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Improved stability of salvianolic acid B from Radix *Salviae miltiorrhizae* in deep eutectic solvents

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Abstract

Deep eutectic solvents (DESs) have numerous chemical applications as environmentally green solvents due to their unique physicochemical property. In the study, the stability of salvianolic acid B (SAB) from Radix Salviae miltiorrhizae were investigated in four kinds of benign choline-based DESs modified by different hydrogen-bond donor (ethylene glycol, 1,2-propanediol, glycerol and 1,4-butanediol), and the degradation products of SAB were analyzed by high performance liquid chromatography coupled with electrospray ionization tandem mass spectrometry (LC-MS/MS). Obviously, the stability test demonstrated that SAB was more stable in DESs than in water or ethanol solution under room temperature or high temperature. And optimum experiment proved that the stabilizing capacity of DESs suffered major influence from the water contents in DESs solution, minor influence from the structure of hydrogen-bond donor and minimal influence from the molar ratio of quaternary ammonium salts to hydrogen-bond donor. Finally, choline chloride-glycerol (molar ratio 1:2) was optimized to offer satisfactory enhancement effect for the stability of SAB. Moreover, the mechanism of improving stability of SAB in DESs was also discussed by analyzing the content variation trends of degradation products. And the interaction between SAB and DESs molecules were also demonstrated by the FT-IR spectrum. Therefore, DESs with stabilizing capacity has great prospect for their applications in extraction of SAB, even may be further developed as carriers for cosmetic and liquid oral medicines.
Keywords: Deep eutectic solvents, Salvianolic acid B, Stabilizing capacity, Degradation mechanism.
1. Introduction

Radix *Salviae miltiorrhizae* (named danshen in Chinese) is widely used as traditional medicine for cardiovascular diseases. Danshen is mainly used as a decoction in traditional Chinese medicinal prescription.\(^1\)\(^2\) Therefore, the water-soluble phenolic acids should be responsible for the therapeutic effects of this medicinal plant. Salvianolic acid B (SAB) is the most abundant compound in water-soluble ingredients, which has been reported to display diverse pharmacological properties such as anti-platelet activity, anti-inflammatory, anti-tumor and free radicals scavenging activity.\(^3\)\(^4\) However, SAB is composed of three units of tanshinol and one unit of caffeic acid. The ester linkages in SAB are unstable and easily hydrolyzed in aqueous solution, especially in neutral and alkaline system.\(^5\)\(^6\) What is more, the hydrolysis products resulted in the loss of the clinical efficacy of SAB products. At present, SAB could be used limit in solid formulation, and the unstable of SAB becomes a bottleneck in the field of clinical application as a liquid formulation.\(^5\) Therefore, it is necessary to develop a new solvent which can enhance the stability of SAB.

Deep eutectic solvents (DESs) are thermodynamically stable, clear liquid mixtures of two or more components together by hydrogen bonding after abidingly heating and stirring, and DESs have lower melting point than either of the individual components.\(^7\)\(^8\) As a type of environmentally benign and designer media, DESs have several advantages over traditional solvents, such as negligible volatility, adjustable
viscosity, wide polarity range, and high solubilization strength.\textsuperscript{9,10} Compared with ionic liquids, DESs (especially choline-based DESs) offer advantages in terms of biodegradability, sustainability, low-toxicity, low cost, and simple synthetic method.\textsuperscript{11,12} These unique physicochemical characteristics make DESs applied in various fields instead of conventional volatile organic solvents. Up to now, they have been widely used in extraction,\textsuperscript{13} electrochemistry,\textsuperscript{14} catalytic\textsuperscript{15} and organic synthesis.\textsuperscript{16,17} In addition, it is reported that DESs appear around plant cell membranes and play the role of solubilization and storage of poorly water-soluble or unstable compounds.\textsuperscript{10,18} Hence, DESs have a great potential as solvent to improve stability of compounds, but only few research groups have been study on the stabilization ability of DES for natural products.\textsuperscript{19,20} Therefore, it is important to further study the stability of unstable natural products in DESs and its stabilization mechanism.

