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CHALCONE AS A POTENT FLXIBLE MOIETY FOR VARIOUS PHARMACOLOGICAL ACTIVITIES

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ABSTRACT

Chalcones are pharmacologically important active heterocyclic compound, chemically they are derivatives of 1,3- diphenylprop-2-en-1-one. They are considered as the precussor for both flavonoids and isoflavonoids. They are found to be important for the pigmentation of flowers so that they act as attractants to the pollinators. Since they are the precussors for flavonoid synthesis, chalcons also plays major role in defense against pathogens and insects. This review aims to summerizze the antimicrobial and anticancer activities of chalcon and their derivatives.

Keywords: Chalcones, antibacterial, Antileishmanial, anticancer activities

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INTRODUCTION

Chalcone is a sweet-smelling ketone and an enone that structures the focal center for an assortment of significant natural mixes, which are referred to as chalcones or chalconoids. Elective names for chalcone incorporate benzylideneacetophenone, phenyl styryl ketone, benzalacetophenone, β-phenylacrylophenone, γ-oxo-α,γ-diphenyl-α-propylene, and α-phenyl-β-benzoylethylene. Countless manufactured courses have been accounted for the union of chalcones, the most old style and general being the Claisen—Schmidt condensation. This review is to portray the ongoing endeavors of researchers in pharmacological screening of natural and synthesized chalcones. Chalcone constitute an impartment group of natural products and some of them possess a wide range of biological activities such as antimicrobial, anticancer (1, 2).

The general Method of synthesis of chalcone as shown below (Fig-1):

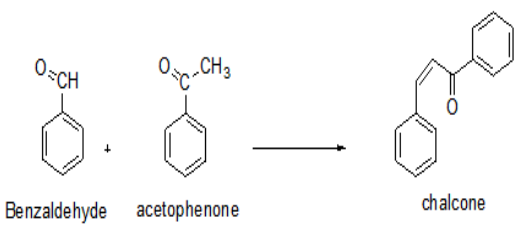

Fig-1 synthesis of chalcone

Physical Properties of Chalcone

The physical properties of chalcone are as follows:-

Molecular formula : C15H12O; Molar mass : 208.26 g mol−1; Exact mass : 208.088815;

Density : 1.071 g/cm3; Melting point : 55–57 °C; Boiling point : 345-348 °C

Pharmacological Activities of Chalcone

Chalcones and its subordinates have been used effectively during the most recent couple of decades because of utilization of such ring framework as the core structure in many medication covering wide scope of pharmacological activities. some of these are discussed below:-

Antimicrobial Activity

Nagaini et al., effectively combined another homologues arrangement of chalcone subsidiaries (Fig-2) as antimicrobial and the anti-bacterial action against E. coli where the presence of hydroxyl group at the ortho position**(1)** demonstrated better antimicrobial activity than with para position**(2)** (3).

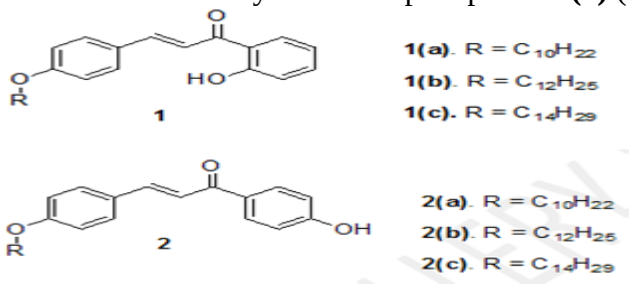

Fig-2 chalcone subsidiaries

Nowakowska *et al*., synthesized and tested 40 substituted chalcones (Fig-3) for studying their *in vitro* antifungal and antibacterial activities. Out of these 40 chalcon substituents compounds **3**, **4** and **5** exhibited good antibacterial property against *Staphylococcus aureus*, *Enterococcus faecalis* and *Bacillus subtilis* (4).

