activities and serves to synthesis various heterocyclic analogs like pyrimidine since they act as outstanding intermediates for formation of wide varied of analogs like pyrazole, pyrimidines. The Chalcones act as a precursor to synthesis flavonoids biologically. They are obtained from plants which are found to be palatable. It is found that certain groups when inserted into chalconoid moiety enhance their pharmaceutical potential. Thus chalcones keep on drawing in extensive logical consideration on account of their relationship with an assortment of natural pharmacological activities [7]. Chalcones, which brought about an assortment of organic and pharmacological interests. Chalcones have numerous biological activities presumably because of their little structures which allows them to get hold of various organic atoms and prompt them to stay attached thereby increasing the activity of such analogue. Therapeutic potential of chalcones incorporate anti-tumor action, malignant growth precaution impacts, anti-inflammatory, antibacterial action, anti-tuberculosis movement, antidiabetic action, anti-leishmanial action, antimicrobial action, antiviral action, antimalarial movement, neuroprotective impacts, anti- HIV, antibacterial, and anticancer activities [8]**.**

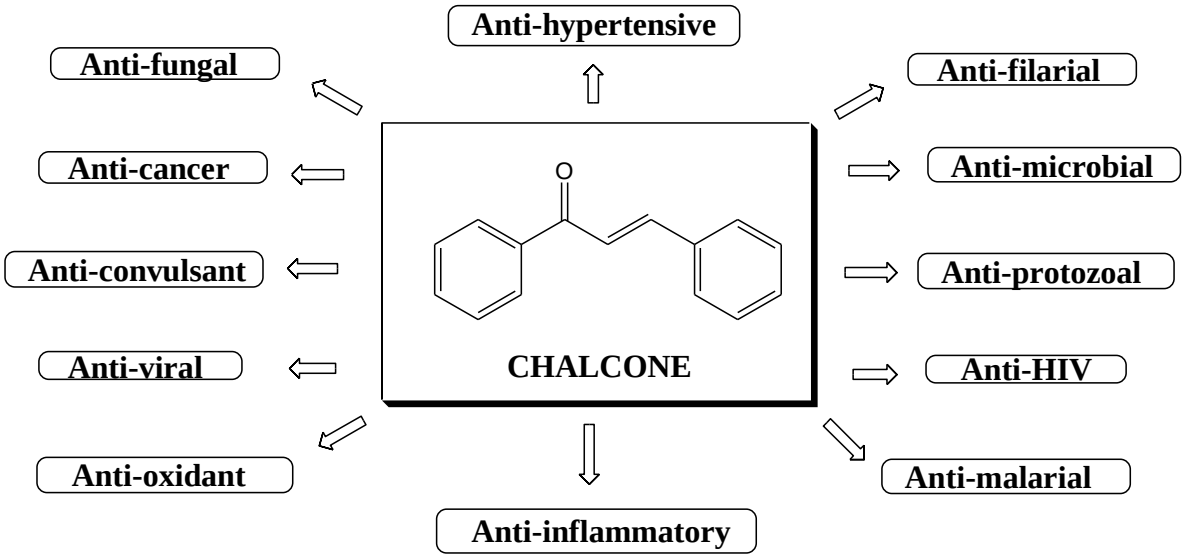
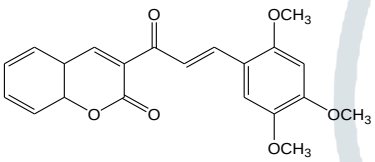
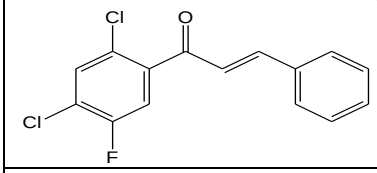
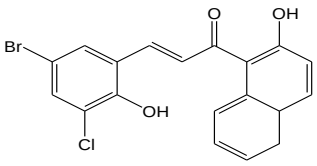
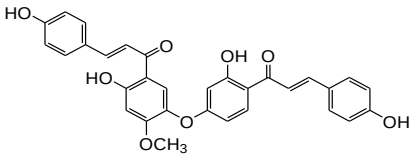
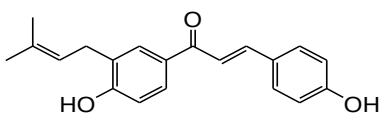
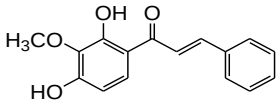
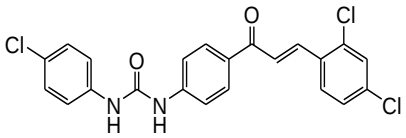
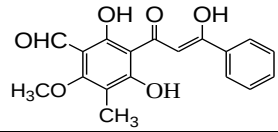
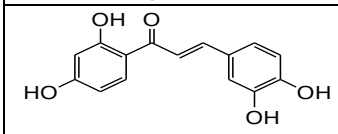
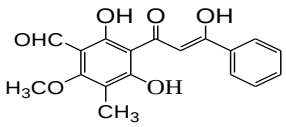
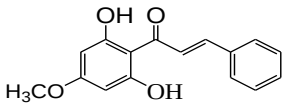
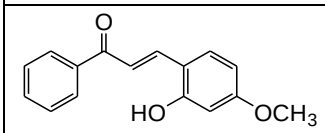
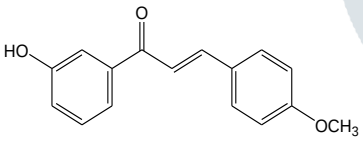
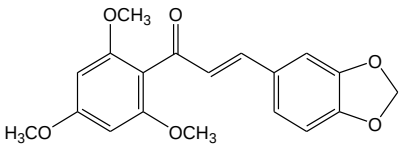
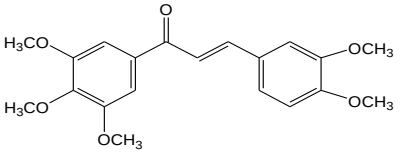
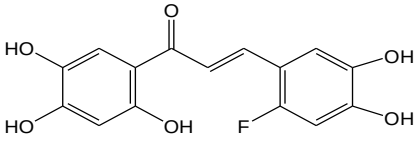


