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ARTICLE

Study on Interaction of Drug to Bovine Serum Albumin and Serum by UV-Visible Spectroscopy

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ABSTRACT

The interaction of drugs (troxerutin, dibazol and reserpine) to bovine serum albumin (BSA) and serum was investigated by UV-visible spectroscopy under simulative physiological conditions. The results showed that there is a kind of new complex between drugs and bovine serum albumin and serum. Comparing the absorption spectra of interaction between three drugs and bovine serum albumin, it can be concluded that there is a large interaction in the system of reserpine with bovine serum albumin and there is a large blue in the system of dibazol and bovine serum albumin. It is significant to study the interaction between drugs and bovine serum albumin and serum for understanding of troxerutin's toxicity and its distribution in the organism.

KEYWORDS

Bovine serum albumin, Serum, Troxerutin, Dibazol, Reserpine, UV-visible spectroscopy.

INTRODUCTION

Serum albumins are one of the most abundant proteins in blood plasma, which play an important role in the transportation and deposition of many drugs molecules in the blood [1]. It is known that the binding ability of drug-albumin may have a significant impact on distribution, free concentration and the metabolism of drug [2]. Hence, studies on the interaction of drugs and serum albumins are significant for elucidating action mechanism, toxicity and dynamic of drugs at the molecular level. Among the serum albumins, bovine serum albumin (BSA) has a wide range of physiological functions involving the binding, transportation and delivery of fatty acids, porphyrins, bilirubin, steroids, *etc*. It is considered to be good compound for specific binding sites for metals, pharmaceuticals and dyes. Bovine serum albumin is a single-chain 582 amino acid globular nonglycoprotein cross-linked with 17 cystine residues (eight disulfide bonds and one free thiol) [3].

Many drugs, including anticoagulants, tranquillizers and general anaesthetics, are transported in the blood while bound to serum albumins [4]. The binding ability of drug-albumin in blood stream may have a significant impact on distribution, free concentration and metabolism of drug. It is then important to study the binding parameters in order to know and try to control the pharmacological response of drugs and design of dosage forms.

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We have already reported the spectroscopic studies to characterize the interaction drug (troxerutin, dibazol and reserpine) and bovine serum albumin by fluorescence spectroscopy [5-8]. The present paper deals with the interaction between drug (troxerutin, dibazol and reserpine) and bovine serum albumin (and serum) by UV-visible spectroscopy and discusses the characteristics of absorption spectra. This kind of studies may provide salient information for understanding of drug's toxicity and its distribution in the organism and hence become an important research field in chemistry, life science and clinical medicine.

EXPERIMENTAL

Bovine serum albumin was purchased from Boquan Biochemical Technology Co., Ltd. (Nanjing, China) and used without further purification. Troxerutin was obtained from Shanxi Yabao Pharmaceutical Group Co. Ltd. (Shanxi, China). Reserpine was obtained from Guangdong Bangmin Pharmaceutical Group Co., Ltd. (Jiangmen, China). Dibazol was obtained from Shanghai Qingping Pharmaceutical Group Co., Ltd. (Shanghai, China). Bovine serum albumin stock solution (7.9×10^{-4} mol L^{-1}) was prepared in pH 7.4 phosphate buffer solution containing 0.1 mol L^{-1} NaCl. The troxerutin, dibazol and reserpine solution (6.0×10^{-4} mol L^{-1}) was prepared in pH 7.4 phosphate buffer solution, respectively. All other chemicals were of analytical reagent grade and double distilled water was used throughout.

The absorption spectrum was recorded with a UV-3600PC spectrophotometer (Shimadzu, Japan) equipped with 1.0 cm quartz cell.

Procedures: A quantitative analysis of the potential interaction between drug (troxerutin, dibazol and reserpine) and bovine serum albumin was performed by fluorimetric titration. About 3 mL solution containing appropriate concentration of bovine serum albumin (1.0×10^{-6} mol L^{-1}) was titrated by successive additions of 6.0×10^{-5} mol L^{-1} stock solution of drug. Titrations were done manually by using micro-injector. The absorption spectra were recorded at room temperatures.

RESULTS AND DISCUSSION

Fig. 1 shows the UV-visible spectra of bovine serum albumin and it's interaction with drug (troxerin, dibazol and reserpine). According to Fig. 1, the absorption peak and absorbance of absorption spectra of the drug and bovine serum albumin system have significantly changed, which reveals that there are different complexes between three drugs and bovine serum albumin.

The maximum absorption wavelength of bovine serum albumin is about 278 nm, which is mainly produced by tryptophan (containing conjugated double bonds). B absorption bands was formed after bovine serum albumin absorbing UV light and producing $\pi \rightarrow \pi^*$ transitions, resulting in 278 nm absorption peak. For troxerutin-bovine serum albumin system, the absorption peak of the system is about 270 nm, which shows that the maximum absorption wavelength of system occurs about 8 nm blue shift *versus* bovine serum albumin and the absorbance of system has been enhanced. For dibazol-bovine serum albumin system, the absorption peak of the system is about 269 nm, which shows that the maximum absorption wavelength of system occurs about 9 nm blue shift *versus* bovine serum albumin and the absorbance of system has been enhanced. For reserpine-bovine serum albumin system, the absorption peak of the system is about 272 nm, which shows that the maximum absorption wavelength of system occurs about 6 nm blue shift *versus* bovine serum albumin and the absorbance of system has been enhanced.