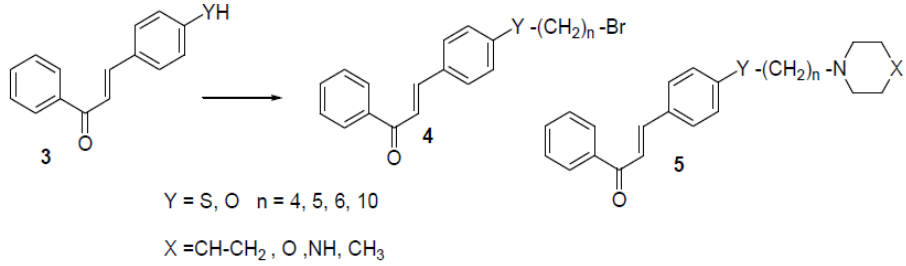

Fig-3 40 substituted chalcones

The proficient and easy synthesis of 17-chalconyl derivatives of pregnenolone (Fig-4) and their assessment as antimicrobial agents were screened by Abid et al (5).

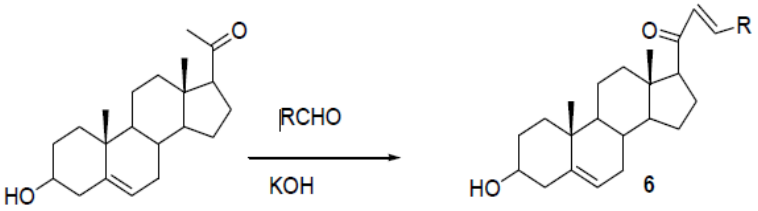

Fig-4 17-chalconyl derivatives of pregnenolone

Swamy *et al.*, reported the antimicrobial activity of 3- hydroxy benzofuran substituted chalcones (Fig-5). It was evident that most of the compounds are very weakly active and few are moderately active against *Staphylococcus aureus* and *Escherichia coli* but compounds **7c, 7d** possessed very good activity against fungi *Aspergillus flavus* and compound **7b** showed moderate activity (6).

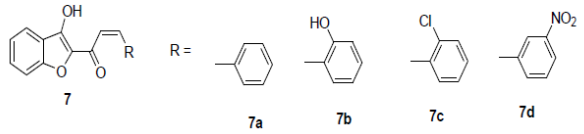

Fig-5 3- hydroxy benzofuran substituted chalcones

Mayekar *et al*., reported that a series of chalcones and its cyclohexenone derivatives (fig-6) were derived from 6-methoxy-2-naphthaldehyde. The compounds **8b** and **8c** showed comparatively good activity against all the bacterial and fungal strains like *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Penicillium marneffei*, *T. mentagrophytes*, *A. flavus* and *A. fumigates* when compared to standard drugs like Ampicillin, Itraconazole (7)**.**

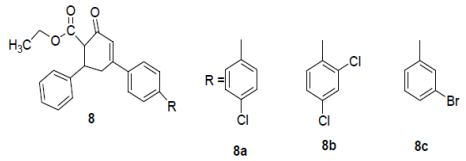

Fig-6 chalcones and its cyclohexenone derivatives

Liaras *et al.*, synthesized a new class of structurally novel derivatives, that incorporate two known bioactive structures a thiazole and chalcone (Fig-7), to yield a class of compounds with interesting antimicrobial properties and antifungal properties and evaluation of antibacterial activity showed that almost all the compounds **9a-j** exhibited greater activity than reference drugs and thus could be promising novel drug candidates (8).

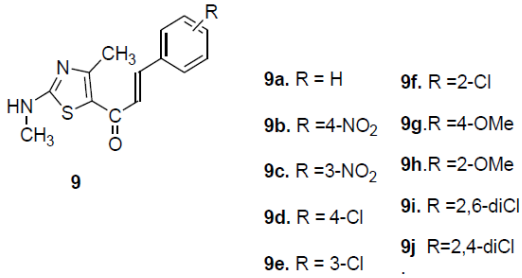

Fig-7 bioactive structures a thiazole and chalcone

Ávila *et al*., described the antibacterial activity of thirty-one chalones (Fig-8) against *Pseudomonas aeruginosa* ATCC 27853, *Bacillus cereus* ATCC 11778, *Staphylococcus aureus* ATCC 25923, and *Escherichia coli* ATCC 25922. From these 31 chalcones, Some showed significant activity against Gram-positive bacteria (9).

