

Poster n. 9

Flavonoid-induced gastric relaxation: structure-activity relationship and mechanism of action.

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Flavonoids comprise a large group of polyphenolic compounds widely distributed in the plant kingdom, abundantly present in the human diet, which exhibit various biological activities, including relaxing effects on various smooth muscles. The cellular effects of flavonoids may be independent of classical antioxidant capacity, but rather they may be mediated by their interaction with specific proteins central to intracellular signalling cascades.

The aims of this study were: i) to investigate the effects of six flavonoids (apigenin, genistein, quercetin, rutin, naringenin and catechin), belonging to different classes, on the gastric tone in mouse isolated stomach; ii) to determine the structure activity-relationship; iii) to examine the mechanism of action of apigenin and quercetin.

Intraluminal pressure recordings from the isolated stomach *in vitro* were performed and the mechanical responses induced by flavonoids before and after different pharmacological treatments were analyzed.

Our results suggest that all flavonoids tested produced a concentration-dependent relaxation which is influenced to a great extent by the structure of the molecules. The action of apigenin and quercetin on the mouse stomach seems not to be dependent on neural action potentials, NO/prostaglandin production, activation of K⁺ channels and does not involve adenylate cyclase or phosphodiesterase, but it can be attributed, at least partly, to a blockade of Ca²⁺ entry through voltage-dependent Ca²⁺ channels.

Poster n. 10

Apoptosis during early development of sea urchin

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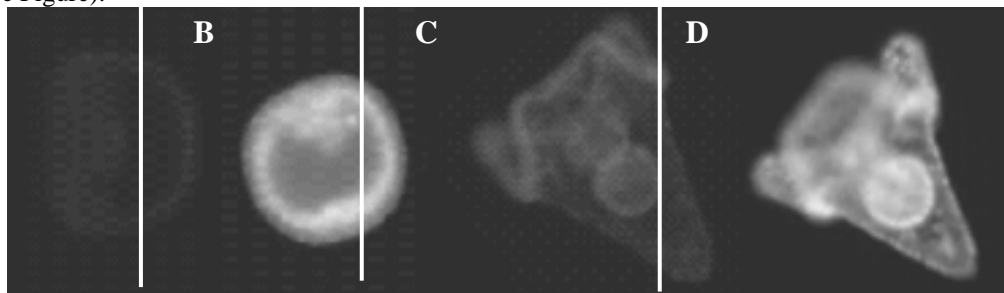
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Apoptosis is a genetic program of cell death that eliminates superfluous or compromised cells during development and adult life of many organisms. In sea urchin embryos, apoptosis is not only a physiological event during larval metamorphosis, but also a process induced by cadmium accumulation or other stressor like TPA (12-O-tetradecanoylphorbol-13-acetate) followed by an increase of temperature to 31°C. Apoptosis is a highly conserved process usually operated by a proteolytic cascade that involves caspase activation by two different pathways: extrinsic and intrinsic. The first one involves membrane death receptors, while the second involves mitochondria.

In this work we analyzed the possible involvement of extrinsic and intrinsic apoptotic pathways in physiological and stressful conditions in *Paracentrotus lividus* embryos. By fluorescent TUNEL assays we demonstrate that apoptosis is part of cadmium and TPA+31°C stress response. We find that Cd and TPA+31°C treatments induce apoptosis through caspase-3 activation, while caspase-7 is the main effector of physiological apoptosis. Caspase-10 is active only in physiological apoptosis, while caspase-8 is mainly involved in stress-induced apoptosis. In addition, we did not find any involvement of mitochondria.

Moreover we observed, in Cd-treated embryos, a Reactive Oxygen Species (ROS) increase, that could be related to the induction of apoptosis (see Figure).

ROS detection in whole embryos:
A) Control 17 h
B) 17 h CdCl₂ 1 mM
C) Control 42 h
D) 42 h CdCl₂ 100 μM



Poster n. 11

Manganese Toxicity: sea urchin embryos and Stress Response Effects

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