Int. J. Chem. Sci.: 11(2), 2013, 1137-1145
ISSN 0972-768X
www.sadgurupublications.com

SPECTROPHOTOMETRIC ANALYSIS OF BOVINE SERUM ALBUMIN IN PRESENCE OF SOME 1-(NAPHTHALEN-3-YL)-3-PHENYLPROP-2-EN-1-ONES

S. GARG and N. RAGHAV*

Department of Chemistry, Kurukshetra University, KURUKSHETRA – 136119 (Haryana) INDIA

ABSTRACT

A series of 1-(naphthalen-3-yl)-3-phenylprop-2-en-1-ones synthesized successfully under solvent free conditions in presence of base were characterized by their IR and PMR spectral data. Thereafter, effect of differently substituted 1-(naphthalen-3-yl)-3-phenylprop-2-en-1-ones was observed on bovine serum albumin in solution. We have found that the synthesized 1-(naphthalen-3-yl)-3-phenylprop-2-en-1-ones interacted with bovine serum albumin irrespective of the nature and position of the substituent.

Key words: Bovine serum albumin, Interaction studies, 1-(naphthalen-3-yl)-3-phenylprop-2-en-1-ones.

INTRODUCTION

Albumin synthesized as preproalbumin, first converted into proalbumin by the cleavage of an N-terminal peptide. After its release from rough endoplasmic reticulum followed by its conversion to albumin in golgi appratus is a soluble, monomeric protein which comprises about one-half of the blood serum protein. Albumin functions primarily as a carrier protein for steroids, fatty acids, and thyroid hormones and plays a role in stabilizing extracellular fluid volume.

Chalcones, the immediate precursors of flavonoids known to possess antioxidant, chemoprotective property[1] are abundantly present in nature starting from ferns to higher plants[2]. Chalcones and their derivatives have been reported to exhibit a wide variety of pharmacological effects including antimalarial[3-6], antiplatelet[7], antiviral[8-10], antibacterial[11-14], antitubercular[15,16], antifungal[17], antitumor[18], antileishmanial[19], analgesic[20, 21], antiulcerative[22], antihyperglycemic[23], antioxidant[24], antiinvasive[25] and cytotoxic[26]. The most common chalcones found in foods are phloretin and its glucoside phloridzin (phloretin 2′-O-β-glucopyranoside), and chalconaringenin. Studies on the bioavailability of chalcones from

*Author for correspondence; E-mail: nraghav.chem@gmail.com

food sources are limited, but synthetic chalcones have been reported to have a wide range of biological properties. In an effort to develop a potent anti-inflammatory and cancer chemopreventive agents a series of chalcones were synthesized[27]. These compounds were tested for their inhibitory effects on the activation of mast cells, neutrophils, macrophages, and microbial cells. It is conceivable that mast cells, neutrophiles, and macrophages are important players in inflammatory disorders[27]. A number of chalcone derivatives have also been identified for their role in inhibition of several important enzymes in cellular systems, such as epoxide hydrolase[28], protein tyrosine kinase[29], xanthine oxidase[30], alkaline phosphatase[31] and quinone reductase[32].

We have reported the interaction of some series of chalcones with BSA. In continuation of our previous work, with 1-(5'-chloro-2'-hydroxyphenyl)-3-(4"-substituted phenyl)-prop-2-en-1-one and their methoxy derivatives[33], 1-phenyl-3-(substituted phenyl)-prop-2-en-1-one[34], 1-(2'-furyl)-3-(substitutedphenyl)-prop-2-en-1-one[35], 1-(2'-thienyl)-3-(substitutedphenyl)-prop-2-en-1-one[36], 1-(4-hydroxyphenyl)-3-(substitutedphenyl)-2-propen-1-ones and 1-(4-nitrophenyl)-3-(substitutedphenyl)-2-propen-1-ones[37], 1-biphenyl-3-(substituted phenyl)-2-propen-1-ones[38], bischalcones[39] with bovine serum albumin. We here report the interaction of bovine serum albumin with 1-(naphthalen-3-yl)-3-(substitutedphenyl)-2-propen-1-ones. This protein is involved in the transportation of a number of compounds including drugs. It is also reported that there is about 80% primary sequence identity between bovine serum albumin and human serum albumin[40]. It is also suggested that the present study performed with BSA can give an insight about the interaction of chalcones with human serum albumin.

