CHALCONE: SYNTHESIS, CHRACTERIZATION AND ANTIMICROBIAL ACTIVITY

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ABSTRACT:

Chalcones have sparked a lot of curiosity in recent years. Chalcones are a key component of many natural sources, and they have a wide range of biological functions. Chalcones, also known as α,β-unsaturated ketones, are an important class of chemical compounds with a wide range of biological activity including antibacterial, antifungal, anticancer and anti-inflammatory properties.

A plethora of research articles have been published and Chalcones continue to show promise in the development of novel drugs. The Claisen–Schmidt condensation process was used to make Chalcone derivatives. UV and IR were used to confirm the structure of the synthesised. Antimicrobial activity was also investigated.

Keywords: Claisen-Schmidt condensation, Chalcone, synthesis, antimicrobial activity.

1. Introduction

The Chemistry of Chalcones has sparked a flurry of research all across the world. The synthesis and biodynamic activities of Chalcones have piqued people's interest. The name "Chalcones" was given by Kostanecki and Tambor [1].Chalcones or benzylideneacetophenone are the important constituents of natural sources. It was first isolated from Chinese liquorice (*Glycyrrhizae inflata*) [2].

Two aromatic rings are connected by an aliphatic three-carbon chain in Chalcones. Chalcones and their derivatives are a class of natural products that have been shown to have a wide range of biological and pharmacological action. Yuh-Heei *et al*. (2002) synthesized different series of Chalcone derivatives, which are having 90% inhibitory activity against ***Mycobacterium tuberculosis***.

Chalcones is a generic term given to compounds bearing the 1, 3-diphenyl-2-propen-1-one framework and it belongs to the flavonoid family. Chemically they are open-chain flavonoid in which the two aromatic rings are joined by a three carbon α, β-unsaturated carbonyl system. Chalcones are readily synthesized in the laboratory by various synthetic methods. Structural modification of chalcones template can be readily achieved.

Different methods are available for the preparation of chalcones [3-5].The most convenient method is the Claisen-Schimdt condensation of equimolar quantities of arylmethylketone with arylaldehyde in the presence of alcoholic alkali [6].

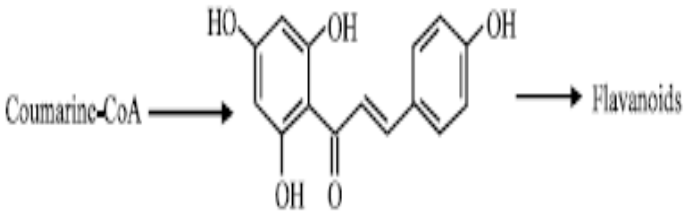

Fig. 1: Biochemical changes of chalcones

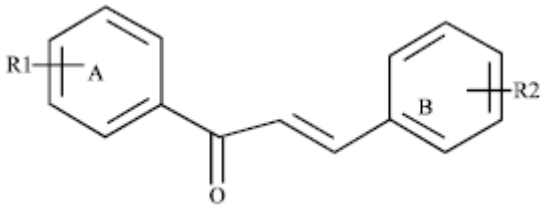

Fig. 2: Parent nucleus of chalcone derivatives

Aromatic aldehydes can be condensed with aliphatic or aromatic ketones in the presence of aqueous alkali in the Claisen-Schmidt condensation reaction to generate Chalcones, which are unsaturated ketones. The first step in this method is aldol condensation, which involves the nucleophilic addition of carbanion generated from aryl ketones to the carbonyl carbon of the aromatic aldehydes. Dehydration of the hydroxy ketones to form the conjugated α, β unsaturated ketones or Chalcones (Fig. 2) (Yerra *et al*., 2004).

Chalcones have been reported to possess many useful properties, including anti-inflammatory [7], antifungal [8-10], antioxidant [11], cytotoxic [12] and anticancer [13-16] activities.Many chalcones have been reported as having high antimalarial activity, probably as a result of Michael addition of nucleophilic species to the double bond of the enone [17,18].

