Available online at https://www.sjomr.org

SCIENTIFIC JOURNAL
OF MEDICAL RESEARCH

Vol. 6, Issue 21, pp 43-46 , 2022

ISSN: 2520-5234

REVIEW ARTICLE

Synthesis, Pharmacological Activity and Uses of Chalcone Compounds: A Review

Ban H. Taresh*

Department of Clinical Laboratories, College of Applied Medical Sciences, University of Kerbala, Karbala, Iraq

ARTICLE INFORMATIONS

Article history:

Received: 27 November 2021

Revised: 02 January 2022

Accepted: 10 January 2022

Published: 25 March 2022

Keywords:

Aldol,
Chalcone,
Medical Application,
Reaction,
Synthesis.

Corresponding author:

Ban H. Taresh

Email: ban.tarsh@uokerbala.edu.iq

Department of Clinical Laboratories, College of Applied Medical Sciences, University of Kerbala, Karbala, Iraq

ABSTRACT

Chalcones as a chemical compound has piqued attention in a variety of sectors (academia besides and industry). Many chalcones derivatives are now being used to treat viral infections, cardiovascular infections, parasite toxicity, pain, gastritis, stomach tumors, and food flavors and cosmetic formulation elements. However, much of the chalcones' medical potential is still untapped. This survey aims to discuss the importance of chalcones, their applications, preparations, and reactions, as well as scientists involved in the pharmacological screening of formatted chalcones, studying the importance of chalcones, and preparing pharmacologically active chalcones with biological activities. Although naturally occurring chalcones have long been used in traditional medicine, recent scientific breakthroughs have revealed that these chemicals exhibit a wide spectrum of biological activity in a variety of animals. It is possible to obtain these natural chemicals. Chalcones are chemical compounds having a wide range of biological activity used in agriculture to control weeds and undesired pests.

INTRODUCTION

Chalcone is a ketone and an aldehyde (enone) that generates the central core of chalcones, which are a group of significant biological compounds. Benzylidene acetophenone, phenyl styryl ketone, benzalacetophenone, phenylacrylophenone, oxo, diphenyl, propylene, and -phenyl-benzoylethylene are some of the several names for chalcone.[1-3] The ketoethylenic group (–CO–CH=CH-) is one of them (Figure 1).

Chalcones[4-14] are used to make a variety of cyclic derivatives,[15-20] such as pyrazolines and isoxazole.

Properties of Chalcone: As a solid-state reaction, this reaction (aldole) can be carried out without the use of any solvent. In high-temperature water (200 to 350°C), the reaction between substituted aldehydes and ketones can be achieved using the same starting materials. Substituted chalcones were also produced using a piperidine-mediated process to prevent side reactions such as numerous condensations, polymerizations, and rearrangements. The preparation of chalcones can be done

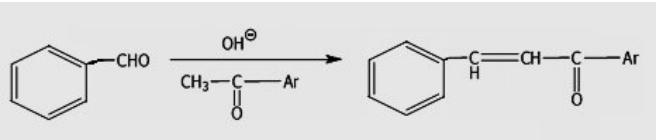

Figure 1: Formula of Chalcone

CITATION: Taresh BH. "Synthesis, Pharmacological Activity and Uses of Chalcone Compounds: A Review". Sci. J. Med. Res. 2022;6(21):43-46.
DOI: 10.37623/sjomr.v06i21.9

in a number of ways.[21] Claisen–Schmidt condensation in (base or acid)- medium under homogenous conditions was used to find chalcones.[22-23] With modest success, heterogeneous catalysts have been used in the Claisen–Schmidt reaction utilizing Lewis acids, Bronsted acids, or solid bases. The most important of them are dependent on the presence of certain catalysts. Claisen-Schmidt reactions to generate chalcones have previously been described using particular catalysts, such as KF-Al_2O_3 or 2-2-bipyridine complex to Co $(OAc)_2$ as the basic medium.[24-27]

Synthesis Methods of Chalcone: The catalysts are either powerful or weak (bases or acids). The chalcone is created from the aldol product in basic medium (base catalysis) via dehydration in (an enolate) - mechanism, whereas in acidic medium (acid catalysis), it is produced via (an enol)-mechanism. The main disadvantage of this method is the sluggish response time; the reaction takes a few days to complete,[28-30] as shown in Figure 2.

