B015  
DIFFERENTIAL MODULATION OF OXIDATIVE AND NITROSATIVE STRESS PATHWAYS BY RED WINE POLYPHENOLS, PROVINOLS™, IN TISSUES FROM ZUCKER FATTY RATS (FA/FA)

A. AGOUNI 1, A. H. LAGRUE-LAK-HAL 1, M. SLADKOVÁ 1, 2, O. PECHANOVÁ 2, M. C. MARTÍNEZ 1, R. ANDRIANTSITOHAINA 1
1 UMR CNRS 6214-Inserm U771, Angers, France
2 Institute of Normal and Pathological Physiology, Bratislava, Slovak Republic

Obesity is associated with numerous complications including significantly increased risks of diabetes and cardiovascular diseases. Epidemiological studies report an inverse association between dietary flavonoid consumption and mortality from cardiovascular diseases. The aim of this work was to study the effects of dietary supplementation of red wine polyphenols extract, Provinols™, on the regulation of both NO and O2- pathways in different tissues in an experimental model of obesity, the Zucker fatty rats (ZF).

Rats received normal diet (n = 6) or supplemented with Provinols™ (20 mg/kg/day, n = 6) for 8 weeks. Then, NO and superoxide anion (O2-) production was measured in heart, lung, and liver by electronic paramagnetic resonance after animals being scarified.

Also, tissues were dissected and homogenized for western blot assays protein expression. 

Table 1: Western blots analysis of protein expression in tissues from Provinols™ treated rats compared to controls. ns, no significant change.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>p65</th>
<th>p-IκκBα</th>
<th>g6s</th>
<th>p70S6ks</th>
<th>p90S6ks</th>
<th>Mn</th>
<th>Cu/Zn</th>
<th>EC</th>
<th>SOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td></td>
</tr>
</tbody>
</table>

Regarding NO, we found that Provinols™ increased its release in both heart and lung, but not in liver. However, Provinols™ reduced O2- production in lung and liver without change in heart.

In conclusion, Provinols™ differentially affect the balance between NO and O2-, as well as the associated regulation of protein expression, in tissues from obese rats.

B016  
IMPACT OF A 14-NIGHT INTERMITTENT HYPOXIA (IH) EXPOSURE ON METABOLIC AND CARDIOPULMONARY ADAPTATIONS TO EXERCISE IN HEALTHY SUBJECTS

J. TONINI 1, 2, 3, A.-S. MICHALLET 1, 2, P. FLORE 1, 2, H. NESPOULET 1, 2, J.-L. PEPIN 1, 2, B. WUYAM 1, 2, P. LEVY 1, 2, R. TAMISIER 1, 3
1 Inserm ERI17, Laboratoire Hypoxie Physiopathologie (HP2), Grenoble, France
2 Joseph Fourier University, REx-S, IFR1, Grenoble, France
3 CHU de Grenoble, Clinique de Physiologie, Sommeil et Exercice, Grenoble, France

Introduction – Modifications in exercise tolerance have been reported in obstructive sleep apnea (OSA) patients. Also specific mechanisms have been speculated related to intermittent hypoxia (IH), hypertension, obesity or metabolic disturbance associated to OSA may play a significant role in exercise limitation. In order to eliminate these confounding factors we aimed to evaluate the effects of IH exposure during 14 nights in healthy subjects on exercise capacity, cardio-respiratory response and substrate oxidation during exercise.

Methods – 12 healthy subjects (BMI: 21.8 ± 0.5 kg.m-2) were exposed to repetitive sequences of hypoxia – re-oxygenation during sleep in a hypoxic tent with appropriate cyclic re-oxygenation (rate: 30 desaturations.h-1). Maximal and sub-maximal exercise tests were performed before and after exposure in order to investigate cardio-respiratory variables and substrate oxidation parameters.

Results – IH did not modify maximal exercise parameters (VO2, heart rate, power output) nor ventilatory threshold (VTh). But this was achieved with a significant PETCO2 reduction and a VE/VCO2 increase during both maximal (Pre IH vs Post IH at VTh and Max, p<0.05) and sub-maximal (Pre vs Post at 30% and 60% Pmax, p<0.05) exercise tests, indicating hyperventilation. At the 1st min recovery after submaximal exercise test, diastolic arterial blood pressure (DBP) was higher after IH exposure (Pre: 60 ± 3 vs Post: 78 ± 2 mmHg) in favour of a delayed DBP recovery following acute exercise. During sub-maximal exercise, subjects reached maximal lipid oxidation at higher power output and presented a decreased blood lactate at the same percentage of relative power after IH exposure.

Conclusion – Exposure to 14 days of nocturnal IH is associated with an increased ventilatory response to subsequent exercise at sea level. Furthermore, delayed DBP recovery after exercise is in favor of early IH-induced cardiovascular modifications. This observation related to muscular exercise adaptations confirms the efficacy of the model in reproducing early cardiovascular alterations occurring in OSA. Moreover, this model induces metabolic adaptations as soon as 14 nights of exposure.

Jeudi 2 avril 2009, de 10 h 00 à 11 h 30
C — STRESS OXYDANT, NO, VIEILLISSEMENT

C001  
SENSIBILITÉ DE LA FONCTION ENDOTHÉLIALE AU STRESS OXYDANT CHEZ UN MODÈLE DE RATS EXPOSÉS À UNE POLLUTION DE TYPE CITADINE AU CO

C. REBOUL 1, G. MEYER 1, J. BOISSIERE 1, S. GAYRARD 1, P. OBERT 1
1 EA4278, Physiologie et Physiopathologie des Adaptations Cardiovasculaires à l’Exercice, Avignon, France

Objectif – Evaluer les effets d’une pollution de type citadine au monoxyde de carbone (CO) sur la fonction endothéliale, chez une population de rats. Cette évaluation sera réalisée dans des conditions standard, puis consécutivement à un stress oxydant aigu.

Méthodologie – Des rats Wistar (250-280 g) ont été placés dans un environnement simulant une pollution de type urbaine au CO (30 ppm 12 h/jour + 5 pics à 100 ppm) pendant 4 semaines. La fonction vasculaire a été évaluée sur des anneaux d’aorte thoracique isolés et placés dans une cuve à organe. La vasorelaxation endothélium-dépendante a été évaluée sur anneaux pré-contractions par l’ajout de doses croissantes d’acétylcholine en condition standard, puis après un stress oxydant (incubation dans la cuve de peroxyde d’hydrogène, H2O2, 200 μM, 20 min). Cette incubation a été réalisée en présence ou non d’un inhibiteur spécifique de la NOS2...