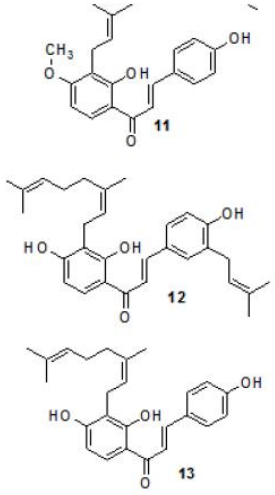

Fig-8 new thirty-one chalones

Chitra *et al*., synthesized four copolyesters from 3,3- (1,4-phenylene)bis(1-(4-hydroxyphenyl)prop-2-en-1- one (THAP) (fig-9) and 3,3-(1,4-phenylene)bis(1-(4-hydroxy-3- methoxyphenyl)prop-2-en-1-one (TMAP) and showed potential bactericidal activity against pathogenic bacteria (10).

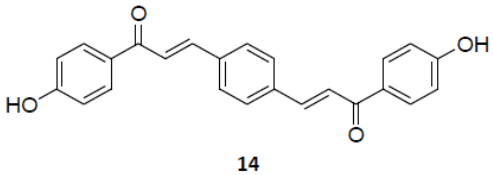

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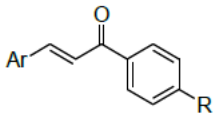
Fig-9 copolyesters from 3,3- (1,4-phenylene)bis(1-(4-hydroxyphenyl)prop-2-en-1- one

Different mini libraries were developed by Bhatia *et al.*, for antibacterial activity. The mini-libraries **15{1a, 2a–d}, 15{1b, 2a–d}, 15{1a–f, 2a}** and **15{1a–f, 2c}** (fig-10) were showing good antibacterial activity. Out of these 4, 3-(4-chlorophenyl)-1-(4- methoxyphenyl)prop-2-en-1-one exhibited more activity than others (11).



R (a-f) = OCH_3 , Cl, CH_3 , Br, NO_2, $N(CH_3)_2$

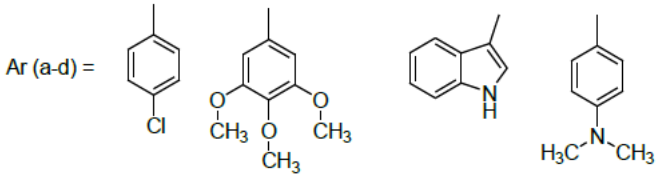


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Fig- 10 4, 3-(4-chlorophenyl)-1-(4- methoxyphenyl)prop-2-en-1-one derivatives

Nitrogen and sulfur heterocyclic mimics of furano flavonoids (fig-11) synthesized and screened for antibacterial activity by Yadav *et al* (12).

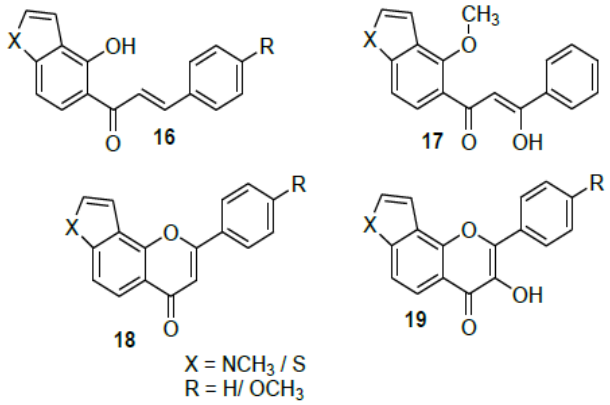


Fig-11 sulfur heterocyclic mimics of furano flavonoids

To determine the antibacterial activity Mokle *et al*., evaluated Some important novel compounds (fig-12) were evaluated and studied their effect on seed germination of wheat (Triticum aestivum). It was found that compound **21e, 21f, 21g, 22b, 22e, 22f** and **22g were found to** exhibit good antibacterial activity against all bacteria at a concentration of 100µg/ml (13)**.**

