International Journal of Botany Studies
www.botanyjournals.com
ISSN: 2455-541X
Received: 03-11-2021, Accepted: 19-11-2021, Published: 04-12-2021
Volume 6, Issue 6, 2021, Page No. 685-693

A review on plant chalcones a recent approach

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Abstract
Most of the medicinal plants are a very good source of primary and secondary metabolites. Lot of phytochemicals are obtained from the plant sources that are used as medicinal agents in current pharmaceutical systems. Flavones are one of the important secondary metabolites present in many leaves, flowers, glucosides, and various vegetables, spices and natural foods. Chalcones considered as best intermediated in flavonoid biosynthesis but they do not accumulate to an appreciable degree in most plants. Chalcones are a group of plant-derived polyphenolic compounds belonging to the flavonoids family that possess a wide variety of anti oxidant, antitubercular, antibacterial, antifungal, and modulatory functions, which may have therapeutic potential for several diseases. The largest number of natural chalcones has been isolated from species of the Leguminosae, Asteraceae and Moraceae species with valuable for variety of nutrceutical, cosmetic and medicinal applications. Chalcone can isolated from different plants parts by suitable extraction process and separated by coloumn chromatographic techiniques. The purpose of this review is to summarize the various naturally occurring chalcone compounds which have been isolated from different plants and to describe the recent efforts of scientists in a pharmacological screening of chalcones, studying importance of chalcones and their biological activities.

Keywords: chalcones, anti-tubercular, antifungal, anti-bacterial

Introduction

An interesting feature of chalcones pharmacophore is that they serve as starting materials for the synthesis of five and six- membered heterocyclic compounds such as Pyrimidines, Pyrazolines, Flavones, Flavonols, Flavonones, Aurones and Benzoyl coumarones as well as certain compounds like Deoxybenzoins and Hydantoins which are of some therapeutic application [1]. Chalcones and their derivatives find application as artificial sweeteners, scintillators, polymerization catalysts, fluorescent whitening agents, organic brightening agents, stabilizers against heat, visible light, ultraviolet light and aging [2]. Chalcone containing plants have also been used for a long time in traditional medical practice. The use of herbal medicines continues to expand rapidly across the world. As a result of pharmacological studies [3], several pure chalcones isolated from different plants have been approved for clinical trials for treatment of cancer, viral and cardiovascular disorders or have been included as ingredients in cosmetic preparations. Polyphenols represent one of the most prevalent classes of compounds found in our daily diet. Over the last ten years [4], increasing attention has been dedicated to chalcones because of their interesting biological activities. Indeed, chalcones constitute an important group of natural compounds that are especially abundant in fruits (*e.g.*, citruses, apples), vegetables (*e.g.*, tomatoes, shallots, bean sprouts, potatoes) and various plants and spices (*e.g.*, licorice), many of which have been used for centuries in traditional herbal medicine. The majority of the content of chalcones in citrus fruits and various plants is mediated through the formation of 4,2′,4′,6′-tetrahydroxychalcone (also known as naringenin chalcone by chalcone synthase. Naringenin chalcone also plays an essential role in the flavonoid biosynthetic pathway and contributes significantly to the total amount of plant flavonoids [5].

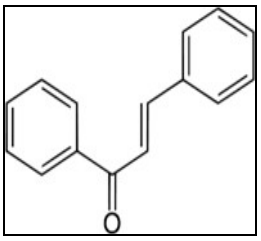

Fig 1: Structure of Chalcone

The chemistry of chalcones has generated intensive scientific studies throughout the world. Especially interest has been focused on the synthesis and biodynamic activities of chalcones [6]. The name “Chalcones” was given by Kostanecki and Tambor. These compounds are also known as benzalacetophenone or benzylidene acetophenone. In chalcones, two aromatic rings are linked by an aliphatic three carbon chain. Chalcone bears a very good synthon so that variety of novel heterocycles with good pharmaceutical profile can be designed. Chalcones are -unsaturated ketone containing the reactive ketoethylenic group –CO-CH=CH-. These are coloured compounds because of the presence of the Chromophore -CO-CH=CH-, which depends in the presence of other auxochromes. Chalcones and their

derivatives demonstrate wide range of biological activities such as anti-diabetic, anti-neoplastic, anti-hypertensive, anti-retroviral, anti-inflammatory, anti-parasital, anti-histaminic, anti-malarial, anti-oxidant, anti-fungal, anti-obesity, anti-platelet, anti-tubercular, immunosuppressant, anti-arrhythmic, hypnotic, anti-gout, anxiolytic, anti-spasmodic, anti-nociceptive, hypolipidemic, anti-filarial, anti-angiogenic, anti-protozoal, anti-bacterial, etc.

Synthetic approach

Claisen-schmidt reaction

A variety of methods are available for the synthesis of chalcones, the most convenient method is the one that involves the Claisen-Schmidt condensation of equimolar quantities of a substituted ketone [7] with substituted aldehydes in the presence of aqueous alcoholic alkali. In the Claisen-Schmidt reaction, the concentration of alkali used, usually ranges between 10 and 60 %.

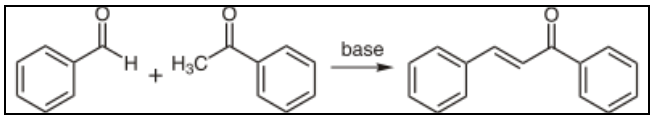

Fig 2

Molecular Graphics and Docking

The process of discovery of a new drug is a very difficult task. Pharmaceutical and biotechnology companies need to make huge investments in the discovery of a single drug that may cure a disease or simply alleviate the symptoms of another. These are businesses like any other, where profits fuel their growth and provide the investments for future discoveries. Modern drug discovery is mainly based *Insilico* -chemicobiological approach where, computer plays very important role in discovery of new drugs, not only it can save money but also time. Use of computational techniques in drug discovery and development process is rapidly gaining in popularity, implementation and appreciation [8]. Both computational and experimental techniques have important roles in drug discovery and development and represent complementary approaches. CADD (Computer Aided Drug Discovery) entails:

