CHAPTER V

CONCLUSION

In Vitro Studies.

The simple and rapid high-performance liquid chromatographic analysis of serum methotrexate utilized apparatus, and analytical condition as follow:

column : radial μ Bondapak C18

detector : ultraviolet spectrophotometer, at 303 nm

solvent : 0.01 M KH_2PO_4 pH 4.5/acetonitrile = 82/18

IS : 8-chlorotheophylline

extraction: Sep pak

The HPLC analysis could be used for monitoring serum methotrexate concentration to prevent the toxicity.

In Vivo Studies.

From pharmacokinetic study, single dose of 1 mg/ml of methotrexate intravenous injection was studied in 11 patients suffering from head and neck cancer. Serum methotrexate levels were determined by the HPLC. Individual serum profile were analyzed according to two-compartment model using PCNONLIN computer program. The distribution rate constant, elimination rate constant, biological half-life, and mean peak serum

concentration were 4.15 hr^{-1} (1.8 - 6.2 hr^{-1}), 0.19 hr^{-1} (0.09 - 0.3 hr^{-1}), 4.2 hours (2.3 - 7.5 hours), and 6.7 mcg/ml (3.6 - 8.4 mcg/ml), respectively. Besides these, pharmacokinetic equation which calculated serum methotrexate concentration at any times was elaborated. Average volume of distribution and total clearance were 23.7 L, and 4.5 L/hr, respectively.

Tumor responses for methotrexate subsequent by irradiation in Thai patients suffering from head and neck cancer were 100% with complete response rate of 57.1% and partial response rate of 42.9%.