Synthesis, Characterisation and Antibacterial Activity of Novel Chalcones

Venkatachalam. H, Jayashree B.S, and Vignesh Shetty

Abstract — A few of the novel chalcones were synthesised and characerised by IR, NMR and Mass spectra. They were screened for their antibacterial activities against gram positive bacteria such as *Enterococcus*, *Staphylococcus aureus*, and gram negative bacteria such as *Escherichia coli and Pseudomonas aeruginosa* by agar diffusion method. Out of the six compounds tested, all the test compound showed moderate antibacterial activity against *Enterococcus* strain, while, JMC-13 showed zone of inhibition at 16mm at a concentration of 20 mg/mL. All the six compounds were further screened against *Enterococcus* strain at concentrations of 2000 µg, 5000 µg and 10000 µg per mL where, compound JMC 14 showed maximum inhibition at 2000 µg/ mL.

Keywords— Anti-bacterial activity, Chalcones

I. Introduction

Chalcones are 1,3-diaryl propen-1-ones, and serve as precursors in the synthesis of benzopyrones. Benzopyrones exhibit variety of biological activities and beneficial for human health [1]. Hence synthesis of chalcones is an important research field not only because they are precursors of flavonoids but also because of their wide range of biological activities such as antioxidant [2] antibacterial [3], anticancer [4], [5], antidiabetic [6], anti-inflammatory activities [7], [8].

II. Materials and Methods:

A. Synthesis

Traditionally, chalcones are prepared by Claisen-Schmidt condensation of equimolar concentrations of aryl aldehydes and acetophenones in the presence of a base [9]. In the present work, 0.001 moles of substituted 2-methoxyacetophenone was dissolved in 15 ml of methanol and was thoroughly stirred with 2 ml of 20% alcoholic solution of sodium hydroxide. After stirring the reaction mixture for 30 minutes, 0.001 moles of substituted benzaldehyde was added in portions. Stirring was continued until the completion of the reaction. The progress of the reaction was monitored by TLC using n-hexane: ethylacetate (7:3). The reaction mixture was then suspended in ice cold water and the resulting solution was acidified with dilute hydrochloric acid. The product which precipitated was collected by filtration and dried in air and stored in a desiccator. Fig. 1 represents the scheme of synthesis. The substitutions are given in Table I.

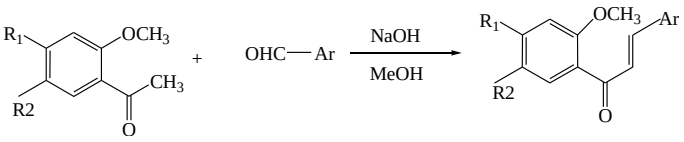
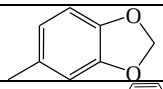
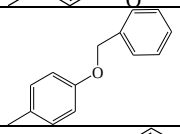
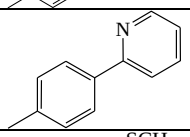
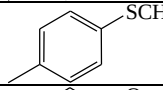
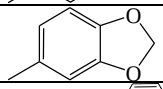
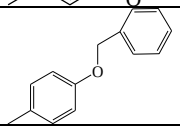


Fig. 1: Scheme of synthesis of Chalcones

TABLE I
THE SUBSTITUTIONS AT VARIOUS POSITIONS OF CHALCONES

Compound	Ar	R_1	R_2
JMC10		OCH_3	H
JMC11		OCH_3	H
JMC12		OCH_3	H
JMC13		OCH_3	H
JMC14		H	OCH_3
JMC15		H	OCH_3

The compounds were purified by recrystallization and the analyzed by IR (Shimadzu), Mass (GCMS-QP5050A, Shimadzu, Japan), NMR (Bruker) spectra. Further, these compounds were evaluated for their antibacterial activity by agar diffusion method [10], [11]. In this technique, melted agar inoculated with microorganisms is poured into Petri dishes. Wells were made in the agar plate and a specific volume of the antimicrobial substances were placed in them, plates were incubated at a temperature of 37°C for the respective time. The antimicrobial substance diffuses through agar around its well and produces a clear zone of inhibition. The diameter of this zone gives an estimation of the degree of activity of the antimicrobial substance.