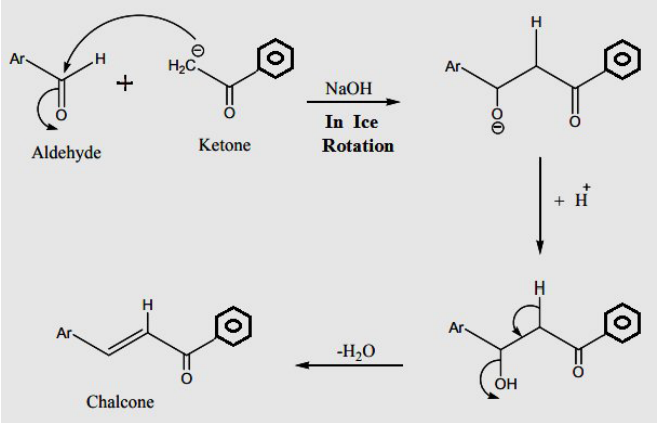

Figure 2: Mechanism of Chalcone Synthesis

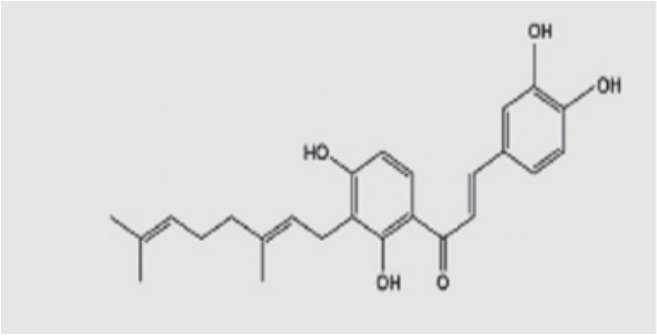

Figure 3: Chalcone derivative with antiviral effect

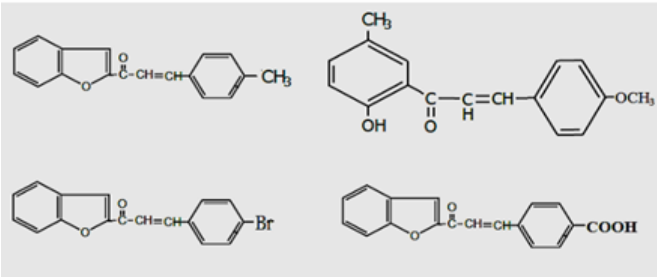

Figure 4: Chalcone derivatives with antibacterial effect

General Procedure for Chalcone: Place (1 mol-as-a-weight) of any aldehyde in a conical flask on a magnetic spin plate, add (1-mole) of the ketone, then (1-mL of absolute ethanol or 95% ethanol) to the mixture, stir, then add (0.10 mL of a 15 Molar NaOH solution) to the flask, stir at room temperature until it solidifies. After that, the majority of the formatted chalcone will precipitate out of the solution. Break up the solid and dilute with 3 mL of ice water with a spatula. Transfer the mixture to another (3 mL) of ice water in a tiny beaker. Suction filter, wash with cold water and dry the yield after completely stirring. Recrystallization from 95 percent ethanol should be used to purify chalcone-(aldol) condensation products.

Applications in Biological Fields

Chalcones and their derivatives have attracted a lot of attention in recent years. Many research studies have been published on chalcones, and fresh pharmacological studies are still being conducted. Researchers have investigated new methods for producing chalcone derivatives, which offer many pharmacological and biological properties. The Figure 3 shows that these chalcone compounds have significant antiviral activity.[3] Other chalcone compounds had higher antibacterial activity,[31,32] although Figure 4.