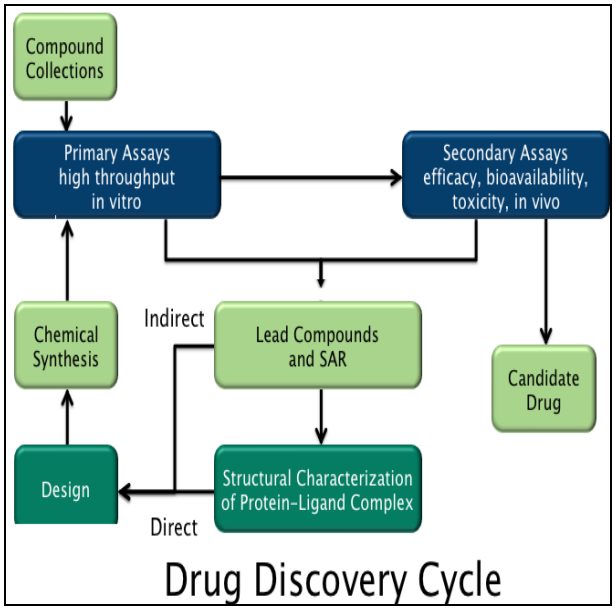

Fig 3: Schematic representation of drug discovery cycle

1. Use of computing power to streamline drug discovery and development process.
2. Advantage of chemical and biological information about ligands and/or targets to identify and optimize new drugs.
3. Design of *Insilico* filters to eliminate compounds with undesirable properties (poor activity and/or poor Absorption, Distribution, Metabolism, Excretion and Toxicity, (ADMET)) and select the most promising candidate. Fast expansion in this area has been made possible by advances in software and hardware computational power and sophistication.
4. Identification of molecular targets and an increasing database of publicly available target protein structures like the protein data bank www.pdb.org. CADD is being utilized to identify hits (active drug candidates), select leads (most likely candidates for further evaluation), and optimize leads i.e. transform biologically active compounds into suitable drugs by improving their physicochemical, pharmaceutical, ADMET/PK (pharmacokinetic) properties [9].
5. Virtual screening is used to discover new drug candidates from different chemical scaffolds by searching commercial, public, or private 3-dimensional chemical structure databases.

Molecular Docking

In the field of molecular modeling, docking is a method, which predicts the preferred orientation of one molecule to a second when bound to each other to form a stable complex. Knowledge of the preferred orientation in turn may be used to predict the strength of association or binding affinity between two molecules using scoring functions [10]. The associations between biologically relevant molecules such as proteins, nucleic acids, carbohydrates, and lipids play a central role in signal transduction. Furthermore, the relative orientation of the two interacting partners may affect the type of signal produced. Therefore docking is useful for predicting both the strength and type of signal produced.

Docking is frequently used to predict the binding orientation of small molecule drug candidates to their protein targets in order to in turn predict the affinity and activity of the small molecule. Hence docking plays an important role in the rational design of drugs. The modeling of bimolecular complexes by computational docking using the known structures of their constituents is developing rapidly to become a powerful tool in structural biology. It is especially useful in combination with even limited experimental information describing the interface. Molecular docking involves the prediction of ligand (small molecule) conformation and orientation, referred as 'pose', within the active site of the molecular target. Virtual screening based on molecular docking has become an integral part of many modern structure-based drug discovery efforts.

Hence, it becomes a useful endeavor to evaluate existing docking programs, which can assist in the choice of the most suitable docking algorithm for any particular study.

The protein-ligand docking procedure can be typically divided into two parts: rigid body docking and flexible docking.

Rigid Docking

This approximation treats both the ligand and the receptor as rigid and explores only six degrees of translational and rotational freedom, hence excluding any kind of flexibility. Most of the docking suites employ rigid body docking procedure as a first step.

Flexible Docking

A more common approach is to model the ligand flexibility while assuming having a rigid protein receptor, considering thereby only the conformational space of the ligand. Ideally, however, protein flexibility should be taken into account, and some approaches in this regard have been developed.