Venkatachalam. H, Department of Chemistry, Manipal Institute of Technology, Manipal University, India.venkatachalam.h@manipal.edu

Jayashree. B.S, Department of Pharmaceutical Chemistry, Manipal College of Pharmaceutical Sciences, Manipal University, India. jayashree.sy@gmail.com (Corresponding Author)

Vighnesh, Enteric Diseases Division, Central Research Laboratory, KMC Manipal, Manipal University, India, vigneshshetty2009@yahoo.co.in

III. Results And Discussion

Spectral Data:

JMC10:

IR (KBr) 1651 (C=O), 1598 (C=C), 1249 (O-CH_3), 1112 cm^{-1} (C-O-C).

^{1}H NMR (400MHz, DMSO) δ 3.59 (3H, s, H-OCH_3), 3.85 (3H, s, H-OCH_3), 3.913, (1H, d, H-CH=CH), 3.918, (1H, d, H-CH=CH), 6.055 (2H, s, H-O-CH_2-O), 6.6-7.7 (6H, m, H-Ar),

Mass (C I) m/z 313 $(M+1)^+$

JMC11:

IR (KBr) 1653 (C=O), 1598 (C=C), 1261 (O-CH_3), 1133 cm^{-1} (C-O-C).

^{1}H NMR (400MHz, DMSO) δ 3.55 (3H, s, H-OCH_3), 3.85 (3H, s, H-OCH_3), 3.913, (1H, d, H-CH=CH), 4.428, (1H, d, H-CH=CH), 5.143 (2H, s, H-O-CH_2-C_6H_5), 6.6-7.7 (12H, m, H-Ar)

Mass (C I) m/z 375 $(M+1)^+$

JMC12: IR (KBr) 1653 (C=O), 1598 (C=C), 1509 (C=N), 1261 (O-CH_3), 1133 cm^{-1} (C-O-C).

^{1}H NMR (400MHz, DMSO) δ 3.55 (3H, s, H-OCH_3), 3.85 (3H, s, H-OCH_3), 4.07, (1H, d, H-CH=CH), 4.48, (1H, d, H-CH=CH), 6.6-8.7 (11H, m, H-Ar)

Mass (C I) m/z 346 $(M+1)^+$

JMC13: IR (KBr) 2948 (S-CH_3), 1655 (C=O), 1604 (C=C), 1261 (O-CH_3), 1133 cm^{-1} (C-O-C).

^{1}H NMR (400MHz, DMSO) δ 3.55 (3H, s, H-OCH_3), 3.84 (3H, s, H-OCH_3), 3.95, (1H, d, H-CH=CH), 4.42, (1H, d, H-CH=CH), 6.6-7.7 (7H, m, H-Ar)

Mass (C I) m/z 315 $(M+1)^+$

JMC14: IR (KBr) 1671 (C=O), 1608 (C=C), 1281 (O-CH_3), 1105 cm^{-1} (C-O-C).

^{1}H NMR (400MHz, DMSO) δ 3.57 (3H, s, H-OCH_3), 3.75 (3H, s, H-OCH_3), 3.97, (1H, d, H-CH=CH), 4.46, (1H, d, H-CH=CH), 6.056 (2H, s, H-O-CH_2-O), 6.93-7.22 (6H, m, H-Ar),

Mass (C I) m/z 313 $(M+1)^+$

JMC15:

IR (KBr) 1682 (C=O), 1607 (C=C), 1281 (O-CH_3), 1170 cm^{-1} (C-O-C).

^{1}H NMR (400MHz, DMSO) δ 3.53 (3H, s, H-OCH_3), 3.75 (3H, s, H-OCH_3), 3.973, (1H, d, H-CH=CH), 4.463, (1H, d, H-CH=CH), 5.14 (2H, s, H-O-CH_2-C_6H_5), 7.05-7.43 (12H, m, H-Ar)

Mass (C I) m/z 375 $(M+1)^+$

The infra-red absorptions of the carbonyl groups were in the range of 1650 – 1682 cm^{-1}, characteristic of α, β-unsaturated carbonyl group. The aromatic protons of all the test compounds resonate at δ 6.6 – 7.7, except JMC12 in which the protons resonate at δ 6.6 – 8.7. In the case of JMC13, the singlet corresponding to the protons of SCH_3 group, got merged with the solvent (DMSO) peak.

