Pharmacokinetic study to assess the bioavailability of phenolics from an olive leaf extract

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Ethical review	Approved WMO
Status	Completed
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON37716

Source
ToetsingOnline

Brief title
Bioavailability of phenolics from olive leaf extract

Condition

- Cardiac disorders, signs and symptoms NEC
- Bone disorders (excl congenital and fractures)
- Vascular injuries

Synonym
cardiovascular disease, osteoporosis

Research involving
Human

Sponsors and support

Primary sponsor: Bio-Actor

Source(s) of monetary or material Support: bedrijf (Bio-Actor)

Intervention

Keyword: hydroxytyrosol, oleuropein, olive leaf extract, phenolics

Outcome measures

Primary outcome

The primary aim of the study is to evaluate the bioavailability and pharmacokinetics of the phenolics present in the olive leaf extract and the metabolites which are formed upon administration of a dose which was previously shown to have biological activity. Assessment and evaluation will be done by analyzing the plasma and urinary concentrations of the main study parameter: the olive phenolics oleuropein, hydroxytyrosol, tyrosol and their human metabolites in the plasma and urine following a single oral consumption of the olive leaf extract. To do this, blood samples will be collected pre-dose and after 30 min, 1h, 2h, 3h, 4h, 6h, 8h, 12h, 16h and 24h. Urine will be collected and pooled as follows: 0-4h, 4-8h, 8-12h, 12-16h and 16-24h.

Secondary outcome

Secondary study parameter 1: A first secondary aim, the bioavailability will be compared for premenopausal and postmenopausal women, as differences in circulating levels have been shown for specific phenolic compounds. As both populations are of interest as target population for the olive extract under study, comparison of potential differences in circulating metabolites is important for extrapolation of the observed biological activity towards both groups. To do this, pharmacokinetic parameters of the main circulating phenolic metabolites in plasma will be compared for both groups.

Secondary study parameter 2: As second secondary study aim, the effect of the bioavailable phenolics on the processes of osteoblastogenesis and adipogenesis will be investigated in mesenchymal stem cells (MSCs) from human bone marrow. To do this, blood samples collected from the individuals will be combined with MSC cells in an ex vivo approach. This additional aim is included to obtain a mechanistic link between the circulating levels of phenolics upon ingestion of the product and the previously observed biological activity in relation to bone formation processes.

Study description

Background summary

Olives, olive oils and products derived from olive trees (e.g. leaf extracts) have generated significant interest due to their association with various health-protective and therapeutic activities, into a large extent related to the presence of high amounts of phenolic micronutrients such as oleuropein, hydroxytyrosol and tyrosol. However, previous research has also shown that the final bioavailability and biological activity greatly depends on the matrix in which the olive phenolics are ingested (e.g. oil versus extract). Within a certain matrix, e.g. olive leaf extracts, bioavailability may further be influenced by the physical properties of the matrix, such as solubility under aquatic conditions and the concentration in which the product is administered. As only the bioavailable fraction of the olive phenolics may have biological activity in the body, the amount of activity which reach systemic circulation may have final health effects. Furthermore, as bioavailability of specific phenolics has been shown to depend on circulating levels of female estrogens, this may influence the final bioactivity of the olive phenolics, and therefore selection of the study population can be of great importance.

Study objective

The objective of the study is to obtain information on the bioavailability and pharmacokinetics of the phenolics present in an olive leaf extract (Bonolive®, dose 250 mg), standardized on 40% oleuropein, and to identify the composition of the metabolites which circulate in the body. This information will be used to support the previously generated data regarding biological activity of the

extract in view of European Food Safety Authority (EFSA) health claim submission. Moreover, differences in these parameters depending on the target population will be assessed.

Study design

Parallel study design in which the olive leaf extract is administered to two study groups of equal size (8 complete datasets per group). The intervention will comprise the oral intake of a single capsule containing 250 mg of the olive leaf extract.

Intervention

The study will consist of 1 study day in which each subject will consume the olive leaf extract once.

Study burden and risks

After an overnight fasting, a catheter is placed in the arm of each subject for repeated blood collection. During the study day, 11 times 12mL blood sample will be taken. The participants are to refrain from products containing olives or olive-derived products (e.g. olive oil or olive fruit or leaf extracts), all sorts of alcohol, tea and vinegars for a period starting 3 days prior to the start of each study day. The participants are asked not to change their normal dietary habits before the study period. No adverse effects are expected. Participants will not benefit directly from participation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-Female adults between 18 and 75 years old
-The study will consist of 8 premenopausal and 8 postmenopausal women.
-Only non*smoking individuals can participate. Non*smoking individuals are hereby defined as individuals who did not smoke during at least 6 months before the start of the study. Individuals who did not smoke for minimum 3 months prior to the study could also be included, upon evaluation and decision by the investigators.
-The participants are capable and willing to sign the Informed Consent Form at voluntary basis, after having received detailed information.
-The volunteers are considered healthy based on their medical history as questioned by the investigator during an interview and a general physical examination by the investigator.
-Female volunteers do not intend to become pregnant prior to or during the study and using adequate contraception.
-Premenopausal women should be on monophasic oral anti conception and the test day should not be in the pause week or in the first 3 days of pill use, in order to obtain a constant level of estrogen.
-The postmenopausal women should be at least 2 years post menopausal to ensure a homogeneous population

Exclusion criteria

-Clinically significant abnormal liver functioning (serum alanine and aspartate aminotransferase).
-Clinically significant abnormal serum creatinin.
-Abnormal BMI (i.e. lower than 18 or higher than 30).
-Use of concomitant medications or supplements.
-Blood donation during the last 4 weeks prior to the first dosing till 4 weeks after the last dosing.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	24-01-2012
Enrollment:	31
Type:	Actual

Ethics review

Approved WMO Date:	05-12-2011
Application type:	First submission
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	26-03-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 21153
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
Other	10566
CCMO	NL38388.068.11
OMON	NL-OMON21153