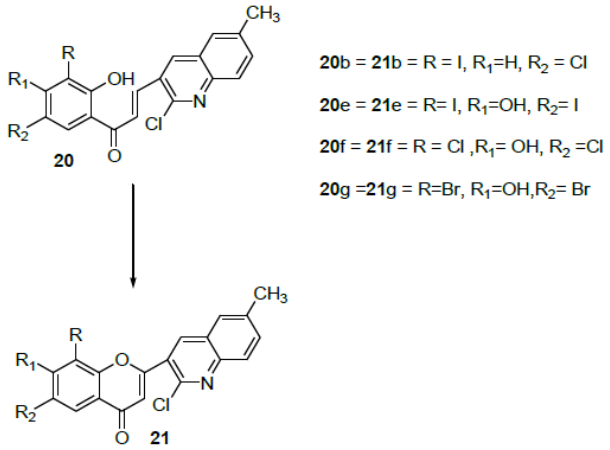


Fig-12 important novel compounds

Hussain *et al*., synthesized a series of new 3-[4-(1*H*-imidazol-1-yl)phenyl]prop-2- en-1-ones (fig-13) were evaluated for the anti-fungal activity. Few of them showed good activities (14)**.**

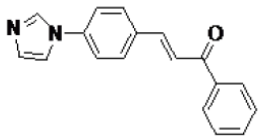


Fig-13 new 3-[4-(1*H*-imidazol-1-yl)phenyl]prop-2- en-1-ones

Antileishmanial Activity

Paula et al., were contemplated the eighteen analogs of a functioning common chalcone were integrated utilizing xanthoxyline and a few subsidiaries, and these analogs were tried for specific action against both promastigotes and intracellular amastigotes of Leishmania amazonensis in vitro. Three analogs (23a, 23b, and 23c) containing nitro, fluorine or bromine groups, individually, showed increased movement against the parasites when compared with the regular chalcone.

The nitrosylated chalcone 23a was likewise tried intralesionally in an infected mice and was seen as same as effective as th Pentostan reference tranquilize at a portion multiple times higher than that of the chalcone in controlling both the lesion development and the parasite burden (15).

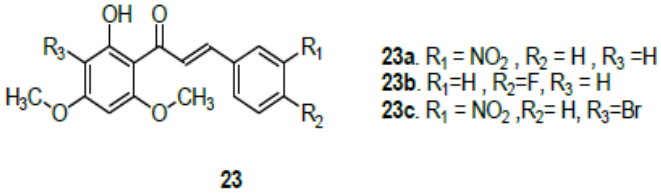


Fig-14 analogs (23a, 23b, and 23c) containing nitro, fluorine or bromine groups

One new amide (24) just as two known chalcones and one known flavanone (Fig-15) were confined from P. hispidum leaves by Ruiz et al. The outcomes indicated that the known chalcone displayed the most strong antileishmanial action with an IC50 of 0.8 µM (amphotericin B: IC50 = 0.2 µM) (16).

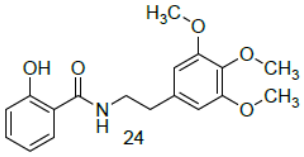
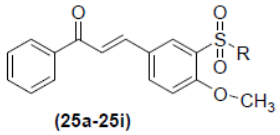


Fig-15 chalcones and one known flavanone

Carla et al., demonstrated another arrangement of sulfonamide 4-methoxychalcone subsidiaries (25a–25i) (Fig-16) were orchestrated and which indicated antileishmanial movement against Leishmania braziliensis promastigotes and intracellular amastigotes and decided its cell harmfulness profile. Strangely all compounds displayed a fixation subordinate antileishmanial profile and the benzylamino subsidiary (25i) indicated a natural action superior to pentamidine (17).



