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Importance and Bioactivity of the Microbial *trans*-Resveratrol Metabolites Dihydroresveratrol and Lunularin

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Background:
Over the last two decades, the phytochemical *trans*-Resveratrol (*trans*-3,5,4‘-trihydroxystilbene; *t*-RES) gained enormous scientific and public attention due to postulated, positive health effects. Dietary sources of *t*-RES are peanuts, grapes, wine, some berries, and Itadori tea. *T*-RES is considered to mimic the positive effects of calorie restriction, which may prevent or reverse the detrimental effects of obesity, type 2 diabetes, hypertension, chronic inflammation, and other age-associated metabolic diseases. In a former human intervention study with 12 healthy human volunteers the formation of three microbial-derived metabolites of *t*-RES (dihydroresveratrol, 3,4’-dihydro-*trans*-stilbene, and lunularin; Fig. 1) were detected. These metabolites were detected both in vivo and in vitro (Fig. 2; Bode *et al*. 2013).

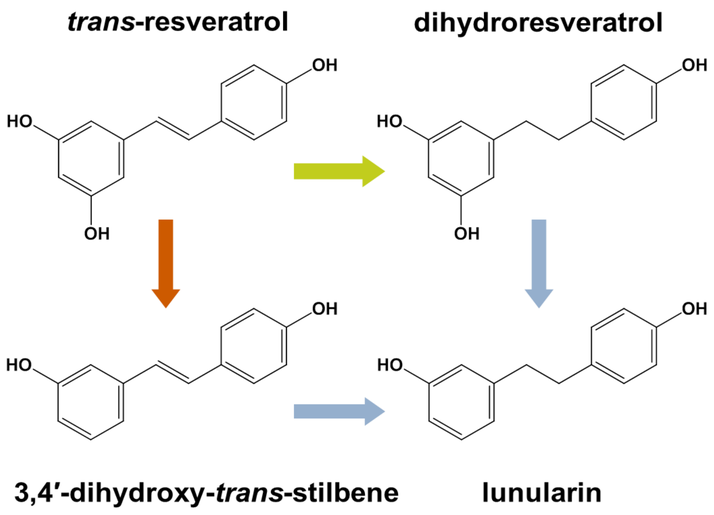

Fig. 1: Formation of *trans*-resveratrol metabolites by the human gut microbiota

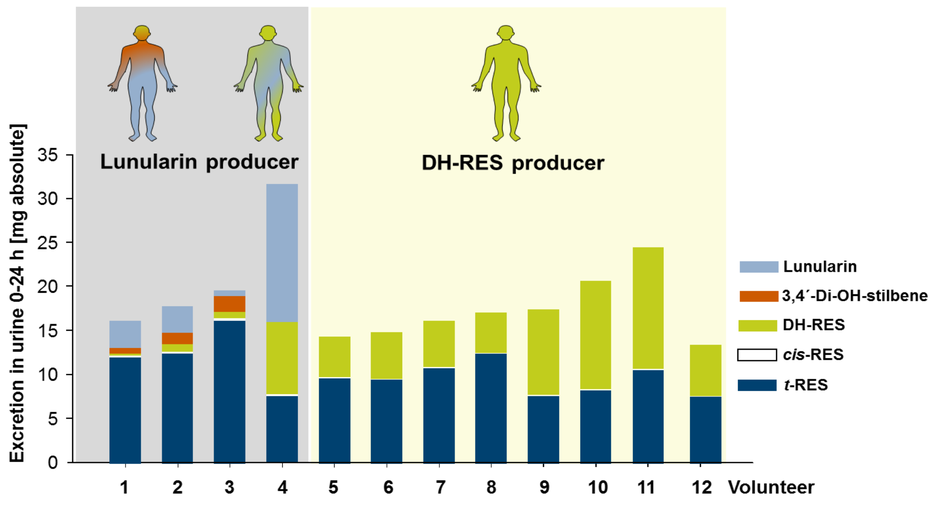

Fig. 2: Metabolites detected in human urine Samples after an oral dose of *t*-RES (Bode *et al*. 2013)

PhD project:

The objective of this PhD project is to clarify the importance of the microbial *t*-RES metabolites dihydroresveratrol and lunularin in human adults by means of a human intervention study that is based on a larger cohort (n = 100). In this human intervention study 1 mg *t*-RES/kg body weight is administered to the volunteers. They will donate urine (spot urine before intervention, $t_{0 - 24h}$ and $t_{24 - 48h}$), blood (sub-group: n = 12; t_{0h}, $t_{1,5h}$, t_{24h} and t_{48h}), and fecal samples during or after the study (Fig. 3).

