



Relationship between Lactone Ratios of 9-Nitrocamptothecin and their Lactone/Carboxylate Equilibria *In Vitro* and *In Vivo*

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SUMMARY. The aim of this study was to evaluate the effect of lactone ratios on the lactone/carboxylate equilibria of 9-nitrocamptothecin (9-NC) *in vitro* and *in vivo*. The interconversion of lactone and carboxylate forms of 9-NC was studied. Then the lactone ratio vs time profiles of these 9-NC solutions were further investigated in pH 7.4 PBS, rat plasma and blood. 9-NC solutions with different lactone ratios (lactone ratios=100 %, 75 %, 50 %, 25 % and 0 %, respectively) were obtained by modifying the pH of solution and it was found that the effects on lactone/carboxylate equilibrium were in the order: blood cells > plasma albumin > pH. After i.v. administration, between the groups of 100 % and 75 % lactone ratios, the AUC_{0-t} values of lactone 9-NC were almost equal. Therefore, there might be no difference between the anticancer activities of 9-NC solution in the range of 75~100 % lactone ratios.

KEY WORDS: 9-nitrocamptothecin, Intravenous injection, Lactone, Pharmacokinetics.

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