1.1. Nomenclature:

At various times, multiple nomenclature systems for Chalcone were proposed. The American Chemical Society's publication "Chemical Abstracts" has adopted the following pattern. (See Figure 3)

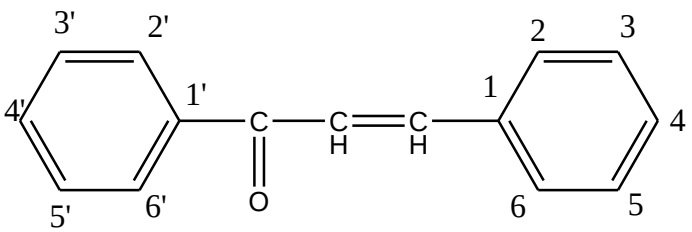

Fig.3: Nomenclature 1

The following system was used by the British Chemical Abstract and Journal of Chemical Society. (See Figure 4)

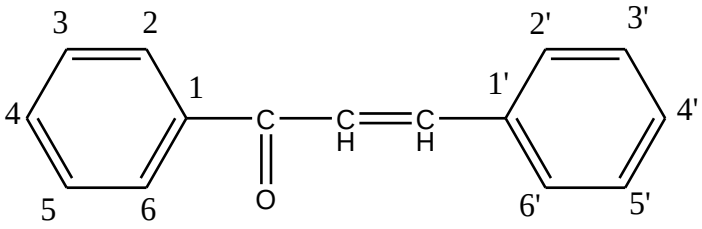

Fig.4: Nomenclature 2

1.2. Objectives:

***** The Claisen-Schmidt condensation process of 4-methoxyacetophenone and benzaldehyde in the presence of KOH was used to make Chalcone.

* The yield of the synthesised chemical will be determined,

* The product will be recrystallized. The melting point will be used to determine purity.

* IR and UV will be used to confirm the structure of the synthesised molecule.

*The purpose of this research is to learn more about the biological features of the Chalcone derivative.

2. Experimental

2.1. Methodology:

Chalcones can be synthesised using a variety of techniques. The Claisen-Schmidt condensation of equimolar amounts of substituted acetophenone with substituted aldehydes in the presence of aqueous alcoholic alkali is the most practical approach.

2.2 General synthesis of chalcone:

Chalcones **(3)** are prepared by simple condensation of simple aromatic aldehyde **(1)** with simple acetophenone **(2)** in the presence of alkali.

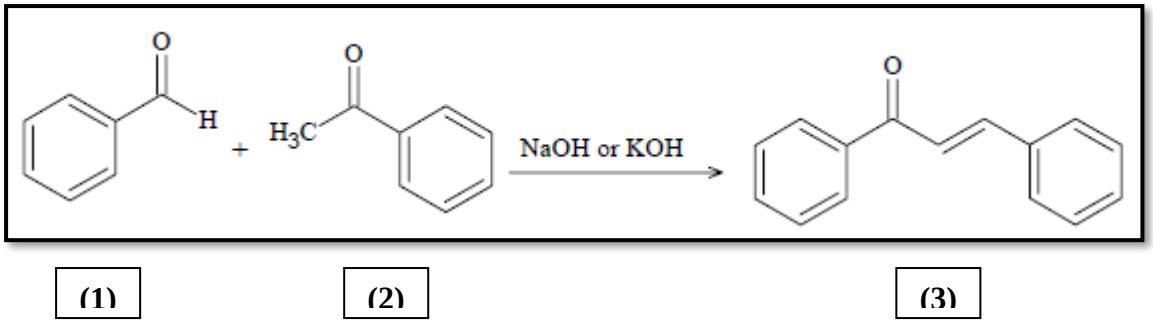

Fig.5: General synthesis of chalcone

2.3 Synthesis of Chalcone Derivative (GK2)

A solution of 4-methoxyacetophenone (0.1 mol) in ethanol (15 ml) and benzaldehyde (0.1 mol) in ethanol (15 ml) was mixed together with constant stirring. To this mixture aqueous solution of potassium hydroxide (60%) was poured gradually with constant stirring and the stirring was continued for 4 hrs. Then it was poured into 400 ml of cold distilled water with constant stirring and then refrigerated for 14 hrs. The precipitate was filtered and washed with ice cold water.

3. Results and Discussion

The synthesis of the Chalcone is a single step method. The structure of the synthesized Chalcone derivative was confirmed by IR. The yield of the synthesized derivative was found. The derivative was also characterized by UV and the biological activity was also carried out.

