superior stability to the semiquinone radical over the nitro respectively. Indeed, in agreement with their reduction potentials.

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PP58

Preventive effect of Ellagic acid on blood pressure, oxidative stress and cardiac remodelling in L-NAME induced hypertensive rats

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The aim of this study was to investigate the preventive effect of Ellagic acid (EA), a potent antioxidant agent, on blood pressure, oxidative markers and cardiac wall remodelling in L-NAME induced hypertensive rats. Male Sprague-Dawley rats were given L-NAME (40 mg/kg/day) to induce hypertension, and simultaneously treated with EA 15 mg/kg/day for 4 weeks (L-NAME + EA group), or a vehicle (L-NAME group). Age-matched rats served as a control group. Systolic blood pressure (SBP) was monitored using a tail cuff method once a week throughout the experiment. After 4 weeks of treatment, the rats were weighed, anaesthetized with peritoneal injection of pentobarbital-sodium (60 mg/kg) and scarified by exsanguinations. The heart was isolated. The left ventricular weight (LVW), heart weight (HW), relative heart weight (LVW/BW), cardiac wall thickness and ventricular cross-sectional area were determined as ventricular hypertrophy index. Plasma malonyldialdehyde (MDA) and vascular superoxide production were also analysed. EA significantly reduced SBP of L-NAME treated rats when compared to those of the L-NAME group (167.96 ± 1.21 vs. 197.91 ± 7.95 mmHg; $p < 0.05$). The prevention of increase in SBP of L-NAME + EA was associated with a decrease in superoxide production in carotid arteries (65.67 ± 4.48 vs. 109.91 ± 8.45 counts/min/mg dry weight; $p < 0.05$) and MDA (6.74 ± 0.4 vs. 9.56 ± 1.01 μM; $p < 0.05$). However, there were no significant difference of rat body weight, HW, LVW and LVW/BW ratio among groups. The left ventricular wall thickness of L-NAME treated with EA was slightly smaller than those in L-NAME rats but not reach a statistically significant level. The cross-sectional area of left ventricle in L-NAME and L-NAME treated with EA were significantly greater than those in control group, but there were no significant difference in cross-sectional area between these two groups. In conclusion, EA has antihypertensive and antioxidant properties in nitric oxide deficiency model, but has no effect on a cardiac wall remodelling.

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PP59

Ability of silybin and its derivatives to prevent protein oxidation in different model systems

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Flavonolignan silybin is a major component of silymarin isolated from seeds of the milk thistle (*Silybum marianum*). Natural silybin is a mixture of two diastereoisomers - silybin A and silybin B. Besides hepatoprotective effects, silybin was lately reported as anticancer, chemoprotective, dermatoprotective and hypocholesterolemic agent. Silybin plays an important role as antioxidant and free radical scavenger as well. Therefore, the antioxidant activity of silybin, dehydrosilybin, 23-*O*-butanoyl and 23-*O*-palmitoyl esters of silybin (respectively C4 and C16) was investigated. Especially their ability to prevent activation of hemoglobin (Hb) to highly reactive hypervalent heme protein species (ferrylHb and perferrylHb) was examined. Indeed, Hb cytotoxicity has been associated with the generation of protein radicals, which are formed when the ferric iron of Hb (Fe^{3+}) is oxidised by H_2O_2 to (Fe^{4+}) to form perferrylHb and ferrylHb, with the later also bearing a radical on its protein. The relationship between the structural properties of silybin and its derivatives and their ability to prevent oxidation of Hb was investigated in model system in the presence or the absence of lipids. The antioxidant activities of silybin, dehydrosilybin, 23-*O*-butanoyl and 23-*O*-palmitoyl silybin derivatives were correlated with their interaction with Hb species. Results are discussed in relation to the potential of dehydrosilybin, silybin and C4 and C16 derivates to prevent activation of Hb to hypevalent heme protein species.