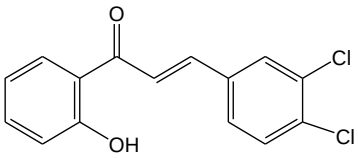
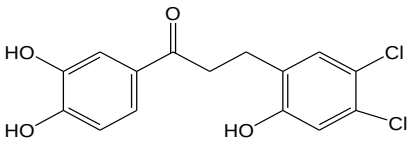
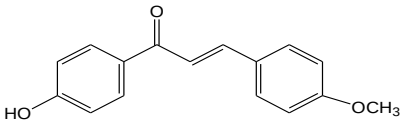
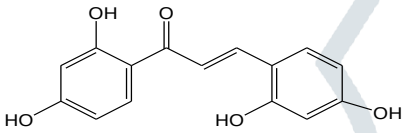
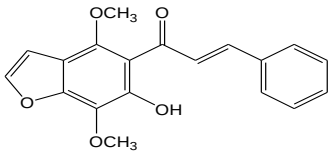
Fig. 4: Chalcones with multiple pharmacological activities

Recent chalcones as pharmacological active agents

In the past few years, many chalcones and its derivate isolated naturally or synthesized and showed prominent biological profile. Few important compounds of this class are listed in Table 1.

Structure of chalcone	Name	Pharmacol. activity
	3-[1-oxo-3-(2, 4, 5-trimethoxyphenyl)-2-propenyl]-2H-1-benzopyran-2-ones	antimicrobial activity against *B.subtilis, B.pumilis* and *E.coli* [9]
	3-aryl-1-(2,4-dichloro5-fluorophenyl)-2-propen-1-ones	antimicrobial activity, due to the possess favorable lipophilic character of halogens [10]
	3-(5-bromo-3-chloro-2-hydroxyphenyl)-1-(2-hydroxy-4a,5-dihydronaphthalen-1-yl)prop-2-en-1-one	antifungal activity against *A.niger* and *R.oryzae.*[11]
	retrochalcone	Isolated from from *G. infanta* exhibited prominent antibacterial activity [12].
	1-(4-hydroxy-3-(3-methylbut-2-enyl)phenyl)-3-(4-hydroxyphenyl)prop-2-en-1-one	Isolated from the leaves of *Malclura tinctoria* possessing antifungal activity [13]

	2’ , 4’-dihydroxy-3’ -methoxychalcone	from the methanolic extract of *Zuccagnia punctata* exhibited antifungal activity [14].
	1-(4-chlorophenyl)-3-(4-(3-(2,4-dichlorophenyl)acryloyl)phenyl)urea	exhibited antimalarial activity [15]
	2,4-dihydroxy-3-(3-hydroxy-3-phenylacryloyl)-6-methoxy-5-methylbenzaldehyde	exhibited the anti-HIV activity [16]
	1-(2,4-dihydroxyphenyl)-3-(3,4-dihydroxyphenyl)prop-2-en-1-one	exhibited the anti-HIV activity [17]
	2,4-dihydroxy-3-(3-hydroxy-3-phenylacryloyl)-6-methoxy-5-methylbenzaldehyde	exhibited the anti-HIV activity [18]
	1-(2,6-dihydroxy-4-methoxyphenyl)-3-phenylprop-2-en-1-one	showed significant anti-leishmanial activity [19]
	3-(2-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one	exhibited anti-tubercular activity [20]
	1-(3-hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one	exhibited anti-mycobacterial activity [21]
	3-(benzo[d][1,3]dioxol-5-yl)-1-(2,4,6-trimethoxyphenyl)prop-2-en-1-one	isolated from the stem bark of *Millettia leucantha* showed cytotoxicity [22]
	3-(3,4-dimethoxyphenyl)-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one	possessing good cytotoxic activity [23]
	3-(2-fluoro-4,5-dihydroxyphenyl)-1-(2,4,5-trihydroxyphenyl)prop-2-en-1-one	exhibited anti-cancer activity [24]