3.1 Yield

The yield of the synthesized Chalcone derivative was 85% and the colour of the product obtained was Yellow.

3.2 FTIR

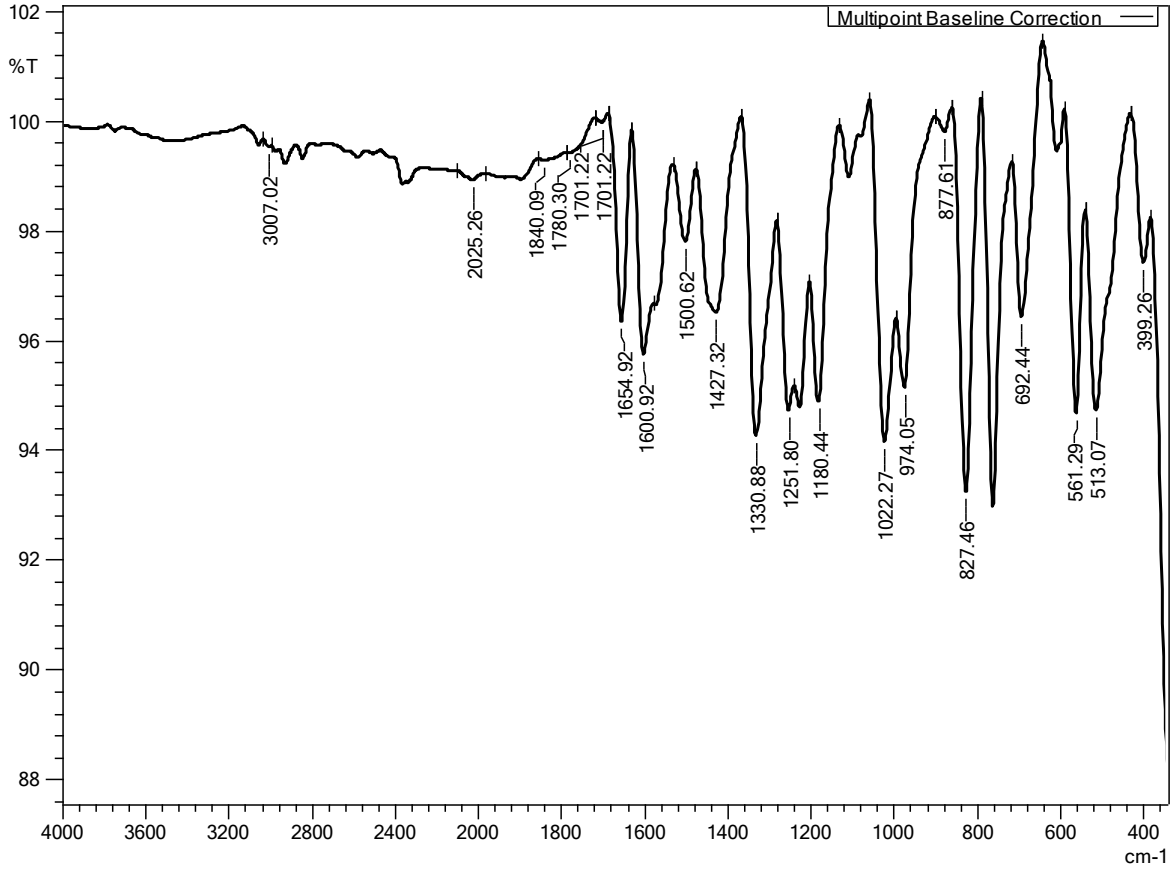

Fig.6: FTIR of synthesized Chalcone derivative

The strongest peak should be the ester C=O stretch, this normally appears at 1750-1735 cm^{-1}but conjugation with the ring shifts the peak to 1654.92 cm^{-1}. The carbonyl stretching vibrations for the enones (=C-C=O) was found at 1654.92 cm^{-1}.The weaker band at 1330.88 cm^{-1} was the ether CO stretch of the OCH_3.

