IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 4, May 2023

Review on Synthesis of Chalcone and its Derivatives with their Biological Activities

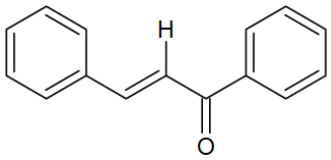
Mr. Dipak P. Solanke[1], Mr. Saurabh S. Shisve[2], Mr. Yash H. Hadage[3], Mr. Rohit B. Auti[4], Miss. Madhavi R. Mhase[5], Miss. Vaishali A. Bhutambare[6], Dr. Santosh D. Ghule[7]

Students, Samarth College of Pharmacy, Belhe, Pune, Maharashtra, India[1,2,3,4,5]
Professor, Samarth College of Pharmacy, Belhe, Pune, Maharashtra, India[6]
Principal, Samarth College of Pharmacy, Belhe, Pune, Maharashtra, India[7]

Abstract: *In a new and efficient antimicrobial agents, substituted chalcones have been synthesized by condensing benzaldehyde derivatives with acetophenone derivati ves in dilute ethanolic sodium hydroxide solution at room temperature according to Claisen Schmidt condensation. Chalcones are a valuable molecule of medicinal importance due to presence of reactive keto ethylenic group – CO–CH=CH–, belonging to the flavonoid family. 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 in chalcones are responsible for their biological activity. This review is focused about different methods of synthesis and versatile biological activity of chalcones including antimicrobial, anticancer, antioxidant, antimalarial, antituberculosis etc.*

Keywords: Chalcones, synthesis, Antibacterial activity, biological activity, Claisen-Schmidt reaction.

I. INTRODUCTION



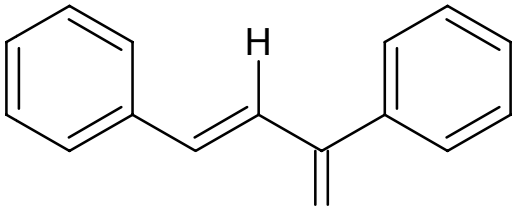
(2E)-1,3-diphenylprop-2-en-1-one

Chalcone compounds are -unsaturated ketone involving the reactive keto-ethylenic group (CO-CH=CH-) which gave colored compounds due to the presence (CO- CH=CH) the chromophore group. “Chalcone” which have another name like (benzalacetophenone or benzylidene acetophenone). Chalcones are starting material to synthesize many cyclic derivatives like pyrazolines isoxazoles. The framework 1,3-diphenylprop-2-en-1-one is well known by the generic term ‘‘chalcone,’’ a name coined by Kostanecki and Tambor It is also known as benzalacetophenone and benzylidene acetophenone. Chalcones belong to the flavonoid family. The versatile molecule chalcone is an α, β-unsaturated ketone thatcontains the reactive keto-ethylenic group –CO– CH=CH–, a chromophore responsible for the color in chalcone compounds, depending on the presence of other auxochromes.

Chalcone has conjugated double bonds with absolute delocalization and two aromatic rings that possess an p-electron system, which gives them relatively low redox potential and a greater chance of undergoing electron transfer reactions. A number of chalcones having hydroxy, alkoxy groups in different position have been reported to possess anti-bacterial, antiulcer, antifungal, antioxidant, vasodilatory, antimitotic, antimalarial, antileishmanial and inhibition of chemical mediators release, inhibition of leukotriene B4, inhibition of tyrosinase and inhibition of aldose reductase activities. Appreciation of these findings motivated us to synthesize chalcones as a potential template for anti microbial agents. There are several methods for the preparation of chalcones, the most convenient of which is the Claisen-Schmidt condensation of equimolar quantities of aryl methyl ketone and aryl aldehyde in the presence of alcoholic alkali. Typically, high-alkaline media such as KOH, NaOH and Ba(OH)2, as well

DOI: 10.48175/IJARSCT-9858

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 4, May 2023



O(2*E*)-1,3-diphenylprop-2-en-1-one

Chalcone compounds are -unsaturated ketone involving the reactive keto-ethylenic group (CO-CH=CH-) which gave colored compounds due to the presence (CO- CH=CH) the chromophore group. "Chalcone" which have another name like (benzalacetophenone or benzylidene acetophenone). Chalcones are starting material to synthesize many cyclic derivatives like pyrazolines isoxazoles. The framework 1,3-diphenylprop-2-en-1-one is well known by the generic term ''chalcone,'' a name coined by Kostanecki and Tambor It is also known as benzalacetophenone and benzylidene acetophenone. Chalcones belong to the flavonoid family. The versatile molecule chalcone is an α, β-unsaturated ketone thatcontains the reactive keto-ethylenic group –CO– CH=CH–, a chromophore responsible for the color in chalcone compounds, depending on the presence of other auxochromes.

