



New Formulation of Resveratrol, a Natural Compound with Anti-fatigue Effect:

Thermosensitive Hydrogels Preparation and Pharmacokinetics Assessment

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Abstract

Introduction: Resveratrol (RES), a natural polyphenolic compound, exerts an anti-fatigue activity, but its administration is complicated by its low water solubility, short half-life ($t_{1/2}$) and rapid **in vivo** metabolism. Our previous study has demonstrated that the anti-fatigue effect of RES could be manifested through improving its water solubility and oral bioavailability. In order to overcome the shortcoming of short $t_{1/2}$ and **in vivo** metabolism, RES was loaded in thermosensitive hydrogels to extend the $t_{1/2}$ and improve the bioavailability of RES.

Methods: The thermosensitive hydrogel composed of 20% (w/w) Poloxamer 407 and 2.5% (w/w) Poloxamer 188 was prepared using cold method. Sol-gel transition temperature range of the hydrogel was 32°C and the RES release from the hydrogel was mainly controlled by Fickian diffusion. RES plasma concentration was quantified by the currently developed and validated high-performance liquid chromatography with electrochemical detection method.

Results: The pharmacokinetics result indicated that RES-loaded hydrogel has been significantly prolonged the $t_{1/2}$ by 4.2 fold and reduced the clearance of RES by 2.3 fold. Furthermore, pharmacokinetic studies revealed an improvement in $AUC_{0-\infty}$ by 2.4 times of RES released from RES-loaded hydrogel in comparison with the RES solution.

Conclusions: According to our results, we concluded that RES-loaded hydrogel offers a new approach to extend the $t_{1/2}$ and improve the bioavailability of RES. The hydrogel will be further processed for future studies in anti-fatigue activity and rat exercise performance evaluation.

Keywords: Resveratrol, Thermosensitive hydrogel, Pharmacokinetics, Bioavailability