In this study, DESs were studied as stabilizing media for SAB from Radix \textit{Salviae miltiorrhizae}, and four kinds of benign choline chloride-based DESs modified by different hydrogen-bond donor including ethylene glycol, 1,2-propylene glycol, glycerol and 1,4-butylene glycol were investigated in this experiment. SAB and its degradation products were analyzed by LC-MS/MS. The stabilizing capacity of DESs was assessed by optimizing the structure of hydrogen-bond donor, the molar ratio of quaternary ammonium salts to hydrogen-bond donor and the water contents in DESs solution. Moreover, the mechanism of improving stability of SAB was also discussed.
2. Experimental methods

2.1 Materials

SAB was bought from Chengdu Must Bio Technology Co., Ltd (Chengdu province, China). Methanol, ethanol and acetic acid of HPLC grade were purchased from MREDA (MREDA Technology Inc., USA). Water was deionized water quality. Choline chloride (ChCl), ethylene glycol (EG), 1,2-propanediol (PDO), glycerol (GL) and 1,4-butanediol (BDO) were purchased from Tianjin Dengfeng Chemical Reagent Factory (Tianjin province, China) with purity > 99.8%.

2.2 Solvent and sample preparation

All the DESs including choline chloride-ethylene glycol (ChCl-EG), choline chloride-1,2-propanediol (ChCl-PDO), choline chloride-glycerol (ChCl-GL) and choline chloride-1,4-Butanediol (ChCl-BDO) were prepared by continuous stirring at 100°C.

SAB solutions were prepared by dissolving SAB in each solvent (water, ethanol, methanol and DESs) with sufficient mixing for 5 min at room temperature. All of the samples were filtered through a 0.45 µm cellulose membrane.

2.3 Stability tests

The effects of temperature, storage time, and water content in DESs on the stability of SAB were investigated with the methods described below, and each experiment was duplicated three times.
The effect of storage time was investigated in 25°C water bath, and three tubes of each group were tested using HPLC at 1, 3, 5, 7, 9, 11, 13, 15, 30, 45, and 60 days, respectively.

For high temperature accelerated experiment, SAB solutions were put in glass vials with screw caps and placed in a water bath at 60 and 90°C, respectively. Three tubes of each group were rapidly cooled to room temperature and assessed by HPLC after incubating 0, 3, 6, 9 and 12 hours.

The effect of water content (0 vol%, 25 vol%, 50 vol%, 75 vol%, and 100 vol%) in DES on the stability of SAB was investigated at 90°C water bath for 0, 3, 6, 9 and 12 hours, respectively.

2.4 Apparatus and analysis

The stability tests of SAB were analyzed by an Agilent 1260 HPLC system (Agilent Technologies, Waldbronn, Germany) equipped with an online degasser, a G1311C quaternary-pump, a G1329B auto-sampler, a G1314B VWD detector with wavelength of 286 nm, and a GT-30 column temperature controller maintained at 40°C. Chromatographic separation of SAB and its degradation products were performed on a Zorbax SB-C18 reversed-phase column (4.6 × 150 mm, 5 µm, Agilent, USA). The mobile phase consisted of water (A) and methanol (B) in a linear gradient elution of 10-20% B at 0-10 min, 20-40% B at 10-20 min, and 40-50% B at 20-30 min. The flow rate was 1.0 mL min⁻¹ and the sample injection volume was 5 µL. All
samples were filtered through 0.45 µm cellulose membranes prior to HPLC analysis. Acquisition and analysis of data were performed by Agilent OpenLAB CDS Chemstation edition Software Ver. C. 01. 07.

A Thermo Scientific Q Exactive LC-MS/MS (Thermo Fisher Scientific Inc., USA) equipped with an HESI source was used for structural analysis of analytes. The TOF-MS analysis worked in negative mode and mass range was set at \( m/z \) 100-1500. The optimal of HESI source parameters were as follow: the spray voltage were from -2.5 to -3.5 kV; capillary temperature was set to 320°C; sheath gas, 35 psig; spray current, -100–100 A; probe heater temperature were -300–300°C; The mobile phase consisted of water (A) and methanol (B) in a linear gradient elution of 10-40% B at 0-6.67 min, 40-50% B at 6.67-13.33 min, and 50-100% B at 13.33-20 min. the sample injection volume was 5 µL, the flow rate of 2.1 mL min\(^{-1}\), and the detector wavelength was set to 286 nm. All the operations, acquisition and analysis of data were controlled by Thermo Xcalibur Software.

