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ORIGINAL ARTICLE

Short-term supplementation with a specific combination of dietary polyphenols increases energy expenditure and alters substrate metabolism in overweight subjects

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BACKGROUND AND OBJECTIVES: Impaired regulation of lipid oxidation (metabolic inflexibility) is associated with obesity and type 2 diabetes mellitus. Recent evidence has indicated that dietary polyphenols may modulate mitochondrial function, substrate metabolism and energy expenditure in humans. The present study investigated the effects of short-term supplementation of two combinations of polyphenols on energy expenditure (EE) and substrate metabolism in overweight subjects.
SUBJECTS AND METHODS: Eighteen healthy overweight volunteers (9 women, 9 men; age 35 ± 2.5 years; body mass index 28.9 ± 0.4 kg m^{-2}) participated in a randomized, double-blind cross-over trial. Combinations of epigallocatechin-gallate (E, 282 mg day^{-1}) + resveratrol (R, 200 mg day^{-1}) and E + R + 80 mg day^{-1} soy isoflavones (S) or placebo capsules (PLA) were supplemented twice daily for a period of 3 days. On day 3, circulating metabolite concentrations, EE and substrate oxidation (using indirect calorimetry) were measured during fasting and postprandial conditions for 6 h (high-fat-mixed meal (2.6 MJ, 61.2 E% fat)).
RESULTS: Short-term supplementation of E + R increased resting EE (E + R vs PLA: 5.45 ± 0.24 vs 5.23 ± 0.25 kJ min^{-1}, $P = 0.039$), whereas both E + R (699 ± 18 kJ 120 min^{-1} vs 676 ± 20 kJ 120 min^{-1}, $P = 0.028$) and E + R + S (704 ± 18 kJ 120 min^{-1} vs 676 ± 20 kJ 120 min^{-1}, $P = 0.014$) increased 2–4 h-postprandial EE compared with PLA. Metabolic flexibility, calculated as the postprandial increase to the highest respiratory quotient achieved, tended to be improved by E + R compared with PLA and E + R + S only in men (E + R vs PLA: 0.11 ± 0.02 vs 0.06 ± 0.02, $P = 0.059$; E + R + S: 0.03 ± 0.02, $P = 0.009$). E + R + S significantly increased fasting plasma free fatty acid ($P = 0.064$) and glycerol ($P = 0.021$) concentrations compared with PLA.
CONCLUSIONS: We demonstrated for the first time that combined E + R supplementation for 3 days significantly increased fasting and postprandial EE, which was accompanied by improved metabolic flexibility in men but not in women. Addition of soy isoflavones partially reversed these effects possibly due to their higher lipolytic potential. The present findings may imply that long-term supplementation of these dosages of epigallocatechin-gallate combined with resveratrol may improve metabolic health and body weight regulation.

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Keywords: polyphenols; human substrate metabolism; resveratrol; epigallocatechin-gallate

INTRODUCTION

Disturbances in lipid metabolism have a key role in the development of obesity, type 2 diabetes mellitus and cardiovascular disease. A mismatch between energy supply and expenditure as well as intrinsic disturbances in the capacity to adapt fuel oxidation to fuel availability (defined as metabolic inflexibility) in adipose tissue and skeletal muscle are the major causes of obesity-related complications.[1]

Impairments in the lipid-buffering capacity of adipose tissue may lead to lipid accumulation in non-adipose tissues (ectopic fat deposition) in conditions where oxidative capacity is insufficient.[2] It is well-established that lipid accumulation in the liver and skeletal muscle is strongly associated with insulin resistance.[3] Indeed, decreased fasting lipid oxidation and impaired switching between lipid and carbohydrate fuels in response to insulin, dietary stimuli or exercise has been observed in conditions of insulin resistance.[1,4,5] Underlying mechanisms for metabolic inflexibility may be a reduced mitochondrial function or capacity,[6] although recent studies indicate that glucose disposal rather than mitochondrial dysfunction is a determinant of substrate utilization during insulin stimulation.[7]

Lifestyle interventions, aiming at reducing (saturated) fat intake and increasing physical activity, have been demonstrated to efficiently counteract disturbances in lipid metabolism and seem to improve metabolic flexibility.[8,9] However, lifestyle interventions have been shown to be ineffective in about 30% of the subjects, indicating the need for additional preventive strategies.

Reversal of metabolic impairments by means of dietary supplementation may be a good strategy to increase the success of lifestyle interventions. Dietary polyphenols are natural components of fruits and vegetables that have recently been shown to alter substrate and energy metabolism.

Resveratrol (R), an activator of silent mating type information regulation 2 homolog 1 (SIRT1, a member of the NAD+ dependent deacetylases family of sirtuins) and peroxisome proliferator-activated receptor gamma co-activator 1 alpha

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