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Stability and Toxicology of the Controlled-release Tablets of Sasanquasaponin-Casein

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Abstract. The light stability, wet stability and thermal stability of the controlled-release tablets of sasanquasaponin (SQS)-casein were studied, respectively. The median lethal dose of SQS and the controlled-release tablets of SQS-casein were studied respectively. After strong light illumination the controlled-release tablets of SQS-casein for 5 days and 10 days respectively and placement the controlled-release tablets of SQS-casein for 5 days and 10 days respectively in humidity being 75±5, respectively, the release rates of the controlled-release tablets of SQS-casein meet the requirements of United States Pharmacopoeia, and the controlled-release tablets of of SQS-casein release SQS by slowness and constant in 12h. When humidity were 90±5% , the release rates of the controlled-release tablets of SQS-casein meet the requirements, but the controlled-release tablets of of SQS-casein do not release SQS by constant in 12h. When temperatures were 40±2℃ and 60±2℃ respectively, the release rates of the controlled-release tablets of SQS-casein does not meet the requirements. The anti-high temperature and moistureproof measures are required in production, packaging, transportation and storage of the controlled-release tablets of SQS-casein. The toxicity of the controlled-release tablets of SQS-casein is much lower than that of SQS.

Introduction

Casein is the main component of milk protein, which not only has a good nutrition, but also has good biocompatibility with the human body. Casein can be used for accessories [1]. Sasanquasaponin (SQS) has a very abundant origin source in China and other Asian Countries, which is a traditional Chinese herb's effective component obtained from camellia oleifera [2, 3]. SQS is a kind of saponin, whose chemical structure is similar to those of ginseng saponin and other saponins [2-4]. SQS has many pharmacological effects similar to ginseno-side, including anti-inflammation, anti-hyperlipidemia and anti-effusion [5-7]. SQS suppressed the cardiac arrhythmias, prevented against ischemiain-duced decrease in contract force and promoted the force recovery from reperfusion [2, 3]. It is known that SQS has multifunctional pharmacolo-gicalactions including its anti-arrhythmia, anti-ischemia, and antihyperlipi-demia, antihypertension and other cardioprotective effects. SQS is a hopeful candidate for development of new therapeutic drugs. When SQS was used as medicine of cardiovas- cular system, the half-life of SQS was short [2]. The controlled-release tablets of SQS were prepared with SQS to solve the problem of short the half-life of SQS [8]. Studies of the stability and toxicity of the controlled-release tablets of SQS-casein have important significance for clinical application of the controlled-release tablets of SQS-casein.

In this paper, the light stability, wet stability and thermal stability of the controlled-release tablets of SQS-casein were studied, respectively. The median lethal dose of SQS and the controlled-release tablets of SQS-casein were studied respectively.

Experimental

The controlled-release tablets of SQS-casein were prepared according to [1] using the following procedure. Weighed amount of SQS, casein and guar gum were mixed, screening mixed 30 times, ground and got the controlled-release powders. Weighed amounts of the controlled-release powders, the controlled-release powders were putted into Φ = 1.3mm model of stainless steel, pressed into tablet with 1MPa pressure. The composition of the controlled-release tablets of SQS-casein were SQS: casein: guar gum = 60: 30: 15 (mass ratio).

The strong light test, humidity test and high-temperature test of the controlled-release tablets of SQS-casein were tested on Binder APT-COM pharmaceutical stability chamber, respectively. Release rates of the controlled-release tablets of SQS were determined before and after the strong light tests, humidity tests and high-temperature tests, respectively.

Release rates of the controlled-release tablets of SQS were determined as the Chinese Pharmacopoeia Appendix XD first method, dissolution test used installation of the second method [9]. The release rates of the controlled-release ctablets of SQS-casein were determined by SR8-Plus release ratetester. Distilled water of degasification 500ml was added in release cup, water temperature was 37±0.1℃, mixing speed at 50r/min, took 3ml suction at 1h, 3h, 6h, 9h, 12h, respectively. The amount of SQS was determined with vanillin colorimetric method [1], calculated the cumulative release rate.

The toxicology of the controlled-release tablets of SQS-casein were studied using the following procedure. 48 C57BL6J male mice (8～10 weeks old) were randomly divided into two experimental groups. One experimental group of mice were fed with SQS, another experimental group of mice were fed with SQS-casein, once a day and for a week. The drug concentrations were 0, 100, 300 and 500mg/kg (100, 300, 500 times of normal concentrations), respectively.

Results and discussion

Fig.1 shows the results of the strong light test of the controlled-release tablets of SQS-casein. As can be seen in Fig.1, after strong light illumination the controlled-release tablets of SQS-casein for 5 days and 10 days respectively, the release rates of the controlled-release tablets of SQS-casein meet the requirements of United States Pharmacopoeia at dissolution time being 3h, 6h and 12h respectively, the requirements of United States Pharmacopoeia are that the release rate of the controlled-release tablet are in 20～40%, 45～75% and >75%, respectively at dissolution time being 3h, 6h and 12h respectively. And the controlled-release tablets of SQS-casein release SQS by slowness and constant in 12 h. Because the effects of strong light illumination on release rate of the tablets of SQS-casein was little, not need protective light illumination measures in production, packaging, transportation and storage of the controlled-release tablets of SQS-casein.

