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First International Congress on Biotechnology and Bioengineering

International initiatives for a Sustainable Development

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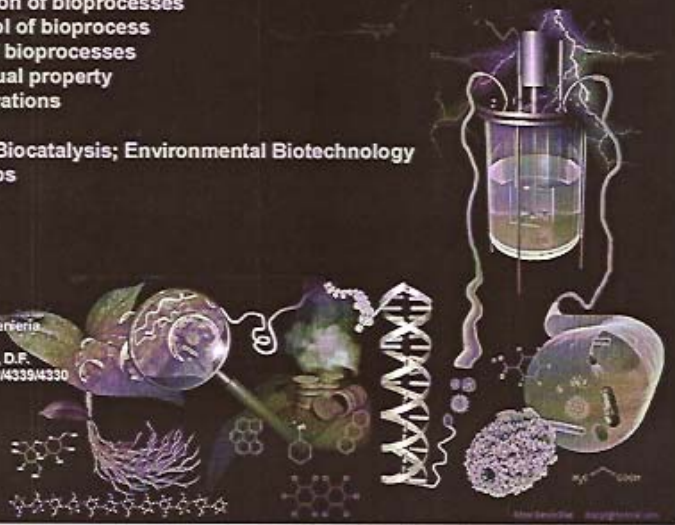
Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional (CINVESTAV - IPN)

CONFERENCE THEME:

- International initiatives for a Sustainable Development
- Governmental initiatives for solving local state problems (TBC)

Topics:

- Environmental Biotechnology
- Biofuels
- Food Biotechnology and Bioengineering
- Biocatalysis technologies
- Plant biotechnology
- Nanobiotechnology
- Biopolymers
- Bioprocesses
- Bioinformatics
- Biosafety issues and bioethics
- Modelling and simulation of bioprocesses
- Supervision and control of bioprocess
- Design and scale up of bioprocesses
- Patenting and Intellectual property
- Biotechnological innovations
- Round tables on:
  Bioprocesses; Biocatalysis; Environmental Biotechnology
- Courses and Workshops



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BIOACTIVITY OF COCOA FLAVONOIDS IN HUMAN HEPATOMA CELLS. ANTIOXIDANT EFFECTS AND MECHANISMS OF ACTION AGAINST OXIDATIVE STRESS-INDUCED APOPTOSIS.

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Cocoa (*Theobroma cacao* L.) is an important dietary source of polyphenols, mostly flavanols and procyanidin oligomers, which have shown a powerful in vitro antioxidant activity, providing protection against oxidation. Oxidative stress plays a pivotal role in ageing, as well as in the pathogenesis of several diseases such as cardiovascular and inflammatory diseases, cancer, neurodegenerative disorders, etc. *In vitro* and *in vivo* studies have suggested a beneficial action of cocoa flavonoids against oxidative stress-related diseases associated to their antioxidant effect. We investigated the protective effect of a cocoa polyphenolic extract (CPE) on cell viability and antioxidant defences of cultured human HepG2 cells submitted to oxidative stress induced by *tert*-butyl hydroperoxide (*t*-BOOH). Furthermore, the protective effect of the CPE against *t*-BOOH-induced apoptosis and the molecular mechanisms involved in this process were also studied.

Cells were treated with increasing concentrations of CPE within a physiological range (0.05-50 µg/mL) for 2 or 20h. Cell viability, reactive oxygen species (ROS), glutathione (GSH) and malondialdehide (MDA) levels, and activity of antioxidant enzymes (glutathione peroxidase -GPx- and glutathione reductase -GR-) were determined after treatment of cells with *t*-BOOH. Also, the activity and/or levels of proteins involved in survival/proliferation pathways or cell death were determined (namely ERKs, AKT, JNKs, caspase-3) after 20h treatment with a selected CPE dose.

CPE completely prevented the cell damage and ROS generation associated to the oxidative stress induced by *t*-BOOH. CPE also diminished MDA levels and modulated the activity of antioxidant enzymes, increased after *t*-BOOH treatment, partly recovering the depleted GSH levels. Incubation of HepG2 cells with *t*-BOOH induced apoptosis as evidenced by caspase-3 activation, together with a transient activation of the extracellular-regulated kinases (ERKs) and a sustained activation of the c-jun N-amino terminal kinases (JNKs). Pre-treatment of cells with CPE prevented apoptosis through the reduction of ROS generation and the modulation of the apoptotic pathways activated by *t*-BOOH. CPE treatment also activated survival signalling proteins such as protein kinase B (AKT) and ERKs, and increased the activity of GPx and GR.

These findings show that CPE, in concentrations within a realistic physiological range, is an effective cytoprotective agent against oxidative stress-induced apoptosis, up-regulating cell survival/proliferation pathways. Therefore, cocoa may play an important role in the protection against oxidative stress-related diseases and ageing.