17β-Estradiol (E2) and testosterone (T) exert actions in most tissues, including skeletal muscle. In aging, this tissue can present pathologies as sarcopenia which is associated to low hormone levels that cause a deregulation of apoptosis. We previously showed that E2 and T inhibit H_2O_2-induced apoptosis in C2C12 cells. The aim of our research is to deepen the understanding of the molecular mechanisms involved in the antiapoptotic action of both hormones. Here we demonstrate that E2 up-regulates the expression and activity of manganese superoxide dismutase (MnSOD). Pharmacological and immunological assays indicate that the estrogen receptor (ER) mediates these events. In addition, the expression of MnSOD decreases when cells are treated with H_2O_2, effects that are reversed with E2 pretreatment. Moreover, we showed that the apoptotic action of hydrogen peroxide requires PKCδ; and JNK activation which is abolished when the cells were pretreated with E2. Experiments with the antagonist flutamide involved the androgen receptor (AR) in the antiapoptotic action of T. Biochemical and immunological data support mitochondrial and microsomal localizations of the AR in the C2C12 cells. Sucrose gradient fractionation demonstrates its presence in rafts and caveolae. Besides, the AR interacts with caveolin-1, association that is lost after T treatment, suggesting AR translocation from the membrane to inner cellular compartments. Our studies contribute to elucidate the mechanism by which these hormones regulate signaling cascades, throwing light on the molecular basis of myopathies associated with deregulation of apoptosis by sex hormone deficiency states.

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Mechanism of action of alendronate in vascular system

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Bisphosphonates (BP) are frequently used in postmenopausal osteoporosis treatment. Although the risks attributed, hormone replacement therapy with estrogens combined with synthetic progestins remains as an alternative therapy to counteract menopause signs and symptoms. The aim of this work was to investigate the mechanism of action of alendronate (ALN) in vascular tissue in the presence or absence of synthetic or endogenous ovarian hormones such as estrone (E1) or medroxyprogesterone acetate (MPA). Endothelial cell (EC) and vascular smooth muscle cell (VSMC) cultures obtained from aortic strips of Wistar rats were employed. ALN treatment markedly increased EC nitric oxide (NO) production. In the presence of a MEK inhibitor (PD98059), the stimulatory action of ALN on NO was suppressed (220 ± 20 vs 345 ± 38, 210 ± 21 vs 221 ± 18 nmol de NO/mg prot; C vs ALN, C + PD vs ALN + PD; $p < 0.05$). The effect of ALN on NO synthesis was dependent on extracellular calcium influx, since preincubation of EC with the channel blocker verapamil (V) blunted BPs action (238 ± 19 vs 245 ± 16 nmol de NO/mg prot; C + V vs ALN + V; $p < 0.05$). In combined treatments, the simultaneous exposure to ALN + E1 enhanced the individual effect of each agonist on NO synthesis (90, 60, 58% above control; ALN + E1, ALN, E1; $p < 0.05$). Higher improvement effect was obtained with ALN + MPA co-treatments (56, 80, 250% above control; ALN, MPA, ALN + MPA; $p < 0.02$). Using wound healing assays, we showed that 48 h of exposure to ALN partially prevents MPA-induced cell motility (344 ± 39 vs 219 ± 24 cells/field; MPA vs MPA + ALN; $p < 0.001$). In conclusion, BP has a positive effect on vascular homeostasis, improved by the presence of ovarian hormones.

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Nano-hydroxyapatite for use in bone tissue repair

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Bone can be considered as a biological hybrid material composed of organic and inorganic components: collagen and rod-shaped hydroxyapatite (HAP) of 20–50 nm lengths. The synthetic hydroxyapatite ($Ca^{10}(PO^4)^6(OH)^2$) has been extensively used as a bone substitute material due to its chemical and structural similarities with natural mineral bone. One way to obtain HAP nanoparticles is by using self-assembled amphiphilic molecules as structure directors. This study involves different hexadecyltrimethylammonium bromide (CTAB) micellar-block copolymer organized networks. Inorganic precursors were added in sequence to the CTAB-polymer solution, followed by a hydrothermal treatment. The final product was separated from the suspension by filtration and then dried. The X-ray diffraction and infrared spectroscopy pattern of the materials synthesized corresponds to the HAP pattern. Transmission and scanning electron microscopy microphotographs show a fiber network composed by 37 nm length HAP nanorods. After treatment with simulated body fluid (SBF) a layer of HAP nanocrystals grew on the material surface; that is related to the bioactivity of the material. To confirm the samples' biocompatibility, calvarial osteoblasts obtained from neonatal rats were exposed to the material and then, viability and cell adhesion were evaluated. A new method of HAP nanocrystals with similar shape, morphology and chemical characteristics of bone were developed. After SBF immersion, material revealed a spherulitic-like HAP layer that implies a positive physiological response and good bond ability to the host tissue. Therefore, nanomaterials obtained by the proposed synthesis could have a wide range of biomedical applications.