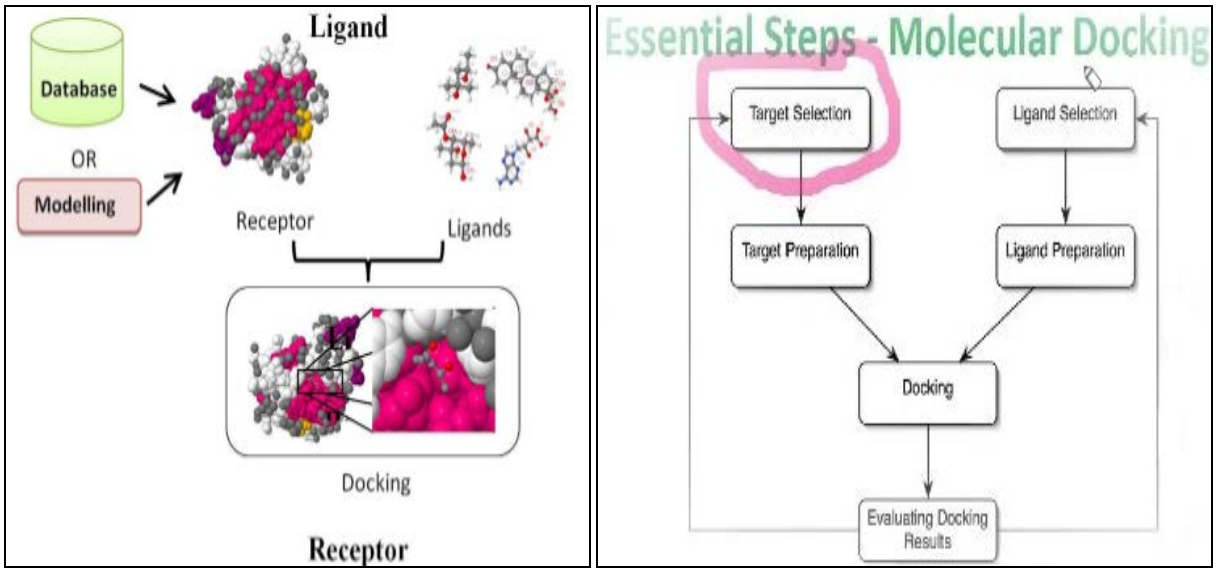

Fig 4: Drug receptor binding and docking steps

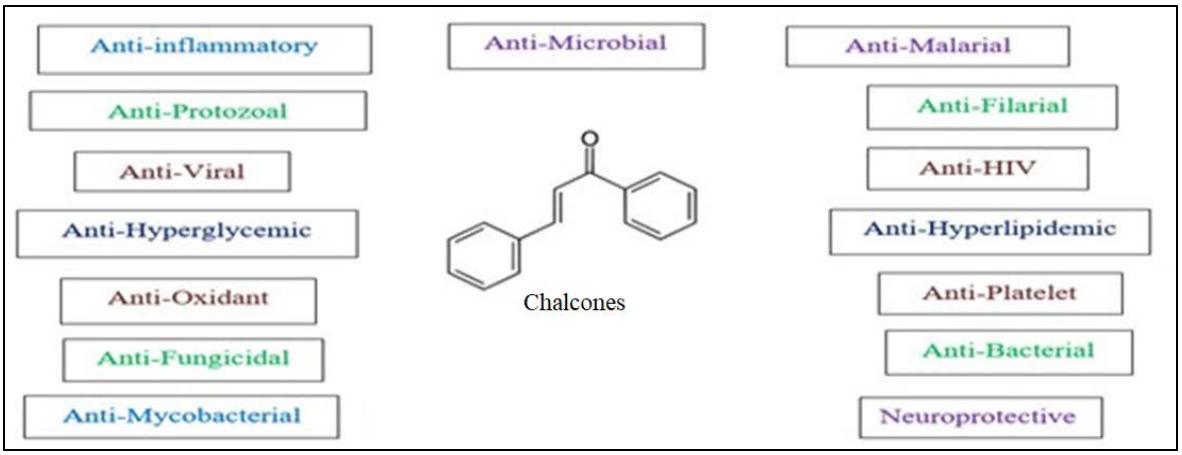

Fig 5: Biological activity of chalcones

Antimicrobial activity

The isolation and development of new and different antimicrobial agents has been a very important step and much of the research program efforts are directed towards development of new as well as modification of existing available drugs, because of the unsatisfactory[12] status of present treatment of microorganism, drug side effects, and the acquisition by the infecting microorganism of resistance to the present drugs. Although considerable advances have been achieved over recent decades in the research and development of new structural proto types as effective antimicrobials, current antimicrobial chemotherapy still suffers from two major limitations. The first is the lack of selectivity of conventional antimicrobial agents, which in turn brings about unwanted side effects. The second is acquisition of multi drug resistance by the microorganism. The design of new agents, active against resistant organism is of critical importance. In the field of natural chemistry, chalcone bearing compounds as antimicrobial agents, have achieved significant improvements in terms of potency, spectrum, and pharmacokinetic properties. The resistance to antimicrobial drugs is wide spread, the development of new antimicrobial agents and understanding their mechanisms of action are becoming vital nowadays [11]. Among the antimicrobial agents discovered in recent years, natural flavones as potent and selective antimicrobial agents showing activity against gram positive and gram negative bacteria [11].

Antitubercular activity

Tuberculosis is a long-lasting granulomatous [16] illness and a foremost health problem in emerging countries. Tuberculosis is an infection produced by the bacterium *Mycobacterium tuberculosis*. TB most generally takes place in the lungs but besides affects other organs, include the skin, bones, digestive tract, central nervous system (brain and spinal cord) lymph nodes, and liver. In tuberculosis, response of a tissue is a classic example of chronic granulomatous inflammation in individuals. About 65% of the population is infected with *Mycobacterium tuberculosis*.

According to World health organization, 1.8 million die of it annually and 8 million people globally develop active TB. In India, it is estimated that about 0.6 million die from it and nearly 1.8 million people develop active disease every year. A different facet got added in the 1982s due to spread of HIV with high occurrence of tuberculosis and *Mycobacterium avium* complex infection with HIV patients. India has a large load of HIV infected people and these patients are especially vulnerable to severe forms of tubercular infection. Every year over 0.5 million cases of multi-drug resistant" TB occur worldwide, which remains as challenge to existing chemotherapy of tuberculosis.

Anti-Oxidant Properties

Oxygen is highly reactive atom that is capable of becoming part of potentially damaging molecule commonly called "free radical." Free radicals are capable of attacking cells of the body, causing them to lose their structure and function. Free radial formation is controlled naturally by various compounds known as antioxidants. It is when the ability of antioxidant is limited that this damage can become cumulative and debilitating.

Antioxidant is substance that prevents or slows the breakdown of another substance by oxygen. Antioxidants are chemical substances that donate an electron to the free radical and convert it to a harmless molecule. Antioxidants are substances used by the body to protect itself from damage caused by oxidation. Oxidation is a process that causes damage in our tissues through the work of free radicals. An antioxidant is a chemical that prevents the oxidation of other chemicals. Natural antioxidants Anti-oxidant compounds in food play an important role as health-protecting factors. Scientific evidence suggests that antioxidants can reduce the risk for chronic diseases including cancer and heart disease. Anti-oxidant can delay or prevent the oxidation of cellular oxidizable substances. Synthetic anti-oxidants, such as butylated hydroxyl anisole and butylated hydroxyl toluene were commonly used for industrial processing to reduce damage to the human body and prolong the storage stability of food. Naturally occurring antioxidants are some enzymes. Reduced glutathione, Superoxide dismutase, Catalase, Glutathione peroxidase. High molecular weight proteins like Albumin, Ceruplasmin, Transferin, Haptoglobin and Low molecular weight compounds like lipid soluble antioxidants, Tocopherol, Carotenoids, Quinine and some poly-phenols, water soluble antioxidants like Ascorbic acid, Uric acid and Some Polyphenols. Minerals like Selenium, Manganese, Copper, Zinc and Vitamin-A, C, and E. Some plants antioxidants:- Apple, Citrus peel, Sesame seed, Grapes and wines, Soyabean, Tomato, Orange, Ashwagandha, Carrot, Liquorice, Amla, Terminalia bellerica, etc. are rich sources of antioxidants. In recent years, researchers have focused on developing effective, safe, and natural anti-oxidants that can resist oxidative stresses.

An antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules. Oxidation is a chemical reaction that transfers electrons from a substance to an oxidizing agent. Oxidation reactions can produce free radicals, which start chain reactions that damage cells. Antioxidants terminate these chain reactions by removing free radical intermediates, and inhibit other oxidation reactions by being oxidized themselves. As a result, antioxidants are often reducing agents such as thiols, ascorbic acid or polyphenols.

Although oxidation reactions are crucial for life, they can also be damaging; hence, plants and animals maintain complex systems of multiple types of antioxidants, such as glutathione, vitamin C, and vitamin E as well as enzymes such as catalase, superoxide dismutase and various peroxidases. Low levels of antioxidants, or inhibition of the antioxidant enzymes, cause oxidative stress and may damage or kill cells. As oxidative stress might be an important part of many human diseases, the use of antioxidants in pharmacology is intensively studied, particularly as treatments for stroke and neurodegenerative diseases. Antioxidants are also widely used as ingredients in dietary supplements in the hope of maintaining health and preventing diseases such as cancer and coronary heart disease. In addition to these uses of natural antioxidants in medicine, these compounds have many industrial uses, such as preservatives in food and cosmetics and preventing the degradation of rubber and gasoline. The term antioxidant originally was used to refer specifically to a chemical that prevented the consumption of oxygen. In the late 19th and early 20th century, extensive study was devoted to the uses of antioxidants in important industrial processes, such as the prevention of metal corrosion, the vulcanization of rubber, and the polymerization of fuels in the fouling of internal combustion engines [66]. The antioxidant activity measured by an individual assay reflects only the chemical reactivity under specific conditions applied in that assay [57]. Depending upon the reactions involved, the assays can be classified into two types: assays based on hydrogen atom transfer (HAT) reactions and assays based on electron transfer (ET). The majority of HAT – based assays applies a competitive reaction scheme, in which antioxidant and substrate compete for thermally generated peroxyl radicals through the decomposition of azo compounds. These assays include inhibition of induced low-density lipoprotein autoxidation, oxygen radical absorbance capacity (ORAC), total radical trapping antioxidant parameter (TRAP), and crocin bleaching assays. ET – based assays include the total phenols assay by Folin – Ciocalteu reagent (FCR), Trolox equivalence antioxidant capacity (TEAC), ferric ion reducing antioxidant power (FRAP), "total antioxidant potential" assay using a Cu (II) complex as an oxidant, and DPPH.

