Effects of \( p \)-Synephin on Hepatic Metabolism and Perfusion Pressure: Calcium- and cAMP-Dependence and Sensitivity to Adrenergic Antagonists

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**INTRODUCTION:** \( p \)-Synephin and *Citrus aurantium* extracts are widely used for weight loss purposes and as appetite suppressants. Considering that the *C. aurantium* (bitter orange) extract is able to affect diverse parameters of liver metabolism and hemodynamics and that \( p \)-synephin is one of the main active components of this extract, the purpose of the present work was to obtain detailed informations about the action of synephin in the liver.

**MATERIALS AND METHODS:** The experimental system was the isolated perfused rat liver. The perfusion fluid was Krebs/Henseleit-bicarbonate buffer, saturated with an \( O_2:CO_2 \) (95:5) mixture, pH 7.4 and at 37 \(^\circ\)C. Metabolites were measured using standard enzymatic procedures. Oxygen uptake was monitored polarographically and pressure was measured by means of a pressure transducer. cAMP was assayed by means of ELISA.

**RESULTS AND DISCUSSION:** \( p \)-Synephin stimulated glycogenolysis, glycolysis, gluconeogenesis and oxygen uptake. The compound also increased the portal perfusion pressure and the redox state of the cytosolic \( NAD^+/NADH \) couple. All these phenomena were \( Ca^{2+} \)-dependent. Similarly, the infusion of \( p \)-synephin produced a stable increment in cAMP release. This phenomenon always occurs in the liver under the influence of agonists whose action is at least partly mediated by cAMP. The metabolic and hemodynamic actions of \( p \)-synephin were strongly inhibited by prazosin (mainly \( \alpha_1 \)-antagonist) and yohimbine (mainly \( \alpha_2 \)-antagonist), moderately affected by propranolol (non specific \( \beta \)-antagonist) and almost not affected by SR59230A (\( \beta_3 \)-antagonist). Propranolol, on the other hand, completely abolished the stimulation of cAMP release.

**CONCLUSIONS:** In conclusion, the results of this work support the proposition that \( p \)-synephin presents important metabolic and hemodynamic effects in the liver, mediated by both \( Ca^{2+} \) and cAMP. These effects are mainly catabolic in nature, probably mediated by adrenergic stimulation, and they could be contributing to the overall stimulation of metabolism that usually occurs during weight loss periods.

Key-words: liver, cAMP, \( Ca^{2+} \), metabolism.

Supported by: CNPq