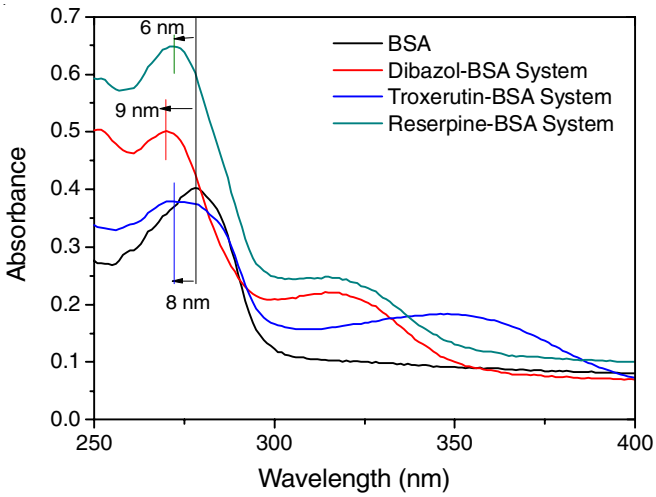

Fig. 1. Absorption sptectra of the interaction of drug (troxerutin, dibazol and reserpine) with bovine serum albumin

According to the previous report [9], the reason of the absorption peak shift is mainly due to impurities in the reagents and solvents in the sample coexistence material, environment and equipment and other factors. During the absorption peak shift, usually accompanied by peak height, peak number, peak shape, especially the fine structural changes of the peak. The absorption peak usually can be divided into interference with absorption, monochromatic nature and measured on properties to change the three categories according to the absorption peak displacement causes. Regardless of the type caused by the absorption peak absorption peak displacement, as long as the light absorbing composition to stimulate the change of the state or ground state energy and the ground state to an excited state energy increases. In both cases, its absorption peak show blue shift otherwise, then a red shift. Accompanied by red shift, peak shape, peak height, there will be changes. The greater the energy change, the consequences become more significant. The absorption peak blue shift of the interaction of bovine serum albumin with drug (troxerutin, dibazol and reerpine) shows that the ground state to an excited to reduce the energy from the energy point of view.

The absorption peak and absorbance of interaction of bovine serum albumin with three drugs (troxerutin, dibazol and reserpine) is about 270 nm, 269 nm, 272 nm and 0.353, 0.499 and 0.353, respectively. The results show that there is a big difference about three absorption spectra. There is a large interaction in the system of reserpine with bovine serum albumin and there is a large blue shift (9 nm) in the system of dibazol and bovine serum albumin.

As shown in Fig. 2, serum's absorption spectroscopy has two peaks in 279 nm and 416 nm, respectively and the

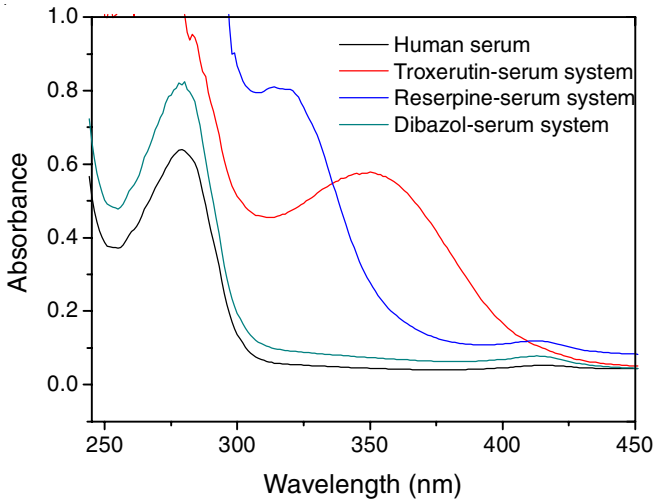

Fig. 2. Absorption spectra of serum and the system of interaction of serum with drug

absorbance of absorption peak located in 279 nm is much larger than located in 416 nm. Two typical absorption peaks at 279 nm and 416 nm, provide an experimental basis for choosing the suitable excitation wavelength to studying the human serum fluorescence spectroscopy. In addition, the light absorption of UV region of serum is much larger than the absorption located in visible light region, especially in the range of 255 to 300 nm. For troxerutin-serum system, the absorption spectroscopy of human serum has obviously changed after interacting with troxerutin. The serum of the two typical absorption peaks at 279 nm and 416 nm merge into an absorption peak at 350 nm and the maximum absorption peak position the red shift (279 nm to 350 nm) and the reasons is that the conformation of the protein is changed. For dibazol-serum system, there is a wave peak at 280 nm and 413 nm, respectively. The results show that the absorption of the system at UV region is much larger than visible light region, which is somewhat similar to human serum. Comparing the absorption spectra before and after serum interacts with dibazol, it can be found that its absorbance changed, but the absorption peak position unchanged. For reserpine-serum system, there is a wave peak at 316 nm and 412 nm. Comparing the serum and reserpine-serum system, the more obvious peaks in the serum by the 279 nm changes to 316 nm; another peak to 412 nm by 416 nm changes. These show that there is an interaction between human serum and reserpine.

Conclusion

In conclusion, this study shows that the absorption spectra of the interaction between drug (troxerutin, dibazol and reserpine) and bovine serum albumin and serum by UV-visible spectroscopy under simulative physiological conditions. The results show that three difference types of complexes between drug and bovine serum albumin (or serum). There a blue shift after drug (troxerutin, dibazol and reserpine) interacts with bovine serum albumin (or serum). The result may help to provide some information for understanding of drug's toxicity, its distribution in the organism and clinical application.

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