Measurement of antioxidant activity

Various methods have been developed to evaluate the antioxidant agents of natural origin. Antioxidant action includes radical scavenging capacity, inhibition of lipid peroxidation, metal ion chelating ability and reducing capacity. Antioxidant activity can be measured using *in-vitro* methods and animal studies. These *in-vitro* methods can be divided into two major categories:-

1. Measuring the ability to donate an electron or hydrogen atom to a specific reactive oxygen species or to any electron acceptor.
2. Testing the ability to remove any source of oxidative initiation, like inhibition of enzymes, chelation of transition, metal ions and absorption of U.V radiation.

DPPH Method (2, 2-diphenyl-1-picryl hydrazyl)

DPPH assay method is based on the reduction of methanolic solution of colored free radical DPPH (2,2-diphenyl-1-picryl hydrazyl) by free radical scavenger. The procedure involves measurement of decrease in absorbance of DPPH at its absorption maxima of 517 nm, which is proportional to concentration of free radical scavenger added to DPPH reagent solution. This is the most widely reported method for screening of antioxidant activity of many drugs.

Hydroxyl radical scavenging activity

This method involves *in-vitro* generation of hydroxyl radicals using Fe^{3+} / ascorbate / EDTA / H_2O_2 system. The hydroxyl radicals formed by the oxidation reaction with DMSO (dimethyl sulphoxide) to yield formaldehyde. Formaldehyde formed will produce an intense yellow colour with Nash reagent (2M ammonium acetate with 0.05M acetic acid and 0.02M acetyl acetone in distilled water). The intensity of yellow color formed is measured at 412 nm spectrophotometrically against a reagent blank. The activity is expressed as % hydroxyl radical scavenging.

Nitric oxide radical inhibition activity

This method is based on the inhibition of nitric oxide radical generated from sodium nitroprusside in buffer saline and Griess reagent. In presence of scavengers the absorbance of the chromophore is evaluated at 546 nm. The activity was expressed as % reduction of nitric oxide.

Superoxide anion scavenging activity

In-vitro super oxide radical scavenging activity is measured by riboflavin / light / NBT (Nitro blue tetrazolim) reduction. Reduction of NBT is the most popular method which involves the measurement of decrease in absorbance of NBT in presence of scavengers. The activity is measured in terms percentage of inhibition.

Anti Fungal Activity

A fungus is a colourless plant lacking chlorophyll fungi that causes disease in humans may be like yeast or mould and are called mycotic infections or fungal infections. The demand for antifungal drug was small since most humans with normally functioning immune system are able to ward off the invading fungi. Recently, research on newer antifungals has increased the incidence of life threatening fungal infections. Fungal infections may be categorized as superficial mycotic infections and systemic mycotic infections. Superficial mycotic infections are[14] those occurring on the surface or just below the skin or nail. Systemic mycotic infections are those occulting inside the body, such as lungs and other body organs. Fungal infections are common, not only as primary disease but also secondary to therapy with oral antibiotics. Individuals suffering from malignancy, diabetes mellitus, those on corticosteroids and immune compromised subjects are more prone to develop fungal infections. *Candida albicans* is normally found as part of the gastrointestinal tract and vagina and it causes diseases like ring worm and athlete's foot. *Trichophyton rubrum* is also a causative agent from ring worm. *Dermatophytes* are fungi causing infections on skin,hair, and nails. Dermatophytic infections known as *tinea* are caused by *Trichophyton*,*Microsporum and Epidermophyton.* Thermally dimorphic fungi are saprophytes which grow in one from at room temperature and indifferent from in host at 37^0C. Some of the most common infectious disease and causative agents are *Histoplasma capsulatum* (Histoplasmosis),*Blastomyces dermatitidus* (Blastomycosis),*Paracoccidiodes brasiliensis* (Paracoccidiomycosis), Coccidioides immitus (Coccidiomycosis). *Aspergillus* spores are present everywhere, inhalation is the most common route of inoculation, but infection through wounds, burns and implanted device such as catheters is also possible. *Aspergillus* is major source of infection in person with leukemia, receiving organ transplants and bone marrow transplants. List of some species contain chalcones has some therapeutic activities

Table 1: List of Chalcones from Medicinal Plants

Species	**Flavones Present**
Pityrogramma triangularis	Triangularin-2′,6′-dihydroxy-4′-methoxy-3′- methylchalcone
Myrica gale	2′,6′-dihydroxy-4′-methoxy-3′,5′- dimethyldihydrochalcone
Derris robusta	Rubone
Psoralea corylifolia	*Bakuchalcone*
Polygonum lapathifolium	dihydrochalcone and three chalcone derivatives lapathinol, lapathone
Brackenridgea zanguebarica	Brackenin
Tephrosia woodii	Mixtecacin
Helichrysum rugulosum	Mixture of 1,3,4- trimethoxy derivatives and dimethyl allyl groups and methoxy derivatives chalcone
Lindera umbellate	2′,6′-dihydroxy-4′-methoxydihydrochalcone and 2,4′,6′trihydroxydihydro chalcone
Glycyrrhizae radix	Isoliquiritin and Licuraside
Angelica keiskei	Xanthangelols B-E
Bidens tripartitus	2'-hydroxy-4, 4'-dimethoxychalcone
Pongamia pinnata	Ponganones I and II
Dalbergia stipulacea	Stipulin
Primula macrophylla	3,3'-dihydroxychalcone
Tephrosia spinosa	Spinochalcones A and B, flemistrictinA
Calythropsis aurea	Calythropsin and dihydrocalythropsin
Boronia inconspicua	2',4,4',6'-tetrahydroxy-5-(E-3,7-dimethylocta-2,6-
Dydimocarpus aurentica	Aurentiacin B and Aurentiacin A
Pityrogramma triangularis	Triangularin-2′,6′-dihydroxy-4′-methoxy-3′- methylchalcone
Myrica gale	2′,6′-dihydroxy-4′-methoxy-3′,5′- dimethyldihydrochalcone
Derris robusta	Rubone

Psoralea corylifolia	*Bakuchalcone*
Polygonum lapathifolium	dihydrochalcone and three chalcone derivatives lapathinol, lapathone
Dydimocarpus aurentica	Aurentiacin B and Aurentiacin A
Lophira alata	Lophirone B and C
Humulus lupulus	Xanthohumol-M, bichalcone humulusol and six known chalcones
Helicrysum zivojinii	Bis-dihydrochalcone
Piper aduncum L.	Cardamonin
Eysenhardtia polystachya	*2′*,4′-dihydroxychalcone-6′-O-β-D-glucopyranoside, α,3,2′,4′-tetrahydroxy-4-methoxy-dihydrochalcone-3′,-C-β-glucopyranosy-6′-O-β-D-glucopyranoside and α,4,4′-trihydroxydihydrochalcone-2′-O-β-D-glucopyranoside
Haematoxylum campechianum	Sappanchalcone and 3-deoxysappanchalcone
Finger root	Two chalcone derivatives
Persicaria lapathifolia	Flavokawain B, pinostrobin and pashanone chalcones