Table-1

Absorption Frequency (cm-1)	Responsible functional group
1654.92 (s)	exhibited characteristics of carbonyl
1600.92 (s)	C=C Olefinic
1500.62 and 1427.32 (m)	aromatic C=C
1330.88 (w)	CO stretch of the OCH_3 group

3.3 UV

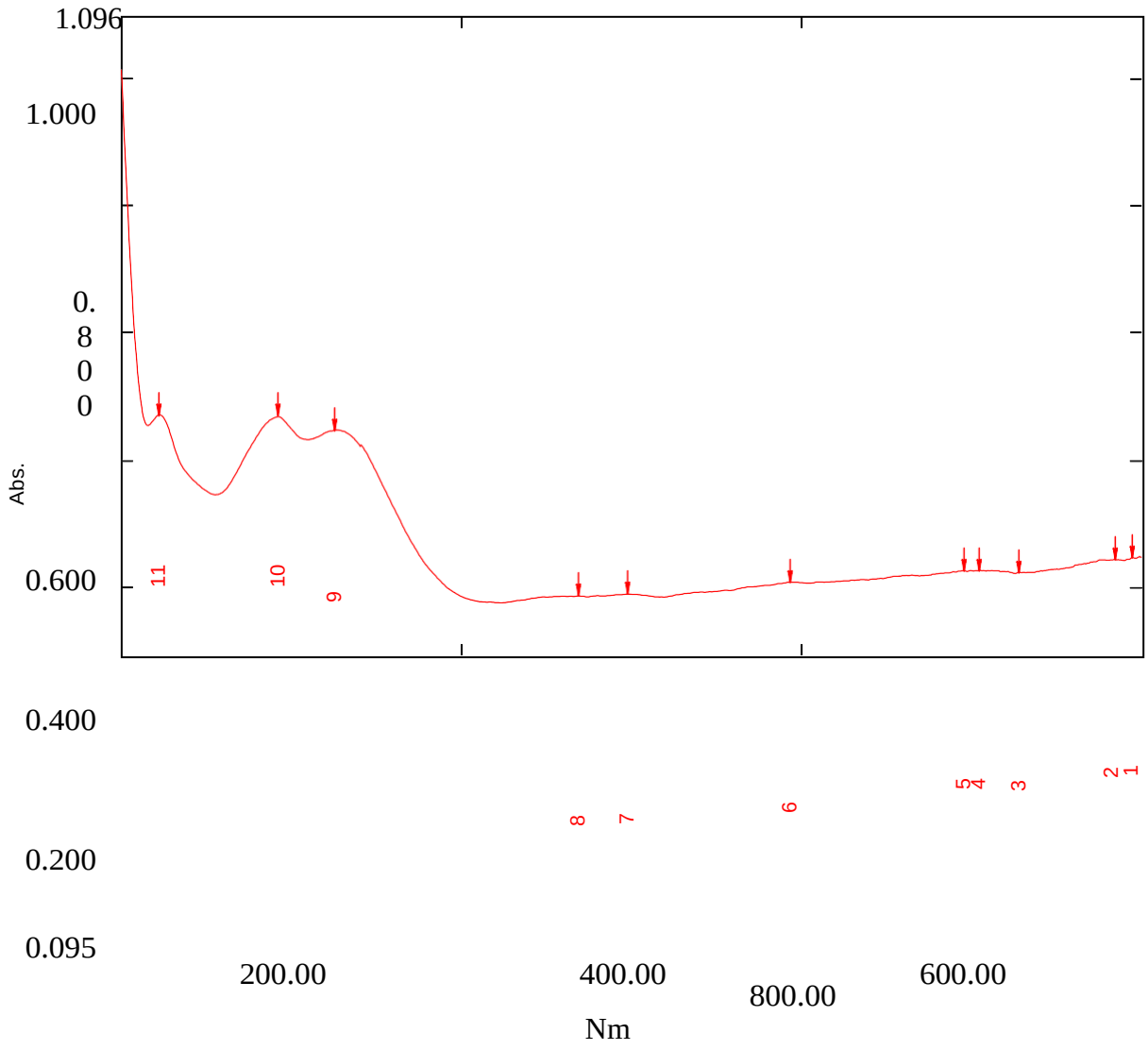

Fig.7: UV of Chalcone derivative

3.4 Antimicrobial activity

Staphylococcus aureus and Escherichia coli were used to test the antibacterial activity of the Chalcone derivative. Candida albicans and Mucor sps were the fungal species used to test the Chalcone derivative's antifungal activity. As a reference antibacterial agent,

Ciprofloxacin was utilised, which is an efficient antibacterial agent against the bacteria studied.

