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Sprague-Dawley 랫트에서 수용성 Surfactin C 제형의 경구흡수율 및 약물동태학적 연구

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Phamracokinetics and bioavailability of Water-soluble formulation of Surfactin C in Sprague-Dawley rats

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실험목적

Surfactin is a macrolide lipeptide produced by Bacillus subtilis (Arima et al. 1968, Sandrin et al. 1990). It has a strong surface tension-lowering activity, together with antitumor, fibrinolytic and antiviral activities. Various pharmacodynamic activities for surfactins have been demonstrated in vitro, but bioavailability of surfactins has not been proven. The aim of the present study was to evaluate systemic bioavailability of new water-soluble formulation of surfactin C and to determine its pharmacokinetic profiles.

재료 및 방법

Surfactin C was extracted and purified from the fermentation products of Bacillus subtilis BC1212 (Korean Patent 10-2004-0092258). The surfactin C-Na, water-soluble formulation form was analyzed after heat-treatment, treatment with proteolytic enzymes and at different pH values. To evaluate the bioavailability and pharmacokinetic profiles of surfactin C, a single dose of surfactin C-Na (25 mg as surfactin C/kg of body weight) was administered to Sprague-Dawley (SD) rats. The concentration of surfactin C in plasma samples were analyzed by liquid chromatography/mass spectrometry. The plasma surfactin C concentration vs. time was analyzed using model-independent standard methods for the derivation of pharmacokinetic parameters.

결과 및 고찰

The stability of surfactin to pH, temperature and protease was evaluated. Surfactin was resistant to high temperature, a wide range of pH and the action of hydrolytic enzymes. The pharmacokinetic natures of surfactin which were shown the short half-life, rapid clearance and poor bioavailability (Table 1 and Fig. 1). The results of study should provide preliminary data of surfactin for further dose-finding studies and for the design of application forms. It is also be important to a context of the safety of surfactin.

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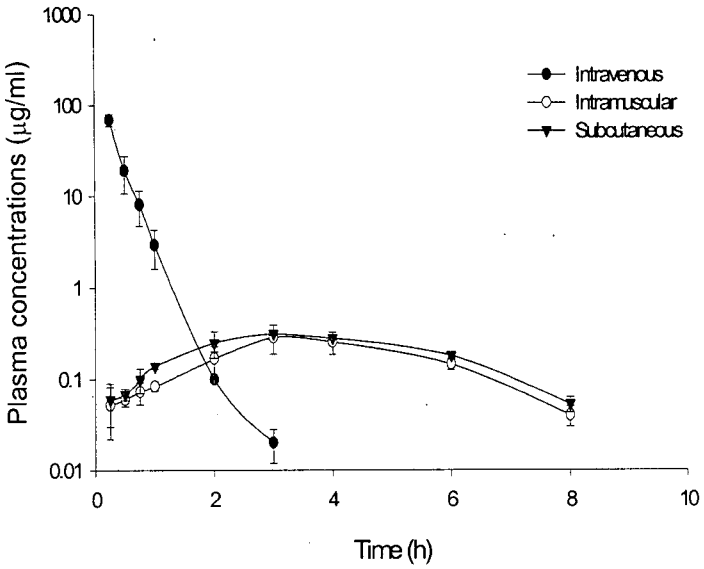

Fig. 1. Plasma concentrationsof surfactin C-Na in SD rats after intravenous, intramuscular and subcutaneous administration with 25 mg/kg of body weight.

Table 1. Pharmacokinetic parameters of surfactin C-Na in SD rats after intravenous, intramuscular and subcutaneous administration with 25 mg/kg of body weight

Pharmacokinetic parameters	Units	The routes of administration		
		Intravenous	Intramuscular	Subcutaneous
t_{max}	h	-	3	3
C_{max}	μg/ml	240.6±33.7	0.31±0.10	0.32±0.06
λ_z	1/h	1.16±0.80	0.51±0.08	0.47±0.11
$t_{1/2\lambda z}$	h	0.63±0.24	1.46±0.54	1.61±0.23
AUC	μg·h/ml	59.4±11.2	1.28±0.56	1.43±0.61
V_z	l /kg	0.12±0.02	-	-
Cl	l /h/kg	0.42±0.08	-	-
MRT	h	0.19±0.07	3.85±1.24	3.81±1.63
V_{ss}	l/kg	0.08±0.05	-	-

† t_{max}, the time to reach peak or maximum plasma concentration C_{max}, peak plasma concentrations; λ_z, terminal elimination coefficient; $t_{1/2\lambda z}$, terminal elimination half-life; AUC, area under curve; V_z, volume of distribution; Cl, total body clearance; MRT, mean residence time; V_{ss}, volume of distribution at the steady state.