B. Anti-bacterial Activity

The synthesized test compounds were evaluated for their anti-bacterial activity against gram positive bacteria such as *Enterococcus*, *Staphylococcus aureus*, and gram negative bacteria such as *Escherichia coli*, *Pseudomonas aeruginosa* by agar diffusion method. All the test compounds showed zone of inhibition for *Enterococcus*, whereas they did not show any significant zone of inhibition for other bacterial strains. All the compounds were tested at a concentration of 20 mg/mL against *Enterococcus*. Test compounds such as JMC10, JMC11, JMC12, JMC13, JMC14 and JMC15 showed zone of inhibition at 15, 12, 14, 16, 15 and 13 mm respectively. These compounds were further screened against *Enterococcus* for the quantification of the efficacy at concentrations of 2000 µg, 5000 µg and 10000 µg per mL. JMC14 showed zone of inhibition of 14 mm at a concentration of 2000 µg/mL, whereas the standard ciprofloxacin at concentration of 50 µg/ml gave a zone of inhibition of 18 mm.

IV. CONCLUSION

The title compounds were synthesized by Claisen-Schmidt condensation and obtained in good yield. These compounds were purified by recrystalisation and characterized by UV-Visible, IR, NMR and Mass spectra. They were further screened for their antibacterial activity against gram positive bacteria such as *Enterococcus*, *Staphylococcus aureus*, and gram negative bacteria such as *Escherichia coli*, *Pseudomonas aeruginosa* by agar diffusion method. The compounds showed zone of inhibition against only one bacterial strain, *Enterococcus*. Hence, all the six compounds were further tested against the bacterial strain, *Enterococcus* at lower concentrations by taking 2000 µg, 5000 µg and 10000 µg per mL where, only JMC14 gave a zone of inhibition of 14mm at concentration of 2000 µg/mL.

References

[1] E. Middleton, K. Chithan, T.C Theoharides. "The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer". *Pharmacol. Rem.* Vol 52, No. 4, pp 673-751, 2000.

[2] H. Haraguchi, H. Ishikawa, K. Mizutani, Y. Tamura, T. Kinoshita, "Antioxidative and superoxide scavenging activities of retrochalcones in Glycyrrhiza inflate", *Bioorg. Med. Chem*, 6, pp 339–347, 1998.

[3] B. Baviskar, S. Patel, B. Baviskar, S. S. Khadabadi, M. Shiradkar, "Design and synthesis of some novel chalcones as potent antimicrobial agent". *Asian J. Research Chem.*, Vol 1, Issue 2, pp 67-69, 2008.

[4] H. Makita, T. Tanaka, H. Fujitsuka, N. Tatematsu, K. Satoh, A. Hara, H. Mori, "Chemoprevention of 4-nitroquinoline 1-oxide-induced rat oral carcinogenesis by the dietary flavonoids chalcone, 2-hydroxychalcone and quercetin", *Cancer Res.*, 56, pp 4904–4909, 1996.

[5] R. J. Anto, K. Sukumaran, G. Kuttan, M. N. A. Rao, V. Subbaraju, R. Kuttan, "Anticancer and antioxidant activity of synthetic chalcones and related compounds" *Cancer Lett.*, Vol 97, issue 1, pp 33–37, 1995.

[6] R. G. Damazio, A. P. Zanatta, L. H. Cazarolli, L. D. Chiaradia, A. Mascarello, R. J. Nunes, R. A. Yunes, F. R. Barreto Silva, "Antihyperglycemic activity of naphthylchalcones"' *Eur. J. Med. Chem.*, Vol. 45, pp 1332–1337, 2010.

[7] H. K. Hsieh, T. H. Lee, J. P. Wang, J. I. Wang, C. N. Lin, "Synthesis and anti-inflammatory effect of chalcones and related compounds", *Pharm. Res*, Vol 15, pp 39–46, 1998.
[8] C. N. Lin, T. H. Lee, M. F. Hsu, J. P. Wang, F. N. Ko, C. M. Teng, "Dihydroxychalcone as a potent chemical mediator and cyclooxygenase inhibitor", *J. Pharm. Pharmacol.*, Vol 49, pp 530–536, 1997
[9] B. S. Jayashree, Noor Fathima Anjum, Yogendra Nayak, D. Vijay Kumar, "Synthesis of substituted 3-hydroxy flavones for antioxidant and antimicrobial activity", *Pharmacologyonline*. Vol 3, pp 586-595, 2008.
[10] Atta-ur-Rahman, M. I. Choudhary, W. J. Thomsen, Bioassay techniques for drug development, Harward Academic Publishers, 2001, Chapter 1.2., pp 14-26.
[11] B.S. Jayashree, Shakeela Yusuf and D. Vijay Kumar, Synthesis of Some Coumarinyl Chalcones of Pharmacological Interest, *Asian Journal of Chemistry*, Vol. 21, No. 8 , pp 5918-5922, 2009.