Natural Occurrence of flavones

Flavokawain B, pinostrobin and pashanone chalcones were isolated from seeds of *Persicaria lapathifolia* two chalcone derivatives isolated from Finger root with nutraceutical potentials [59]. Two chalcones, sappanchalcone and 3-deoxysappanchalcone were isolated from the ethanolic extract obtained from *Haematoxylum campechianum* L. [58]. Six new flavonoids *2′*,4′-dihydroxychalcone-6′-O- β-D-glucopyranoside, α, 3, 2′, 4′-tetrahydroxy-4- methoxy-dihydrochalcone-3′, -C-β-glucopyranosy- 6′- O- β- D-glucopyranoside, 7- hydroxy- 5, 8′- dimethoxy- 6′α- L-rhamnopyranosyl- 8- (3-phenyl- trans-acryloyl)- 1-benzopyran- 2- one, 6′, 7-dihydroxy-5, 8- dimethoxy- 8 (3-phenyl- trans-acryloyl)- 1- benzopyran- 2- one, 9- hydroxy-3, 8- dimethoxy- 4- prenylpterocarpan and α, 4, 4′-trihydroxydihydrochalcone-2′-O-β-D-glucopyrano- side were isolated from bark of *Eysenhardtia polystachya* [57]. Cardamonin, a schistoso- micidal chalcone from *Piper aduncum* L. (Piperaceae) that inhibits *Schistosoma mansoni* ATP diphosphohydrolase [56]. Bis-dihydrochalcone diglucoside containing a cyclobutene ring, a methylene-bridged bischalconeglycoside, both probably dimers of the co-occuring isosalipur- poside, and seven known naringenin, apigenin, kaempferol and luteoline glucoside identified and isolated from extract of the air-dried aerial parts of *Helicrysum zivojinii* [55]. A new prenylated chalcone xanthohumol-M, bichalcone humulusol and six known chalcones were found from *Humulus lupulus* [54]. Chalcone dimers Lophirone B and C compounds were isolated from *Lophira alata* [53]. Three new chalcones, 3, 2'-dihydroxy-4,3'-dimethoxychalcone-4'-glucoside, 4'-O-(2'''-O- caffeoyl)-2',3',3,4-tetrahydroxychalcone and 2',4',3- trihydroxy-3',4-dimethoxychalcone were isolated from *Coreopsis lanceolate* flowers [52]. Nardokanshone A, a new type of sesquieterpenoid- chalcone hybrid isolated from *Nardostachys chinensis*. Two new diprenylated dihydro-chalcones, elastichalcone A1 and elastichalcone B2 were isolated from the leaves of *Artocarpus elasticus* [60]. Bractelactone, a novel chalcone from *Fissistigma bacteolatum* [59]. Three new chalcone dimers oxyfadichacones A, B and C along with four known chalcones, 2',4'- dihydroxychalcone, 2',4',4-trihydroxychalcone, 2'- hydroxy-4'-methoxychalcone and 2',4'-dihydroxy- 4-methoxychalcone, were yielded and identified from *Oxytropis falcata* [58]. A new acetylated chalcone glycoside, trans-2' 6'-dihydroxy- 4'- O-(4"-acetyl-rhamnoside)- 4- methoxychalcone and a new biflavonoid glycosides, 5,3',5", 4'"-tetrahydroxy-3'", 5'"dimethpxy-biflavone (4'→8")- 7- O- ((2- rhamnoside) rhamnoside) were isolated from the ethyl acetate soluble fraction of the methanol extract obtained from *Trigonosciadium brachytaenium* [57]. Four flavonoids were obtained and their structures were identified as 3- hydroxy- 4- methoxylon-chocarpin a new prenylated chalcone, 4-methoxylonchocarpin, isobavachromene and dorspoinsettifolin were isolated from the seeds of *Millettia pachycarpa* [56]. Two new chalcone glycosides 4'-O-(6"-O-galloyl-β-d- glucopyranosyl)- 2',4-dihydroxychalcone and 4'-O- (6"-O-galloyl-β-d-glucopyranosyl)- 2'-hydroxy-4-methoxychalcone together with one known chalcone glycoside 4'-O-β-d-glucopyranosyl- 2'- hydroxy-4-methoxychalcone were isolated from the stems of *Entada phaseoloides* [54]. A new flavanone (mildbone) and a new chalcone (mildbenone) have been obtained from African Erythrina species, *Erythrina mildbraedii* of Cameroon [55]. Eight chalcone derivatives as the active principles, including licochalcone G, licochalcone A, echinantin, 5-prenylbutein, licochalcone D, isoliquiritigenin, licoagrochalcone A and kanzonol C from the *Glycyrrhiza inflata* [53]. Hybrid flavan-chalcones, desmos flavans A and B, together with three known compounds, cardamonin, pinocembrin and crysin were isolated from leaves of *Desmos cochinchinensis* [52]. Two new chalcone derivatives morachalcones B and C were isolated from the leaves of *Mora alba* [51]. The phytochemical analysis of the plant *Bacopa monnierie* reveals that it contains a chalcone type of compound 2, 4, 6-trihydroxy-5-(3,3-dimethyl propenyl)-3-(4-hydroxyphenyl) propiophenone [50]. Isocordoin and 2',4'- dihydroxy-3'-(dimethylallyl)-dihydrochalcone were isolated from the root of *Lonchocarpus xuul* [49]. Three new chalcones, xanthokeismins A, B and C in addition to a known chalcone, Xanthoangelol B from the stem of *Angelica keiskei* [47]. Garcinol, the antioxidant chalcone isolated from *Garcinia indica* [48]. A new flavanone, 7-hydroxy-5,6-dimethoxyflavanone together with three other flavonoids, didymocarpin, 2',4'- dihydroxy- 5' 6'- dimethoxychalcone and isodidymocarpin had been isolated from the methanol extract of the tree bark of *Cryptocarya costata* [46]. 2′-hydroxy-4′, 6′-dimethoxy-3, 4- methylenedioxy chalcone was isolated from the leaves of *Bauhinia variegata* [45]. Two new chalcone 2′, 6′-dihydroxy-4-isopenteniloxy-3, 4-(3″,3″-dimeth- ylpyrano) chalcone and 4,2′,6′-trihydroxy-3′,4′-metilenodioxo-3-isopentenilchalcone were isolated from the wood ethanolic extract of *Beilschmiedia tovarensis* [44]. Three novel chalcone derivatives, malloto- philippens C, D, and E were isolated from the fruits of *Mallotus philippinensis* [43]. Three sweet dihydrochalcone glucosides tribatin 2"-acetate, phloridzin and trilobatin from the leaves of *Lithocarpus pachyphyllus* [42]. Xanthoangelol, isobavachalcone, Xanthoangelol H, laserpitin, isolaserpitin, 3'-senecioyl khellacone, 4'- senecioyl khellactone, selinidin, pteryxin, (3' R)- 3'- hysroxycolumbianidin, mumdulea

