Self-microemulsifying drug delivery system for oral delivery of T1-11

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ABSTRACT SUMMARY
T1-11, isolated from a Chinese medicinal herb Gastrodia elata, in an adenosine analogue that has been shown to delay the progression of Huntington’s disease in an animal model. However, the solubility of T1-11 is poor (< 1 mg/mL) and the oral bioavailability is low. In order to improve the oral bioavailability of T1-11, a solubility enhancement system such as the SMEDDS (Self Microemulsifying Drug Delivery System) was developed. A formulation for T1-11 composed of Labrafac PG (10%), Tween 80 (72%), and 95% alcohol (18%) significantly increased the solubility of T1-11 to 6.94±0.15 mg/mL was developed and evaluated.

INTRODUCTION
SMEDDS is a strategy for the delivery of hydrophobic drugs that are insoluble in water in order to improve the oral bioavailability. SMEDDS spontaneously forms an emulsion in the gastrointestinal tract presenting the drug in a dissolved form, and the small droplet size provides a large interfacial surface area for drug absorption.¹

N6-(4-hydroxybenzyl) adenine riboside (designated T1-11) is originally extracted from the tradition Chinese medicine, Gastrodia elata. T1-11 has been shown to activate the A2AR, and has been shown to delay the progression of a transgenic mouse model of Huntington’s disease (R6/2) in motor coordination.¹

However, due to the poor solubility of T1-11 in water, the oral bioavailability of T1-11 was really low (< 5%). The objectives of this study were to develop and characterize the optimal formulation of SMEDDS that can effectively improve the solubility of T1-11.

EXPERIMENTAL METHODS
- Phase diagram: A pseudo-ternary phase diagram was constructed using the composition of Labrafac® PG, Tween 80 and 95% alcohol as shown in Figure 1. Various ratios of the components were mixed under moderate agitation. SMEDDS could be achieved to form the transparent solution.
- Solubility of T1-11: The saturated solubility of T1-11 in the SMEDDS of different compositions was determined by adding an excess of drug and stirring continuously for at least 24 h to reach the equilibrium. The supernatant was centrifuged at 4000 rpm for 5 minutes.
- Analysis of T1-11: The SMEDDS was analyzed by reversed phase high performance liquid chromatography quipped with a C18 column and the absorbance at 270 nm was monitored via a UV detector. The mobile phase composition was 0.1% tri-fluoroacetic acid and methanol at a ratio of 60: 40 (v/v), and the flow rate was set at 0.5 mL/min.

The particle size distribution was analyzed...
by diluting the SMEDDS with water and analyzed by a N5 Submicron Particle Size Analyzer.

RESULTS AND DISCUSSION

As shown in Figure 1, the shaded area indicated the conditions where SMEDDS could be formed. T1-11 loaded SMEDDS containing 10% (w/w) Labrafac® PG, 72% (w/w) Tween 80, and 18% (w/w) 95% alcohol was chosen and the highest amount of dissolved T1-11 was found in the formation ($6.94 \pm 0.15$ mg/mL). The mean particle size of T1-11 loaded SMEDDS was found between 180 and 250 nm within 28 days of storage at room temperature (Figure 2).

CONCLUSION

A T1-11 loaded SMEDDS was prepared by adding $6.94 \pm 0.15$ mg/mL of the drug into the mixture containing 10% (w/w) Labrafac® PG, 72% (w/w) Tween 80, and 18% (w/w) 95% alcohol. The current SMEDDS can effectively improve the solubility of T1-11.

REFERENCES


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