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Opposite effects of ursodeoxycholic acid and sodium deoxycholate on intestinal calcium absorption

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We have demonstrated that sodium deoxycholate (NaDOC) inhibits the intestinal Ca^{2+} absorption. The aim of this study was to find out if ursodeoxycholic acid (UDCA) could block this effect. Four week old chicks were used: 1) controls, 2) treated with NaDOC, 3) treated with UDCA and 4) treated with UDCA + NaDOC. Intestinal calcium absorption was measured by the ligated intestinal loop technique. Glutathione (GSH), carbonyl content, changes in mitochondria membrane permeability and the activity of alkaline phosphatase (AP) and antioxidant enzymes were determined by spectrophotometry. Ca^{2+}-ATPase pump (PMCA), Na^+/Ca^{2+} exchanger (NCX1) and calbindin D28K (CB) protein and gene expressions were analyzed by RT-qPCR and Western blot. UDCA alone increased the intestinal Ca^{2+} absorption. The combined treatment restored the inhibitory effect caused by NaDOC on the intestinal Ca^{2+} absorption. UDCA increased the protein and gene expression of PMCA, NCX1 and CB and the combined treatment returned the values to control ones. AP activity did not change with UDCA, but decreased with NaDOC, which was prevented by simultaneous UDCA administration. NaDOC decreased the GSH content and increased protein carbonyl content and SOD activity. NaDOC altered the internal mitochondrial membrane permeability, which was avoided by UDCA. In conclusion, UDCA promotes intestinal absorption of Ca^{2+}, while NaDOC produces inhibitory effect. The combined treatment avoids the inhibitory effect of NaDOC because the oxidative stress is blocked. The stimulatory effect of UDCA on the intestinal Ca^{2+} absorption would be through an increase in gene and protein expression of molecules involved in the transcellular Ca^{2+} pathway.

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Effects of osteogenic cells on insulin resistance. Comparative effect in two strains of rats

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Osteocalcin (BGP) is a small protein with three glutamic acid residues exclusively secreted by osteoblasts, which regulate energy metabolism through insulin receptor signal in that cell. The objective of the present study was to determine if obesity could affect BGP effect on insulin resistance. We studied two strains of rats: spontaneous IIMb/Beta obese (OB) and Wistar (W) rats. Three mothers of each strain were fed from the beginning of pregnancy with AIN93 diet containing 0.6 mg% calcium; male weaning rats ($n = 10$ per group) continued with the same diet until 50 days of life. BGP, Cross Laps (CTX) and insulin were evaluated in serum by ELISA; glucose by enzymology colorimetric and HOMA-IR was calculated. Body composition was evaluated according to AOAC methods. Results: (mean ± SD): OB vs. W, respectively: total fat: 39 ± 10 vs. 18 ± 4 g% ($p < 0.01$); ash (g%): 2.6 ± 0.2 vs. 3.2 ± 0.4 ($p < 0.05$); BGP (ng/ml): 375 ± 46 vs. 840 ± 106 ($p < 0.01$); glucose (mg/dl): 152 ± 69 vs. 99 ± 41; insulin (mg/dl): 4.1 ± 1.6 vs. 0.1 ± 0.0 ($p < 0.01$); CTX (ng/ml): 83 ± 8 vs. 94 ± 6 ($p < 0.01$). OB rats presented significantly low mineral content, BGP, insulin and bone resortion but higher glucose values and insulin resistance vs. W group. Conclusion: Obesity induced a reduction in BGP levels and in bone resortion that suggest a decrease biologically active BGP levels. This reduction would increment fasting glucose levels and insulin resistance. UBACyT 20020100100320.

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