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Preparation of Controlled-release Tablets of Sasanquasaponin

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Abstract. The controlled-release tablets of sasanquasaponin (SQS) were prepared by using SQS, hydroxypropyl methyl cellulose, ethylcellulose and lactose as the main drug, skeleton material and fillers, respectively. The effects of the dosage of hydroxypropyl methyl cellulose and ethylcellulose on release rate were studied. The release rate curve of the data of the prescription of the controlled-release tablets of SQS were fitted as zero order, one order and Higuchi equation. The release rate of the controlled-release tablets of SQS were controlled by controlling the dosage of hydroxypropyl methyl cellulose and ethylcellulose. The influence of the dosage of hydroxypropyl methyl cellulose on release rate of the controlled-release tablets of SQS was the biggest factor. The prescription of the controlled-release tablets of SQS contains in each piece: SQS 200mg, hydroxypropyl methyl cellulose 40mg, ethylcellulose 30mg, lactose 30mg. The controlled-release tablets of SQS release SQS by slowness and constant in 12h.

Introduction

Sasanquasaponin (SQS) is a traditional Chinese herb's effective component obtained from Camellia oleifera, which has a very abundant origin source in China and other Asian Countries [1, 2]. SQS is a kind of saponin, whose chemical structure is similar to those of ginseng saponin and other saponins [3-6]. SQS inhibited leukocyte adhesion to endothelial cells induced by heat-stress in HUVECs. This inhibitor effect of SQS was in a dose dependent manner [7, 8]. SQS has very wide and protective actions on cardiovascular system [4]. SQS inhibited the isopreterenol-induced elevation of S-T in electrocardiogram of rat hearts [9]. Total numbers of elevated S-T and mean amplitude of S-T were significantly decreased in SQS-treated group compared with that in I-R-only group. SQS may antagonize the changes of malondialdehyde, superoxide dismutase and glutathione peroxidase induced by isoproterenol, revealing the relationship to a dose-dependence manner. SQS is most likely to possess the capabilities of anti-oxygen free radicals and anti-lipoperoxidation to myocardialis-chemic injury induced by isoproterenol [9].Effects of sasanquasaponin on injury of endothelial cells: SQS has protective effects on injury of endothelial cells induced by hypoxia-reoxygenation and neutrophil adhesion [10]. SQS at high concentrations (>12.5mg/ml) has relative strong inhibitionary effects on straphylocooccuuaureus direcetly [11]. Recent studies from Huang and colleagues also showed that SQS inhibited the ischemia and reperfusion-induced injury by anti- oxygen free radicals and antilioperoxidation in myocardial ischemia in rats [9]. After oral administration of SQS by using the does at 100 mg/kg, 200 mg/kg and 400mg/kg/0.2ml per day for 3 months, there are no toxicity effects found for SQS on liver, kidney and heart and on development of rats [12]. It is known that SQS has multifunctional pharmacologicalactions including its anti-arrhythmia, anti-ischemia, anti-inflammation, and antihyperlipidemia, antihypertension and other cardioprotective effects. SQS may

have no or few deleterious effects even though SQS still need to be received more stringent and systemic pharmacological, pharmaceutical or chemical, and pharmacokinetic investigations. SQS is a hopeful candidate for development of new therapeutic drugs. When SQS was used as medicine of cardiovascular 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 [13, 14].

In this paper, the controlled-release tablets of SQS were prepared by using SQS, hydroxypropyl methyl cellulose (HPMC), ethylcellulose(EC) and lactose as the main drug, skeleton material and fillers, respectively. The effects of the dosage of hydroxypropyl methyl cellulose and ethylcellulose on release rate were studied. The release rate curve of the data of the prescription of the controlled-release tablets of SQS were fitted as zero order, one order and Higuchi equation.

Experimental

The controlled-release tablets of SQS were prepared by the equivalence increase method [13] using the following procedure. Weighed amount of HPMC, EC, lactose, and SQS were mixed, screening mixed 30 times, soft materials were prepared by adding 90% ethanol solution. The soft materials were dried at 50℃ for 3h, 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 2MPa pressure. The controlled-release tablets of SQS were also prepared as control with HPMC, lactose, SQS and EC, lactose, SQS as raw material, respectively.

Release rate 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 [15]. The release rate of the controlled-release tablets of SQS were determined by SR8-Plus release rate tester. 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 [16], calculated the cumulative release rate.

Results and discussion

The release rate with different dosages of HPMC and EC are shown in Fig.1. According to Fig.1, when HPMC and EC is only used as skeleton material in preparing controlled-release tablets of SQS, the release rate of the controlled-release tablets of SQS is too slow and fast respectively.

