Drug Development and Industrial Pharmacy, 2010; 36(11): 1356–1363

informa
healthcare

ORIGINAL ARTICLE

Enhanced oral bioavailability of Wurenchun (*Fructus Schisandrae Chinensis* Extracts) by self-emulsifying drug delivery systems

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Abstract

Background: Wurenchun is the alcohol extract from *Fructus Schisandrae Chinensis*, which has good efficiency in lowering abnormal serum glutamic pyruvic transaminase (SGPT) level of patients suffering from acute or chronic hepatitis. The main purpose of this work is to prepare self-emulsifying drug delivery systems (SEDDS) for enhancing the solubility, dissolution rate, and oral bioavailability of poorly water-soluble traditional Chinese medicines, Wurenchun. *Methods*: Pseudoternary phase diagrams were used to evaluate the efficient self-emulsification domains, and particle size distributions of resultant emulsions were determined. The dissolution test was performed according to the second method of Chinese Pharmacopoeia dissolution procedure. The pharmacokinetic study in rats for the optimized formulation was performed and compared to commercial capsules. *Results*: The optimized formulation for bioavailability assessment consisted of 20% oleic acid, 65% Tween 20, and 15% Transcutol P. The mean droplet size distribution of the optimized SEDDS was approximately 240 nm when diluted with 1000-fold volume of the distilled water. The in vitro dissolution rates of the active components of Wurenchun SEDDS were significantly higher than those of the commercial capsules. SEDDS have significantly increased the C_{max} and area under the curve) (AUC) of Wurenchun compared to reference capsules ($P < 0.05$). And the relative bioavailability of SEDDS for schisandrin and schisandrin B was 292.2% and 205.8% compared to the commercial capsules, respectively. *Conclusion*: The results suggest the potential use of SEDDS to improve oral absorption of the sparingly soluble drugs or traditional Chinese medicine, such as Wurenchun.

Key words: *Bioavailability; schisandrin; schisandrin B; self-emulsifying drug delivery systems; Wurenchun* (Fructus Schisandrae extracts)

Introduction

Schisandra chinensis (*Turcz.*) *Baill* grows wild in most eastern parts of Russia, the Kuril islands, southern Sachlin, and northeastern China, Korea, and Japan[1] and is a monoecious liana[2]. The seeds and fruits of *S. chinensis* have been used in traditional Chinese medicine (TCM) formulations for their antihepatotoxic effect. The major constituents of *S. chinensis* are the schisandra lignans. In most cases, the ethanol extract of *S. chinensis* (commonly referred to as Wurenchun) contains higher levels of these components than other parts. Results of many researches indicated that Wurenchun efficiently lowers the elevated serum alanine aminotransferase levels of patients suffering from chronic viral hepatitis or poisonous diseases and has hepatoprotective effects both in vivo and in vitro[3]. However, schisandra lignans are poorly water-soluble resulting in low solubility and bioavailability (BA) through oral route.

The dissolution rate of poorly water-soluble drugs often becomes a rate-limiting step in their absorption from the gastrointestinal (GI) tract[4]. Various solubilization methods

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(Received 5 Nov 2009; accepted 24 Mar 2010)

ISSN 0363-9045 print/ISSN 1520-5762 online © Informa UK, Ltd.
DOI: 10.3109/03639045.2010.480975

have been used to increase the drug solubility and dissolution properties, including the use of surfactants, water-soluble carriers, polymeric conjugates, and solid dispersions[5–9].

Among the formulations, self-emulsifying drug delivery systems (SEDDS) are a class of emulsion that has received particular attention as a means of enhancing oral BA of poorly absorbed drug[10]. SEDDS are defined as isotropic mixtures of natural or synthetic oils, solid or liquid surfactants, or alternatively, one or more hydrophilic solvents and cosolvents/surfactants[11–14]. Upon mild agitation followed by dilution in aqueous media, such as GI fluids, these systems can form fine oil-in-water emulsions or self-microemulsifying drug delivery systems. Self-emulsifying formulations spread readily in the GI tract, and the digestive motility of the stomach and the intestine provides the necessary agitation for the spontaneity of emulsion formation[15]. In comparison to sensitive and metastable emulsions, SEDDS are physically stable formulations that are easy to manufacture. In recent years, SEDD technology has been widely used in TCM. You et al. developed a new self-emulsifying microsphere of zedoary turmeric oil[16] and Tang et al.[17] prepared a new self-emulsifying formulation of *Ginkgo biloba* extracts for improving the BA of the main active components.