flavanone A, prostratol F, falcarindiol and 5- N- penta-decylresorcinol were isolated from the exudate of *Angelica keiskei* [41]. A new prenylated chalcone Artoindonesianin J isolated from the root bark of *Artocarpus bracteata* Hook [39]. Pure lonchocarpin and derricin were isolated from *Lonchocarpus sericeus* [40]. L-hydroxypandu- ratin A, panduratin A, sakuranetin, pinostrobin, pinocembrin and dihydro-5,6-dehydrokawain were isolated from red rhizome variety of *Boesenbergia pandurate* [38]. Prorepensin was isolated from the extract of the dried powdered twigs of *Dorstenia prorepens. Dorstenia zenkeri* yielded p-hydroxybenzaldehyde, dorsmanin A, 4,2,4-trihydroxychalcone and 4,2,4-trihydroxy-3-prenylchalcone [37]. 2', 3'-Dihydroxy-4' 6'-dimethox- chalcone and the corresponding dihydrochalcone were isolated from the leaves of *Uvaria dulcis* [36]. α-hydroxydihydro- chalcone (α,4,2′-trihydroxy-4′-O-geranyldihydro- chalcone), a new isoflavone norisojamicin have been isolated from the stem bark of *Millettia usaramensis* [35]. Flavonoids, syzalterin, L-farrerol and L- liquiritigenin and the chalcone isoliquiritigenin were isolated from fresh flowering bulbs of *Pancratium maritimum* L. [34]. Munchiwarin, a chalcone with the 2, 2, 6-tri- isoprenyl-cyclohex-5-ene-1, 3-dione skeleton, was isolated from *Crotalaria trifoliastrum* [33]. A new triterpene, methyl-3-epi- betulinate in its native form and 4′,6′-dihydroxy-2′- methoxy-3′,5′-dimethyl chalcone isolated from the aerial parts of *Syzygium samarangense* [32]. Chalcone pedicin, two new condensed chalcones, fissistin and isofissistin were also obtained from ethyl acetate extract of *Fissistigma lanuginosum* [31]. From the aerial parts of *Boronia inconspicua* two novel dihydrochalcones, 2',4, 4', 6'-tetrahydroxy-5-(E-3, 7-dimethylocta-2, 6-dienyl)-3-(3-methylbut-2-enyl) dihydrochalcone and 2',4,4',6'-tetrahydroxy-3,5-di(3-methylbut-2- enyl) dihydrochalcone have been isolated and identified [30]. Two new chalcones, calythropsin and dihydrocalythropsin isolated from the crude extract of *Calythropsis aurea* [29]. Spinochalcones A and B, flemistrictin A chalcones were isolated from roots of *Tephrosia spinosa* [28]. A new dihydroxy chalcone 3, 3' -dihydroxychalcone, 3' -methoxyflavone and beta- sitosterol have been isolated for the first time from the whole plant of *Primula macrophylla* [27]. The structures were characterized as 7-hydroxy- 2'5'-dimethoxy-[6", 6"-dimethylpyrano(2", 3": 4', 3')] chalcone for ponganone-I, and 7-hydroxy-2', 5'-dimethoxy-3, 4-methylenedioxy-[6", 6"-dimethyl- pyrano (2",3",4',3')] chalcone for ponganone II [25]. 2'- hydroxy- 4, 4'- dimethoxychalcone was isolated from green parts and flower heads of *Bidens tripartitus* [24]. New chalcones, xanthangelols B-E were isolated from roots of *Angelica keiskei* [23] Isoliquiritin and licuraside both of which are kinds of chalcones, identified from *Glycyrrhizae radix* [22]. dihydrochalcones, 2′, 6′- dihydroxy-4′-methoxydihydrochalcone and 2,4′,6′-trihydroxydihydrochalcone have been isolated from leaves of *Lindera umbellate* 21. A complex mixture of chalcones and flavanones, 1, 3, 4- trimethoxy derivatives and dimethylallyl groups and methoxy derivatives were obtained from *Helichrysum rugulosum* 20. New prenylated flavanone, oaxacacin, and its chalcone, mixtecacin have been isolated from roots of *Tephrosia woodii* [19]. Several known chalcones, a new isoflavone, a dihydrochalcone and three chalcone derivatives lapathinol, lapathone, angelafolone, valafolone and melafolone were isolated from *Polygonum lapathifolium* [17]. Rubone, a new chalcone isolated from *Derris robusta* seed shells [15]. A new Bakuchalcone, dihydrofuranochalcone has been identified in seeds of *Psoralea corylifolia* [16]. From the fruits of *Myrica gale* the isolation of 2′,6′-dihydroxy-4′- methoxy-3′,5′-dimethyldihydrochalcone, and 4,4,6-trimethyl- 2- (3-phenylpropionyl)-cyclohexane-1,3, 5-trione [14]. Rubone, a new chalcone isolated from *Derris robusta* seed shells [15]. Triangularin-2′, 6′-dihydroxy- 4′- methoxy-3′-methylchalcone has been isolated from the exudate farina of the ceroptin chemotype of *Pityrogramma triangularis* [13].

Results

Importance of Chalcones

They serve as starting materials for the synthesis of five and six- membered heterocyclic compounds such as Pyrimidines, Pyrazolines, Flavones, Flavonols, Flavononones, Aurones and Benzoylcoumarones as well as certain compounds like Deoxybenzoins and Hydantoins which are of some therapeutic application [41]. Chalcone containing plants have also been used for a long time in traditional medical practice. The use of herbal medicines continues to expand rapidly across the world. As a result of pharmacological studies, several pure chalcones isolated from different plants have been approved for clinical trials for treatment of cancer, viral and cardiovascular disorders or have been included a ingredients in cosmetic preparations. chalcones constitute an important group of natural compounds that are especially abundant in fruits (*e.g.*, citruses, apples), vegetables (*e.g.*, tomatoes, shallots, bean sprouts, potatoes) and various plants and spices (*e.g.*, licorice), many of which have been used for centuries in traditional herbal medicine.

Discussion

The biological effects of flavones were found to be dependent on the presence, the number and position of functional groups such as methoxy, glycosides, hydroxyl, and halogens in ring systems. They present a broad spectrum of biological activities such as antifungal [46], antifilarial, larvicidal, anticonvulsant [46], anticancer [47], anti-inflammatory [49], neuroprotective [49], antimalarial [50], antibacterial [51], antilipidemic [52], antihyperglycemic [52], antiviral [53], antimycobacterial [54], antiprotozoal (antileishmanial and antitrypanosoma) [55], antiangiogenic [56], antiplatelet [57], anti-HIV5. Recent studies also showed that heteroaryl-based chalcones are potent MAO-A inhibitors [59].