(25a-25i)

R= **25a** = N(CH3)2

25b = N(CH2CH3)2

25c = Pyrrolidin -1 -Yl

25d = morpholin -4-yl

25e = phenylamino

25f = 4-chlorophenylamino,

25g = 3, 4 -dichlorophenylamino

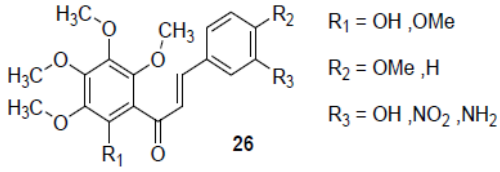
25h = 4 - methoxyphenylamino

25i = benzylamino

Fig-16 sulfonamide 4-methoxychalcone subsidiaries (25a–25i)

A progression of chalcones polyoxygenated on the ring A (with pentamethoxy or 2′-hydroxy-3′, 4′, 5′, 6′-tetramethoxy substitution designs) (Fig-17) was blended from tangeretin, a characteristic Citrus flavonoid. These chalcones were assessed by Quintin et al., for their antiproliferative, enactment of apoptosis, hindrance of tubulin gathering and antileishmanial exercises.

Correlation with the reference practically equivalent to 3′, 4′, 5′-trimethoxylated chalcones demonstrated that such peroxygenated substitution designs on the ring A were less advantageous to these activities (18).



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R_1 = OH ,OMe

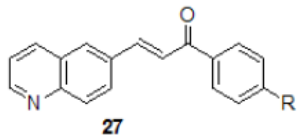
R_2 = OMe ,H

R_3 = OH ,NO_2 ,NH_2

Fig-17 chalcones polyoxygenated on the ring A
(with pentamethoxy or 2′-hydroxy-3′, 4′, 5′, 6′-tetramethoxy substitution designs)

Anticancer Activity

Tavares et al., assessed a series of new 6-quinolinyl and Quinolinyl N-oxide Chalcones (Fig-18) were productively arranged by incorporating all chalcones were tried by insignificant inhibitory focus (MIC) against three types of Candida, Cryptococcus gattii and Paracoccidioides brasiliensis. The impact of these mixes was additionally tried on the endurance and development of the human malignant growth cell lines UACC-62 (melanoma), MCF-7 (bosom), TK-10 (renal) and leukemic cells, Jurkat and HL60.The leukemic cells the mixes 28f, 27g, 28g and 29g have indicated the best action (19).



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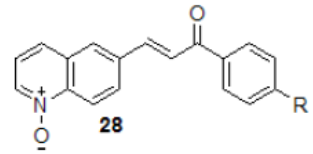

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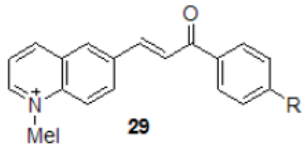

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27a,28a,29a. R =H, **27b,28b,29b.** R =Me , **27c,28c,29c.** R = OMe, **27d,28d,29d.** R =NO_2,

27e,28e,29e. R = F, **27f,28f,29f.** R = Br , **27g,28g,29g.** R =Cl

Fig-18 new 6-quinolinyl and Quinolinyl N-oxide Chalcones

A progression of novel coumarin–chalcone (Fig-19) mixtures were developes and assessed by Sivakumar et al., for their cytotoxicity compound 30 appeared around 30-fold greater selectivity towards C33A (cervical carcinoma) cells over typical fibroblast NIH3T3 cells (20).

