Thesis Title	Pharmacokinetics of Dipyridamole in Thalassemia.
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Degree	Master of Science (Pharmacology)

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Date of Graduation 5 June B.E.2532 (1989)

ABSTRACT

Dipyridamole has been used in alleviating numbers of clinical symptoms related to cardiovascular disorders. The presumed modulating activities of dipyridamole on platalet function suggest its therapeutic potential for hypoxemic syndrome, commonly associated with splenectomized thalassemia patients. The pharmacokinetics data of dipyridamole for proper dosing regimens in thalassemia patients is essentially nonexisted. This study was designed to develop an HPLC-method for monitoring dipyridamole in human blood; both in the plasma and the red blood cells, and study its pharmacokinetic nature

in thalassemia so that an accurate dosage regimen could be develop for this very unique group of individuals.

Being a compound contains chromophore that produces both UV-(max.280 nm) and fluorescence (max.ex.285 & em.475nm) spectra of which the molar absorptivity of the latter is very strong and thus its detecting sensitivity at 1 nanogram level has been satisfactory developed. Under the acidic chromatographic condition the silica-base C-18 column is less affected and is highly favorable over other conventional methods that the sample preparation in complex matrix, i.e. human blood can be accordingly simplified. The use of minimal amounts of Pic-B6 (2uM) is recommended in this study against the traditional use of ralatively high concentration of the pairing reagent (i.e., 5mM). This was found to have additional advantages in term of efficiency, reliability and sensitivity.

The pharmacokinetics parameters of dipyridamole after a single oral dose of 50mg in 8 thalassemia (4 non-splenectomized & 4 splenectomized) and 4 normal volunteers were accordingly determined. It was found that thalassemia patients could absorb less dipyridamole than normal individuals judging from the smaller AUC in thalassemia. The deviated changes of the internal milieu in the gastrointestinal tract in thalassemia was believed to be the contributing cause of delayed in lag time and Tmax of dipyridamole in blood while the absorption rate nor other related pharmacokinetic parameters were not changed. Dipyridamole seems to stay longer in the RBC than the plasma as the $t^{1}/_{2\beta}$ was longer in

the RBC, the site of its therapeutic action. It was proposed that dosage regimen of dipyridamole could be better derived from the pharmacokinetic data of the RBC rather than the parameters commonly taken from the plasma. This would provide a more accurate monitoring and better use of dipyridamole in thalassemia.