EXPERIMENTAL

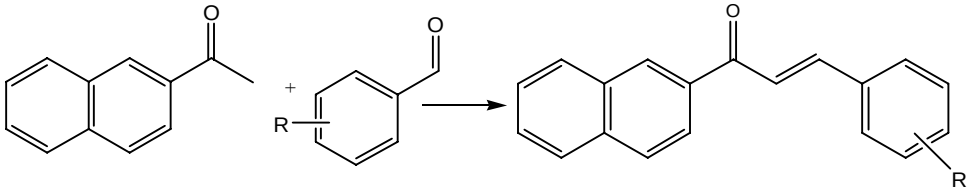
Materials and methods

The reaction progress and purity of products were monitored by thin layer chromatography. Thin layer chromatography was performed with silica-gel G (suspended in $CHCI_3$-EtOH) and plates were viewed under iodine vapors. Melting points were determined by electrochemical capillary Melting points apparatus and are uncorrected. Elisa plate reader, Systronic make was used for measuring absorbance in the visible range. The Lab-India made Spectrofuge (Model 16M) was used for centrifugation purpose.

Synthesis of chalcones

A series of chalcones 1-(naphthalen-3-yl)-3-(substitutedphenyl)-2-propen-1-ones was synthesized by the grinding of substituted benzaldehyde (0.01 mole) with 2-

acetylnapthlene (0.01 mole) in presence of potassium hydroxide (0.01 mole), respectively with a mortar and pestle. The progress of reaction and the purity of the products were confirmed through TLC. The structures were confirmed by their IR and ^{1}HNMR spectra.



2-acetylnapthlene subsituted benzaldehyde 1-(naphthalen-3-yl)-3-(substituted phenyl)-2-propen-1-one

Reaction of chalcones with bovine serum albumin

To 10 mL solution of 0.1 mM BSA, 1 mL solution of 50 mM chalcone solution was added drop wise with constant stirring. After interaction between chalcone and BSA, some albumin gets precipitated. The remaining protein in solution was estimated by biuret method[41]. The results are presented in Fig. 1.

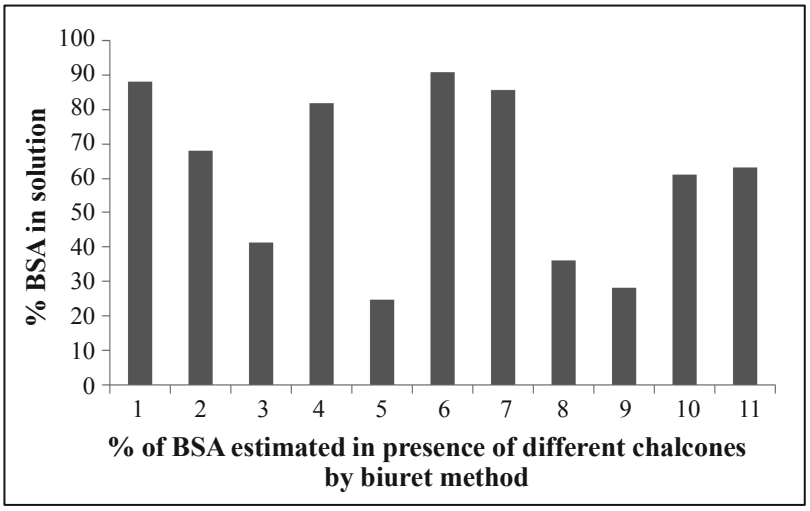


Fig. 1: The results presented are calculated as % of BSA left in solution after interaction with chalcone with respect to control where no chalcone was added but an equal amount of solvent was added

A series 1-(naphthalen-3-yl)-3-phenylprop-2-en-1-ones was synthesized in good yields by Claisen Schmidt reaction between substituted benzaldehydes and 2-acetylnapthlene. Their IR and ^{1}H NMR data are reported in Table 1 and 2.