Fourier-transform infrared spectroscopy (FT-IR) spectra (Bruker FT-IR spectrometer, Germany) were registered at room temperature over the range 4000 to 400 cm\(^{-1}\). The pH value of the diluted DES with 90% (v/v) deionized water was tested with acidometer (Merck, Darmstadt, Germany).

2. Results and discussion

3.1 Physicochemical properties of DESs
Significant physical characters of DESs including viscosity, pH, polarity, melting point and composition of solvents in follow experiment were examined in Table 1. DESs used in this work were identified by FT-IR in Fig. S1. The data showed that viscosity of all tested DESs was higher than that of traditional solvents. Compared with glycerol, the viscosity of ChCl-GL was decreased by formation of hydrogen bonds between glycerol and choline chloride. Because of the large viscosity, the pH of DESs was measured by diluting with 90% (v/v) of water. The result demonstrated that DESs were weak acidity with the pH 4.72-5.95. The melting points of DESs were dramatically reduced after H-bond forming, which was consistent with the literature reported. In addition, densities of these DESs ranged from 1.12 to 1.20 were revealed to be higher than that of traditional solvents. As another important property, polarities of DESs were very similar, and between the polarity of water and alcohol.

3.2 Stability of SAB under ambient conditions

It was reported that water is a common solvent for SAB, and alcohol can enhance the stability of SAB. Thus, ChCl-EG (1:2), ChCl-PDO (1:2), ChCl-GL (1:2), ChCl-BDO (1:2), water, ethanol and methanol were compared as solvents to storage SAB at 25°C for 60 days. As shown in Fig.1, the degradation of SAB followed a pseudo-first-order reaction kinetics in various solvents, and the first-order reaction rate constants (k) were calculated by the following equations:

$$\ln \left( \frac{C_f}{C_0} \right) = -kt$$ (1)
\[ T_{0.9} = -\ln (0.9)/k \]  \hspace{1cm} (2)

\[ T_{1/2} = -\ln (0.5)/k \]  \hspace{1cm} (3)

Where \( C_i/C_0 = A_i/A_0 \), \( A_0 \) is the initial peak area in HPLC of SAB and \( A_i \) is the peak area of compounds after degradation time (t) at a certain temperature. \( T_{0.9} \) means the time of SAB decomposes 10% of the original content.

The results in Table 2 showed that the type of solvents had important influence on the stabilization of SAB. SAB in water showed the highest degradation rate, and the validity period (\( T_{0.9} \)) only 10.13 days. While less than 10% degradation of SAB occurred in all of DESs over a 24-day period. The degradation rate of SAB in different solvents was according to the following sequence: water >> ethanol > methanol ≈ DESs. The result indicated that DESs could significant improve the stability of SAB under ambient temperature.

### 3.3 Screening of hydrogen bond donors in DESs

It is reported that the degradation of SAB were degraded in three pathway including ester hydrolysis, hydrogenation cracking, and opening ring reaction, and the affect factors of the stability of SAB was including the properties of solvent, temperature and pH value.\(^6,^{24,25}\) The structure of hydrogen bond donors (HBD) can significantly affect the formation of inter-molecular interactions with choline chloride, particularly hydrogen bonds, which has considerable influence on the physicochemical properties of DESs.\(^{21,26}\) Thus, different HBD in DESs probably
affect the stability of SAB. Taking into account temperature is also an important factor in the stability of SAB, ChCl-EG (1:2), ChCl-PDO (1:2), ChCl-GL (1:2), ChCl-BDO (1:2) and water were selected to investigate the degradation rate of SAB at 60°C and 90°C, respectively (shown in Fig. 2 and Fig. 3). And the degradation products including caffeic acid (CAF), tanshinol (TAN), protocatechuic aldehyde (PRO), rosmarinic acid (ROS), lithospermic acid isomer (LITI), lithospermic acid (LIT), salvianolic acid A (SAA) and salvianolic acid E (SAE) were analyzed by LC-MS/MS (shown in Fig. S2 and Table S1).