Chalcone has conjugated double bonds with absolute delocalization and two aromatic rings that possess an p-electron system, which gives them relatively low redox potential and a greater chance of undergoing electron transfer reactions. A number of chalcones having hydroxy, alkoxy groups in different position have been reported to possess anti-bacterial, antiulcer, antifungal, antioxidant, vasodilatory, antimitotic, antimalarial, antileishmanial and inhibition of chemical mediators release, inhibition of leukotriene B4, inhibition of tyrosinase and inhibition of aldose reductase activities. Appreciation of these findings motivated us to synthesize chalcones as a potential template for anti microbial agents. There are several methods for the preparation of chalcones, the most convenient of which is the Claisen-Schmidt condensation of equimolar quantities of aryl methyl ketone and aryl aldehyde in the presence of alcoholic alkali. Typically, high-alkaline media such as KOH, NaOH and Ba(OH)2, as well as natural phosphates, are chosen as suitable media for preparation . Even the use of Lewis acid (B2O3, RuCl3, BF3, AlCl3, p-toluene sulfonic acid and dry HCl) has been reported.

II. DRUG PROFILE

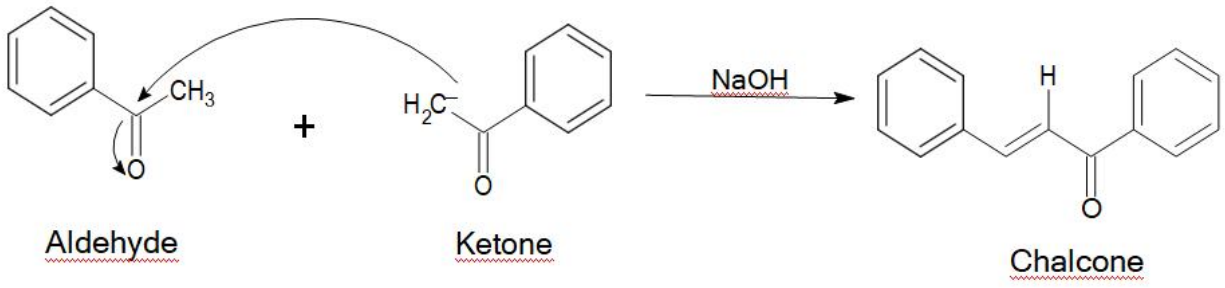
Name of Drug :- Chalcone

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 4, May 2023

Synonym	1,3-Diphenyl-2-Propen-1-One
Structure	O
Molecular Formula	$C_{15}H_{12}O$
Molecular Weight	208.25gm/mol
Colour	Yellow Solid
Nature	Crystalline
Odour	Aromatic Like
Melting point	55 to 57 °C
Boiling point	345 to 348 °C

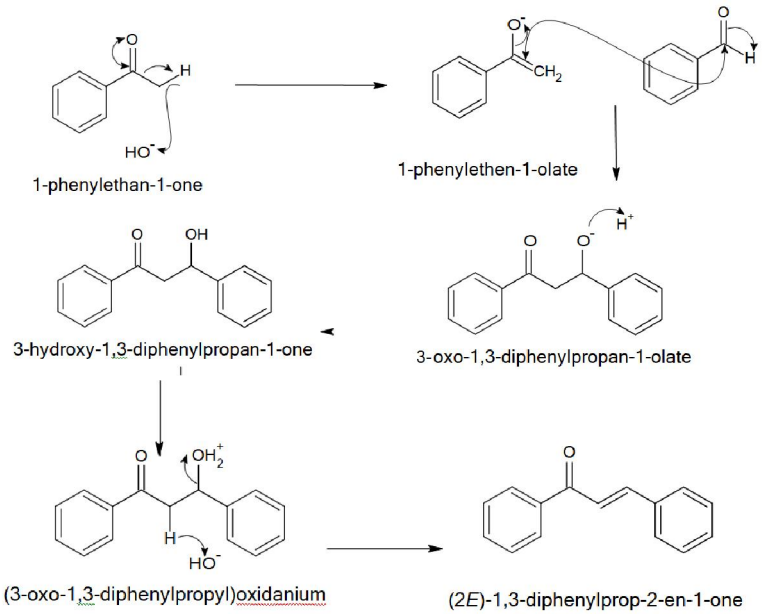
Uses:- The chalcones derivatives show a variety of biological activities including anticancer, antibacterial, anticonvulsant, anti-HIV, antihyperglycemic, anti-inflammatory, antileishmanial, antimicrobial, antioxidant, antiprotozoal, antitubercular and antiviral, anti-ulcerative and helps form a stable chemical structure. Natural aromatic ketone utilized for the biosynthesis of flavones and as a template for bioactive substancesknown as chalcones.