HIV antiviral action Chalcone derivatives have been investigated33 as anti-HIV, with promising results in clinical trials, as shown in Figure 5. Several chalcone compounds showed antibacterial, antifungal, antimalarial, antiviral, anti-inflammatory, antileishmanial, anti-tumor, and anticancer effects in a wide range of pharmacological and biological applications. Chalcones are biologically active because of their alpha, beta-unsaturated carbonyl system (Figure 6).

Anticancer properties Chalcone derivatives have been explored as anticancer medicines with promising findings[34] (Figure 7).

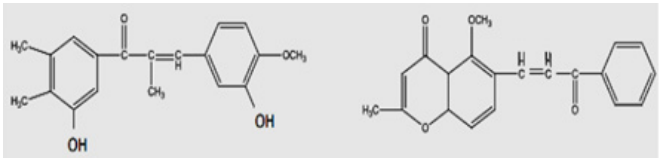

Figure 5: Chalcone derivatives with anti-HIV effect

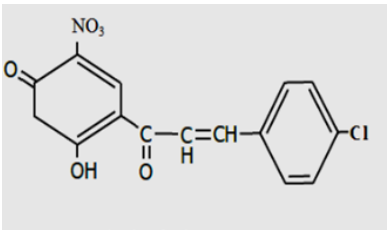

Figure 6: Chalcone derivative with antimalarial effect

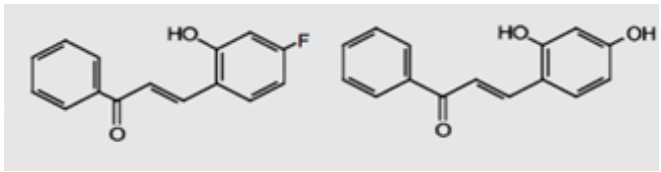

Figure 7: Chalcone derivative with anticancer effect

Chalcones as Useful Intermediates for the Synthesis of Heterocyclic Compounds

Chalcones are versatile precursors for heterocyclic compound synthesis. Chalcones' structural change is dependent on the enone moiety.[35] Micheal addition allows chalcones to react with a nucleophile. It can act as a bi-electrophile in cyclo condensation reactions, reacting with a bi-nucleophile, and this is an appealing method for synthesizing heterocyclic compounds.[36,37] A carbonyl molecule can undergo a carbonyl addition reaction, resulting in hemiacetals, hemiketals, and schiff bases; in all of these reactions, a nucleophile attacks a carbonyl carbon directly. An alternative reaction route is available if the electrophilic carbonyl carbon is -unsaturated; it has a double bond at the carbon position conjugated to the carbonyl group. A resonance structure with a positive charge on the -carbon can be sketched, indicating that it has the potential to be an electrophilic target.

CONCLUSION

Chalcones are versatile molecules that may be used to make a wide range of heterocyclic compounds. Heterocycles have inherent reactivity, allowing for a wide range of rich, diverse, and productive transformations. Given the widespread existence of heterocycles in natural products and pharmaceuticals, developing innovative, quick, and efficient preparative methods for these structures is a pressing need in medicinal chemistry. There are various chalcone-based heterocycles, many of which have been demonstrated to be life-saving therapeutic agents. This essential class of compounds is recognized to enjoy a wide range of research-oriented use, focused on the discovery of new pharmaceutical and therapeutic products due to the inherent pharmacological qualities demonstrated by this important class of compounds.

