

## Concurrent Session 17

### Systemic and airway levels of glutathione and $\alpha$ -tocopherol in asthma

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**Background** - Antioxidant defences are impaired in asthma. Measurement of the reduced and oxidized forms of key antioxidants in the airways will improve our understanding of the role of antioxidants in asthma.

**Objective** - To investigate antioxidant defences in asthma, by measuring the oxidized and reduced forms of key antioxidants (glutathione and  $\alpha$ -tocopherol) in the airways (induced sputum) and systemically (peripheral blood).

**Design** - Induced sputum and peripheral blood were collected from stable asthmatics (n=44) and healthy controls (n=31). Total glutathione (GSht), reduced glutathione (GSHr) and glutathione disulfide (GSSG) concentrations were determined by colorimetric assay.  $\alpha$ -tocopherol and  $\alpha$ -tocopherol quinone levels were measured by HPLC.

**Outcomes** - Concentrations of GSht, GSHr and GSSG in sputum supernatant were elevated in asthma versus controls [GSht (median (IQR)); 15.3 (10.0-22.4) versus 7.0 (4.7-14.3)  $\mu$ M,  $P = 0.002$ , GSHr; 4.1 (1.4-6.8) versus 1.2 (0.0-3.8)  $\mu$ M,  $P = 0.026$  and GSSG; 5.9 (4.0-8.4) versus 2.6 (1.8-5.1)  $\mu$ M,  $P = 0.005$ ]. Sputum supernatant GSSG was inversely associated with FEV<sub>1</sub>/FVC% ( $r = -0.316$ ,  $P = 0.029$ ). Circulating  $\alpha$ -tocopherol levels were low in asthma versus controls [plasma; 7.3 (5.7-8.1) versus 12.5 (6.6-18.6) mg/L,  $P = 0.020$  and whole blood; 2.2 (1.5-2.8) versus 2.8 (2.1-3.7) mg/L,  $P = 0.076$ ]. Subjects with asthma had elevated whole blood levels of  $\alpha$ -tocopherol quinone (2.4 (2.1-3.3) versus 1.6 (1.0-2.5) mg/L,  $P = 0.039$ ) and % $\alpha$ -tocopherol quinone (53.8 (47.2-64.4) versus 44.6 (21.0-51.9)%,  $P = 0.039$ ) and %  $\alpha$ -tocopherol quinone correlated with asthma control score ( $r = 0.804$  and  $P = 0.009$ ).

**Conclusion** - In asthma, the oxidant-antioxidant balance is disturbed both systemically and in the airways. Measurement of the oxidized forms of antioxidants is important, as the oxidized forms of both glutathione and  $\alpha$ -tocopherol are clinically relevant, being associated with worse clinical outcomes in asthma.

### Green tea supplementation alters gene transcripts involved in hepatic fat oxidation and synthesis in rats fed high fat diets

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**Background** - Green Tea has been shown to induce many health related benefits including reductions in bodyweight and waist circumference, decreased insulin resistance and improvement in blood lipid profiles all of which are implicated in the aetiology of non-alcoholic fatty liver disease. However, to date little is known about the effect of green tea on the molecular mechanisms regulating hepatic lipid synthesis, storage and oxidation.

**Objectives** - This study investigated the impact of green tea, tea catechins or black tea supplementation on rodent liver gene transcripts essential for lipid oxidation and synthesis, and on liver fat accumulation.

**Design** - Sprague-Dawley rats were fed a high fat diet and supplemented at 100% of their fluid intake with water as a control (n=7), green tea (n=7), epigallocatechin-3-gallate (EGCG) (n=7) or black tea (n=7) from 4 weeks age for a period of 6 months. Following supplementation the mRNA levels of Peroxisome Proliferator Receptor Alpha (PPAR $\alpha$ ), Carnitine Palmitoyl Transferase 1 (CPT1), Acetyl CoA Oxidase (ACO), Sterol Regulatory Element Binding Protein 1c (SREBP-1c), Fatty Acid Synthase (Fsynth), Malonyl CoA Decarboxylase (MCD) and Acetyl CoA Carboxylase (ACC) were measured. Histology and triglyceride analysis was performed to establish the extent of fatty infiltration in the liver.

**Outcomes** - Green tea and black tea supplementation significantly decreased the rodents fat mass and increased the expression of all genes examined, particularly ACO (GT = 20 fold, BT = 14 fold) and MCD (GT = 12 fold, BT = 13 fold). The supplementation with green and black tea also resulted in greater fatty infiltration of the liver than both the control and the EGCG groups.

**Conclusions** - Green and black tea, but not EGCG, appear to cause an increase in the amount of fatty infiltration in the liver, possibly as a consequence of the increased expression of lipid synthesis genes. The concomitant increase in the expression of genes involved in the metabolism of fat suggests that fatty acid turnover in the liver was increased.