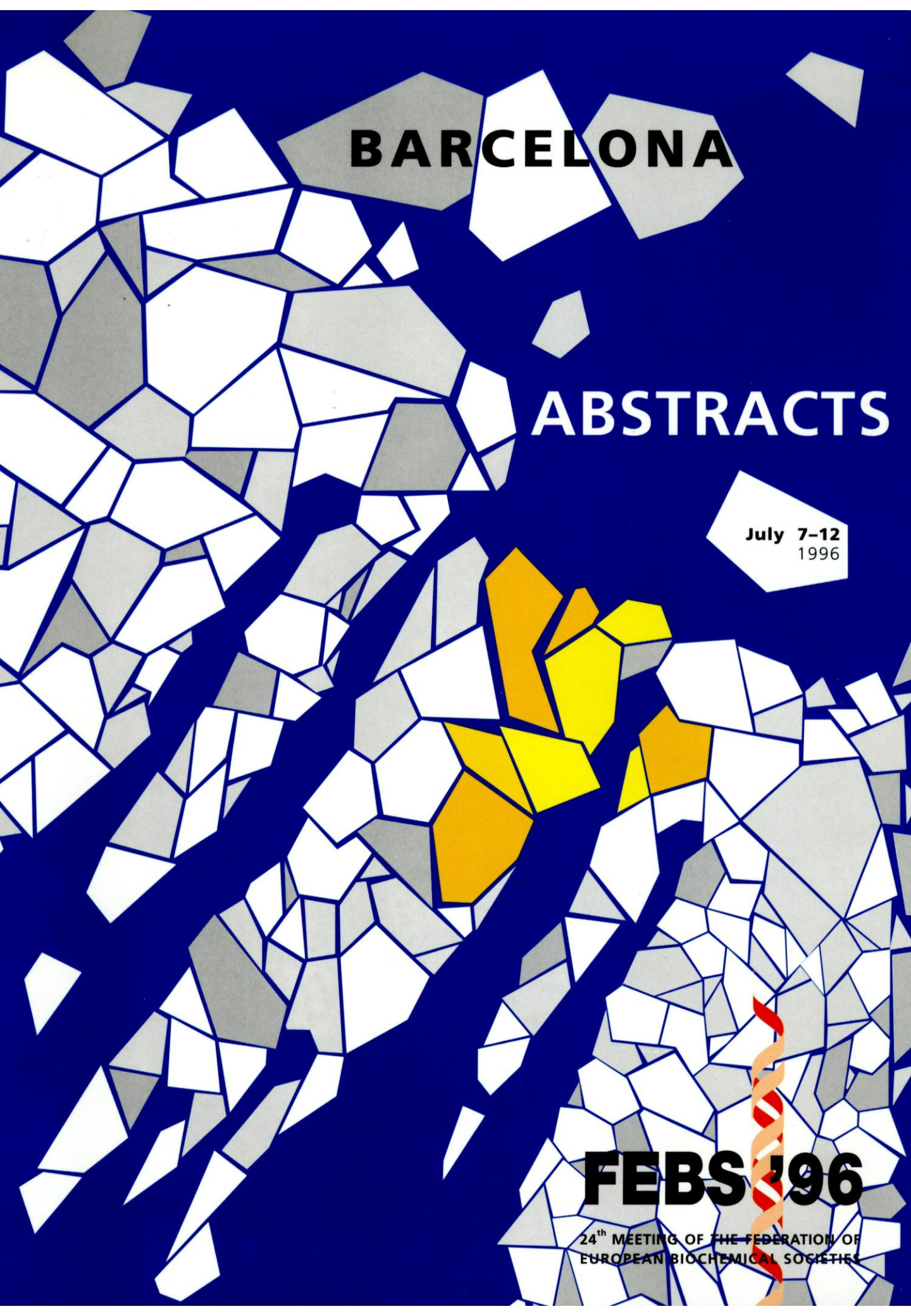
BARCELONA

ABSTRACTS

July 7–12
1996



FEBS '96

24th MEETING OF THE FEDERATION OF EUROPEAN BIOCHEMICAL SOCIETIES

13 GLUTATHIONE STATUS OF PLACENTAE FROM DIFFERENTLY POLLUTED REGIONS OF UKRAINE.

M.Obolenskaya, T.Tschaikovskaya, L.Lebedeva, L.Macewicz, O.Platonov, K.Decker. Inst.Mol.Biol.& Gen., Kiev, Ukraine; Inst.Bioch., Freiburg, Germany.