REFERENCES

1. A j Leusink, J G Noltes, Reaction of Organo-tin hydrides with α, β-unsaturated ketones Tetrahedron letters, 7, 20, p.2221-2226(1966).
2. Zhang Ze, Tanya-Jun, Cs Wang, H Wu, One-pot Synthesis of 3,5-Diphenyl-1H-pyrazoles from Chalcones and Hydrazine under Mechanochemical Ball Milling, Heterocycles, 89, p.103-115(2014)
3. P Venkatesan, S Sumathi, Piperidine mediated synthesis of heterocyclic Chalcones and their antibacterial activity, Journal of Heterocyclic Chemistry, 47, 1, p.81-84(2009).
4. S.J. Won, T.C.T. Liu, L.T. Tsao, J.R.Weng, H.H Ko, J.P. Wang, C.N.Lim, Eur. J. Med. Chem. 40, 103(2005).
5. N. Sharma, D. Mohanakrishnan, U.K. Sharma, R. Kumar, A.K. Richa, D.Sahal Sinha, Eur. J. Med. Chem. 79, 350 (2014) 204.
6. N. Yadav, S.K. Dixit, A. Bhattacharya, L.C. Mishra, M. Sharma, S.K. Awasthi, V.K. Bhasin, Chem. Biol. Drug Des. 80, 340(2012) 203.
7. A. Phrutivorapongkul, V. Lipipun, N. Ruangrungsi, K. Kirtikara, K. Nishikawa et al., Chem. Pharm. Bull. 51(2), 187–190 (2003) 213.
8. C. Nakamura, N. Kawasaki, H. Miyataka, E. Jayachandran, I.H. Kimet al., Bioorg. Med. Chem. Lett. 10(3), 699–706 (2002).
9. E.M. Guantai, K. Ncokazi, T.J. Egan, J. Gut, P.J. Rosenthal, R. Bhampidipati, A. Kopinathan, P.J. Smith, K. Chibale, J. Med. Chem. 54, 3637 (2011).
10. G.M. Cunha, J.B. Fontenele, F.C. De Souza, E.R. Silveira, N.A. Nogueira et al., Phytotherap. Res. 17(2), 155–159 (2003).
11. NJ. Lawrence, A.T. McGown, S. Ducki, J.A. Hadfield, Anticancer Drug Des. 15(2), 135–141 (2000).
12. Chetana B. Patil , S. K. Mahajan, Suvarna A. Katti ., Chetana B Patil et al /J. Pharm. Sci. & Res. Vol.1(3), 2009, 11-22.
13. Khan SA, Ahmed B, Alam T, Pak. J. Pharm. Sci., 2006, Vol.19(4), 290-294 .
14. M. Satyanarayana, Priti Tiwari, Brajendra K. Tripathi, A. K. Srivastava And Ram Pratap, Bioorganic & Medicinal Chemistry 12 (2004) 883–889.
15. Ohad Nerya , Ramadan Musa , Soliman Khatib , Snait Tamir , Jacob Vaya, Phyto chemistry 65 (2004) 1389–1395.
16. Mei Liu, Prapon Wilairat, Simon L. Croft, Bioorganic & Medicinal Chemistry 11 (2003) 2729–2738 Chetana B Patil ,J. Pharm. Sci. & Res.,1(3), 2009, 11-22. 22.
17. Mao Sheng CHENG, Rong Shi LI George KENYON Chinese Chemical Letters, 11, No. 10, pp. 851−854, 2000.
18. Alain Valla , Benoist Valla , Dominique Cartier , Régis Le Guillou , Roger Labia, Loic Florent , Sébastien Charneau , Joseph Schrevel , Pierre Potier European Journal of Medicinal Chemistry 41 (2006) 142–146 .
19. Prasad YR, Kumar PR, Ramesh B. Int. J. Chem. Sci. 2007;5(2): 542-548 .
20. Nidhi Mishra , Preeti Arora , Brajesh Kumar , Lokesh C. Mishra , Amit Bhattacharya , Satish K. Awasthi , Virendra K. Bhasin , European Journal of Medicinal Chemistry 43 (2008) 1530e1535 .
21. Choi O, Wu CZ, Kang SY, Ahn JS, Uhm TB, Hong YS (2011). "Biosynthesis of plant-specific phenylpropanoids by construction of an artificial biosynthetic pathway in Escherichia coli". Journal of Industrial Microbiology & Biotechnology. 38 (10): 1657–65. doi:10.1007/s10295-011-0954-3. PMID 21424580.
22. Kreuzaler F, Hahlbrock K (1972). "Enzymatic synthesis of aromatic compounds in higher plants: formation of naringenin (5,7,4'-trihydroxyflavanone) from p-coumaroyl coenzyme A and malonyl coenzyme A". FEBS Lett. 28 (1): 69–72. doi:10.1016/0014-5793(72)80679-3. PMID 4646877.