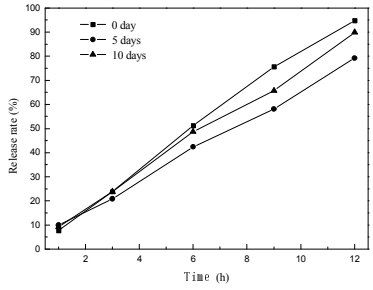

Fig.1 The results of the strong light test of the controlled-release tablets of SQS-casein

Fig.2 shows the results of the humidity test of the controlled-release tablets of SQS-casein. As can be seen in Fig.2a, after placement the controlled-release tablets of SQS-casein for 5 days and 10 days respectively in humidity being75±5 %, the release rates of the controlled-release tablets of SQS-casein meet the requirements of United States Pharmacopoeia at dissolution time being 3h, 6h and 12h respectively, and the controlled-release tablets of of SQS-casein release SQS by slowness and constant in 12 h. As can be seen in Fig.2b, after placement the controlled-release tablets of

SQS-casein for 5 days and 10 days respectively in humidity being 90±5%, the release rates of the controlled-release tablets of SQS-casein meet the requirements of United States Pharmacopoeia at dissolution time being 3h, 6h and 12h respectively, but the controlled-release tablets of of SQS-casein do not release SQS by constant in 12 h. Then, the moistureproof measures are required in production, packaging, transportation and storage of the controlled-release tablets of of SQS-casein.

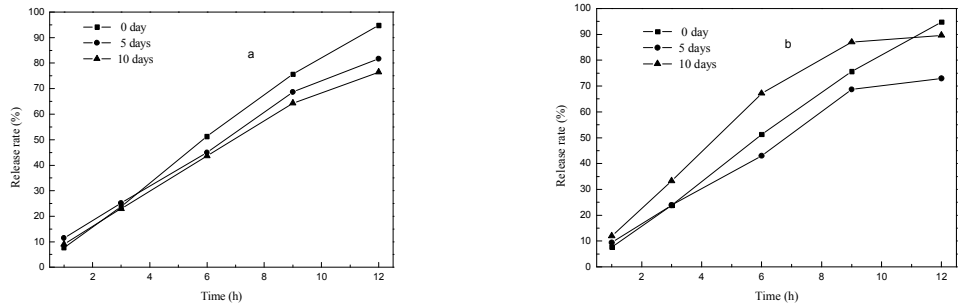

Fig.2: The results of the humidity test of the controlled-release tablets of SQS-casein.
a: 75±5%; b: 90±5%

Fig.3 shows the results of the high-temperature test of the controlled-release tablets of SQS-casein. As can be seen in Fig.3, after placement the controlled-release tablets of SQS-casein for 5 days and 10 days respectively in temperature being 40±2℃ and 60±2℃ respectively, the release rates of the controlled-release tablets of SQS-casein does not meet the requirements of United States Pharmaco-poeia. Then the anti-high temperature measures are required in production, packaging, transportation and storage of the controlled-release tablets of of SQS-casein.

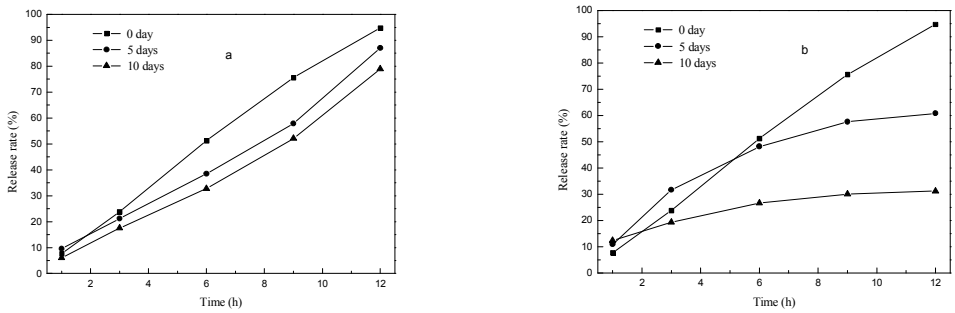

Fig.3 The results of the high-temperature test of the controlled-release tablets of SQS-casein
a: 40±2℃; b: 60±2℃

Fig.3 shows the results of the high-temperature test of the controlled-release tablets of SQS-casein. As can be seen in Fig.3, after placement the controlled-release tablets of SQS-casein for 5 days and 10 days respectively in temperature being 40±2℃ and 60±2℃ respectively, the release rates of the controlled-release tablets of SQS-casein does not meet the requirements of United States Pharmacopoeia. Then the anti-high temperature measures are required in production, packaging, transportation and storage of the controlled-release tablets of of SQS-casein.