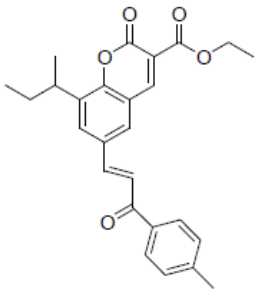

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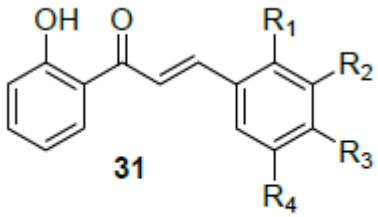
Fig-19 novel coumarin–chalcone

The Synthesized chalcones (Fig-20) and their antitumoral action were examined on HepG2 hepatocellular carcinoma cells and dose-dependent hindrance of cell multiplication by Echeverria et al (21).



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R_1=R_2=R_3=R_4= H

Fig-20 Synthesized chalcones

Kumar et al., developed a progression of indolyl chalcones and assessed in vitro for their anticancer action against three human malignancy cell lines. derivatives 32b–d, 32h, 32j, 32l, 32m, 33g, and 33j (fig-21) demonstrated huge

cytotoxicity, especially, indolyl chalcones 32i and 32m were recognized as the most powerful and specific anticancer agent with IC50 values 0.03 and 0.09 μM, against PaCa-2 cell line, individually (22).

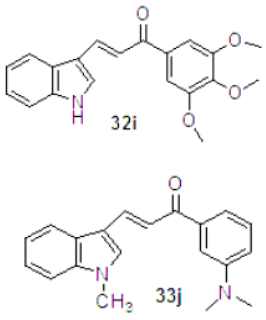

Fig-21 derivatives 32b–d, 32h, 32j, 32l, 32m, 33g, and 33j

Novel (E)- α-benzylthio chalcones (Fig-22) were accounted by Reddy et al., with in vitro activity and demonstrating that few of them are intense inhibitors (practically identical to imatinib, the reference compound) of BCR-ABL phosphorylation in leukemic K562 cells, known to express elevated levels of BCR-ABL. The capacity of such agents to altogether hinder K562 cell multiplication proposes that this framework could be a promising lead for the advancement of anticancer specialists that can block BCR-ABL phosphorylation in leukemic cells (23).

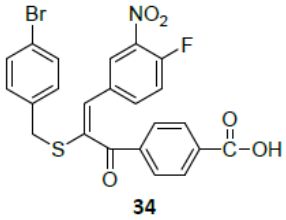

Fig-22 Novel (E)- α-benzylthio chalcones

Another arrangement of benzofuran-2-yl(4, 5-diydro-3, 5-substituted diphenylpyrazol-1-yl) methanone (Fig-23) subordinates were orchestrated by Parekh et al and indicated their antiproliferative action contemplated against human disease cell lines. Compounds a,b,c were shown great MDR reversal activity (24) .

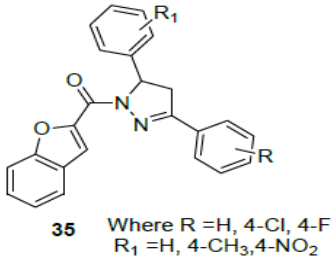

Fig-23 benzofuran-2-yl(4, 5-diydro-3, 5-substituted diphenylpyrazol-1-yl) methanone

Liu *et al*., synthesized *N*-Methylpiperidinylchalcones (fig-24) and determined their antiproliferative activity against human tumour cell lines (25).

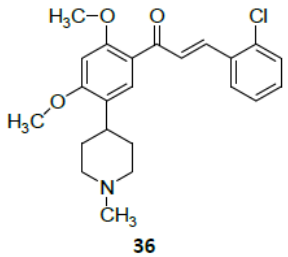

Fig-24 *N*-Methylpiperidinylchalcones

Conclusion

The literature review of chalcone heterocyclic core has demonstrated that it is a flexible core having different pharmacological activities of chalcone derivatives like antimalarial, anticancer, antileishmanial activity and so on. The crucial data given in this article can be used further by specialists in the structure and advancement of novel and powerful medications in the treatment of different diseases which are referenced in this article.

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