ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Spectrophotometric analysis of bovine serum albumin in presence of synthesized 1-(2'-furyl)-3(substitutedphenyl) -2-propen-1-ones

Raghav N * and Malik P

Department of Chemistry, Kurukshetra University, Kurukshetra-136119 (INDIA)

ABSTRACT

Serum albumin interacts with a vast array of chemically diverse ligands at specific binding sites. In the present work we report binding of bovine serum albumin with chalcones. Chalcones are versatile synthetic and natural intermediates for a variety of compounds and possess diverse pharmacological activities. Series of 1-(2'-furyl)-3(substitutedphenyl)-2-propen-1-ones were synthesized by the Claisen-Schmidt condensation and their effect was observed on the concentration of bovine serum albumin. It was found that the synthesized chalcones interacted with bovine serum albumin irrespective of the nature and position of the substituent.

Key words: Bovine serum albumin, interaction, 1-(2'-furyl)-3(substitutedphenyl)-2-propen-1-ones, chalcones

Corresponding author
Email: nraghav.chem@gmail.com

ISSN: 0975-8585

INTRODUCTION

Serum albumin is a major protein component of blood plasma. It is a soluble, monomeric protein and comprises about one-half of the blood serum protein. It serves as a transport protein for several endogenous compounds. Albumin functions primarily as a carrier protein for steroids, fatty acids, thyroid hormones and is also capable of binding a broad spectrum of therapeutic agents. Half life of a drug can be a result of drug binding to serum albumin. Thus, the binding property of drugs to serum albumin is one of the most important factors determining their pharmacokinetics [1].

Chalcones are very versatile molecules due to their ease of synthesis and diverse biological activities these molecules possess. These are also important synthetic intermediates for the synthesis of different types of heterocyclic compounds. Chalcones have been reported to possess various biological activities such as antimicrobial[2], antiviral[3], antileishmanial[4], antitubercular[5], anticancer[6], anti-inflammatory[7], analgesic[8], antiplatelet[9], antiulcerative[10], antimalarial[11], antioxidant[12], antihyperglycemic[13] and immunomodulatory [14], etc.. Chalcones have been found to inhibit release of chemical mediators [15] and of leukotriene B_4 [16]. A number of enzymes are also reported to be inhibited by chalcones such as nitric oxide synthase, cyclooxygenase [17], glutathione-5-transferases (GST) isolated from mouse liver[18], epoxide hydrolases[19], Mitochondrial monoamine oxidase isolated from rat liver [20], cyclic adenosine monophosphate phosphodiesterase [21], liver xanthine oxidase[22, 23], 5-hydroxytryptophan de-carboxylase [24,25], tyrosinase [26] and aldose reductase [27] etc. In this direction we are working with the interaction of serum albumin with chalcones. It is reported that Human serum albumin and bovine serum albumin share about 80% primary sequence identity with each other [28]. Therefore, the present study performed with BSA can give an idea about the interaction of chalcones with HSA, 1-(5'-chloro-2'-hydroxyphenyl)-3-(4"-substituted phenyl)-prop-2-en-1-one and their methoxy derivatives have already been reported to behave similarly towards BSA and Human serum proteins [29].

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 $CHCl_3$-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- The 1-(2'-furyl)-3(substitutedphenyl)-2-propen-1-ones were synthesized from 2-acetylfuran (0.01 mole), substituted aryl aldehydes (0.01 moles) in presence of potassium hydroxide (0.03 mole) by the method used earlier in our laboratory [29]. The

ISSN: 0975-8585

progress of reaction and the purity of the products were confirmed through TLC. The structures were confirmed by their IR data and 1HNMR.

Reaction of chalcones with Bovine Serum Albumin- 1ml solution of 50 mM chalcone solution was added drop wise to 10 ml solution of 0.1mM BSA with constant stirring. The interaction between chalcone and BSA resulted in precipitation of protein from the solution. The remaining protein in solution was estimated by biuret method [30]. The results are presented in figure 1.

