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Intervention study on the effect of quercetin on biomarkers for cardiovascular syndrome in patients with different apolipoprotein E (ApoE) isoforms

Submission date	Recruitment status	[_] Prospectively registered
09/05/2008	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
19/08/2008	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
14/06/2019	Circulatory System	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Intervention study on the effect of quercetin on biomarkers for cardiovascular syndrome in patients with different apolipoprotein E (ApoE) isoforms

Acronym
Quercetin1

Study objectives
Quercetin is a flavonoid naturally occurring in all plant foods, mainly in onions, broccoli, green cabbage, apples and in lower concentrations in black tea and red wine. Ingestion of flavonoids was inversely correlated with the incidence of cardiovascular diseases, like atherosclerosis and stroke and risk factors like hypertension. The polyphenol quercetin is a potent antioxidant but may also regulate gene expression and might act through anti-inflammatory effects, e.g. regulation of the expression of cellular adhesion molecules (inter-cellular adhesion molecule-1 [ICAM-1], vascular cell adhesion molecule-1 [VCAM-1], E-selectin) and of the secretion of pro-inflammatory cytokines (tumour necrotising factor alpha [TNFa]) and chemokines (monocyte chemoattractant protein-1 [MCP-1]), modulation of enzyme acivities and vascular tonus.

Only few human intervention studies with quercetin have been performed so far. In this human trial the effect of quercetin in carriers of the apolipoprotein E (ApoE) type 4 with a high risk for development of atherosclerosis and potentially less protected against oxidative damage due to fewer -SH groups will be studied in comparison to ApoE 3 homozygote. In a cross-over design quercetin and placebo will be applied in random order for eight weeks each, intermitted by a three-week wash-out phase. As dietary fats may change endothelial function, this parameter is tested both in the fasting state and following a fat-rich meal. Metabolic and inflammation parameters will be determined in the fasting and in part postprandial state in blood and urine. Low density lipoprotein (LDL) and chylomicron (CM)/remnants will be isolated and tested for adhesion molecules expression on endothelial cells.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the Ethics Committee of the Medical Faculty of the Christian-Albrechts-University of Kiel (Germany) on the 18th May 2007 (ref: A 120/07).

Study design
A randomised, double-blind, placebo-controlled, cross-over intervention study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Cardiovascular disease

Interventions
Patients are randomised to:
1. Quercetin 150 mg
2. Placebo

Patients will receive two capsules of one of the above three times a day during principal meals (breakfast, lunch and dinner) for a total of 6 capsules (150 mg) total dose per day. Patients will receive this for eight weeks for each intervention (verum and placebo), interrupted by a wash-out period of three weeks.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Quercetin

Primary outcome measure
Endothelial function (PAT-Index) after 56 (±2) days supplementation.

Secondary outcome measures
1. Body mass index (BMI)
2. Waist circumference (WC)
3. Waist to hip ratio (WHR)
4. Blood pressure, pulse

Changes in:
5. Fasting and postprandial triglycerides (AUC)
6. Fasting and postprandial insulin (AUC)
7. Fasting and postprandial glucose (AUC)
8. Homeostasis model assessment of insulin resistance (HOMA-IR) (insulin-glucose-product)
9. HOMA B-cell function
10. Metabolic regulatory parameters, namely: cholesteryl ester transfer protein (CETP), glutathione (GSH)
11. Lipids and apolipoproteins, namely total triglycerides and in very low density lipoprotein (VLDL)/triglyceride-rich lipoprotein (TRL), apoliprotein B100, total, low density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL) cholesterol, free fatty acids, lipoprotein A (LpA)
12. Oxidative modification of lipids and oxidative stress, namely: oxidised LDL, isoprostanes

13. LDL- and CM/remnant-induced adhesion molecule expression on endothelial cells (human umbilical vein endothelial cells [HUVEC])
14. Inflammatory parameters, namely: C-reactive protein (CRP), soluble VCAM (sVCAM), soluble ICAM (sICAM), soluble E-selectin, interleukin-6 (IL-6), TNFa, MCP-1
15. Gene expression profile in monocytes (fasting monocyte isolation), expression of genes which may affect antioxidative status, metabolism and inflammatory responses (arteriosclerosis)

Measurements for the secondary outcome will be made after each intervention period.

Overall study start date
24/05/2007

Completion date
16/05/2008

Eligibility

Key inclusion criteria
1. Healthy male volunteers
2. Aged 45 - 69 years
3. Member of the Metabolic Intervention Cohort Kiel (MICK)
4. Homozygous for ApoE 3 or ApoE 4, or ApoE 3/4 heterozygous
5. Written informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Male

Target number of participants
50 (apoE 3/3 [n = 20], apoE 4/4 [n = 10], apoE 3/4 [n = 20])

Total final enrolment
49

Key exclusion criteria
1. Participation in a clinical study with a medicament or a medicinal product within the last 30 days or simultaneous participation in another clinical examination
2. Inability to understand and to comply with the study protocol
3. Known metabolic or gastro-intestinal diseases, which affect the absorption, metabolism or excretion of food or food components
4. Condition after surgery of the gastro-intestinal tract, which affect gastro-intestinal motility
5. Haemoglobin less than 12 g/dL
6. Ferritin less than 35 µg/L
7. Latex allergy
8. Diabetes (fasting glucose levels greater than 125 mg/dl after repeated determination)

9. Surgery within the last three months, which still affects the current state of health
10. Deformation of finger tips, which inhibits correct recording of the EndoPAT device (measures a Peripheral Arterial Tone [PAT™] signal for assessment of endothelial dysfunction)
11. Illness of thyroid gland, which has metabolic and/or cardiovascular effect
12. Known hepatitis B, hepatitis C, human immunodeficiency virus (HIV) infection or chronic liver disease
13. Kidney malfunction
14. Psychiatric disorders, epilepsy, risk of suicide
15. Drug or alcohol abuse
16. Intake of nitrate and/or calcium antagonists, which affect the blood pressure
17. Intake of drugs affecting the absorption, metabolism or excretion of food components or the gastro-intestinal motility
18. Intake of hormone preparations, particularly cortisone
19. Eating disorders, anorexia, bulimia, unusual outsider dietary habits
20. Legal incapacity

Date of first enrolment
24/05/2007

Date of final enrolment
16/05/2008

Locations

Countries of recruitment
Germany

Study participating centre
Max Rubner-Institute
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Sponsor information

Organisation
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Sponsor type
Government

Website
http://www.mri.bund.de

ROR
https://ror.org/045gmmg53

Funder(s)

Funder type
Government

Funder Name
German Federal Ministry of Education and Research (Bundesministerium Für Bildung und Forschung [BMBF]) (Germany) (ref: 0313856A)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/05/2013	14/06/2019	Yes	No