Extended Abstract Journal of Cancer Biology and Therapeutic Oncology 2021
Vol.5 Issue2

Resveratrol suppresses prostate cancer progression in transgenic mice

Hong Cai
University of Leicester, United Kingdom

Introduction

Resveratrol (trans-3,4',5-trihydroxystilbene) is a naturally occurring antifungal found in a variety of foods including the skin of red grapes and peanuts. Since the seminal report that resveratrol could inhibit multiple stages of carcinogenesis, it has been the subject of extensive preclinical investigations for the treatment and prevention of numerous pathologies including cancer, cardiovascular and Alzheimer's disease, insulin resistance, and diabetes . Attempts to translate these findings to humans have increased in recent years but there are still fundamental gaps in our understanding of the pharmacokinetic pharmacodynamic relations and how plasma/target tissue concentrations correlate with clinical efficacy or beneficial effects on health maintenance . Such information is needed to inform the choice of optimum dose and formulation requirements, and to enhance understanding of the key modes of action for resveratrol in each pathology it is also particularly important given the notoriously low systemic bioavailability of parent resveratrol due to its rapid metabolism, which, if not taken into consideration, would affect its clinical utility.

Background of the Research

Resveratrol has been shown to prevent the development of a variety of malignancies in preclinical rodent models, including colorectal and prostate cancers . Concentrations of parent resveratrol achievable in human colon after oral ingestion of 1 g daily can be as much as 100- to 1000-fold higher than in plasma, and appreciable concentrations are also detected after a far lower intake of 5 mg . Furthermore, the concentrations generated in human colorectal tissue by these doses have been found to elicit changes in pharmacodynamic markers that may be mechanistically linked to cancer-preventive effects of resveratrol . In addition, concentrations of ~5 nmol/g tissue (equivalent to ~5 μM, assuming 1 g tissue has a volume of 1 mL) have been reported in colorectal liver metastases from patients who received 5 g SRT501/d, a micronized formulation of resveratrol designed to improve bioavailability . This dosage caused a significant increase in cleaved caspase-3, a marker of apoptosis, in malignant tissue. Resveratrol metabolites, but not the parent compound, have been detected in resected breast tissue from women undergoing surgery for breast cancer who took capsules containing a mixture of fruit and cocoa extracts plus resveratrol for 6d.

Patients suitable for the study were identified at multidisciplinary team meetings; they were eligible if they required prostate biopsies for suspected prostate cancer or for monitoring of existing low-grade cancer, or surgery for the management of benign prostatic hypertrophy. Patients were >18 y of age and were asked to avoid food and drink containing resveratrol during the trial. Participants also completed a food diary and dosing calendar to monitor compliance. Exclusion criteria included excessive alcohol intake, chemotherapy or use of an investigational drug within 4 wk of tissue sampling, any malabsorption syndrome, chronic use of warfarin or antiepileptic drugs, and evidence of abnormal renal or liver function. All patients were recruited at the University Hospitals of Leicester NHS Trust, where they were randomly allocated into 3 parallel groups of 10 that received either 5 mg resveratrol daily, 1 g (4 × 250 mg) resveratrol daily, or no intervention. A significant body of preclinical evidence suggests resveratrol may have value in the treatment and/or prevention of prostate cancer. Our clinical trial has shown that although resveratrol species can reach prostate tissue after both a dietary-achievable and a pharmacological dose, the metabolites rather than parent resveratrol predominate, suggesting this tissue mirrors the plasma kinetic profile, albeit with lower total concentrations detected (range: 11–34 μM and 0.05– 0.15 μM for 1 g and 5 mg, respectively) than systemic concentrations at the same time point postdosing. This contrasts with our previous analysis of colorectal mucosa where the concentrations of total [14C]- resveratrol equivalents reached the order of 100–600 pmol/mg in certain patients after ingestion of a 1 g dose. Hence, tissue bioavailability of total resveratrol species appears to be ~10-fold higher in the colon than in the prostate, which is consistent with regions of the gastrointestinal tract containing the highest concentrations of resveratrol derivatives after oral administration to rodents.

This work is partly presented 2nd Global Summit on Oncology and Hematology on April 05-06, 2021 | Webinar