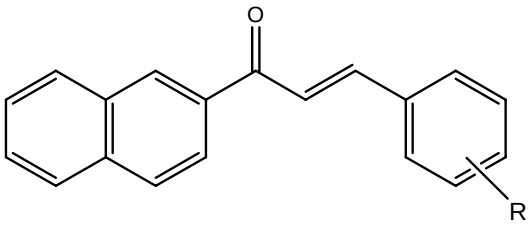


Table 1: IR Data [υ max (cm^{-1})] of Chalcones ($C_{10}H_7$-CO-CH=CH-C_6H_4R)

Comp. No.	R	[C=O]	[C=C]	[CH]	[O-N-O sym]	[O-N-O asym]
1	H	1666	1605	3055	-	-
2	*o*-Cl	1666	1605	3055	-	-
3	*m*-Cl	1659	1605	3078	-	-
4	*p*-Cl	1659	1605	3063	-	-
5	*o*-OCH_3	1659	1597	3063	-	-
6	*m*-OCH_3	1659	1597	3063	-	-
7	*p*-OCH_3	1659	1597	3063	-	-
8	*o*-NO_2	1659	1597	3009	1342	1512
9	*m*-NO_2	1666	1605	2916	1342	1512
10	*p*-NO_2	1659	1605	3070	1350	1528
11	*p*-N(CH_3)	1659	1597	3070	-	-

Table 2: ^{1}H NMR (δ ppm) data obtained for chalcones ($C_{10}H_7$-CO-CH=CH-C_6H_4R)

Comp. No.	R	H-2	H-3	J2-3 (Hz)-	Ar-H	3H, -OCH_3
1	H	7.521 (d)	8.029 (d)	15.6	7.118-8.299 (m)	-
2	*o*-Cl	7.447 (d)	7.685 (d)	15.3	7.199-8.343 (m)	-
3	*m*-Cl	6.678 (d)	7.766 (d)	15.3	7.156-8.456 (m)	-
4	*p*-Cl	7.456 (d)	7.651 (d)	15.1	7.186-8.416 (m)	
5	*o*-OCH_3	7.378 (d)	7.756 (d)	15.6	7.199-8.343 (m)	3.867 (s)

Cont…

Comp. No.	R	H-2	H-3	J2-3 (Hz)-	Ar-H	3H, -OCH_3
6	*m*-OCH_3	7.548 (d)	7.767 (d)	15.6	7.199-8.343 (m)	3.867 (s)
7	*p*-OCH_3	7.587 (d)	8.091 (d)	15.5	7.156-8.456 (m)	3.867 (s)
8	*o*-NO_2	7.652 (d)	7.980 (d)	15.5	7.129-8.526 (m)	-
9	*m*-NO_2	6.965 (d)	7.850 (d)	15.5	7.199-8.343 (m)	-
10	*p*-NO_2	7.357 (d)	8.061 (d)	15.7	7.156-8.456 (m)	-
11	*p*-$N(CH_3)$	7.450 (d)	7.882 (d)	15.7	7.129-8.526 (m)	-

In Table 2, ^{1}H NMR ($CDCl_3$) data of different chalcones are presented. It was observed that C-2 and C-3 protons resonated as doublets with coupling constant ~ 15 Hz. The stereochemistry across C-2, C-3 double bond is Trans. The other protons were revealed at their respective position.

Table 3: Experimental analysis of synthesized chalcones ($C_{10}H_7$-CO-CH=CH-C_6H_4R)

Comp. No.	R-	% of BSA left in solution after interaction with chalcones
1	H	87.90
2	*o*-Cl	67.89
3	*m*-Cl	41.43
4	*p*-Cl	81.74
5	*o*-OCH_3	24.78
6	*m*-OCH_3	90.62
7	*p*-OCH_3	85.5
8	*o*-NO_2	36.23
9	*m*-NO_2	28.42
10	*p*-NO_2	61.11
11	*p*-$N(CH_3)$	63.20

RESULTS AND DISCUSSION

The biological activities exhibited by chalcones and their potential to be used as synthones for the synthesis of large number of heterocyclic compounds have made our interest in the synthesis of a large number of substituted chalcones. The most widely used method used for the synthesis of chalcones involves Claisen-Schmidt condensation of substituted arylaldehyde with the arylmethyl ketones with the help of mortar and pestle by solvent free synthesis. In the present work, we reported solvent free synthesis of a series of chalcones i.e. 1-(naphthalen-3-yl)-3-subsituted phenyl prop-2-en-1-ones by the reaction of substituted benzaldehydes with 2-acetylnapthlene and in the presence of a base.

