מדינת ישראל
STATE OF ISRAEL

MINISTRY OF HEALTH
CHIEF SCIENTIST OFFICE
JERUSALEM

משרד הבריאות
לשכת המדען הראשי
ירושלים

Research Number: 3-12024
Title: The bioavailability of EGCG protected by the milk protein- β-lactoglobulin and its role in prevention of obesity and insulin resistance
Principal Investigator: Prof. Yoav D. Livney
Institute: Technion
Other Author(s): Prof. Eddy Karnieli
Institute(s): Technion
Year (Start): 2016 Year (End):2017

Background: (-)-Epigallocatechin-3-gallate (EGCG), a catechin polyphenol in green tea is a highly potent antioxidant. Studies attributed positive effects of EGCG in prevention of obesity and diabetes. However, EGCG is quickly degraded and its bioavailability is low. To provide it with the necessary protection, we have developed a novel technology for complexation of EGCG with heat-denatured β-Lactoglobulin (β-Lg) from cow milk. These complexes were found to protect EGCG during shelf life and to mask its bitterness and astringency.
Research Hypothesis: Complexation of EGCG with β-Lg may protect it, hence improve its bioavailability. EGCG may improve overall body insulin sensitivity and glucose metabolism.
Aims: We investigated the effect of complexation with β-Lg on EGCG bioavailability in a rat model, and the role of EGCG in milk fortified with EGCG-β-Lg complexes (comp) vs. milk fortified with free EGCG on obesity and insulin resistance, using a mouse model.
Methods: *Bioavailability study:* The pharmacokinetics of EGCG were determined after intragastric administration of EGCG to Sprague-Dawley rats. After 1 hr of fasting, the rats were given a solution of EGCG complexed with β-Lg (and controls of EGCG, β-Lg and phosphate buffer (PB) alone). Blood was periodically taken for 6 hr after the administration and EGCG was quantified. *Biological effects study:* Mice were divided into 2 groups; one was fed a high-fat-diet (HFD) and the other a normal diet (ND), for 12 weeks. Each group was divided to 4 sub-group which received EGCG-β-Lg complexes in milk (1% fat), or EGCG in milk (1% fat), or EGCG in water, or water, as controls. Drink and food intakes were monitored. Body weight was recorded weekly. Fecal lipids and body fat % (by MRI) were determined and glucose and insulin tolerance tests (GTT, ITT) were conducted.
Results and Discussion: *Bioavailability study*: Administration of EGCG-β-Lg complexes enhanced EGCG bioavailability by a factor of 1.73 relative to that of free EGCG solution. *Biological effects study:* Body weight gain and body fat percentage were similar between mice which received milk enriched with EGCG-β-Lg complexes, and mice which received milk enriched by free EGCG. However, during GTT, after 4 weeks of study, the maximal glucose concentration (MGC) in the serum of the HFD comp+milk group was significantly lower compared with that of the HFD EGCG+milk group ($P<0.05$). Moreover, during the GTT after 12 weeks of study, the MGC of the ND comp+milk group and 0-30 minute area under-the-curve were significantly lower compared with those of the ND EGCG+milk group.
Conclusions: β-Lg complexation sustained the release and enhanced the bioavailability of EGCG– thus increasing its level in the blood. Moreover, long-term consumption of milk fortified with EGCG-β-Lg complexes improved glucose homeostasis significantly more than consumption of milk fortified with free EGCG. This study found advantages of diet enrichment with EGCG-β-Lg complexes for preventive medicine.
Key words: EGCG, Beta-lactoglobulin, Bioavailability, Obesity, Diabetes

Israeli Medical Abstracts Repository (IMAR)

Publications associated with the project: (in preparation)

רח' רבקה 29, תלפיות ירושלים. למכתבים: רח' בן-טבאי 2 ירושלים 91010, טלפון 02-5681208/9, פקס 02-6725833
29 Rivka St. Talpiot, Jerusalem, Mailing address: 2 Ben-Tabai St. Jerusalem 91010, Israel
Tel.: 972-2-568-1208/9, Fax: 972-2-672-5833
e-mail address: chief.scientist@moh.health.gov.il