Properties: 1.It is yellowish crystalline solid.
Flavanones can be easily achieved through cyclization of chalcones treated with hydrobromic acid in glacial acetic acid. In this isomerization reaction, partial demethylation and debenzylation may occur.
It is soluble in organic solvents but insoluble in water. like ethanol anddiethyl ether but insoluble in water.
Hence, the formed product chalcone is **non-polar** because the compoundis insoluble in water and it is an alpha-beta unsaturated ketone.
The boiling point for this substance is 345 to 348 °C.
The melting point is 55 to 57 °C.
Reaction of Chalcone



Mechanism of Chalcone
Aromatic aldehyde undergoes condensation reaction with aldehyde or ketone which contain alpha hydrogen atoms in the presence of an alkali. This reaction is called Claisen-Schmidt reaction. In the Claisen-Schmidt reaction, the concentration of alkali frequently ranges between 10 and 60%. The reaction is carried out at around 50 0C for 12–15 h or at room temperature for 1 week. Under these conditions, a Cannizzaro reaction also takes place and thus reduces the yield of the desired product. As a means to avoid the disproportionation of aldehyde, the use of benzylidene-diacetate in place of aldehyde has been reported. Benzalacetophenone the α, β unsaturated ketone also known as Chalcone, can be used to synthesize many useful derivatives. Chalcone can be prepared from benzaldehyde and acetophenone with catalyst sodium hydroxide via aldol condensation. We are interested in this base-catalyzed reaction because the reaction of chalcone formation has been used as a model reaction of aldol condensation.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 4, May 2023