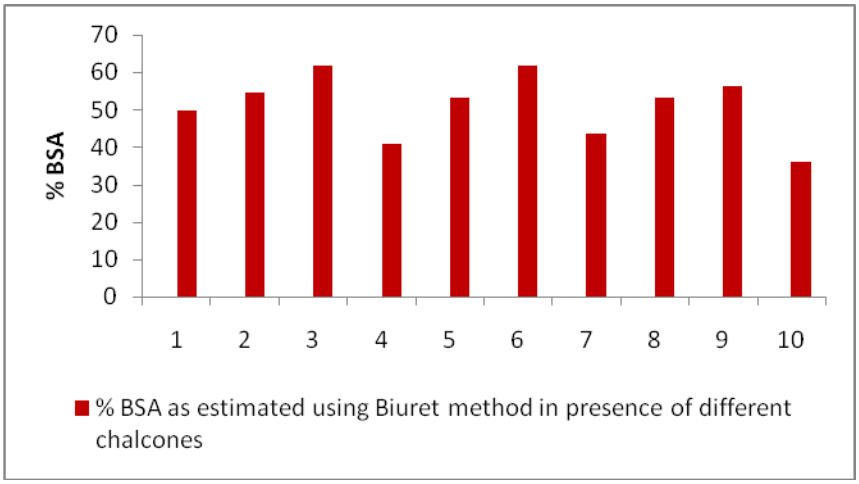


Fig. 1 Effect of 1-(2'furyl)-3-(substituted phenyl) prop-2-en-1-ones on bovine serum albumin

Experimental:

1-(2'-furyl)-3(substitutedphenyl) -2-propen-1-ones were synthesized in good yields by Claisen Schmidt reaction between 2-acetylfuran and substituted benzaldehydes. Their physical parameters such as melting points, Rf values, % yields are reported in Table 1. The given Rf values are determined in benzene. The IR and 1HNMR data of different chalcones is presented in tables 2 and 3 respectively.

Table 1: Physical Parameters of Synthesized Chalcones (C_4H_3O-CO-CH: CH-Ar)

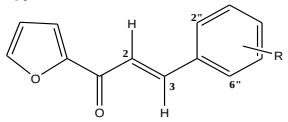
Com pNo	Ar-	Mol. Formula	M. Wt.	M.Pt.(lit) °C	Rf value	% Yield
1	C_6H_5-	$C_{13}H_{10}O_2$	194	90-93 °C	0.581	94.42
2	*o*-Cl-C_6H_4-	$C_{13}H_9ClO_2$	228	62-65 °C	0.605	82.09
3	*m*-Cl-C_6H_4-	$C_{13}H_9ClO_2$	228	60-62 °C	0.593	86.83
4	*p*-Cl-C_6H_4-	$C_{13}H_9ClO_2$	228	120-123°C	0.581	80.20
5	*o*-OMe-C_6H_4-	$C_{14}H_{12}O_3$	234	80-82 °C	0.520	94.97
6	*m*-OMe-C_6H_4-	$C_{14}H_{12}O_3$	234	60-63 °C	0.520	80.48
7	*p*-OMe-C_6H_4-	$C_{14}H_{12}O_3$	234	70-74 °C	0.533	72.76
8	*o*-NO_2-C_6H_4-	$C_{13}H_9NO_4$	239	110-113 °C	0.800	55.56
9	*m*-NO_2-C_6H_4-	$C_{13}H_9NO_4$	239	175-178 °C	0.426	84.57
10	*p*-NO_2-C_6H_4-	$C_{13}H_9NO_4$	239	225-229 °C	0.426	90.61

ISSN: 0975-8585

Table 2: IR Data [$\upsilon_{max}(cm^{-1})$] of Chalcones (C_4H_3O-CO-CH:CH-Ar)

Compound No	Ar-	[C=O]	[C=C]	[CH]	[O-N-O sym]	[O-N-O asym]
1	C_6H_5-	1659	1605	3113	-	-
2	*o*-Cl-C_6H_4-	1659	1605	3087	-	-
3	*m*-Cl-C_6H_4-	1659	1605	3094	-	-
4	*p*-Cl-C_6H_4-	1659	1605	2982	-	-
5	*o*-OMe-C_6H_4-	1651	1589	3132	-	-
6	*m*-OMe-C_6H_4-	1659	1605	3117	-	-
7	*p*-OMe-C_6H_4-	1659	1605	2839	-	-
8	*o*-NO_2-C_6H_4-	1659	1605	3117	1350	1528
9	*m*-NO_2-C_6H_4-	1659	1605	3086	1342	1528
10	*p*-NO_2-C_6H_4-	1659	1605	3150	1345	1530