The objectives of this study were to develop and characterize the optimal formulation of SEDDS containing Wurenchun and to assess the BA compared with the Wurenchun commercial capsules (Gantaixin®) in rats. The in vitro release profiles of the active components from Wurenchun SEDDS and the commercial capsules were compared using high-performance liquid chromatography (HPLC). In this study, the SEDDS formulation of Wurenchun was accordingly developed to improve the solubility, dissolution, and oral absorption and to acquire reproducible blood–time profiles of the active components (schisandrin and schisandrin B) of Wurenchun (structure shown in Figure 1).

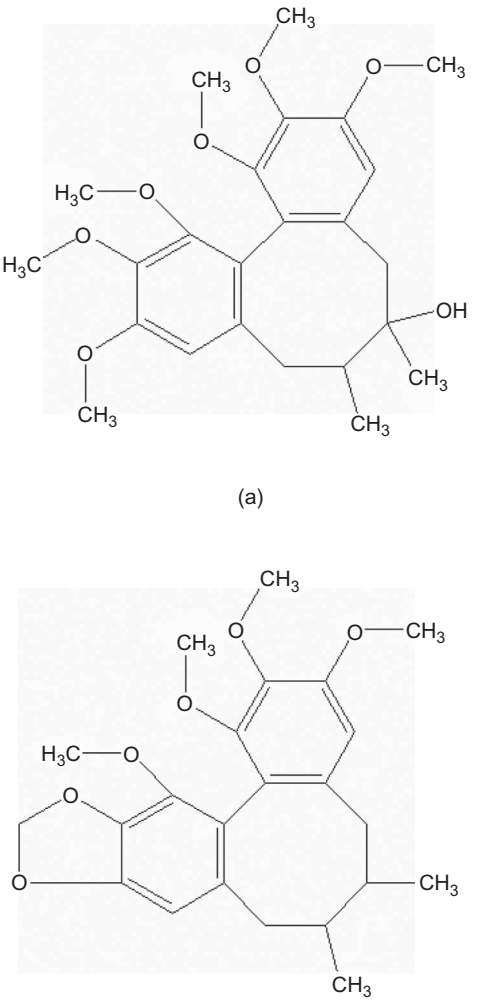

Figure 1. Structure of (a) schisandrin and (b) schisandrin B.

Materials and methods

Materials

Wurenchun (*S. chinensis* extract), which contained schisandrin (3.68%) and schisandrin B (1.66%), was supplied by Xi'an Xiaocao Botanical Science Technology Co., Ltd. (Xi'an, Shanxi, China). Wurenchun commercial capsules (Gantaixin®) were purchased from Guangdong Zaitian Pharm. Co., Ltd. (Qingyuan, Guangdong, China, 0.25 g extract/capsule). Standard substances of schisandrin and schisandrin B were supplied by the National Institute for Control of Pharmaceutical and Biological Products (Beijing, China). Nimodipine was purchased from Kunming Kexiang Biotechnology Co., Ltd. (Kunming, Yunnan, China). Cremophor (RH40, HS15, EL, and ELP) was kindly gifted by BASF Corp. (Ludwigshafen, Germany). Isopropyl myristate, ethyl oleate, and oleic acid were purchased from Sinopharm, Shanghai Chemical Co. (Shanghai, China). Soybean oil, olive oil (food grade), Tween 20, and PEG 400 were purchased from Tianjin Kemi'o Chemical Development Center (Tianjin, China). Tween 80 was purchased from Shanghai Shanpu Chemical Plant (Shanghai, China); 1,2-propylene glycol was obtained from Tianjin Tianda Chemical Plant (Tianjin, China). Transcutol P was gifted by Gattefoss Corp. (Saint-Priest, France). Miglyol 812 was from Condea Chemie GmbH (Witten, Germany). Methyl *tert*-butyl ether was from Tianjin Guangfu Fine Chemical Research Institute (Tianjin, China). All other reagents were of chromatographic grade. Distilled water, prepared from deionized water, was used throughout the study.