Placenta specimens were obtained in "clean"[C], radioactively contaminated[RadCon] and chemically polluted[ChPol] areas. The corresponding indices of glutathione status in these areas were the following: glutathione transferase(GST) activity 50.4±9.0, 17.0±3.0 and 18.0±2.0 mU/mg cytosolic protein; glutathione reductase activity 1.4±0.2, 0.9±0.1 and 0.3±0.05 mU/mg cytosolic protein; total SH-group content 30.2±5.7, 18.5±1.9 and 25.9±1.9 μmol/g; tissue low-molecular thiols 0.25±0.03, 0.35±0.06 and 1.3±0.2 μmol/g tissue. Malonic dialdehyde (MDA) content as a measure of lipid peroxidation was 55.8±7.8 and 59.1±7.3 μmol/g tissue in C and ChPol areas, respectively, in contrast to 128.8± 13.0 μmol/g tissue in RadCon regions. In the specimens from the latter, the distribution of GSTπ-specific antigen along the villi was uneven unlike that in specimens from C regions. The similar decrease of GST activity in both RadCon and ChPol regions of Ukraine may be the cause of a reduced detoxifying activity of placentae while the differences between both areas in the placental glutathione and oxidative status point to different pathogenetic mechanisms of this reduction.

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14 EXPLORING CONNECTIONS BETWEEN ARGININE METABOLISM AND OXIDATIVE RESPONSE IN HUMAN POLYMORPHONUCLEAR LEUCOCYTES.

D.Teixeira, E.Mascarell, V.Meneu, M.P.Merino, M.Ortuño, E.O'Connor and E.Alonso. Dpt. of Biochemistry, University of Valencia (Spain); e-mail: Eulalia.Alonso@uv.es

Circulating levels of arginine and its metabolites may contribute to regulate the oxidative burst elicited by antigens in human polymorphonuclear leucocytes (PMNs). To test this hypothesis and to investigate their biochemical mechanisms we have analyzed, using flow cytometry, the effect of arginine and metabolically related compounds (citrulline and ornithine) on the levels of H_2O_2 and O_2^- under basal conditions and following stimulation with chemotactic factors. Arginine availability increases H_2O_2 generation by PMNs following PMA stimulation. This effect is clearly related to the function of nitric oxide syntetase, since it is blocked by nitroarginine, an inhibitor of this enzyme, while citrulline, another product of this enzyme, decreases the generation of H_2O_2 and O_2^-. Calcium may be involved also in the modulation of the oxidative burst, since it decreases the production of O_2 reactive species and potenciates the inhibitory effect of nitroarginine. In view of these results, it seems feasible that changes in the availability of arginine and citrulline may affect the oxidative response of PMNs under certain physiopathological conditions.

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15 MITOCHONDRIAL DNA DELETION AND OXIDATIVE STRESS

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Different causes can originate in cells oxidative stress. Several Authors have demonstrated in various systems an age-related increase of the reactive oxygen species (ROS) by-produced during oxidative phosphorylation (1). In particular, quite recent studies have shown that mitochondrial DNA (mtDNA) is damaged by such ROS with the production of base modifications, point mutations and large deletions (2). Therefore, the evaluation of the oxidative damage of mtDNA has become more and more important. Especially the quantitation of the 4977 bp long deletion of mtDNA known as the "common deletion" (because of its frequency in disease cases as well as in aging samples) is quite relevant. We have established a method for the determination of the 4977 bp deletion absolute level (3) and we have used it in the specimens of two brain areas from a group of Alzheimer's disease patients versus controls, previously assayed for the OH^{8}dG content of mtDNA. We have measured the 4977 bp deletion level also in skeletal muscle samples, assayed for some respiratory chain enzyme activities, isolated from healthy humans of different ages (4). Furthermore, we tested the "common deletion" level as a marker of an increased mitochondrial oxidative stress in non-primary mitochondrial pathologies involving alteration of mitochondrial metabolism or structure.

1. Sohal, R.S., et al., (1995), Free Rad. Biol. Med., 19, 499.
2. Wallace, D.C., et al., (1995), In: Molecular aspects of aging (Esser K. and Martin G.M. eds) John Wiley & Sons Ltd, pp. 199.
3. Lezza, A.M.S., et al., (1993), Bull. Mol. Biol. Med., 18, 67.
4. Lezza, A.M.S., et al., (1994), Biochem. Biophys. Res. Commun., 205, 772.

16 POTENTIAL NEUROPROTECTANTS WITH ANTIOXIDANT AND CALCIUM UPTAKE INHIBITORY EFFECTS

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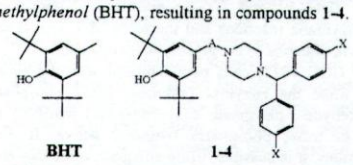
The aim of this study was to attempt the combination of pharmacophores responsible for calcium antagonistic and lipid peroxidation inhibitory effects. The structures of known calcium antagonists *medibazine, lomerizine, cinnarizine* and *flunarizine* were hybridized with that of *2,6-di-tert-butyl-4-methylphenol* (BHT), resulting in compounds **1-4**.



