

## SALICYLATE AND ACETYLSALICYLATE REVERSIBLY INHIBIT 6-PHOSPHOFRUCTO-1-KINASE ACTIVITY

Guilherme Autuori Spitz, Wagner Santos Coelho, Mauro Sola-Penna and Patricia Zancan

Laboratório de Enzimologia e Controle do Metabolismo (LabECoM), Departamento de Fármacos, Faculdade de Farmácia, UFRJ

It has been known for more than a century that salicylates are able to reduce fasting blood glucose in diabetic patients. The cellular and molecular mechanisms of the hypoglycemic activity of these compounds have not been satisfactorily elucidated. Recently, it has been published that these effects of salicylates might directly occur in cell metabolism and not in hormone levels. Cellular glucose metabolism occurs through the glycolytic pathway where 6-phosphofructo-1-kinase (PFK) plays a crucial regulatory role. The aim of this study is to evaluate the effects of salicylate and acetylsalicylic acid (ASA) on PFK activity of purified enzyme, muscle homogenates and erythrocytes lysates. Our results show that both salicylate and ASA promote a dose-dependent inhibition of PFK activity in all the systems employed, presenting an average  $K_i$  of 6 mM. This inhibition decreases at higher concentrations of purified PFK, suggesting the modulation of oligomeric equilibrium of the enzyme by the compounds. ASA is not inducing the acetylation of the enzyme, since its effects are very similar to the effects of salicylate. In conclusion, we can infer that the hypoglycemic effects of salicylate can be due to the inhibition of the regulatory glycolytic enzyme PFK and, consequently, glycolysis.

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