Conclusion

Chalcone is regarded as a privileged structure of great practical interests because these natural and synthetic chalcone derivatives have shown numerous interesting biological activities with clinical potential against various diseases. Chalcones attracted considerable research interest in multiple disciplines [60]. Chalcones are a common scaffold found in many naturally occurring compounds, especially plant-derived natural products. In addition, many chalcone derivatives are prepared due to their easy convenience for synthesis.

Acknowledgments

I wish to acknowledge my thanks Nehru College of Pharmacy and Vinayaka Mission College of Pharmacy for their guidance in every step of our work.

References

1. Paliwal S, Pathak DP. Scholars Academic Journal of Pharmacy (SAJP) ISSN 2347-9531 (Print). Shaw AK and Kulshreshtha DK: Triterpenoids and chalcone from *Syzygium samarangense*. Phytochemistry,1995:38:687-9.
2. Yerragunta V, Kumaraswamy T, Suman D, Anusha V, Patil P, Samhitha T. A review on Chalcones and its importance. PharmaTutor,2013:1(2):54-9.
3. Ramadan MA, Khalifa AA. Acetophenones, a chalcone, a chromone and flavonoids from *P. maritimum*. Phytochemistry,1998:49(8): 2579-83.
4. Kumar G, Jalaluddin MD, Rout P, Mohanty R, Dileep CL. Emerging trends of herbal care in dentistry. Journal of clinical and diagnostic research: JCDR,2013:7(8):1827.
5. Ratapa Y, Karalai C, Lojanapiwatana V, Seechamnanturakit V. A chalcone and a dihydrochalcone from *U. dulcis*. Phytochemistry,2000:53:511-3.
6. Durazzo A, Lucarini M, Souto EB, Cicala C, Caiazzo E, Izzo AA *et al*. Polyphenols: A concise overview on the chemistry, occurrence, and human health. Phytotherapy Research,2019:33(9):2221-43.
7. Reutrakul V, Claeson P, Pongprayoon U, Sematong T, Santisuk T, Taylord WC. Anti- inflammatory cyclohexenyl chalcone derivatives in *Boesenbergia pandurate*. Phytochemistry,2002:59:169-73.
8. Prashar H, Chawla A, Sharma AK, Kharb R. Chalcone as a versatile moiety for diverse pharmacological activities. International Journal of Pharmaceutical Sciences and Research,2012:3(7):1913.
9. Sliwoski G, Kothiwale S, Meiler J, Lowe EW. Computational methods in drug discovery. Pharmacological reviews,2014:66(1):334-95.
10. Jia HP, Dreyer DR, Bielawski CW. Graphite oxide as an auto-tandem oxidation–hydration–aldol coupling catalyst. Advanced Synthesis & Catalysis,2011:353(4):528-32.
11. Liu JK, Qin XD, Wu WL, Chen ZH. Antioxidant activities of three dihydrochalcone glucosides from leaves of *Lithocarpus pachyphyllus*. Z Naturforsch,2004:59:481-4.
12. Chaudhary KK, Mishra N. A review on molecular docking: novel tool for drug discovery. Databases,2016:3(4):1029.
13. Suarez, Vargas OEB. New chalcones from*Beilschmiedia tovarensis*. Rev Col Quim,2005:34:35-41.
14. Katsila T, Spyroulias GA, Patrinos GP, Matsoukas MT. Computational approaches in target identification and drug discovery. Computational and structural biotechnology journal,2016:14:177-84.
15. Hakim EH, Harlim T, Jalaluddin MN, Syah YM, Achmad SA, Takayama H. Cytotoxic chalcones and flavanones from the tree bark of *Cryptocarya costata*. Z Naturforsch,2006:6:184-8.
16. Coates A, Hu Y, Bax R, Page C. The future challenges facing the development of new antimicrobial drugs. Nature reviews Drug discovery,2002:1(11):895-910.
17. Ahmad A, Oswal N, Sarkar FH. Emerging role of Garcinol, the antioxidant chalcone from *Garcinia indica* Choisy and its synthetic analogs. Journal of Hematology & Oncology,2009:2(1):1-13.
18. Borges, Vela-Catzin T, Yam-Puc A, Chan M. Antiprotozoal and cytotoxic studies on isocordoin derivatives. Planta Medica,2009:75(12):1336-8.
19. Drake LA, Dinehart SM, Farmer ER, Goltz RW, Graham GF, Hordinsky MK *et al*. Guidelines of care for superficial mycotic infectionsof the skin: Tinea corporis, tinea cruris, tinea faciei, tinea manuum, and tinea pedis. Journal of the American Academy of Dermatology,1996:34(2),282-286.
20. Zhang T, Xiao L, Yang L, Chen R. Two new chalcones from leaves of *Morus alba* L. Fitoterapia,2010:81:614-16.
21. Ehlers S, Schaible UE. The granuloma in tuberculosis: dynamics of a host–pathogen collusion. Frontiers in immunology,2013:3:411.
22. Nguyen PH, Lee HS, Kim E, Park J, Lim SI, Oh WK. Chalcones as novel influenza A (H1N1) neuraminidase inhibitors from *Glycyrrhiza inflata*. Bioorg Med Chem Lett,2011:21:294-8.
23. Jin J, Lin C, Zhu C, Liu Y, Lin A, Zhang L *et al*. Two new chalcone glycosides from the stem bark of *Entada phaseoloides*. Fitoterapia,2011:82:1102-5.
24. Ali MI, Ahmed G, Afza N, Lateef M, Iqbal L, Waffo AFK *et al*. Potent antioxidant and lipoxygenase inhibitory flavanone and chalcone from *Erythrina mildbraedii* Harms of Cameroon. Z Naturforsch,2012:67:98-102.
25. Li CY, Zhong YJ, Yuan ZP, Li YF, Liang B. A new prenylated chalcone from the seeds of *Millettia pachycarpa*. Chin J Nat Med,2012:10:222-5.
26. Shafaghat A, Salimi F. Novel acetylated chalcone and biflavonoid glycosides from *Trigonosciadium brachytaenium* (Boiss.) Alava. Nat Prod Res,2013:22:2111-7.
27. Li LY, Wang SS, Que S, Yang WZ, Zhang FY, Gong NB *et al*. Oxyfadichalcones A-C: three chalcone dimers fused through a cyclobutene ring from Tibetan medicine *Oxytropis falcata* Bunge. Tetrahedron,2013:69:11074-9.
28. Sureshbabu M, Fang YC, Wu YH, LanYH, Chang FR, Chang YW *et al*. Potent inhibition of human neutrophil activations by bractelactone a novel chalcone from *Fissistigma bracteolatum*. Toxicol Appl Pharmacol,2013:266:399-07.
29. Ran XH, Luo HR, Zheng YM, Liu YQ, Hu JM, Zhou J. Nardokanshone A, a new type of sesquieterpenoid-chalcone hybrid from *Nardostachys chinesis*. Tetrahedron Lett,2013:54:5650.
30. Rahmani M, Kassim NK, Hashim NM, Sukari MA, Akim AM, Go R. New diprenylated dihydrochalcones from leaves of *Artocarpus elasticus*. Phytochem Lett,2013:6:582-5.
31. Oidovsambuu S, Jeon JS, Nho CW, Um BH. Chalcones from the flowers of *Coreopsis lanceolata* and their *in-vitro* antioxidant activity. Planta Med,2013:79(4):295-00.
32. Yakubu MT, Oladiji AT. Cytotoxic, antimutagenic and antioxidant activities of methanolic extract and chalcone dimers (Lophirone B and C) derived from *Lophira alata* (Van Tiegh. Ex Keay) stem bark. Evid Based Complement Alternat Med,2014:19:20-30.
33. Zhang F, Hu Z, Ding H, Tang H, Ma Z, Zhao X. Novel prenylated bichalcone and chalcone from *Humulus*