SQS and HPMC are 200mg/tablet and 40mg/tablet respectively. The influence dosages of EC on release rate of the controlled-release tablets of SQS are shown in Fig.2. According to Fig.2, when dosages of EC are 20mg / tablet and 40mg/tablet, the release rate of the controlled-release tablets of SQS are 44.5% and 41.5% respectively in 3h, overshoot required value of 20%～40%. When the

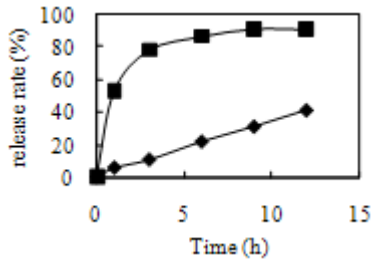

Fig.1 The releasing rate with different dosages of HPMC and EC
◆- SQS: 200mg/tablet, HPMC: 100mg/tablet; ■−SQS: 200mg/tablet, EC: 100mg/tablet

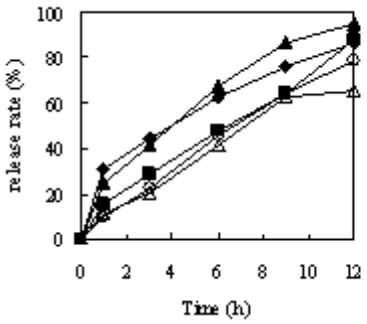

Fig.2 The influence dosages of EC on release rate of the controlled-release tablets of SQS
◆- EC: 20mg/tablet, lactose: 40mg/tablet;
■- EC: 30mg/tablet, lactose: 30mg/tablet;
▲- EC: 40mg/tablet, lactose: 20mg/tablet;
○- EC: 50mg/tablet, lactose: 10mg/tablet;
△- EC: 60mg/tablet

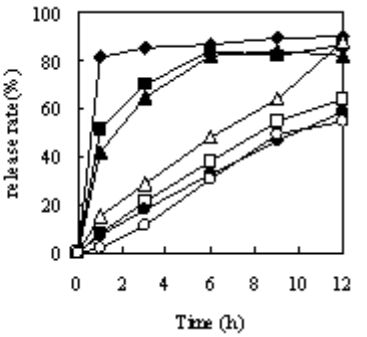

Fig.3 The influence dosages of HPMC on release rate of the controlled-release tablets of SQS
◆- HPMC: 10mg/tablet, lactose: 60mg/tablet;
■- HPMC: 20mg/tablet, lactose: 50mg/tablet;
▲- HPMC: 30mg/tablet, lactose: 40mg/tablet;
△- HPMC: 40mg/tablet, lactose: 30mg/tablet;
□- HPMC: 50mg/tablet, lactose: 20mg/tablet;
●- HPMC: 60mg/tablet, lactose: 10mg/tablet;
○- HPMC: 70mg/tablet

dosage of EC is 60mg / tablet, the release rates of the controlled-release tablets of SQS are 20.3%, 41.5% and 65.5% in 3h, 6h, 12h, respectively, the releasing rates are not required value. When the dosage of EC are 30mg / tablet and 50mg/tablet respectively, the releasing rates are required value, the linearity of release rate curve of the dosage of EC is 30mg / tablet is better than that of the dosage of EC is 50mg / tablet.

SQS and EC are 200mg/tablet and 30mg/tablet respectively. The influence dosages of HPMC on release rate of the controlled-release tablets of SQS are shown in Fig.3. According to Fig.3, the release rates of the controlled-release tablets of SQS are controlled by controlling the dosage of HPMC and EC. The influence of the dosage of HPMC on release rate of the controlled-release tablets of SQS is the biggest factor, with the increase in the dosage of HPMC release rate growing slowly. When dosages of HPMC are 10mg/tablet, 20mg / tablet and 30mg/tablet, the releasing rates overshoot large required value. When dosages of HPMC are 50mg/tablet, 60mg / tablet and 70mg/tablet, the releasing rates are less than that of required value. When the dosage of HPMC is 40mg/tablet, the releasing rate is required value; the linearity of release rate curve is well. The prescription of the controlled-release tablets of SQS contains for each piece: SQS 200mg, HPMC 40mg, EC 30mg, lactose 30mg.

The release rate curve of the data of the prescription of the controlled-release tablets of SQS are fitted as zero order, one order and Higuchi equation, the results shown in Table 1. As can be seen in Table 1, the correlation of zero order equation is the best; the controlled-release tablets of SQS release SQS by slowness and constant in 12 h.

Table 1 Kinetics of the controlled-released tablets

Type of equation	Formula	Correlation coefficient
zero order equation	y=6.6408t+8.851	r=0.998
one order equation	In(1-y)=-0.1672t+4.7812	r=0.947
Higuchi equation	y=28.715t1/2-18.183	r=0.982

Conclusions

The controlled-release tablets of SQS are prepared by using SQS, HPMC, EC and lactose as the main drug, skeleton material and fillers. The releasing rate of the controlled-release tablets of SQS are controlled by controlling the dosage of HPMC and EC. The influence of the dosage of HPMC on release rate of the controlled-release tablets of SQS is the biggest factor. The prescription of the controlled- release tablets of SQS contains for each piece: SQS 200mg, HPMC 40mg, EC 30mg, lactose 30mg. The controlled-release tablets of SQS release SQS by slowness and constant in 12 h.

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