The synthesis of different chalcones was established by their spectral data. In the IR spectra of chalcones (1-11) as mentioned in Table 1, the peak at 1651-1659 cm-^{1} represent >C=O stretching vibrations which indicate the presence of carbonyl group in conjugation with highly unsaturated system and the results suggests the presence of α, β-unsaturated carbonyl group in the synthesized compounds. The synthesis of chalcones is characterized by the presence of two doublets around δ 7.6-6.6 and δ 8.2-7.5. These represents C-2 and C-3 protons and the geometry across the double bond has been found out to be trans as doublets with coupling constant $J_{2,3}$ is ~ 15.9-15.0 Hz. The aryl and other protons were revealed at their respective position. After establishing the structures of 1-(naphthalen-3-yl)-3-subsituted phenyl prop-2-en-1-ones, their effect were observed on BSA in solution.

We have earlier reported spetrophotometric analysis of BSA in presence of different series of chalcones[33-39]. In the present work, the results are presented on the basis of interaction of serum protein with synthesized 1-(naphthalen-3-yl)-3-subsitutedphenylprop-2-en-1-ones (Fig. 1). The chalcones possess α, β-unsaturated ketone moiety and are therefore highly reactive. The moiety reacts with most nucleophilic group available and therefore has been used as synthons for the synthesis of different types of heterocycles[42]. In proteins also, a number of side chain groups such as thiol, amino, imidazole, alcohol etc. are available. Any of these side chain containing nucleophilic groups can react with α, β-unsaturated ketone group. We propose that nucleophilic groups of BSA react with α, β-unsaturated group in an effective manner. The results suggest that 1-(naphthalen-3-yl)-3-(2-methoxyphenyl)-prop-2-en-1-one is most reactive chalcone as it decreased the availability of BSA in solution to maximum extent. The resulting interactions may cause a change in the three dimensional structure of albumin under study and finally resulting its precipitation out of solution.

CONCLUSION

To conclude, we have synthesized a series i.e. 1-(naphthalen-3-yl)-3-subsituted phenyl prop-2-en-1-ones; by Claisen-Schmidt condensation successfully under solvent free conditions and has been characterized with the help of IR and ^{1}H NMR spectra. These α, β-unsaturated compounds may possess diverse biological activities as reported with this class of compounds. It has been found that these chalcones interact with the bovine serum albumin, a protein mainly responsible for the transportation of a number of compounds.

ACKNOWLEDGEMENT

The authors are thankful to Department of Science and Technology and UGC, New Delhi, for providing financial assistance.

REFERENCES

1. S. M. Kuo, Critical Reviews^{TM} in Oncogenesis, **8**, 47 (1997).
2. C. Mark and D. Nagarathnam, J. Nat. Prod., **54**, 1656 (1991).
3. T. Narender, Shweta, K. Tanvir, M. S. Rao, K. Srivastava and S. K. Puri, Bioorg. Med. Chem. Lett., **15**, 2453 (2005).
4. J. N. Dominguez, J. E. Charris, G. Lobo, N. G. Dominguez, M. M. Moreno, F. Riggione et al., Eur. J. Med. Chem., **36**, 555 (2001).
5. R. Li, G. L. Kenyon, F. E. Cohen, X. Chen, B. Gong and J. N. Dominguez., J. Med. Chem.; **38**, 5031 (1995).
6. M. Liu, P. Wilairat and M. L. Go, J. Med. Chem., **44**, 4443 (2001).
7. L. M. Zhao, H. S. Jin, L. P. Sun, H. Piao and Z. S. Quan., Bioorg. Med. Chem. Lett., **15**, 5027 (2005).
8. S. Cheenpracha, C. Karapai, C. Ponglimanont, S. Subhadhirasakul and S. Tewtrakal., Bioorg. Med. Chem., **14**, 1710 (2006).
9. J. H. Wu, X. H. Wang, Y. H. Yi and K. H. Lee., Bioorg. Med. Chem. Lett., **13**, 1813 (2003).
10. J. E. Wood, M. H. G. Munro, J. W. Blunt, N. B. Perry, J. R. C. Walker and J. N. Ward, J. Bot., **37**, 167 (1999).

11. M. Paramesh, M. S. Niranjan, S. Niazi, S. Shivaraja and M. S. Rubbani, Int. J Pharmacy Pharmaceut. Sci., **2(2)**, 113-117 (2010).

12. H. P. Avila, E. D. Fatima, A. Smania, F. D. Monache and A. S. Junior, Bioorg. Med. Chem., **16**, 9790 (2008).

13. S. F. Nielsen, M. Larsen, T. Bosen, K. Schonning and H. Kromann, J. Med. Chem., **48**, 2667 (2008).

14. D. Batovska, S. T. Parushev, A. Slavova, V. Bankova, I. Tsvetkova, M. Ninova et al., Eur. J. Med. Chem., **42**, 87 (2007).