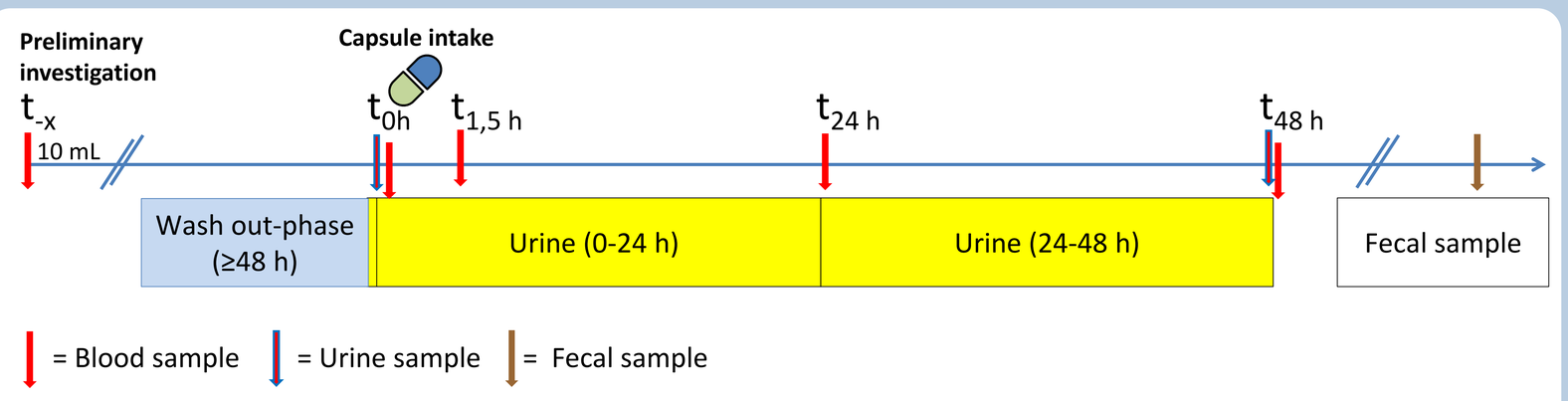

Fig. 3: Timeline of the human intervention study

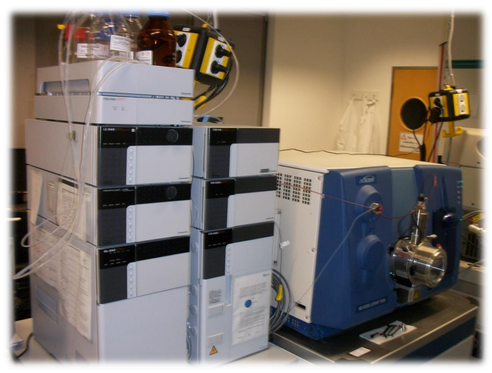

Fig. 4: LC-MS system

Based on their urinary *t*-RES metabolite profiles the volunteers will be grouped in “lunularin producers” and “non-lunularin producers”. Moreover, human blood samples will be used to investigate the phase-II-metabolites (mainly the glucuronates and sulfates) of *t*-RES, 3,4’-dihydro-*trans*-stilbene, and lunularin by LC-MS (Fig. 4). Fecal samples from “lunularin producers” will be used to isolate new *t*-RES metabolising bacteria by cultivating these bacterial strains on solid and liquid media under strict anaerobic conditions using the Hungate technique (Fig. 5).

The fecal samples of the volunteers will be used to compare the fecal microbiota of “lunularin producers” and “non-lunularin producers” by 16S rRNA gene high-throughput sequencing (Fig. 6) and DGGE (Fig. 7). In addition to this approach, qRT-PCR (Fig. 8) will be performed to enumerate total eubacteria as well as the dominant groups of the fecal microbiota.

Fig. 5: (A) Anaerobic bench and (B) Hungate tube

Fig. 6: NGS system

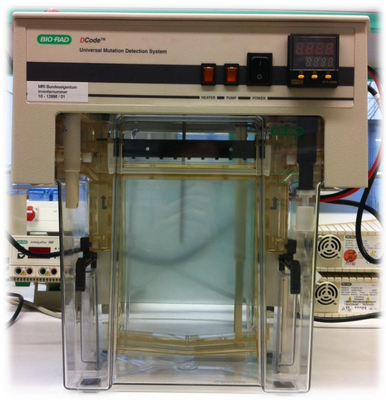

Fig. 7: DGGE system

Fig. 8: qRT-PCR system

References: Bode, L.M., Bunzel, D., Huch, M., Cho, G.S., Ruhland, D., Bunzel, M., Bub, A., Franz, C.M.A.P., Kulling, S.E., 2013. Am J Clin Nutr 97, 295-309.

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