Solubility of Wurenchun

An excess amount of Wurenchun was added to various oils, surfactants, and cosurfactants and mixed by vortexing. The mixture was then kept at 25°C for 7 days to get to equilibrium. The equilibrated sample was centrifuged at 5000 × *g* for 10 minutes to remove the undissolved Wurenchun. The supernatant was taken and diluted with methanol for quantification of the main active components of Wurenchun by HPLC system (Waters Corp., Milford, Massachusetts, USA) consisting of 510 pump and 486 UV spectrometer (Waters Corp.), which were controlled by Millenninum®32 software. The samples were separated on an RP-C_{18} column (Diamondsil™, 200 × 4.6 mm, 5 μm; Dikma, Beijing, China) using a mixture of methanol and water (75:25, v/v) as mobile phase. The mobile phase was filtered through 0.45 μm membrane filter and eluted at a flow rate of 1.0 mL/min and the injection volume was 10 μL. The detection was performed at 220 nm for schisandrin and schisandrin B. Calibration curves were linear over the range of 2.19–24.09 and 2.15–23.65 μg/mL for schisandrin and schisandrin B, respectively. The coefficient of determination was >0.999 in all cases. Precision was 0.99% and 1.51%, respectively. A recovery between 100.4% and 100.6% was calculated for the two substances.

Preparation of self-emulsifying formulation

The amount of main active components of Wurenchun, schisandrin and schisandrin B, in the commercial formulations is 2.523 and 0.773 mg, respectively. A series of self-emulsifying blank formulations were prepared in each of the formulations with varying concentrations of oil (5–65%), surfactant (30–70%), and cosurfactant (5–25%). Components of SEDDS that contained oil, surfactant, cosurfactant, and Wurenchun (20%, w/w of the vehicle) were accurately weighed into glass beaker and heated at 40°C in an air-oscillator until Wurenchun dissolved. At the optimized formulation, the fill volume of a size 1 capsule containing 0.05 g Wurenchun was used for dissolution and BA studies.

Visual observations and droplet size determination

A visual test to assess the self-emulsification properties reported by Kommuru et al.[18] and Tang et al.[17] was modified and adopted in this study. Briefly, the formulation (0.1 mL) was introduced into 100 mL of water in a glass beaker at 37°C, and the contents were blended gently by a magnetic stir bar. The tendency to emulsify spontaneously and the progress of emulsion droplets were observed. The tendency to form an emulsion was judged as 'good' when droplets spread easily in water and formed a fine emulsion that was clear or slightly opaque in appearance, and it was judged 'bad' when the corresponding performance was poor or there was poor emulsion formation or mixtures layered before adding to water. A phase diagram was constructed to identify the good self-emulsifying region. All studies were repeated in duplicate, with similar observations being made between repeats.

The droplet size and the distribution of the resultant emulsions were determined using a Nano Particle Size and Electric Potential Analyzer (Malvern Corp., Malvern, UK). The particle size analyzer can measure sizes from 2 to 3000 nm.

Dissolution test

The dissolution test was performed in an apparatus (Hanson Research Corporation, Chatsworth, CA, USA) according to the second method of Chinese Pharmacopoeia dissolution procedure. Briefly, Wurenchun commercial capsules or SEDDS capsules were put into a sinker. This sinker was loaded into 500 mL of hydrochloric acid (0.1 mol/L) at 37 ± 0.5°C with paddle speed of 100 rpm/min. Each sample (5 mL) was withdrawn at 5, 15, 30, 45, and 60 minutes and then an equal volume of temperature-equilibrated blank media was added into the beaker. The samples were filtered and 10 μL was used for the determination of the amount of schisandrin and schisandrin B to compare the dissolution behavior of the active components of the SEDDS capsules or commercial capsules. The quantification procedure of schisandrin and schisandrin B by HPLC is described above. Calibration curves were linear over the range of 1.158–7.72 and 0.306–2.04 μg/mL for schisandrin and schisandrin B, respectively. The coefficient of determination was >0.9997 in all cases. The lower limit of quantitation (LLOQ) of the method was 0.306 μg/mL for schisandrin B and the accuracy and precision at LLOQ were less than 1% and 2%, respectively.