Fig.4 shows the results of the median lethal dose test of the controlled-release tablets of SQS-casein. As can be seen in Fig.4, as the concentration of SQS and the controlled-release tablets of SQS-casein being same, mice of oral the controlled-release tablets of SQS-casein mortality are much lower than that of oral SQS. The toxicity of the controlled-release tablets of SQS-casein is much lower than that of SQS.

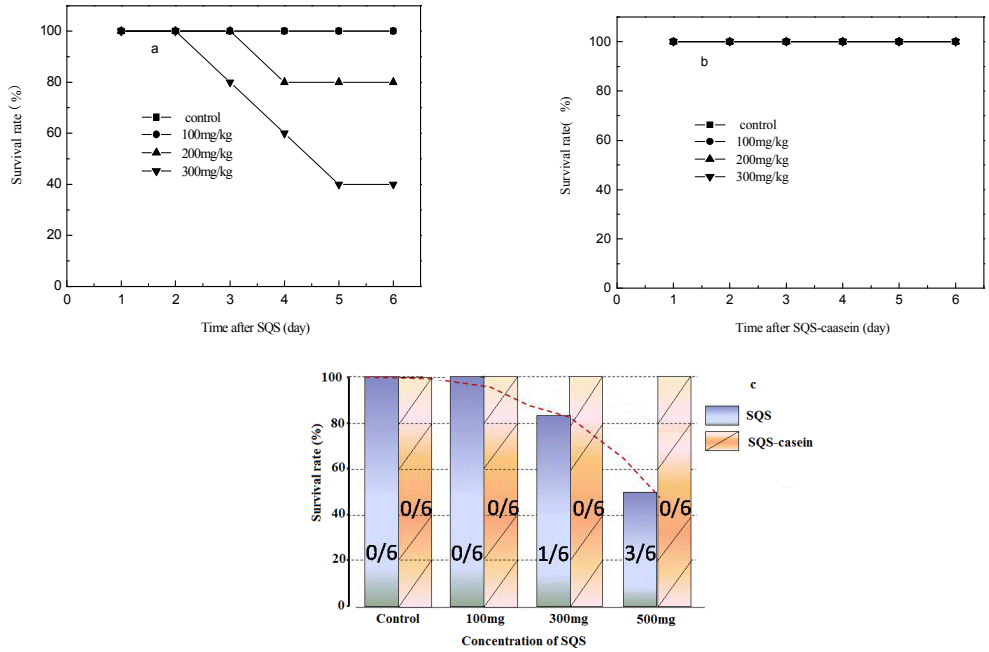

Fig.4: The results of the median lethal dose test of the controlled-release tablets of SQS-casein a: SQS; b: SQS-casein; c: mice mortality by different SQS concentrations

Conclusions

After strong light illumination the controlled-release tablets of SQS-casein for 5 days and 10 days respectively and placement the controlled-release tablets of SQS-casein for 5 days and 10 days respectively in humidity being75±5%, respectively, the release rates of the controlled-release tablets of SQS-casein meet the requirements of United States Pharmacopoeia, and the controlled-release tablets of of SQS-casein release SQS by slowness and constant in 12h. When humidity and temperature were 90±5%, the release rates of the controlled-release tablets of SQS-casein meet the requirements, but the controlled-release tablets of of SQS-casein do not release SQS by constant in 12h. When temperature were 40±2℃ and 60±2℃ respectively, the release rates of the controlled-release tablets of SQS-casein does not meet the requirements. The anti-high temperature and moistureproof measures are required in production, packaging, transportation and storage of the controlled-release tablets of of SQS-casein. The toxicity of the controlled-release tablets of SQS-casein is much lower than that of SQS.

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References

[1] X.Z. Liu, J.H. Yang, L.L. Song, Z.F. Lai and X.Q. Zhu: Spectroscopy and Spectral Analysis. Vol.32 (2012), p. 1650

[2] Z.F. Lai, Y.Z. Chen, J. Chen and X.Z Liu: Chinese Herbal Drug Research Trends. Nova Science Publishers, Inc. NY (2007), p.147

[3] Z.F. Lai, Z.Q. Shao, Y.Z. Chen, M. He: J. Pharmacol. Sci. Vol. 94 (2004), p. 313

[4] Q.R. Huang, S.Y. Cao, M. He, P. Li and W.J. Peng: Chinese Journal of Clinical harmacology and Therapeutics. Vol.8 (2003), p. 170

[5] J. Chen, D. Liu and H.P. Chen: Chinese Pharm. Bulletin. Vol. 23 (2007), p. 724

[6] Q.R. Huang, M. He and Y.C. He: Chinese Traditional and Herbal Drugs. Vol. 36(2005), p.1831

[7] Q.R. Huang, Y.C. Dai, M. He and Y.M. Luo: Chinese Pharmacological Bulletin. Vol.21 (2005), p. 1092

[8] X.Z. Liu, J. Chen and Z.F. Lai: ZL200810042744.4, 2008-9-11

[9] State Pharmacopoeia Commission: Chinese Pharmacopoeia, 2005 edition. Chemical Industry Press. Beijing (2005).