# Effect of AST-120 on Endothelial Dysfunction in Adenine-Induced Uremic Rats

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(アデニン尿毒症ラットにおける血管内皮障害に対する AST-120 の効果)

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Abstract

Chronic kidney disease (CKD) is an independent risk factor for development of cardiovascular disease (CVD) and CKD represents often endothelial dysfunction.
Indoxyl sulfate (IS) is a uremic toxin that accelerates the development of CKD. Serum levels of IS are elevated in patients with CKD, and appear to be correlated with CKD progression. Oral adsorbent AST-120 retards deterioration of renal function, reducing accumulation of IS. In the present study, we determined the monocyte adhesion in the adenine-induced uremic rats *in vivo* and effects of AST-120 in the adhesion and alterations of-adhesion molecules.

Twenty-four rats were divided into four groups as follows: control, control+AST-120, adenine and adenine+AST-120 groups. Body weight and blood pressure were measured on days 0, 21 and 49. Blood samples were taken on days 0, 21 and 49 in each group from the tail vein and by heart puncture under ether anesthesia on day 49. The number of monocyte adherent to the endothelium of thoracic aorta at arterial bifurcation by imaging the entire endothelial surface and the mRNA expressions of adhesion and atherosclerosis-related molecules were examined on day 49. The mRNA expressions of ICAM-1 and VCAM-1 in human umbilical vein endothelial cells were also examined. The adenine-treated rats indicated increases of serum urea nitrogen (s-UN) and creatinine (s-Cr) compared with those in control rats. AST-120 decreased the elevated IS levels in the adenine-treated rats. Adenine increased the number of adherent monocytes, and AST-120 suppressed the increase. The monocyte adhesion was related to serum creatinine and IS in sera. Over-expression of VCAM-1 and TGF-ß1 mRNA in the arterial walls were observed in uremic rats. IS induced increase of the ICAM-1 and VCAM-1 mRNA expressions *in vitro*. In HUVEC, ICAM-1 and VCAM-1 mRNA were accelerated by IS in a dose-dependent manner.

It appears that uremic condition introduces the monocyte adhesion to arterial wall and AST-120 might inhibit increasing the monocyte adherence with CKD progression.