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

Jun CHEN 1*†, Rongrong HU 1†, Xixiong YANG 2, Rong TIAN 1, Wei GU 1, Zhipeng CHEN 1 & Baochang CAI 1

1 College of Pharmacy, Nanjing University of Chinese Medicine, Nanjing 210046, China.
2 College of Chemical Engineering and Pharmacy, Jingchu University of Technology, Jingmen 448000, China.

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\textsubscript{0-4} 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.

* Author to whom correspondence should be addressed. E-mail: chenjun75@163.com
† Contributed equally to the project and are considered to be co-first authors