Animal studies

Experimental protocols were approved by the Animal Care Committee of Harbin Medical University. Twelve male Sprague–Dawley rats weighting 180–220 g were provided by the Experimental Animal Center of the Second Affiliated Hospital of Harbin Medical University (Harbin, Heilongjiang, China), and they were randomly divided into two groups. Wurenchun SEDDS or commercial capsules were given to six fasted SD rats by intragastric administration at a dose of two capsules. Blood samples (~0.25 mL) were collected into heparinized tubes at 0, 1, 2, 4, 6, 7, 8, 9, 10, 12, 14, and 24 hours after drug administration. The plasma samples were separated by centrifugation at 5000 × *g*/min for 10 minutes and stored at –20°C until analysis. The concentration of

schisandrin and schisandrin B was determined by liquid chromatography-electrospray ionization tandem mass spectrometry (LC–ESI–MS/MS). Liquid chromatographic separations were achieved by XTerra®MS-C_{18} column (2.1 × 150 mm, 3.5 μm) at 30°C with the mobile phase of acetonitrile–water–formic acid (80:20:0.2, v/v) at a flow rate of 0.2 mL/min in a run time of 8.5 minutes. The chromatographic system consisted of a Waters 2695 pump that was controlled by Masslynx 4.0 software (Waters Corp.). A triple quadrupole micromass spectrometer (Waters Corp.) fitted with Z-spray ion interface was used for all analyses. Ionization was achieved using electrospray in positive ion mode. The following parameters were optimized for the analysis of schisandrin, schisandrin B, and internal standard (IS): capillary voltages 3.6 kV; cone voltages 28, 35, and 28 V for schisandrin, schisandrin B, and nimodipine (IS), respectively; collision voltages 15, 22, and 15 V, respectively; source temperature 105°C; and desolvation gas (nitrogen) heated to 300°C and delivered at a flow rate of 400 L/h. The other parameters were fixed as the tuning file. Quantification was performed using multiple reaction monitoring of m/z 433.2 → 415.2 for schisandrin, m/z 401.2 → 300.2 for schisandrin B, and m/z 419.3 → 343.3 for IS.

An aliquot of 100 μL mobile phase and 100 μL nimodipine (400 ng/mL in mobile phase) was added to a 100 μL plasma sample in 5 mL EP tubes. The mixture was extracted with 2 mL methyl *tert*-butyl ether. After vortex-mixing for 3 minutes and centrifugation at 2000 × *g*/min for 10 minutes, the organic layer was separated and evaporated to dryness at 40°C under a gentle stream of nitrogen. The residue was reconstituted in 100 μL mobile phase followed by vortex-mixing. A 10 μL aliquot of the supernatant was injected into the LC–MS/MS system. The method showed excellent reproducibility with intraday and interday precision of less than 13.8% (RSD), as well as excellent accuracy between 93.5% and 107.2% for schisandrin and schisandrin B. The LLOQ of schisandrin and schisandrin B was 40.0 and 20.0 ng/mL, respectively, and the extraction recovery was 63.49 ± 5.98% and 62.8 ± 9.09%, respectively. The extraction recovery of IS was 71.4 ± 4.24%.

Pharmacokinetic data analysis

The chromatographic data were automatically processed to obtain peak area ratios of the compound to the internal standard and fitted to a weighed ($1/C$) linear regression relationship. The maximum plasma concentration (C_{max}) and the time to reach this maximum concentration (T_{max}) were determined by visual inspection of the experimental data. The elimination rate constant (K_e) was calculated by applying the least-squares regression technique to the data for the last three or four points of the plasma concentration–time curve, and the half-life ($t_{1/2}$) of the drug was obtained by 0.693/K_e. The relative BA of SEDDS (test formulation) to the commercial capsules (reference formulation) was calculated using the following equation:

$$\text{Relative BA (\%)} = \frac{\text{AUC}_{\text{test}}}{\text{AUC}_{\text{reference}}} \times \frac{\text{Dose}_{\text{reference}}}{\text{Dose}_{\text{test}}}.$$

The data were presented as mean with standard error (SE) for the individual groups. An unpaired Student's *t*-test was used to determine any significant differences. Differences were considered to be significant at $P < 0.05$.

