Thesis Title : Kinetic Study of D-Galactosamine, 6-Azauridine and 5-Fluorouridine in chemotherapy of hepatoma.

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ABSTRACT

6-AzaUrd, 5-FUrd and Urd in ascitic fluid and AS-30D cells were analysed by reversed phase HPLC system and detected with coupled UV spectrophotometre. The concentration determined by peak-height analysis were used for kinetic analysis of drugs.

The studies with AS-30D ascitic hepatoma cells *in vivo* revealed the rapid increase of 6-azaUrd or 5-FUrd level in both ascitic fluid and cells after administration of the respective drugs. The exponential decrease was observed after 30 min of administration for both drugs in ascitic fluid . In cells, 5-FUrd level declined rather sharply, whereas the level of 6-azaUrd decreased at slower rate. Pretreatment with GalN and 6-azaUrd significantly accerelated the rate of reduction of 5-FUrd in both

ascitic fluid and cells. In addtition, pretreatment was followed by UTP depletion to the minimum level within 60 to 90 min. This interval seems to be the most suitable time for sequential administration of 5-FUrd in chemotherapy.

Experimental chemotherapy of intrahepatic tumor bearing rat was performed with doses of drugs adjusted from the kinetic study. The schedule employed was GalN (100 mg/kg) and 6-azaUrd (30 mg/kg) at 0 min and 5-FUrd (15 mg/kg) at 60 min later. The treatment was started on the fifth day after transplantation and every second day, totally 7 times. The tumor bearing rats receiving GalN, 6-azaUrd and 5-FUrd in combination as scheduled had an extended median survival time over the untreated and the animals treated with other regimens.