15. Y. M. Lin, Y. Zhou, M. T. Flavin, L. M. Zhou, W. Nie and F. Chen, Bioorg. Med. Chem., **10**, 2795 (2002).

16. F. C. Chen, Bioorg. Med. Chem., **10**, 2795 (2002).

17. K. L. Lahtchev, D. I. Batovska, P. Parushev, V. M. Ubiyvovk and A. A. Sibirny, Eur. J. Med. Chem., **43**, 2220 (2008).

18. S. K. Kumar, E. Hager, C. Pettit, H. Gurulingappa, N. E. Davidson and S. R. Khan, J. Med. Chem, **46**, 2813 (2003).

19. S. N. Suryawanshi, N. Chandra, P. Kumar, J. Porwal and S. Gupta, Eur. J. Med. Chem., **43**, 2473 (2008).

20. E. J. Leon, M. J. Alcaraz, J. N. Dominguez, J. Charris and M. C. Terencio, Inflamm. Res., **52**, 246 (2003).

21. G. S. Viana, M. A. Bandeira and F. J. Matos, Phytomedicine, **10**, 189 (2003).

22. S. Murakami, M. Muramatsu, H. Aihara and S. Otomo, Biochem. Pharmacol., **42**, 1447 (1991).

23. M. Satyanarayana, P. Tiwari, B. K. Tripathi, A. K. Srivastava and R. Pratap, Bioorg. Med. Chem., **12**, 883 (2004).

24. R. N. Gacche, N. A. Dhole, S. G. Kamble and B. P. Bandgar, J. Enzyme Inhib. Med. Chem., **23(1)**, 28 (2008).

25. S. Mukherjee, V. Kumar, A. K. Prasad, H. G. Raj, M. E. Bracke, C. E. Olson et al., Bioorg. Med. Chem., **9**, 337 (2001).

26. D. N. Dharn, The Chemistry of Chalcones and Related Compounds, Wiley, New York (1981) p. 213.

27. S. J. Won, C. T. Liu, L. T. Tsao, J. R. Weng, H. H. Ko, J. P. Wang et al., Eur. J. Med. Chem., **40**, 103 (2005).

28. C. Morisseau, G. Du, T. W. Newman and B. D. Hammock, Arch. Biochem. Biophys., **356**, 214 (1998).

29. S. Khatib, O. Nerya, R. Musa, M. Shmuel, S. Tamir and J. Vaya, Bioorg. Med. Chem., **13**, 433 (2005).

30. C. N. Khobragade, R. G. Bodade, M. S. Shine, R. R. Deepa, R. B. Bhosale and B. S. Dawane, Enzym. Inhib. Med. Chern., **3**, 341 (2008).

31. N. Raghav, S. Jangra, M. Singh, R. Kaur and A. Rohilla, Int. J Pharmacy Pharmaceut. Sci., **4(2)**, 288 (2012).

32. C. L. Miranda, G. L. M. Aponso, J. F. Stevens, M. L. Deinzer and D. R. Buhler, Cancer Lett., **149**, 21 (2000).

33. Meetu and N. Raghav, Asian J. Chem., **1(7)**, 5475 (2009).

34. N. Raghav and P. Malik, Adv. App. Sci. Res., **2(5)**, 410 (2011).

35. N. Raghav and P. Malik, Res. J. Pharmaceut. Biol. Chem. Sci., **2(4)**, 755 (2011).

36. N. Raghav and P. Malik, Int. J. Appl. Biol. Pharmaceut. Technol., **2(4)**, 218 (2011).

37. N. Raghav and S. Garg, Int. J. Pharm. Pharmaceut. Sci., **4(4)**, 264 (2012).

38. N. Raghav and S. Garg, I. Ravish, Int. J. Pharm. Pharmaceut. Sci., **5(1)**, 372 (2013).

39. N. Raghav, S. Garg and M. Singh, Int. J. Appl. Biol. Pharmaceut. Technol., **2(4)**, 20 (2013).

40. T. J. R. Peter, Adv. Protein Chem., **37**, 161 (1985).

41. A. J. Gornall, C. J. Bradwill and M. M. David, J. Biol. Chem., **177**, 751 (1949).

42. D. N. Dhar, The Chemistry of Chalcones and Related Compounds, Wiley Interscience, New York (1981) p. 228.

Accepted : 24.05.2013