Results and discussion

Vehicles selection

The major constituents of Wurenchun are the schisandra lignans and they are sparingly soluble in ether and water. In most literatures, schisandrin, deoxyschizandrin, or schisandrin B was used as quantitative indicator[19–22]. In this study, schisandrin which is the higher content and schisandrin B which is highly fat-soluble of the schisandra lignans were chosen as quantitative indicators.

The self-emulsifying formulations consisted of oil, surfactants, cosolvent, and drug; it should be a clear and homogeneous liquid at ambient temperature and should have good solvent properties to allow presentation of the drug in solution[23]. Drug amount loaded in each formulation is a very critical factor, dependent on the drug apparent solubility in a variety of vehicles. In addition, the volume of the formulation should be minimized to deliver the therapeutic dose of the drug in an encapsulated form. Vehicles selected for the formulation should have the ability to solubilize the drug to a great extent to obtain a concentrative form of the emulsions. Wurenchun solutions appear brown after dissolution, so the amount of soluble Wurenchun in various vehicles could be estimated by visual observations, and the data of solubility in several good vehicles were determined and some efficient dissolving vehicles by visual observations were selected to do blank formulation compatibility test (Table 1). We found that only No. 6 blank formulation was not layered and formed homogeneous liquid at the ratios. Thus, the No. 6 blank formulation was developed for further characterization.

Visual observations and droplet size analysis

The visual test is a measure of the apparent spontaneity of emulsion formation. A series of SEDDS were prepared

Table 1. Blank formulations compatibility test (vehicle compositions for screening SEDDS formulations).

No.	Oil	Surfactant	Cosurfactant	Homogeneous	Delamination (after 24 hours)
1	IPM	RH40	Transcutol P	Y	Y
2	IPM	ELP	1,2-Propylene glycol	Y	Y
3	IPM	Tween 20	PEG 400	Y	Y
4	Oleic acid	RH40	1,2-Propylene glycol	N	Y
5	Oleic acid	ELP	PEG 400	Y	Y
6	Oleic acid	Tween 20	Transcutol P	Y	N
7	Olive oil	RH40	PEG 400	N	Y
8	Olive oil	ELP	Transcutol P	N	Y
9	Olive oil	Tween 20	1,2-Propylene glycol	N	Y

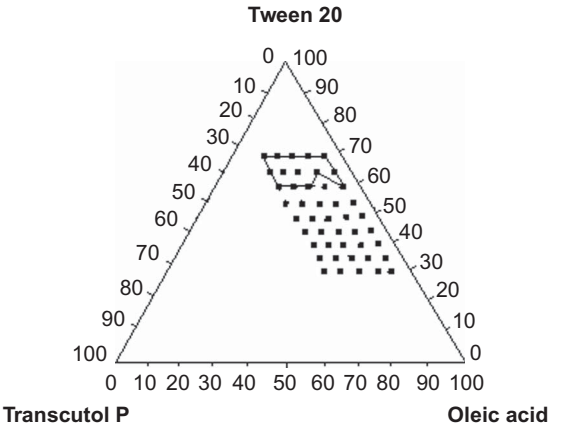

Figure 2. Pseudoternary phase diagrams indicating the efficient self-emulsification region with oleic acid as oil, Tween 20 as surfactant, and Transcutol P as the cosurfactant. Key: the region of efficient self-emulsification is bound by the solid line; and the filled squares represent the composition which were evaluated.

and their self-emulsifying properties were observed through naked eyes. A pseudoternary phase diagram was constructed to identify the self-emulsifying regions and also to acquire the optimum levels of oil, surfactant, and cosurfactant. The phase diagrams of the systems containing oleic acid, Tween 20, and Transcutol P are shown in Figure 2. Efficiency of emulsification was good when the surfactant concentration was more than 55%, and increasing the surfactant concentration (from 30% to 70%) enhanced the spontaneity of the self-emulsification process and decreased the mean droplet size. This may be due to excess penetration of water into the bulk oil causing massive interfacial disruption and ejection of droplets into the bulk aqueous phase[24]. More surfactant can stabilize the oil–water interface, thus resulting in a decrease in droplet size. Furthermore, the decrease in the mean droplet size reflects the formation of a better close-packed film of the surfactant at the oil–water interface, thereby stabilizing the oil droplets[25].