The result of Fig. 2a showed that SAB in water was much less stable than in DESs at 60°C, and the order of degradation rate of SAB was water > ChCl-BDO (1:2) > ChCl-PDO (1:2) ≈ ChCl-GL (1:2) ≈ ChCl-EG (1:2). With the continuous degradation of SAB for 12 h, the contents of degradation products including TAN, ROS, LITI, LIT, SAA and SAE were increased. Obviously, the content of ROS (Fig. 2c) increased fastest in water, and then in ChCl-BDO (1:2). The content of LITI (Fig. 2d) had in a similar manner increased in water and ChCl-PDO (1:2), and the content of LIT was increased in water, but the variation trends in DESs were relatively flat. The content of SAE (Fig. 2F) was little in water, and the variation trend of other degradation products in different solvents was basically the same. Based on the above results, it was speculated that SAB in DESs were mainly open ring to produce SAE, LITI and SAA. While SAB in water were degraded in all of the three pathways, and SAE in water were quickly further degraded to SAA.
In order to intensive analyze the degradation mechanism, two solvents of phosphate buffer (pH 5) and glycerol were added at 90°C stability test comparing with water and ChCl-GL respectively. It was clearly seen that the contents of CAF (Fig. 3b), PRO (Fig. 3d) and ROS (Fig. 3e) in water were increased faster than in phosphate buffer (pH 5), but not detected in other solvents. It was inferred that in aqueous solution, SAB was hydrocracked to form ROS, and then further gradated to CAF and PRO under high temperature, while this degradation pathway of SAB was inhibited in the DESs. The content of LIT was increased in water and phosphate buffer (pH 5), but little increased in DESs. The increase trends of SAA (Fig. 3h) in the ChCl-GL and glycerol were similar, and this phenomenon demonstrated the hydrogen bond donor could affect property of deep eutectic solvents in some degree. However, compared to glycerol, the formation of hydrogen bond between choline chloride and glycerol can significantly enhance the stability of SAB. The variation trends of content of SAE (Fig. 3i) in water and phosphate buffer (pH 5) were relatively flat. Differ from in aqueous solution, SAE in DESs increased at first, but then decreased after 6 hours under high temperature. It was also demonstrated that SAB in DESs principally generated SAE, LITI and SAA, and the further degradation of SAE probably inhibited in DESs in the beginning. This phenomenon may be because DESs with weakly acid could provide protons which promoted the open loop reaction of SAB. But as a non-water system, DESs was not conducive to hydrolysis reaction. Finally, the proposed degradation pathway of SAB both in water and DESs
was concluded in Fig. S3, and the difference of degradation pathway in DESs probably result in the stability enhancement of SAB by comparing with SAB in water.

Compared Fig. 2a and Fig. 3a, SAB was much more stable in all DESs than in water, and the degradation rate of SAB in ChCl-GL was much slower than in other DESs (shown in Table S2). According to the stability test at 60°C and 90°C, the degradation of SAB dissolved in DESs and water was not only conforming to the first-order kinetics, but also strengthen with the increasing of temperatures. What is more, the gaps of degradation rate of SAB at 60°C were not obvious than 90°C. Therefore, 90°C and ChCl-GL were selected for the further experiment.

3.4 Optimistic the ratio between choline chloride and hydrogen-bond donor in DESs

The ratio of hydrogen-bond acceptor and hydrogen-bond donor also plays an important role in the stabilization capacity of DESs. Different ChCl/HBD ratios were compared, including ChCl-GL (1:1), ChCl-GL (1:2), ChCl-GL (1:3), and ChCl-GL (1:4). Fig. 4 demonstrated that degradation trends of SAB were basically the same in four types of DESs, and ChCl-GL (1:2) as solvent obtained a slight advantage for storing SAB. This phenomenon is probably due to the similarity physicochemical properties of four DESs (shown in Table 1). Overall, ChCl-GL (1:2) was adopted in the following optimization.

3.5 Stability of SAB in DES with different water contents
The diluted DESs by adding pure water can dramatically convert their viscosity and inter-molecular interaction, which can obvious impact their solubilization ability and maybe further affect the stabilization capacity.\textsuperscript{28,29} Hence, the effect of the water content on the stability of SAB was evaluated in the water-DESs mixture at 90°C. A series of concentrations of water at 0 vol\%, 25 vol\%, 50 vol\%, 75 vol\% and 100 vol\% were mixed with ChCl-GL (1:2) in this experiment. The results shown in Fig. 5 indicated that the concentration of SAB decreased sharply with the increase of water content. Apparently, the addition of pure water was not conducive to stability of SAB. It was supposed that diluted DESs was increased basicity and broke the inter-molecular interaction between SAB and DESs molecules,\textsuperscript{30} which may facilitate to the ester hydrolytic reaction of SAB. Finally, the best solvent ChCl-GL (1:2) was obtained to enhance the stability of SAB.