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PP60

Disruption in energy metabolism and mitochondrial function in a cellular model of inflammation-induced acute kidney injury

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Sepsis is a very complex clinical condition characterized by stimulation of a systemic inflammatory response due to an infection. It has a profound deleterious effect on kidney functions leading to sepsis-induced acute kidney injury (AKI). This failure seems to occur

through complex mechanisms involving the immune system response, inflammatory pathways, cellular dysfunction and hemodynamic instability. To study the role of cellular energetic metabolism dysfunction and mitochondrial impairment in the occurrence of AKI during sepsis, we developed an inflammation-induced *in vitro* model using proximal tubular epithelial cells (HK-2) exposed to a bacterial endotoxin (lipopolysaccharide, LPS). This investigation has provided key features on the relationship between endotoxic stress and mitochondrial respiratory chain assembly defects. Firstly, we have shown that renal cells subjected to LPS are no longer capable to use adequately the available oxygen to maintain their metabolic functions. One hypothesis of this down-regulation suggests that impairment in mitochondria oxidative phosphorylation could prevent cells from using oxygen for adenosine triphosphate (ATP) production and potentially could cause sepsis-induced organ failure. Our study has then investigated this possible mitochondrial impairment to explain the decreased O_2 consumption rate observed in LPS-treated HK-2 cells. After exposure to LPS, functionality of mitochondria was affected without any disturbance in their spatial organization. LPS seemed rather to interrupt mitochondrial oxidative phosphorylation by blocking cytochrome c oxidase activity. As a consequence, disruptions in the electron transport and the proton pumping across the system occurred, leading to a decrease of the mitochondrial membrane potential, an electron leakage as the form of superoxide anion, a release of cytochrome c in the cytosol and a decrease in ATP production. This irreversible defect in the production of cellular energy would support the concept that kidney failure in sepsis may occur on the basis of cytopathic hypoxia.

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PP61

Role of glyoxalases system in skin aging and in response to dicarbonyl mediated stress

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During aging and in certain pathologies linked to oxidative stress, the proteins irreversibly modified by carbonylation, conjugation with lipid peroxidation products or glycation, accumulate due to a failure of the protein maintenance systems. Glycation occurs when glucose reacts with amines of proteins leading to the formation of advanced glycation end products (AGE) but AGE can also be produced when the dicarbonyl compounds glyoxal (GO) and methylglyoxal (MG) react with proteins.

The most important detoxification system of these compounds is the glyoxalases system composed of two intracellular enzymes glyoxalase 1 (Glo1) and glyoxalase 2 (Glo2) [1]. The involvement of these two enzymes in the aging process has been studied. Indeed, Glo1 activity is reduced during replicative senescence [2] and its overexpression increases longevity in several animal models [3,4]. However, their role in human skin remains poorly studied.

The aim of this work is to better understand the role of Glyoxalases in skin, in particular in the detoxification of compounds GO and MG in response to oxidative stress, and to study their role in the protection of proteins during skin aging.

To first analyse the regulation of Glyoxalases in skin during aging and UV exposition, an immunohistochemistry study was performed on photoprotected or photoexposed skin sections of 10 young donors and 10 old donors. Our results show that Glo1 is expressed exclusively in the undifferentiated keratinocytes of the epidermis basal layer and is increased in aged skins compared to young skins. Regarding protein glycation, we found that AGE accumulate with age and UV exposition in the dermis but carboxymethyllysine modified proteins are more present in the epidermis of young compared to old subjects.

The transcription factor NF-E2-related factor 2 (Nrf2), which is a key factor in the cellular response to stress, has been shown to regulate the expression of Glo1 [5]. Expression of Nrf2 analysed by IHC on the same samples show a decrease in aged keratinocytes suggesting that Glo1 is regulated by a different pathway in the epidermis progenitors. To better understand the role of glyoxalase enzymes during stress, HaCaT cells were subjected to sublethal and lethal concentrations of GO and MG for 24 hours.

A significant increase of glycated proteins was observed immediatly after stress, together with a decreased activity of Glo1 with no change of its expression. A 24 h recovery leads to a reactivation of the enzyme.

We have currently isolated cellular clones with overexpression or inhibition of Glyoxalases which will allow the identification of preferential protein targets of glycation through proteomic studies.

We expect that our study may contribute to decipher the role of glyoxalases in protein maintenance which is a key element of cellular homeostasis and to identify whether these enzymes could be targets for future anti-aging strategies.

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PP62

In Vitro and In Vivo UV Light Skin Protection by an Antioxidant Derivative of NSAID Tolfenamic Acid

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Moderate doses of UV light are beneficial for the skin, with anti-rachitic, anti-depressive effects, while they may also assist the treatment of skin diseases such as psoriasis. In contrast, elevated doses induce erythema, ageing and carcinogenesis. The common ground for all these skin diseases/ageing is initially inflammation.

The first line of therapy for skin inflammation is the class of corticosteroids, with their known side effects, while non-steroidal anti-inflammatory drugs (NSAIDs) are mainly used as analgesic and secondarily against skin inflammation. Some substances or mixtures with antioxidant properties like resveratrol and curcumin seem to