TRANSFORMATION PRODUCTS OF EXTRACELLULAR NAD^+ IN THE RAT LIVER: KINETICS OF FORMATION AND METABOLIC ACTION

Bracht, A.[1], Kangussu, M.[1], Sá-Kanishi, A.B., Lopez, C.H.[1], Kelmer-Bracht, A.M.[1], Broetto-Biazon, A.C.[1]
Departamento de Bioquímica, Universidade Estadual de Maringá, 87020900 Maringá, Brazil

Extracellular NAD^+ is a paracrine agent in the liver. Its main effects are increases in portal perfusion pressure and glycogenolysis and transient inhibitions of oxygen consumption and gluconeogenesis. Extracellular NAD^+ is also extensively transformed in the liver. The purpose of the present work was to determine the main products of extracellular NAD^+ transformation and to quantify their contribution as paracrine agents. The experimental system was the isolated perfused rat liver. The NAD^+ transformation was monitored by HPLC. The single pass transformation of 100 μM NAD^+ ranged between 75% at 1.5 minute after starting infusion to 95% at 8 minutes. The most important products of single pass NAD^+ transformation in the outflowing perfusate were ADP-ribose > uric acid ≈ inosine. Cyclic ADP-ribose (cADP-ribose) as well as adenosine were not detected in the outflowing perfusate. The metabolic effects of ADP-ribose were essentially those already described for NAD^+. These effects were sensitive to suramin (P2 purinergic receptor) but insensitive do 3,7-dimethyl-1-(2-propynyl)-xanthine (A2 purinergic receptor antagonist). Inosine, a known purinergic A3 agonist, was equally active on metabolism, but uric acid was inactive. It was concluded that the metabolic and hemodynamic effects of extracellular NAD^+ are caused mainly by interactions with purinergic receptors with a significant participation of its transformation products ADP-ribose and inosine.

Financial support: CNPq/Fundação Araucária.