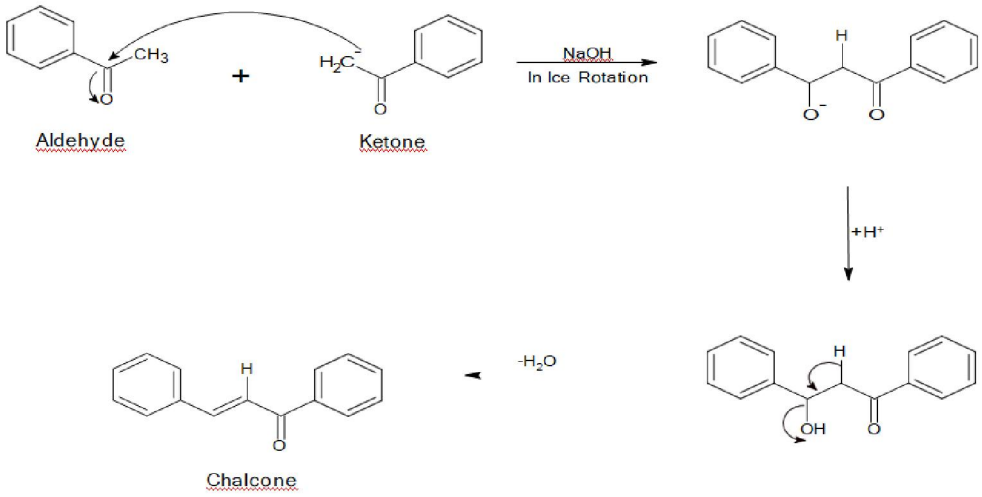


Various Conventional Methods for Synthesis of Chalcone:-

Preparation of Chalcone

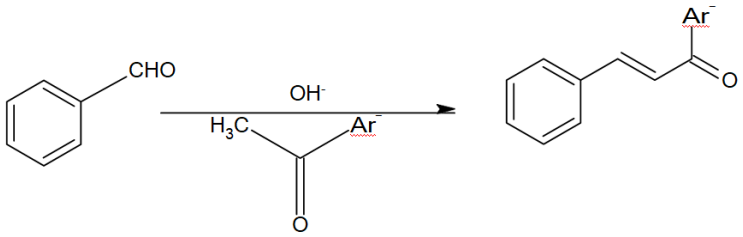
Claisen-Schmidt Reaction **:**

This method for the preparation of chalcones is the classical Claisen- Schmidt summarized by condensation of ketone with aldehyde in the presence of aqueous alkaline bases or in the presence of alcoholic alkali.Synthesis of chalcones by an aqueous solution of an appropriate concentration of (30, 40, 50 or 70) %. Hydrochloric acid or Alkali as condensing agent.

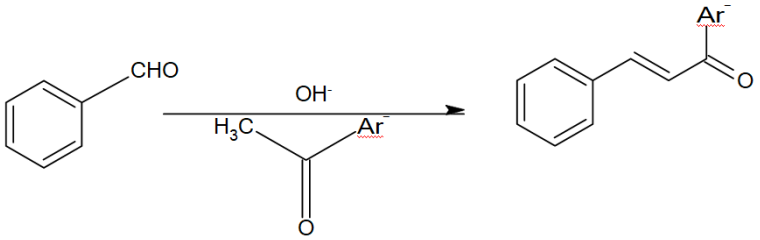


Reaction of ketones and aromatic aldehyde (Aldol Reaction) prepared chalcones in basic medium by reaction of ketones witharomatic aldehyde in ethanol.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 4, May 2023

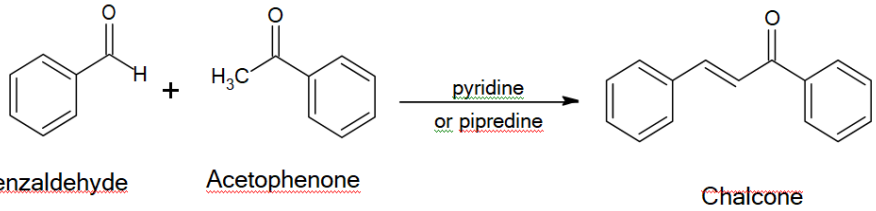


Reaction of ketones and aromatic aldehyde (Aldol Reaction) prepared chalcones in basic medium by reaction of ketones witharomatic aldehyde in ethanol.



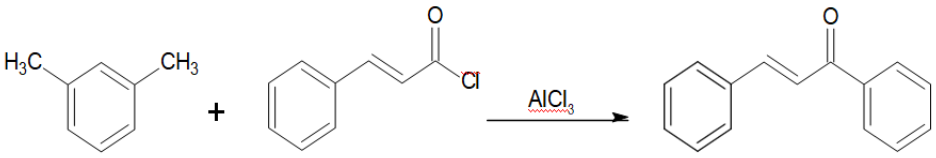
New Method

Prepared chalcone by reaction through condensation between aldehyde andketone with pyridine or pipredine as catalyst, which gave high product



By Fridel –Craft Reaction

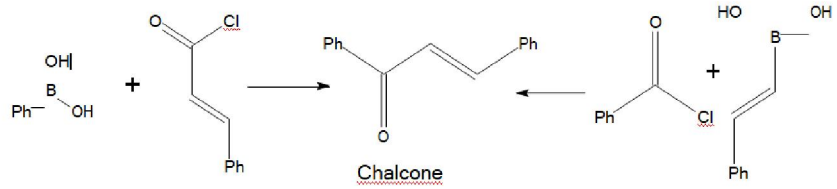
By reaction with aluminum chloride AlCl3



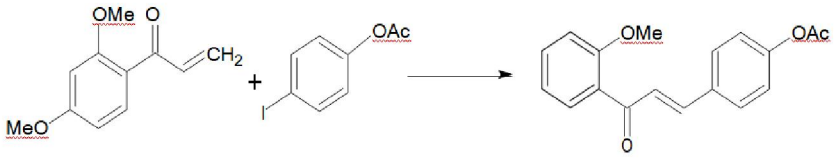
Suzuki reaction And Heck reaction

Chalcones can be prepared by Suzuki through a reaction between phenyl boronic acid and cinnamyl chloride or benzoyl chloride and phenyl vinyl boronic acid. Chalcones and other flavonoids can be prepared by coupling an aryl vinyl ketone with an aryl iodide under Heck reaction conditions.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 4, May 2023



