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**Toxicity in rats of a betaine/glycerol Natural Deep Eutectic Solvent (NADES) for phenolic compounds extraction****Christine Feillet-Coudray, Melha Benlebna, Mariana Ruesgas-Ramon, Beatrice Bonafos, Gilles Fouret, Erwann durand, François Casas, Charles Coudray and María Cruz Figueroa-Espinoza**  
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**Statement of the Problem:** NaDES (Natural Deep Eutectic Solvents) are new natural solvents in green chemistry and have been shown to allow better extraction of plant bioactive molecules, particularly phenolic compounds, by comparison to conventional solvent. NaDES would allow higher phenolic compounds absorption in rodents following oral administration. However, there is a lack of information regarding their in vivo safety. The purpose of this short study was to verify the safety in rats of a mixture of polyphenols extracted from green coffee beans with NaDES.

**Materials & Methods:** Green coffee phenolic compounds at 10 mg of chlorogenic acid equivalent/mL were extracted by NaDES betaine:glycerol (mole ratio 1:2) + 10 water (v/v). Twelve 6-weeks-old male Wistar rats were randomized into two groups of 6 animals and gavaged for 14 days either with water or with phenolic NaDES extract. Rat body weight, food consumption and drinking were determined every two days. Rats were then sacrificed and blood and tissues collected. Plasma/serum routine biochemical analyses were performed (glucose, creatinine, lipids, ASAT/ALAT, uric acid and urea). Lipid (TBARS), protein (thiols and AOPP) and glucose oxidation (AGEs) products were measured in plasma and liver. Liver lipid and glycogen content were also quantified.

**Findings:** Oral administration of phenolic NaDES extract induced mortality in 2 rats. In addition, it induced excessive water consumption, reduced dietary intake and weight loss, hepatomegaly, plasma oxidative stress associated with high blood lipid levels.

**Conclusion & Significance:** This work demonstrated the toxicity of oral administration of the NaDES: betaine/glycerol, under the acute conditions tested. This occurs despite the fact that this NaDES extract contains polyphenols, the beneficial effects of which have been shown to be numerous. Therefore, complementary work is needed to find the best dose and formulation of NaDES that are safe for the environment, animals and ultimately for humans.

**Recent Publications**

1. Fouret G, Gaillet S, Lecomte S, Bonafos B, Djohan YF, Barea B, Badia E, Coudray C & Feillet-Coudray C (2018) Twenty-week follow-up of hepatic steatosis installation and liver mitochondrial structure and activity and their interrelation in rats fed a high fat-high fructose diet. *Br J Nutr*; 119(4): 368-380.
2. Coudray C, Fouret G, Lambert K, Ferreri C, Rieusset J, Blachnio-Zabielska A, Lecomte J, Ebabe Elle R, Badia E, Murphy MP & Feillet-Coudray C (2016) A mitochondrial-targeted ubiquinone modulates muscle lipid profile and improves mitochondrial respiration in obesogenic diet-fed rats. *Br J Nutr*; 115(7): 1155-66.

**Biography**

Christine Feillet-Coudray has graduated from Montpellier Biological and Food Engineering School in 1991 and obtained PhD in 1995 at the Faculty of Medicine of Montpellier. She works at the National Institute of Agronomic Research. Her research interests range over both micronutrients and oxidative stress physiopathology, and more generally malnutrition and its relation to the development of metabolic syndrome components.

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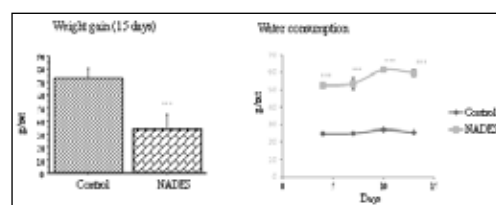


Figure-1: Rats weight gain at the end of the study and water consumption along the study.