ラット脂肪組織のcGMP阻害型，低Km cAMP分解酵素活性に対するバナデートの増強効果

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Stimulatory Effect of Vanadate on 3′, 5′-Cyclic Guanosine Monophosphate-Inhibited Low Michaelis-Menten Constant 3′, 5′-Cyclic Adenosine Monophosphate Phosphodiesterase Activity in Isolated Rat Fat Pads

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ABSTRACT When isolated rat fat pads were incubated with vanadate, the low Michaelis-Menten constant (Km) cAMP phosphodiesterase (PDE) activity in the microsomal fraction was increased in a time- and dose-dependent manner with vanadate. 3′, 5′-Cyclic GMP inhibited the vanadate-stimulated PDE activity with similar profile to the insulin-stimulated one. The stimulatory effect of vanadate was inhibited by inhibitors of tyrosine kinases such as amiloride, biochanin A, and genistein to various extents. Vanadate and insulin both showed the full effect in the absence of either K^+, Na^+, or Ca^{2+} in the medium, while preincubation of the fat pads with a chelator of inracellular Ca^{2+} inhibited the vanadete action in a dose-dependent manner. The insulin action was not inhibited by it at tested concentrations. These results suggest that vanadate action, in contrast to the insulin one, is dependent on the intracelluar level of Ca^{2+}. Preincubation of the fat pads with inhibitors of protein kinase C such as 1- (5-isoquinoline sulfonyl) -2-methylpiperazine (H-7) and staurosporine inhibited, in part, the vanadate action but not insulin one. Furthermore, vanadate increased the protein kinase C activity in fat pads but insulin did not increase. H-7 and amiloride showed a significant inhibition of stimulation of protein kinase C activity by vanadate.

These results suggest that vanadate stimulates, in part, the 3′, 5′-cyclic GMP-inhibited low K_m cAMP PDE activity in the microsomal fraction of fat pads through the activation of tyrosine kinase and protein kinase C-mediated processes.

抄録 ラット脂肪組織とバナデートを反応させるとミクロソーム画分に存在するインスリン感受生cAMP分解酵素活性が特異的に増強された。この増強作用は，チロシンキナーゼおよびC－キナーゼ阻害剤や細胞内Ca^{2+}キレーターによって種々の程度に阻害された。ミクロソーム画分のC－キナーゼ活性は，バナデートによって著しく上昇しかつこれらの阻害剤によってcAMP分解酵素の場合と同様な阻害を受けた。これらの結果から，バナデートは受容体のチロシンキナーゼに作用後，C－キナーゼの活性化を介する過程を経てcAMP分解酵素の活性増強作用を示す事が確認された。