To compare the result, the antibiotic Ciprofloxacin, which is an effective antibacterial agent against the selected bacteria, was utilised as a reference antibacterial agent. As a reference antifungal agent, the medication Amphotericin B was utilised, which is an effective antifungal agent against the fungal species studied.

Antibacterial analysis was followed using standard agar well diffusion method to study the antimicrobial activity of compounds [19, 20, 21]. Each bacterial and fungal isolate was suspended in Brain Heart Infusion (BHI) broth and diluted to approximately 105 colony forming unit (CFU) per ml. They were flood-inoculated onto the surface of BHI agar and then dried. Five-millimeter diameter wells were cut from the agar using a sterile cork-borer and 30 µL (5µg compound in 500 µL DMSO) of the sample solution were poured into the wells. The plates were incubated for 18 h at 37qC for bacteria and at room temperature for fungi. Antimicrobial activity was evaluated by measuring the zone of inhibition in mm against the test microorganisms. DMSO was used as solvent control. Ciprofloxacin was used as reference antibacterial agent. Amphotericin B was used as reference antifungal agent. The tests were carried out in triplicates.

3.4.1 Antibacterial activity chalcone derivative

Antimicrobial activity of the synthesized chalcone derivative was determined by disc diffusion method [27-29].The activity of all human pathogenic microorganisms, including Staphylococcus aureus and Escherichia coli, was determined. The conventional process for preparing nutrition broth, subculture, base layer medium, agar medium, and peptone water was followed. The results of antibacterial studies are given in Table 1.

Table-2 Antimicrobial activity

S.No.	Microorganisms	Control	GK2	Ciprofloxacin
		Zone of inhibition in mm		
1.	*Staphylococcus aureus*	-	08	35
2.	*Escherichia coli*	-	10	12