Table 3: ^{1}HNMR ($CDCl_3$) Data Obtained for Chalcones (C_4H_3O-CO-CH:CH-Ar) δ:



Comp. No	Ar-	H-2	H-3	J_{2-3}(Hz)	Ar-H and Furyl-H	3H,-OCH_3
1	C_6H_5-	6.671 (d)	7.546 (d)	15.3	6.613-7.721(m)	-
2	*o*-Cl-C_6H_4-	7.397 (d)	8.287 (d)	15.3	6.629-7.796(m)	-
3	*m*-Cl-C_6H_4-	7.412 (d)	7.818 (d)	15.3	6.628-7.844(m)	-
4	*p*-Cl-C_6H_4-	7.439 (d)	7.837 (d)	15.0	6.625-7.864(m)	-
5	*o*-OMe-C_6H_4-	7.548 (d)	8.217 (d)	15.9	6.599-7.660(m)	3.940 (s)
6	*m*-OMe-C_6H_4-	7.450 (d)	7.866 (d)	15.6	6.615-7.677(m)	3.878 (s)
7	*p*-OMe-C_6H_4-	7.357 (d)	7.873 (d)	15.6	6.602-7.659(m)	3.876 (s)
8	*o*-NO_2-C_6H_4-	7.652 (d)	7.720 (d)	15.3	6.913-8.621(m)	-
9	*m*-NO_2-C_6H_4-	7.587 (d)	7.687 (d)	15.6	6.652-8.537(m)	-
10	*p*-NO_2-C_6H_4-	6.965 (d)	7.682 (d)	15.9	6.616-8.141(m)	-

RESULTS AND DISCUSSION

The profound biological activities possessed by chalcones and their potential to be used as synthones for the synthesis of large number of heterocyclic compounds have generated considerable interest in the synthesis of a large number of substituted chalcones. One of the most widely used method employed for the synthesis of chalcones involved Claisen-Schmidt condensation of substituted arylaldehyde with the arylmethyl ketones. In the present work we report the synthesis of 1-(2'-furyl)-3(substitutedphenyl) -2-propen-1-ones from 2-acetylfuran and substituted benzaldehydes in the presence of a base.

$$C_4H_3OCOCH_3 + R\text{-}C_6H_4\text{-}CHO \xrightarrow{KOH} C_4H_3OCOCH{:}CHC_6H_4\text{-}R$$

R= H-, *o*-Cl-, *m*-Cl-, *p*-Cl-, *o*-OCH_3, *m*-OCH_3, *p*-OCH_3, *o*-NO_2, *m*-NO_2, *p*-NO_2

The synthesis of different chalcones was established by their spectral data. In the IR spectra of chalcones 1-10 as mentioned in table 2, 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. 1HNMR ($CDCl_3$) data of different chalcones is presented in table 3. 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 the 1-(2'-furyl)-3(substitutedphenyl)-2-propen-1-ones; their effect was observed on BSA in solution. Figure 1 represents the results of the serum protein left in solution after interaction with chalcones. The synthesized 1-(2'-furyl)-3(substitutedphenyl)-2-propen-1-ones possessing α,β-unsaturated ketone moiety are 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 [31]. In proteins also, a number of side chain groups such as thiol, amino, imidazole, alcohol etc. are available. Any of these side chain 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 resulting interactions may cause a change in the three dimensional structure of albumin under study and finally resulting its precipitation out of solution.

CONCLUSION

In summary, we have synthesized 1-(2'-furyl)-3(substitutedphenyl)-2-propen-1-ones by Claisen-Schmidt condensation successfully, which were characterized by TLC, melting point, IR and 1HNMR spectroscopy. The synthesized chalcones may be assumed to have diverse biological activities as has been found in 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.

ACKNOWLEDGEMENTS

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

REFERENCES

[1] Kragh-Hansen U, Chuang VTG and Otagiri M. Biol Pharm Bull 2002; 25: 695.
[2] Mokle SS, Sayeed MA, Kothawar and Chopde. Int J Chem Sci 2004; 2(1): 96.
[3] Onyilagna JC, Malhotra B, Elder M and Towers GHN. Can J Plant Pathol 1997; 19: 133.
[4] Nielsen SF, Chen M, Theander TG, Kharazmi A and Christensen SB. Bioorg Med Chem Lett 1995; 5: 449.

