Z-2-(β-D-GLUCOPYRANOSYLOXY)-3-PHENYLPROPENOIC ACID, AN α-HYDROXY ACID FROM ROOIBOS (ASPALATHUS LINEARIS) WITH HYPOGLYCEMIC ACTIVITY

Muller CJ, Joubert E, Pheiffer C, Ghoor S, Sanderson M, Chellan N, Fey SJ, Louw J

The South African plant, Aspalathus linearis, better known as rooibos, has become popular as a herbal tea on the global market. Contributing to the increased popularity is the health-promoting properties which are mainly attributed to the polyphenolic compounds. In particular, the glucose-lowering effect of its major flavonoid, the dihydrochalcone C-glucoside aspalathin, has highlighted the pharmaceutical potential of such compounds in preventing and treating metabolic diseases which includes type 2 diabetes mellitus. The identification of another major monomeric phenolic compound, Z-2-(β-D-glucopyranosyloxy)-3-phenylpropenoic acid (PPAG), an enolic phenylpyruvic acid glucoside, which rarely occurs in other plants, prompted further investigation. 3-Phenylpyruvic acid (PPA), a chemical compound related to PPAG, but without the sugar moiety and in a keto form instead of the enolic form, was shown to induce insulin release from rat pancreatic islets and enhance glucose uptake in muscle cells. As the glycoside moiety is a key active structure, we anticipated that PPAG could enhance the observed effects demonstrated for phenylpyruvic acid on glucose metabolism. In-vitro studies confirmed that PPAG enhanced glucose uptake. A concentration-response study in Chang cells showed that PPAG enhanced glucose uptake in the concentration range 1.0 to 31.6 µM (EC50 = 3.6 µM). In obese insulin resistant rats, oral administration of PPAG lowered fasting glucose concentrations and improved oral glucose tolerance values. Messenger RNA expression demonstrated up-regulation of genes involved in insulin signalling, glucose utilisation and lipid metabolism in the liver, offering a plausible mechanistic explanation for the observed hypoglycaemic effect of PPAG. This suggests that PPAG has potential as a new class of anti-diabetic therapeutic.
CONSORTIUM OF HEALTH-ORIENTATED RESEARCH IN TRANSITIONING SOCIETIES (COHORTS) INVESTIGATORS. BIRTH STATUS, CHILD GROWTH, AND ADULT OUTCOMES IN LOW- AND MIDDLE-INCOME COUNTRIES

Stein AD, Barros FC, Bhargava SK, Hao W, Horta BL, Lee N, Kuzawa CW, Martorell R, Ramji S, Stein A, Richter L

The prevalence of preterm births and small for gestational age (SGA) births remains high in many populations. Although preterm birth and SGA status have been associated with under nutrition at age 2 years, the later growth patterns of children born preterm have not been examined extensively, especially in low- and middle-income countries. Growth failure in childhood is usually measured as stunting (height-for-age < 2.0 SDs compared with the reference population), and associated with short stature in adulthood along with lower schooling attainment. Growth during the first two years of life is strongly associated with adult height, but not with elevated blood pressure (BP) or glucose levels, and growth later in childhood and through adolescence, especially weight gain, is associated with increased risk for hypertension and impaired fasting glucose. Understanding whether postnatal growth patterns affect risk differentially for individuals born preterm or SGA has implications for managing these infants. In an analysis of child growth and adult health in five low- and middle-income countries (Brazil, Guatemala, India, the Philippines, and South Africa) we investigated the association of preterm status and weight for gestational age (GA) with later growth, schooling attainment, and cardiometabolic outcomes. In the study population of 4518 adults, 12.8% of males and 11.9% of females were born preterm, and 26.8% of males and 22.4% of females were born term but SGA. Adults born preterm were 1.11 cm shorter (95% CI, 0.57-1.65 cm), and those born term but SGA were 2.35 cm shorter (95% CI, 1.93-2.77 cm) compared with those born at term and appropriate size for GA. Blood pressure and blood glucose levels did not differ by birth category. Compared with those born term and at appropriate size for GA, schooling attainment was 0.44 years lower (95% CI, 0.17-0.71 years) in those born preterm and 0.41 years lower (95% CI, 0.20-0.62 years) in those born term but SGA. Being born preterm or term but SGA is associated with persistent deficits in adult height and schooling, but is not related to BP or blood glucose levels in low- and middle-income settings. Increased postnatal growth is associated with gains in height and schooling regardless of birth status, but not with increases in BP or blood glucose levels.

MITOCHONDRIAL SUBHAPLOGROUPS AND DIFFERENTIAL RISK OF STAVUDINE-INDUCED LIPODYSTROPHY IN MALAWIAN HIV/AIDS PATIENTS

Kampira E, Kumwenda J, Van Oosterhout JJ, Dandara C

Lipodystrophy remains a significant problem in HIV/AIDS patients especially those on regimens containing either protease inhibitors or thymidine analogues (stavudine or zidovudine). Many of the manifestations of lipodystrophy have been linked to mitochondrial dysfunction. We set out to investigate whether mitochondrial DNA variation is associated with development of stavudine induced lipodystrophy among adult Malawian HIV/AIDS patients on antiretroviral therapy (ART) which included stavudine. This study was undertaken to explore the role of mtDNA subhaplogroups in susceptibility to developing lipodystrophy in 117 adult HIV/AIDS patients on stavudine treatment. They were recruited from the antiretroviral therapy (ART) clinic at the Queen Elizabeth Central Hospital, Malawi. Patients were categorized according to whether or not they had developed lipodystrophy after being on a stavudine-containing ART regimen for at least 6 months. Whole mtDNA-coding regions of each patient were sequenced and correlated with clinical characteristics. Lipodystrophy was apparent in 16% (n=19) of the participants. In multivariate analysis, age above 40 years (odds ratio: 4.43; 95% CI: 1.36--14.47; p=0.014) was significantly associated with the presence of lipodystrophy. The mtDNA subhaplogroup L3e appeared to be protective against lipodystrophy, as none of 11 subjects with this subhaplogroup presented with lipodystrophy. This study provides indications that susceptibility to lipodystrophy in HIV/AIDS patients on stavudine-containing ART is mtDNA subhaplogroup and population specific.
Admixture occurs when two or more previously separated population groups produce offspring. Admixture can result in inflated false positive findings in genetic association studies of admixed populations, unless one uses genome-wide data to adjust for the effects of admixture in statistical models. Obtaining genome-wide data is expensive, and a cost-effective alternative would be to use ancestry informative markers (AIMs). The predominant population group in the Western Cape, South Africa, is the admixed group known as the South African coloured (SAC), which has five source populations. To date, none of the published lists of AIMs is well suited to this population because of its unique and highly complex ancestry. Using genome-wide data to find polymorphisms with large allele frequency differences between the source populations of the SAC, we developed a panel of AIMs by experimenting with various selection strategies. Subsets of different sizes were evaluated by measuring the correlation between ancestry proportions estimated by each AIM subset with ancestry proportions estimated using genome-wide data. We showed that a panel of 96 AIMs can be used to assess ancestry proportions and to adjust for the confounding effect of the complex five-way admixture that occurred in the South African coloured population.
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