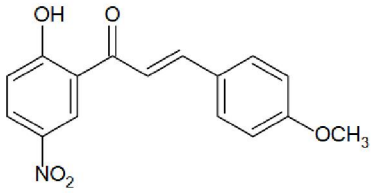
Chalcones by Suzuki coupling



Chalcones by Heck coupling

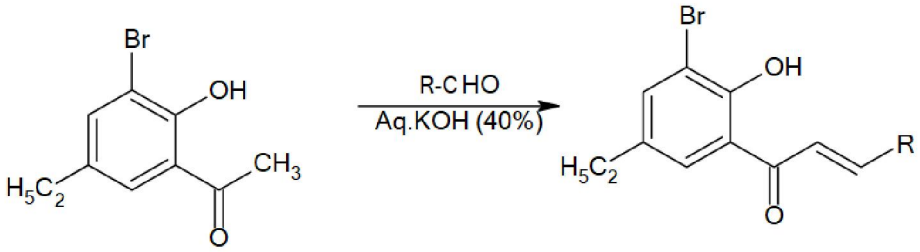
Preparation of hydroxy-nitro chalcone

Several hydroxy-nitrochalcones have been prepared using dry hydrogenchloride gas. Onoda and Sasaki reported the use of hydrochloric acid to synthesize hydroxy-nitrochalcone from 2-hydroxy-5-nitroacetophenone and p-anisaldehyde. Alkali metal alkoxide, magnesium tert-butoxide, borax, piperidine, aluminium chloride, boron trifluoride, amino acids and perchloric acid are other condensing agents which have been employed in several studies



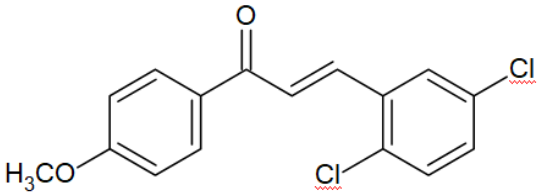
Preparation of a chalcone derivative using 2-hydroxy-3-bromo-5-ethyl acetophenone

A chalcone derivative was synthesized from 2-hydroxy-3-bromo-5-ethyl acetophenone.



Microwave-assisted synthesis of chalcones

microwave technique to synthesize chalcones (Fig. 8). Heterogeneous catalysts including potassium carbonate, barium hydroxide, p-Toluene sulfonic acid, KF-Al2O3, zirconium tetrachloride, piperidine and aqueous alkali have been used for the synthesis of chalcones and their analogs using microwave irradiation



IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 4, May 2023

III. BIOLOGICAL ACTIVITIES OF CHALCONE

1) Antibacterial Activity And Antimicrobial activity

Antimicrobial activity of all synthesized compounds were determined by disc diffusion method. All human pathogenic bacteria viz Staphylococcus aureus , Pseudomonas aeruginosa, E. coli. Compounds with electron releasing groups such as methoxy and hydroxyl showed better antibacterial activity than the others not having such groups. Compounds having pharmacophores such as chloro, dichloro and fluoro groups have exhibited more antifungal activity on all the three fungi than the others. Chalcone derivatives with these substituents showing greater antimicrobial activity.

Anti parasitic Activity (Antileishmanial activity) And Anticancer activity

Antimicrobial activity of all synthesized compounds were determined by disc diffusion method. All human pathogenic bacteria viz Staphylococcus aureus , Pseudomonas aeruginosa, E. coli. Compounds with lectron releasing groups such as methoxy and hydroxyl showed better antibacterial activity than the others not having such groups. Compounds having pharmacophores such as chloro, dichloro and fluoro groups have exhibited more antifungal activity on all the three fungi than the others. Chalcone derivatives with these substituents showing greater antimicrobial activity.

2) Anti parasitic Activity (Antileishmanial activity) And Anticancer activity

Conventional structure activity relationships show that antileishmanial activity is favored by chalcones with more hydrophilic character, with the most active members found among 40-hydroxychalcones. The good antileishmanial activities of the naphthalenyl and pyridinyl derivatives. Chalcone derivatives have been studied as anticancer which showed good results in studies as a drugs.