It was observed that increasing the concentration of the cosurfactant (Transcutol P) within the self-emulsifying region increased the spontaneity of the self-emulsification process. When the cosurfactant is added to the system, it can not only dissolve more drug (Table 2) but also further lower the interfacial tension between the oil and water interface and influence the interfacial film curvature, which thereby readily deforms around oil droplets[18]. Therefore, a little more concentration of Transcutol P is required.

Table 2. Solubility of Wurenchun in various vehicles at 25°C.

	Solubility	
Vehicle	Schisandrin	Schisandrin B
Water	0.425 ± 0.002	0.0346 ± 0.004
Oleic acid	7.681 ± 0.095	3.669 ± 0.073
IPM	13.286 ± 0.058	5.948 ± 0.556
Tween 20	3.006 ± 0.038	1.421 ± 0.026
Transcutol P	15.558 ± 0.158	7.243 ± 0.262

$n = 3$; mean ± SD, mg/mL.

Based on the in vitro self-emulsification properties, the formulation (0.3 g/capsule) containing oleic acid (20%), Tween 20 (65%), Transcutol P (15%), and Wurenchun (20%, w/w of the vehicle) was selected for the dissolution and BA studies. The mean droplet size distribution of the optimized SEDDS was approximately 240 nm with polydispersity 0.38 when diluted with 1000-fold volume of distilled water.

In vitro dissolution study

Dissolution studies were performed for SEDDS and the commercial capsules. The dissolution rates of the active components of Wurenchun from these dosage forms were evaluated in hydrochloric acid (0.1 mol/L). The release percentages of the active components of schisandrin B from the SEDDS were significantly higher than those of the commercial capsules, but there was no significant difference for schisandrin between the two formulations (Figure 3). The equilibrium solubility of schisandrin and schisandrin B was 0.810 ± 0.008 and 0.0524 ± 0.006 mg/mL in the dissolution medium (0.1 mol/L hydrochloric acid) at 37 ± 0.5°C, respectively. The amount of main active components of Wurenchun,