23. Cain CC, Saslowsky DE, Walker RA, Shirley BW .(1997). "Expression of chalcone synthase and chalconeisomerase proteins in Arabidopsis seedlings". Plant Mol. Biol. 35 (3): 377–81. doi:10.1023/A:1005846620791. PMID 9349261.
24. Crosby KC, Pietra BA, Gadella TW, Winkel BS (2011). "Förster resonance energy transfer demonstrates a flavonoid metabolon in living plant cells that displays competitive interactions between enzymes". FEBS Lett. 585(14): 2193–8. doi:10.1016/j.febslet.2011.05.066. PMID 21669202.
25. Austin MB, Noel JP (February 2003). "The chalcone synthase superfamily of type III polyketide synthases". Nat Prod Rep. 20 (1): 79–110. CiteSeerX 10.1.1.131.8158. doi:10.1039/b100917f. PMID 12636085.
26. Saslowsky D, Winkel-Shirley B (2001). "Localization of flavonoid enzymes in Arabidopsis roots". The Plant Journal. 27 (1): 37–48. doi:10.1046/j.1365-313x.2001.01073.x. PMID 11489181.
27. Dao TT, Linthorst HJ, Verpoorte R (September 2011). "Chalcone synthase and its functions in plant resistance". Phytochem Rev. 10 (3): 397–412. doi:10.1007/s11101-011-9211-7. PMC 3148432. PMID 21909286.
28. Whitehead JM, Dixon RA (1983). "Chalcone synthase from cell suspension cultures of Phaseolus vulgaris L". BiochimBiophysActa. 747 (3): 298–303. doi:10.1016/0167-4838(83)90109-7.
29. Napoli C, Lemieux C, Jorgensen R (1990). "Introduction of a Chimeric Chalcone Synthase Gene into Petunia Results in Reversible Co-Suppression of Homologous Genes in trans". Plant Cell. 2 (4): 279–289. doi:10.1105/tpc.2.4.279. PMC 159885. PMID 12354959.
30. Van Blokland R, Van der Geest N, Mol JNM, Kooter JM (1994). "Transgene-mediated suppression of chalcone synthase expression in Petunia hybrida results from an increase in RNA turnover". Plant J. 6 (6): 861–77. doi:10.1046/j.1365-313X.1994.6060861.x.
31. H. Suwito, A. N. Kristanti and N. N. Tri Puspaningsih, "Chalcone: Synthesis, Structure, Diversity and Pharmacological Aspects ", Journal of Chemical and Pharmaceutical Research, 6(5), pp.1076-1088, 2014.
32. Mieaad Mohamd , Nagham Mahmood Aljamali , Wassan Ala Shubber, Sabreen Ali Abdalrahman .," New Azomethine- Azo Heterocyclic Ligands Via Cyclization of Ester " ., Research J. Pharm. and Tech. 11, 6 , 2018.
33. A. V. Leovezijn, W. I. Iwema and A. Stoit, "Arylsulfonyl Pyrazoline Carboxamide Derivatives as 5-HT6 Antagonists", US Patent, 0011775A1, 2014.

34. P. Page, F. Gaggini and B. Laleu, "Pyrazoline Dione Derivatives as NADPH Oxidase Inhibitors ", US Patent, 0172352 A1, 2012.
35. Suwito, H., Jumina, J., Kristanti, A.N., Mustofa, M. and Puspaningsih, N.N.T. Chalcones: synthesis, structure diversity and pharmacological aspects. J. Chem. Pharm. Res. 6(5) (2014) 1076-1088.
36. Schramm, O.G. Multi-component heterocycles synthesis based on Sonogashira Coupling Isomerisation, Desertation, Rieprecht-Karls University, Heidelberg, Germany, (2006) 1-20.
37. Kazlauskas, R.J., and Bornscheuer, U.T. 2012. Synthetic methods VI-Enzymatic and Semi-enzymatic in Comprehensive Chirality. Elsevier Ltd., 7 (2012) 350-371