3) Anti-inflammatory And Hypoglycemic activity

Activated macrophages play a key role in inflammatory responses and release a variety of mediators, including nitric oxide (NO). NO is a potent vasodilator that facilitates leukocyte migration and formation of edema, as well as leukocyte activity and cytokine production. Non-insulin dependent diabetes mellitus (NIDDM, type-II diabetes) is a chronic metabolic disease characterized by insulin resistance, hyperglycemia and hyperinsulinemia. The disease is often associated with obesity, dyslipidemia and hypertension leading to cardiovascular risks.

4) Antitubercular activity And Anti-HIV activity

some of chalcone derivatives tested them for anti-inflammatory, analgesic and Antitubercular activities. Chalcone derivatives have been screened as anti- HIV which indicated to good results in studies as a drugs. Several chalcone derivatives appeared a broad spectrum of pharmaceutical and biological effectiveness like antimicrobial, antifungal, antimalarial, antiviral, anti-inflammatory, antileishmanial anti-tumor and anticancer properties . The alpha , beta - unsaturated carbonyl system in chalcones makes them biologically active.

5) Antioxidant activity

The many free radicals and oxygen species produced during biological processes can damage DNA, proteins and lipids via their oxidation, and have been implicated in the initiation of several degenerative processes related to aging, cancer and atherosclerosis. Hence the removal of free radicals from biological systems is vital to cell sustainability. Antioxidants are well known as free radical scavengers and tend to trap free radical species, specifically inhibiting or delaying the oxidation of oxidizable substrates in the chain reactions.

IV. CONCLUSION

It is found that this chalcone molecule is yet to fully explore for its biological potential. The compounds had been synthesized with an attempt to potentiate them by fulfilling the structural requirement for special biological activities. Almost all the synthesized compounds were found to be active against both Gram positive and Gram negative bacteria.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 4, May 2023

Compound was found to show best activity while other synthesized compounds have also shown comparable activity when compared with standard used. Based on the activity obtained, some conclusion has been made upon the type of substituent's that can be in order to increase the activity chalcone were screened for their possible in vitro antibacterial and anticancer activity by well diffusion method with the help of different bacterial strain like E.coli and S. aureus.

REFERENCES

[1]. B.P. Bandga, S.A. Patil, B.L. Korbad, S.H. Nile, C.N. Khobragade, Eur. J. Med. Chem. 45, 2629–2633 (2010)
[2]. N. Sunduru, A. Agarwal, S.B. Katiyar, Nishi, N. Goyal, S. Gupta, P.M.S. Chauhan, Bioorg. Med. Chem. 14, 7706–7715 (2006).
[3]. Tatsuzaki, K.F. Bastow, K. Nakagawa-Goto, S. Nakamura, H. Itokawa, K.- H. Lee, J. Nat. Prod. 69(10), 1445–1449 ,(2006) .
[4]. J.-M. Yun, M.-H. Kweon, H. Kwon, J.-K. Hwang, H. Mukhtar, Carcinogenesis 27(7), 1454–1464 (2006).
[5]. V. Calvino, M. Picallo, A.J. Lpoz Peinado, R.M. Martin-Aranda, C.J. Duran-Valle, Appl. Surface Sci. 252(17), 6071–6074 (2006).
[6]. Nowakowska, Z. Structural assignment of stilbenethiols and chalconethiols and differentiation of their isomeric derivatives by means of 1H- and 13C- NMR spectroscopy. Spectrosc Lett 38: 477-485, 2005.
[7]. Campos-Buzzi F, Campos JP, Tonini PP, Correa R, Yunes RA, Boeck P, Cechinel-Filho V. Antinociceptive effects of synthetic chalcones obtained from Xanthoxyline. Arch Pharm Chem Life Sci 339: 361-365, 2006.
[8]. Kozlowski D, Trouillas P, Calliste C, Marsal P, Lazzaroni R, Duroux JL. Density functional theory study of the conformational, electronic and antioxidant properties of natural chalcones. J Phys Chem A 111: 1138-1145, 2007.
[9]. Nowakowska Z. A review of anti-infective and anti-inflammatory chalcones. Eur J Med Chem 42 (2): 125-137, 2007.