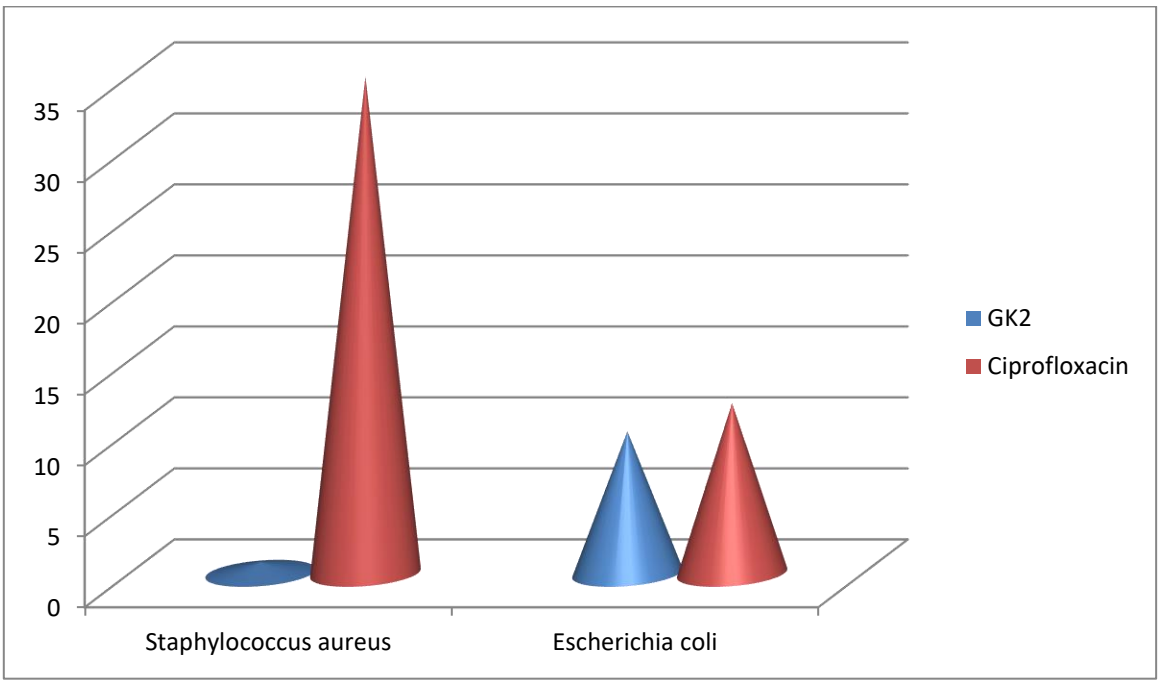

Fig. 8: The antibacterial activity of synthesized Chalcone derivative

The antibacterial activity of the produced Chalcone derivative is shown in Table 2 and Figure 8. The derivative demonstrated some efficacy against the bacterial species, but it was less than the standard antibiotic, Ciprofloxacin, according to the observations.

Fig.9 & 10: Antimicrobial activity of Chalcone derivative

3.4.2 Antifungal activity chalcone Derivative

Table 3 and Figures 10 and 11 show the results of the investigational derivative's tests against Candida albicans and Mucor sps.

Table-3 Antifungal activity

S.No.	Microorganisms	Control	GK2	Amphotericin-B
		Zone of inhibition in mm		
1.	*Mucor sps*	-	14	12
2.	*Candida albicans*	-	09	08

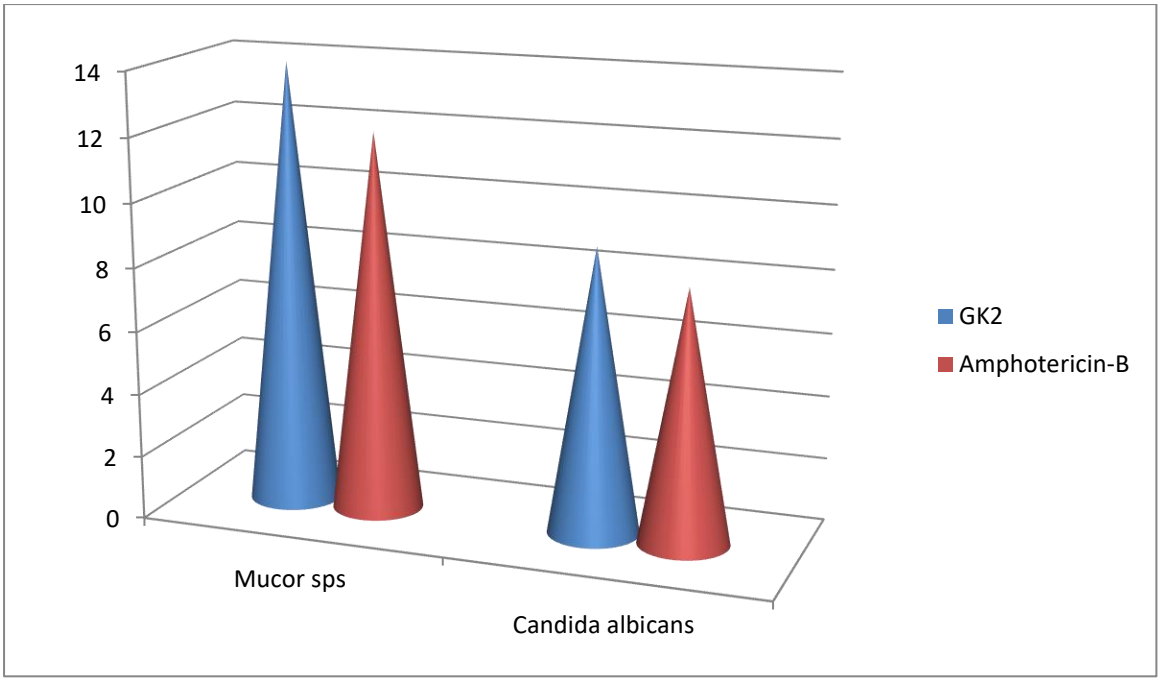

Fig 11: The antifungal activity of synthesized Chalcone derivative

The antifungal activity of the produced derivative is shown in Table 3 and Figure 11. According to the findings, the inhibition was stronger for both Mucor sps and Candida albicans in the event of activity against fungus, as evidenced by derivative. The zone of inhibition against Mucor sps and Candida albicans was found to be substantially higher than that of the conventional medication.