lupulus and their quinone reductase induction activities. Fitoterapia,2014:93:115-20.
34. Vuckovic I, Jadranin M, Pesic M, Dordevic I, Podolski-Renic A, Menkovic N *et al*. Two structurally distinct chalcone dimers from *Helichrysum zivojinii* and their activities in cancer cell lines. Phytochemistry,2014:98:190-6.
35. Costa PS, Laktin GT, de Carvalho PH, Geraldo RB, de Moraes J, Pinto PL *et al*. Cardamonin, a schistosomicidal chalcone from *Piper aduncum* L. (Piperaceae) that inhibits Schistosoma mansoni ATP diphosphohydrolase. Phytomedicine,2015:22(10):921-8.
36. Garcia-Campoy AH, Muniz- Ramirez A. Properties of flavonoids isolated from the bark of *Eysenhardtia polystachya* and their effect on oxidative stress in streptozotocin-induced Diabetes Mellitus in mice. Oxidative medicine and cellular longevity, 2016, 1-13.
37. Lobato-Garcia CE, Alejandro Zamilpa ID, Gomez-Rivera A, Tortoriello J, Gonzalez-Cortazar M. Homoisoflavonoids and chalcones isolated from *Haematoxylum campechianum* L., with spasmolytic activity. Molecules,2017:22:1-10.
38. Abdullah HD, Nadeem AM, Hamid H. Characterization of two chalcone derivatives isolated from Finger root with nutraceutical potentials. Int Journal of Advanced Research,2018:6(11):1089-94.
39. Feyera M, Deyou T, Abdissa N. Antimicrobial chalcones from the seeds of *Persicaria lapathifolia*. Biochem Pharmacol,2018:7(1):1-4.
40. www.knigozal.com/gb/search.xml?q=Chalcones.
41. Muratov E, Pereira M, Peixoto J, Rosseto L, Cravo P, Neves B. Chalcone derivatives: promising starting points for drug design. Molecules, 2017, 1-25.
42. Sikorski JA. Recent advances in therapeutic chalcones. Expert Opinion on Therapeutic Patents,2004:14(12):1669-91.
43. Tasdemir D, Golais F, Dicato M, Diederich M. Dietary chalcones with chemopreventive and chemotherapeutic potential. Genes Nut,2011:6(2):125-47.
44. Ramirez AM, Sauceda JV. Review: The potential of chalcones as a source of drugs. Afr J Pharm Pharmacol,2015:9(8):237-57.
45. Joshi AS, Nimrod AC, Walker LA, Clark AM. Antifungal chalcones from *Maclura tinctorial*. Planta Med,2001:67:87-9.
46. Huang CT, Liu SM, Wang B, Guo J, Bai JQ. Licochalcone A exerts antitumor activity in bladder cancer cell lines and mice models. Trop J Pharm Res,2016:15(6):1151-7.
47. Motomiya T, Ito M, Honda G, Lida A, Kiuchi F, Tokuda H *et al*. Anticarcinogenic compound in the Uzbek medicinal plant, *Helichrysum maracandicum*. J Nat Med,2008:62:174-8.
48. Phillips A, Butler M, Rossi M, Jennifer MP. The plant derived chalcone 2,2′,5′- Trihydroxychalcone provides neuroprotection against toll- like receptor 4 triggered inflammation in microglia. Oxidative medicine and cellular longevity, 2016, 1-10.
49. Fabre N, Roumy V, Gornitzka H, Bourdy G, Chevalley S, Sauvain M *et al*. Activity-guided isolation of antiplasmodial dihydro- chalcones and flavanones from Piper hostmannianum var. berbicense. Phytochemistry,2007:68:1312-20.
50. Armstrong N, Dougnon TV, Fah L, Hounsa E, Bankole HS, Loko F *et al*. Antibacterial activity of chalcone and dihydrochalcone compounds from *Uvaria chamae* roots against multidrug resistant bacteria. Biomed Res International, 2018, 1-10.
51. Wang D, Song X, Zhang Y, Ding W, Peng X, Zhang X *et al*. Natural prenylchalconaringenins and α-amylase inhibition and *in- vivo* antihyperglycemic and antihyperlipidemic effects. J Agric Food Chem,2017:65(8):1574-81.
52. Malhotra B, Elder M, French CJ, Towers GHN. Comparative studies of inhibitory activities of chalcones on tomato ringspot virus (ToRSV). Canadian journal of plant pathology,1997:19(2):133-7.
53. Chen M, Fursted K, Christensen SB, Kharazmi A. *In-vitro* antimycobacterial and antilegionella activity of Licochalcone A from Chinese Licorice roots. Planta Medica,2002:68(5):416-9.
54. Kiderlen AH. *In-vitro* Leishmanicidal activity of naturally occuring chalcones. Phytotherapy Research,2001:15(2):148-52.
55. Becker H, Eicher T, Herhaus C, Kapadia G, Bartsch H, Gerhauser C. Inhibition of endothelial cell functions by novel potential cancer chemopreventive agents. Biochem Biophys Res Commu,2004:3(1):287-95.
56. Leal LKAM, Ferreira MAD, Viana GSB, Silveira ER. Antiplatelet effect of lonchocarpin and derricin isolated from *Lonchocarpus sericeus*. Pharm Biol,2005:43:726-31.
57. Wang XH, Yi YH, Lee KH. Anti-AIDS agents 54, A potent anti-HIV chalcone and flavonoids from genus Desmos. Bioorg Med Chem Lett,2003:13:1813-15.
58. Telerman A, Erlank H, Mordechay S, Rindner M, Rivka O, Kashman Y. Protective and antioxidant effects of a chalconoid from *Pulicaria incisa* on brain astrocytes. Oxid Med Cell Longey, 2013, 1-10.
59. Haridas A, Suresh J, Mathew EG, Ucar G, Jayaprakash V. Monoamine oxidase inhibitory action of chalcones: A mini review. Central Nervous System Agents in Medicinal Chemistry,2016:16(2):120-36.
60. Cseke LJ, Kirakosyan A, Kaufman PB, Warber S, Duke JA, Brielmann HL. Natural products from plants. CRC press, 2016.