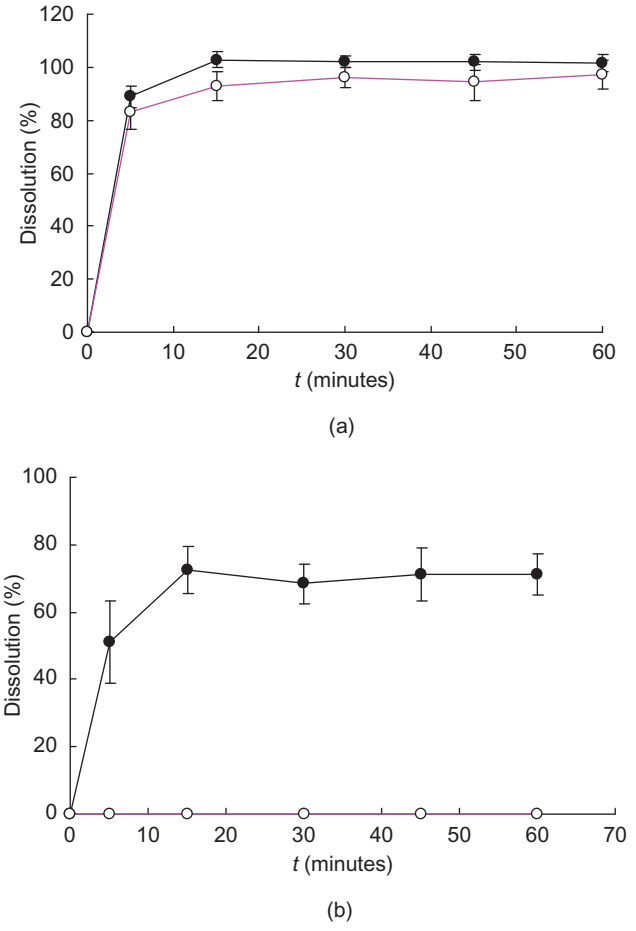

Figure 3. Dissolution profiles of schisandrin and schisandrin B from SEDDS (●) and the commercial capsules (○). (a) Schisandrin; (b) schisandrin B. Tests were conducted in 500 mL of hydrochloric acid (0.1 mol/L) at 37 ± 0.5°C with a rotation speed of 100 rpm/min. Each value is the mean ± SD (n = 6).

schisandrin and schisandrin B, in the commercial formulations is 2.523 and 0.773 mg, respectively. So the dissolution studies were performed in the sink condition. The LLOQ of the method was 0.306 μg/mL for schisandrin B. For the commercial capsules, the dissolution rate of schisandrin B was so slow that the amount of dissolution could not reach the LLOQ. However, the release percentages of schisandrin B for SEDDS capsules reached 71.3% at 45 minutes. It was suggested that the active components of Wurenchun from the SEDDS could be rapidly released because of the small droplet size and increased contact surface with dissolution media.

Bioavailability studies

The plasma profiles of schisandrin and schisandrin B in rats following oral administration of the reference capsule (25.25 and 7.75 mg/kg) and self-emulsifying formulation (18 and 8.924 mg/kg) of Wurenchun were determined. The plasma concentration profiles of schisandrin and schisandrin B for SEDDS presented significantly greater improvement in oral absorption than the commercial capsules (Figures 4 and 5). The main pharmacokinetic parameters for each of the components of the two formulations are summarized in Table 3. The small T_{max} values of SEDDS for all two determined components demonstrated fairly rapid onset compared to the conventional capsules. For schisandrin, the reduction in T_{max} values from 5.83 ± 0.65 hours for capsules to 3.67 ± 0.33 hours for SEDDS was statistically significant ($P < 0.05$) and for schisandrin B, this difference was almost 3.5 hours (capsules: 8.5 hours; SEDDS: 5 hours; $P < 0.05$). Marked differences were also observed for the C_{max}. For schisandrin, the C_{max} value was 2716.18 ng/mL for SEDDS and 1526.72 ng/mL for capsules; for schisandrin B, it was

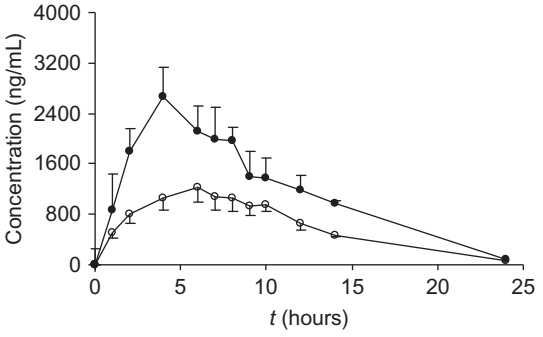

Figure 4. Schisandrin plasma concentration–time profiles of SEDDS (●) and commercial capsules (○) following oral administration at a single dose of two capsules in rats. Each value is the mean ± SE (n = 6).

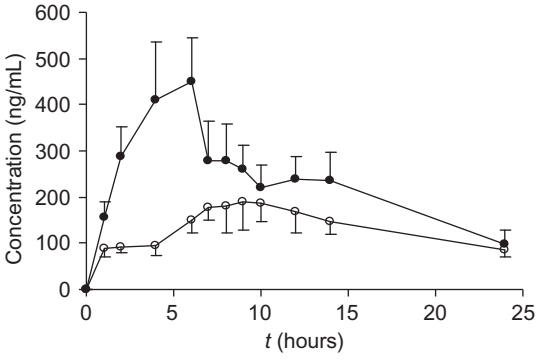

Figure 5. Schisandrin B plasma concentration–time profiles of SEDDS (●) and commercial capsules (○) following oral administration at a single dose of two capsules in rats. Each value is the mean ± SE (n = 6).