	3-(3,4-dichlorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one	possessing anti-inflammatory and cancer chemopreventive activity [25]
	3-(4,5-dichloro-2-hydroxyphenyl)-1-(3,4-dihydroxyphenyl)propan-1-one	exhibited cyclooxygenase-2 inhibitory activity [26]
	4’ -hydroxy-4- methoxychalcone	exhibited anti-hyperglycemic activity [27]
	1,3-bis(2,4-dihydroxyphenyl)prop-2-en-1-one	showed potent tyrosine- kinase inhibitory activity [28]
	1-(6-hydroxy-4,7-dimethoxybenzofuran-5-yl)-3-phenylprop-2-en-1-one	exhibited potassium channel modulatory activity [29]

Heterocyclic compounds with core nuclei of chalcone

Many heterocyclic compounds has been synthesized by using chlacone moiety. 5 or 6 membered heterocyclic compound synthetic view is given in Fig. 5.

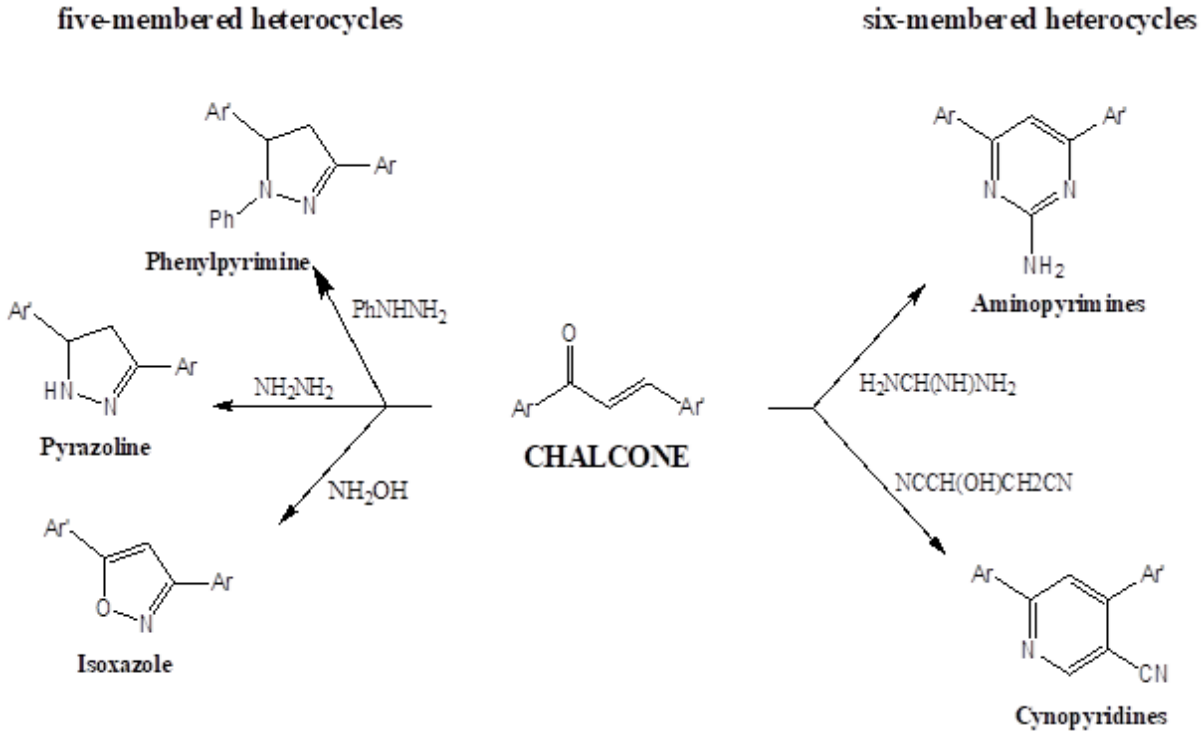


Fig. 5: Chalcone a core nuclei for heterocycles

Conclusion:

This short review highlights the pharmacological potentials of chaconne and its derivatives. Chalcone derivatives received attention by researchers, scientist and pharmaceutical companies due to their anti-cancer, anti-bacterial, anti-fungal, anti-malarial, anti-oxidant, anti-in?ammatory and anti-tubercular activities. It is also a known precursor for the synthesis of variety of heterocycliccompounds.

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