3.6 Preliminary study on the interaction between DESs and SAB

In order to further study the mechanism of the interaction between DESs and SAB, IR spectra of ChCl-GL (1:2), SAB, SAB dissolved in ChCl-GL (1:2) were measured (Fig. 6). The positions and intensities of absorption band attributed to carbonyl group could be considered as the key factors to estimate the influence of solvent on solute. The stretching vibration absorption band of carbonyl group was shifted from 1722 to 1731 cm\(^{-1}\). The reason for the blue shift may be due to ChCl-GL (1:2) formed inter-molecular force with the oxygen atom connected with carbonyl group, and the solvent effect destroyed a p-\pi conjugated system of O=C-O in the solid state, leading
to the enhancement of energy change of the C=O stretching vibration. In addition, the peak intensity of C=O stretching vibration in 1731 cm\(^{-1}\) increased compared with the absorption band in 1613 cm\(^{-1}\) of the stretching vibration of aromatic ring. This phenomenon indicated that the inter-molecular force formed between molecular of ChCl-GL (1:2) and the oxygen atom connected with carbonyl group result in the increase of carbonyl group vibration strength and the large dipole moment of the C=O bonds.

3. Conclusion

In this work, a range of environmentally friendly ChCl-based DESs mixed with different HBDs were developed and validated for enhancing stability of SAB. Different from water, which was commonly used as traditional solvent, the novel proposed DESs were obtained satisfactory stabilization capacity for SAB under ambient temperature and even under high temperature. With the optimization of H-bond donor, salt/HBD ratio and the water content, ChCl-GL (1:2) was chosen as the best solvent for storing SAB in this experiment. In addition, the types of H-bond donor and the water content had some impact on the stability performance of DESs for the target compound. According to comparing variation trends of degradation products, the mechanism of degradation pathway of SAB was different in water and in DESs. DESs as solvents maybe inhibited the ester hydrolysis and hydrocracking of SAB. And FT-IR spectra demonstrated the interaction between solute and DESs molecular. In conclusion, DESs with low toxicity and good capacity of improving stability have
great prospect for storing and extracting SAB, and even be extended to develop benign drug carrier for cosmetic and medicine.

Acknowledgements

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Supporting Information Available

FT-IR spectrums of DESs used in the experiment were provided in Figure S1. HPLC-UV chromatogram of SAB and its degradation products in different solvent was shown in Figure S2. The proposed degradation pathways of salvianol acid B was shown in Figure S3. LC-MS/MS accurate measurements for the SAB and its degradation products were given in Table S1. The observed rate constant (k), half-life ($T_{1/2}$) and shelf-life ($T_{0.9}$) for SAB in different solvents at different temperature were described in Table S2.
References

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Figure Captions

Figure 1 First-order plots for the degradation of salvianolic acid B in different solvents at 25°C.

Figure 2 Content variation trends of salvianolic acid B and its degradation products in different solvent at 60°C.

Figure 3 Content variation trends of salvianolic acid B and its degradation products in different solvent at 90°C.

Figure 4 First-order plots for the degradation of salvianolic acid B in DESs with different salt/HBD ratio at 90°C.

Figure 5 First-order plots for the degradation of salvianolic acid B in DESs with different water content at 90°C.

Figure 6 IR spectra of (a) ChCl-GL (1:2), (b) SAB in solid phase, (c) SAB dissolved in ChCl-GL (1:2).
Figure 1
Figure 2
Figure 3
Figure 4
Figure 5
Figure 6
Table 1 Physical property of solvents used in the experiment.