[5] Siva Kumar M, Geetha Babu SK and Mukesh D. Chem Pharm Bull 2007; 55(1): 44.
[6] a) Francesco E, Salvatore G, Luigi M and Massimo C. Phytochem 2007; 68: 939.
b) Beutler JA, Cardellina JH II, Gray GN, Prather TR, Shoemaker RH, Boyd MR, Lin CM, Hamel E and Cragg GM. J Nat Prod 1993; 56: 1718.
c) Wattenberg LW, Coccia JB and Galbraith AR. Cancer Lett 1994; 83: 165.
d) Yit CC and Das NP. Cancer Lett 1994; 82: 65; Ramanthan R, Tan CH and Das NP. Cancer Lett 1992; 62: 217; Satoni Y. Int J Cancer 1993; 55: 506.
[7] Hsieh HK, Tsao LT and Wang JP. J Pharm Pharmacol 2000; 52: 163.
[8] Viana GS, Bandeira MA and Matos F. J Phytomed 2003; 10: 189.
[9] Zhao LM, Jin HS, Sun LP, Piao HR and Quan ZS. Bioorg Med Chem Lett 2005; 15: 5027.
[10] Mukarami S, Muramatsu M, Aihara H and Otomo S. Biochem Pharmacol 1991; 42: 1447.
[11] Liu M, Wilairat P and Go LM. J Med Chem 2001; 44: 4443.
[12] Miranda CL, Aponso GLM, Stevens JF, Deinzer ML and Buhler DR. J Agric Food Chem 2000; 48: 3876.
[13] Satyanarayana M, Tiwari P, Tripathi K, Srivastava AK and Pratap R. Bioorg Med Chem 2004; 12: 883.
[14] Barford L, Kemp K, Hansen M and Kharazmi A. Int Immunopharmacol 2002; 2: 545.
[15] KO HH, Tsao LT, Yu KL, Liu CT, Wang JP and Lin CN. Bioorg Med Chem 2003; 11: 105.
[16] Deshpande AM, Argade NP, Natu AA and Eckman. Bioorg Med Chem 1999; 7: 1237.
[17] Ahmad S, Sraf DA, Lajis NHj, Shaari K, Mohamed H, Wanab AA, Arifin KT, Hoo WY, Aziz NA, Kadir AA, Sulaiman MR, and Somchit MN. Eur J Pharmacol 2006; 188: 538.
[18] Miyamoto T, Silva M and Hammock BD. Arch Biochem Biophys 1987; 203: 254.
[19] Mullin CA and B. D. Hammock BD. Arch Biochem Biophys 1982; 423: 216.
[20] Tanaka S, Kuwai Y, and Tabata M. Planta Med 1987; 5: 53.
[21] Nikaido T, Ohmoto T, Nomura T, Fukai T and SankawaU. Chem Pharm Bull 1984; 32: 4929.
[22] Martin GJ, Beiler JM and Avakian S. US Patent 1956; 2,769,817; Chem Abst 1957; 51: 14815d.
[23] Beiler JM, Graff M and Martin GJ. Am J Digestive Diseases 1952; 19: 333; Chem Abst 1953; 47: 1198e.
[24] Kamoda M, Chiba T, Mori K and Ito N. Botyu Kagaku 1953; 18: 117; Chem Abst 1954; 48: 778c.
[25] Yuwiler A, Geller E and Elduson S. Arch Biochem Biophys 1969; 89: 143; Chem Abst 1960; 54: 21222c.
[26] Khatib S, Nerya O, Musa R, Shmnel M, Tamir S and Vaya J. Bioorg Med Chem 2005; 13: 433.
[27] Severi F, Benvenuti S, Costantino L, Vampa G, Melegari M and Antolini L. Eur J Med Chem 1998; 33: 859.
[28] Peters TJr. Advances in Protein Chemistry 1985; 37: 161.
[29] Meetu and Raghav N. Asian J Chem 2009; 21(7): 5475.
[30] Gornall AJ, Bradwill CJ and David MM. J Biol Chem 1948; 177: 751.
[31] Dhar DN. The Chemistry of chalcones and related compounds, Wiley Interscience, New York, 1981; 228.