Fig.12 & 13: Antifungal activity of chalcone derivative

4. Conclusion

The chemistry of heterocyclic compounds is still a significant subject in medical chemistry. Finding effective treatment for any disease is the most crucial and integral component of the primary kind's history. To produce a novel class of agents, the standard technique is to look for a representative moiety, which could be a recognised synthetic or natural medicinal agent. Because of their importance as a pioneer in the biosynthesis of flavanoids abundantly available in plants, the preparation of Chalcones (which include a reactive–CO-CH=CH- keto ethylenic group) is of great interest for various investigations. The ability to impart diverse properties in the composition of Chalcones by changing various substituents has piqued the interest of specialists in a variety of sectors. Apart from its value as a starting material in organic and inorganic chemistry, as well as in the therapeutic field (pharmacological proxy showing a large number of actions like antibacterial and antifungal activities). The present work was developed because of the aforesaid qualities and applications of related compounds, and the chemical was synthesised, described, and biological activity was assessed for 4-methoxyacetophenone benzaldehyde derivative. This aids in the development of new modern synthetic pharmaceuticals for a wide range of biological applications.

5. References:

[1] Kostanecki and Tambor S. V. *J. Chem Ber.* , 32, 1921 **1899.**

[2] Yerra, K.R., S. Fang and Y.M. Tzeng,. Synthesis of 2 oxygenated chalcones. Bioorg. Med. Chem., 12, 2679-2686 **2004**.

[3] Rupe H and Wasserzug D, *J. Chem Ber.* , 34, 3527 **1901.**

[4] Hermes S.A, *Chem Ber.* , 70, 9642 2h **1969.**

[5] Breslow D.S and Houser C.R, *Chem Ber.* , 62, 2385 **1940.**

[6] Kazauki K, Hitayama K, Yokomor S and Soki T, *Chem Abstr.* , 85, 591 **1976.**

[7] Z. Nowakowska, Eur. J. Med. Chem. 42, 125 **2007** CrossRef Google Scholar.

[8] S. Lopez et al., Bioorg. Med. Chem. 9, 1999 **2001** CrossRef Google Scholar.

[9] P. Boeck et al., Arch Pharmacy 338, 87 **2005** CrossRef Google Scholar.

[10] H.N. Elsohly, A.S. Joshi, A.C. Nimrod, L.A. Walker, A.M. Clark, Planta Medica 67, 87 **2001** CrossRef Google Scholar.

[11] N. Yayli et al., J. Photochem.Photobiol. A 169, 229 **2005** CrossRef Google Scholar.

[12] M.V.B. Reddy et al., Bioorg. Med. Chem. 16, 7358 **2008** CrossRef Google Scholar.

[13] G. Saydam et al., Lukemia Research 27, 57 **2003** CrossRef Google Scholar.

[14] M. Cabrera et al., Bioorg. Med. Chem. 15, 356 **2007** CrossRef Google Scholar.

[15] C. Nakamura et al., Bioorg. Med. Chem. 10, 699 **2002** CrossRef Google Scholar.

[16] A. Modzelewska, C. Pettit, G. Achanta, N.E. Davidson, P. Huang, S.R. Khan, Bioorg. Med. Chem. 14, 3491 **2006** CrossRef Google Scholar.

[17] L. Troeberg et al., Mol. Med. 6, 660 **2000** Google Scholar.

[18] V.J. Ram, A.X. Saxena, S. Srivastava, S. Chandra, Bioorg. Med. Chem. Lett. 10, 2159 **2000** CrossRef Google Scholar.

[19] Perez, C., Pauli, M. and Bazerque, P.(1990). An antibiotic assay by the agar-well diffusion method. Acta Biol. Med. Exp. 15: 113- 115.

[20] Erdemogßlu, N., Ku¨ Peli, E., Yes, E. and Ilada, R. (2003). Antiinflammatory and antinociceptive activity assessment of plants used as remedy in Turkish folk medicine. J. Ethnopharmacol.89: 123.

[21] Bagamboula, C.F., Uyttendaele, M. and Debevere, J. (2004). Inhibitory effect of thyme and basil essential oils, carvacrol, thymol, estragol, linalool and p-cymene towards Shigella sonnei and S. flexneri. Food Microbiol. 21: 33-42.

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