<table>
<thead>
<tr>
<th>DESs</th>
<th>Compositions</th>
<th>molar ratio</th>
<th>Viscosity (cP)</th>
<th>pH $^a$</th>
<th>$T_m$ (°C)</th>
<th>Density</th>
<th>$E_r^{(30)}$ (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ChCl-EG</td>
<td>Choline chloride:</td>
<td>1:2</td>
<td>37 (25°C)</td>
<td>5.95</td>
<td>-66.01</td>
<td>1.12</td>
<td>56.7</td>
</tr>
<tr>
<td></td>
<td>Ethylene glycol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ChCl-PDO</td>
<td>Choline chloride:</td>
<td>1:2</td>
<td>-</td>
<td>5.03</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1,2-Propanediol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1:1</td>
<td></td>
<td>-</td>
<td>5.21</td>
<td>-</td>
<td>1.16</td>
<td>58.6</td>
</tr>
<tr>
<td>ChCl-GL</td>
<td>Choline chloride:</td>
<td>1:2</td>
<td>376 (20°C)</td>
<td>4.72</td>
<td>-36.15</td>
<td>1.18</td>
<td>58.2</td>
</tr>
<tr>
<td></td>
<td>Glycerol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1:3</td>
<td></td>
<td>450 (20°C)</td>
<td>5.55</td>
<td>-36.25</td>
<td>1.20</td>
<td>58.0</td>
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<tr>
<td></td>
<td>1:4</td>
<td></td>
<td>503 (20°C)</td>
<td>5.12</td>
<td>-</td>
<td>-</td>
<td>57.9</td>
</tr>
<tr>
<td>ChCl-BDO</td>
<td>Choline chloride:</td>
<td>1:2</td>
<td>-</td>
<td>5.02</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td></td>
<td>1,4-Butanediol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GL</td>
<td>Glycerol</td>
<td>-</td>
<td>1412 (20°C)</td>
<td>-</td>
<td>17.8</td>
<td>1.26</td>
<td>57.9</td>
</tr>
<tr>
<td>H$_2$O</td>
<td>Water</td>
<td>-</td>
<td>1.00 (20°C)</td>
<td>7.00</td>
<td>0</td>
<td>0.9982</td>
<td>63.1</td>
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<tr>
<td>EtOH</td>
<td>Ethanol</td>
<td>-</td>
<td>1.20 (20°C)</td>
<td>-</td>
<td>-114.1</td>
<td>0.789</td>
<td>52.1</td>
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<tr>
<td>MeOH</td>
<td>Methanol</td>
<td>-</td>
<td>0.58 (20°C)</td>
<td>-</td>
<td>-98</td>
<td>0.791</td>
<td>55.5</td>
</tr>
</tbody>
</table>

$^a$ the pH value were detected with 90% (v/v) water dilution of DESs.
Table 2: The observed rate constant (k), half-life (T_{1/2}) and shelf-life (T_{0.9}) for SAB in different solvents at 25°C.

<table>
<thead>
<tr>
<th>solvent</th>
<th>k (/day)</th>
<th>R²</th>
<th>T_{1/2} (days)</th>
<th>T_{0.9} (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ChCl-EG (1:2)</td>
<td>0.0034</td>
<td>0.9836</td>
<td>203.82</td>
<td>31.00</td>
</tr>
<tr>
<td>ChCl-PDO (1:2)</td>
<td>0.0043</td>
<td>0.9841</td>
<td>161.16</td>
<td>24.51</td>
</tr>
<tr>
<td>ChCl-GL (1:2)</td>
<td>0.0023</td>
<td>0.9720</td>
<td>301.30</td>
<td>45.83</td>
</tr>
<tr>
<td>ChCl-BDO (1:2)</td>
<td>0.0040</td>
<td>0.9926</td>
<td>173.25</td>
<td>26.35</td>
</tr>
<tr>
<td>Water</td>
<td>0.0104</td>
<td>0.9969</td>
<td>66.63</td>
<td>10.13</td>
</tr>
<tr>
<td>EtOH</td>
<td>0.0060</td>
<td>0.9951</td>
<td>115.50</td>
<td>17.57</td>
</tr>
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<td>MeOH</td>
<td>0.0042</td>
<td>0.9986</td>
<td>165.00</td>
<td>25.10</td>
</tr>
</tbody>
</table>
Environmentally deep eutectic solvents were developed for enhancing the stability of salvianolic acid B from Radix *Salviae miltiorrhiza*. 

Salvianolic Acid B 

![Graphical Abstract](image)

100°C stirring 

Deep eutectic solvents 

Traditional solvents 

**Graphical Abstract**

Environmentally deep eutectic solvents were developed for enhancing the stability of salvianolic acid B from Radix *Salviae miltiorrhiza*. 

Salvianolic Acid B