Table 3. Main pharmacokinetic parameters of schisandrin and schisandrin B after a single oral dose of two capsules of SEDDS or commercial capsules in rats.

		Schisandrin	
Parameters	Unit	SEDDS	Commercial capsules
C_{max}	ng/mL	2716.18 ± 414.33*	1526.72 ± 166.37
T_{max}	hours	3.67 ± 0.33*	5.83 ± 0.65
K_e	h^{-1}	0.224 ± 0.059	0.320 ± 0.101
$t_{1/2}$	hours	6.17 ± 2.85	3.22 ± 0.76
$AUC_{0-24\,hours}$	ng/mL·h	28,035.8 ± 5611.58*	14,675.0 ± 1148.32
F	%	292.2 ± 81.4	100
		Schisandrin B	
C_{max}	ng/mL	514.12 ± 113.61*	266.82 ± 49.53
T_{max}	hours	5.00 ± 0.45*	8.50 ± 0.56
K_e	h^{-1}	0.085 ± 0.024	0.047 ± 0.011
$t_{1/2}$	hours	11.50 ± 2.83	18.7 ± 3.52
$AUC_{0-24\,hours}$	ng/mL·h	5618.8 ± 1129.31*	3117.9 ± 492.85
F	%	205.8 ± 76.51*	100

Mean ± SE, $n = 6$, *$P < 0.05$.

514.12 versus 266.82 ng/mL, for SEDDS and capsules ($P < 0.05$), respectively. Moreover, for schisandrin, $AUC_{0-24\,hours}$ values of 28,035.8 versus 14,675.0 ng/mL·h for SEDDS and commercial capsules, respectively, were found to be statistically significantly different ($P < 0.05$). For schisandrin B, the $AUC_{0-24\ hours}$ for SEDDS was 5618.8 ng/mL·h and that for the capsules was 3117.9 ng/mL·h ($P < 0.05$). The relative BAs of SEDDS to commercial capsules for schisandrin and schisandrin B were 292.2% and 205.8%, respectively.

Recently, more and more studies confirmed that SEDDS could improve the BA of the lipophilic drug[26–28], especially in TCM[17,29]. Our results were similar to those and SEDDS obviously improved the relative BAs of schisandrin and schisandrin B of Wurenchun. In this study, the BA of schisandrin between commercial capsule formulation and self-emulsifying formulation was significantly different. However, for the dissolution rate of schisandrin, there was no significant difference between the two formulations. Schisandrin B in commercial capsule still showed limited absorption. But based on its dissolution profile in Figure 3b, schisandrin B cannot be released. This phenomenon may be due to the mutual transformation of the lignans in Wurenchun under the enzyme of the liver. Wang et al. had researched the transformation of deoxyschizandrin in vitro by cell culture experiment with rat liver. Schisandrin B (the content is about 30%) was detected when deoxyschizandrin was determined[30]. However, it should be further studied whether schisandrin is transformed or whether the other lignans are transformed to schisandrin or schisandrin B. The different dissolution rates of the two formulations perhaps affect the biotransformation of the lignans. It would be useful to research the effect of SEDDS on the metabolism and transformation of the lignans and absorption kinetics of the active components of Wurenchun. In a word, it was suggested that SEDDS could improve the rate and extent of the oral absorption of the active components of Wurenchun in this study.

Conclusions

Wurenchun can efficiently lower the elevated serum alanine aminotransferase levels of patients suffering from chronic viral hepatitis or poisonous diseases and has hepatoprotective effects either in vivo or in vitro. The active components of Wurenchun (the schisandra lignans) have low solubility and BA by oral administration because of poor water solubility. Self-emulsifying formulation developed in this study shows significantly greater extent of dissolution and oral absorption than the commercial capsule based on the in vitro dissolution test and in vivo BA studies. The relative BA of SEDDS for schisandrin and schisandrin B was 292.2% and 205.8%, compared to the reference capsules, respectively. In conclusion, our studies illustrated the potential use of SEDDS for the delivery of sparingly soluble drugs or TCM such as Wurenchun by the oral route.

Declarations of interest

We are grateful to the financial support by the Health Department of Heilongjiang Province, No. 2009-245. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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