BHT **1-4**

1 A: CH_2; X: H
2 A: CH_2; X: F
3 A: CH=CH-CH_2; X: H
4 A: CH=CH-CH_2; X: F

The effects of the parent and hybrid compounds were measured in the following tests: NADPH-induced lipid peroxidation in rat brain microsome and Fe^{2+}-induced lipid peroxidation in rat brain homogenate, K^+-induced and veratrine-induced ^{45}Ca uptake in synaptosomes and 2,2-diphenyl-2-picrylhydrazyl reduction. The new compounds showed strong lipid peroxidation inhibitory and free radical scavenging effects retaining the calcium antagonistic properties.

Meanwhile Alcon Laboratories Inc. published the results of their similar approach that was pursued independently (1).

[1]Hellberg,M. *et al.* (1995) WO 95/15958

17 OXIDATIVE STRESS INVOLVEMENT IN DOXORUBICIN TOXICITY

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The possible involvement of oxidative stress in doxorubicin (DOX) toxicity was investigated in Balb/c mice. DOX was injected s.c. (30 mg/kg) and the activities of superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx), NADPH oxidase as well as the level of thiobarbituric acid reactive substance (TBARS) and lipid peroxides was determined in the liver, heart, lung and kidney. Four days after DOX injection, soluble SOD activity decreased in the kidney and lung and did not changed in the liver and heart. Mitochondrial SOD activity decreased in the lung and kidney and did not changed in the liver. Catalase activity decreased in the liver and lung, increased in the heart and did not changed in the kidney. GPx activity increased in the heart, decreased in the liver and kidney and did not changed in the lung. NADPH oxidase activity decreased in the liver and did not changed in the other tissues. The level of soluble TBARS increased in the liver and did not changed in the other tissues, while the level of mitochondrial TBARS increased in the lung and did not changed in the other tissues. The level of soluble peroxides increased in all tissues except the kidney. The results suggest that the liver and the lung will be more susceptible to reactive oxygen species (ROS) as indicated by increase in TBARS and lipid peroxides. The heart seems more resistant to ROS compared to other tissues. These results suggest that antioxidants could protect these tissues against the toxic effects of DOX, and this possibility is being further studied in our laboratory.

18 INFLUENCE OF OXIDATIVE STRESS PRODUCED BY NITRITE IN THE ACTIVITY OF METHAEMOGLOBIN REDUCTASE IN TWO DIFFERENT SPECIES OF FISH

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Nitrite induces the oxidation of the haemoglobin forming methaemoglobin, which is nonfunctional. To oppose this formation fishes have an enzyme that reverses the process called methaemoglobin reductase (1). *In vitro* activity of the methaemoglobin reductase was determined, in the presence and absence of nitrite in two marine fishes (toadfish, *Halobatrachus didactylus* and gilt head sea bream, *Sparus aurata*). The K_M and V_{max} were determined through the Eisenthal and Cornish-Bowden Plot. The basis for this study is that the methaemoglobin reductase system has very active ferricyanide reductase activity (2). *Halobatrachus didactylus* showed a significant decrease in its values of methaemoglobin reductase activity with the increase in nitrite concentration (38.9; 16.3; 14.5; 14.0 and 12.3 mmol NAD^+/min/gHb respectively to 0; 1; 3; 6 and 9 mM NO_2^-). In *Sparus aurata*, the nitrite didn't induced significant variations in the methaemoglobin reductase activity (27.8; 27.1; 25.3; 22.3 and 18.7 mmol NAD^+/min/gHb gHb respectively to 0; 1; 3; 6 and 9 mM NO_2^-). This results probably indicate fish to have other paths opposing to the formation of methaemoglobin, rather than the enzymatic system of the methaemoglobin reductase. At the moment the meaning of this of this different behaviour is not known.

(1) Jensen, F.B. (1993) Fish Physiol. Biochem., 12, 111
(2) Board, P.G. (1981) Clin. Chim. Acta, 109, 233

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FEBS '96 SECRETARIAT

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7th May 1996

Reference: **PW07-18**

Dear Dr.,

I am pleased to inform you that the abstract entitled "Influence of oxidative stress produced by nitrite in the activity of methaemoglobin reductase in two different species of fish" by Anibal Jaime Miguel has been accepted as a poster communication in the FEBS ´96 Meeting.

The presentation of your poster has been scheduled for **Tuesday, 9th July.** Please, follow the instructions enclosed.

I would remind you that as stated in our 2nd Announcement, accepted abstracts will also be published in the WWW pages on the Meeting (http://www.bq.ub.es/febs96/). A keyword search engine has been designed to allow easy access to the desired abstracts. I would encourage you to consult these pages. We are certain that through this new facility, the exchange of information in poster sessions will be much more efficient. Participants will be able to organize visits to the posters before coming to Barcelona, and even arrange informal meetings during the congress. The abstracts have been added to the WWW pages after the required format conversion. If you detect any mistake that may affect the understanding of your work please let us know.

Looking forward to meet you in Barcelona

Yours sincerely

Josep Ll. Gelpí
FEBS ´96 Scientific Secretariat