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Evaluation of the potential beneficial effects of the administration of Ferula communis extract, containing ferutinin, a natural phytoestrogen, in counteracting postmenopausal dysfunctions, in a cohort of 64 women

Submission date
15/07/2024

Recruitment status
No longer recruiting

Registration date
16/07/2024

Overall study status
Completed

Last Edited
06/09/2024

Condition category
Nutritional, Metabolic, Endocrine

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims

Menopause is marked by a disruption in the menstrual cycle and a decrease/stoppage in the production of estrogen and progesterone hormones in the ovaries. The physical health of women experiencing peri-menopausal discomfort can be negatively affected by both physiological and behavioral changes, leading to symptoms such as hot flashes, night sweats, palpitations, sleep disorders, atrophic vaginitis, and sexual dysfunction. Estrogen and progesterone-based hormone therapy can effectively alleviate menopausal symptoms, but estrogen supplementation may have negative health effects. Hormone replacement therapy has been tested using natural compounds for peri-menopausal disorders, but their effectiveness is still uncertain. In preclinical studies, the administration of low-concentration sesquiterpene ferutinin showed significant antioxidant effects on cardiomyocytes by reducing free radicals and modulating the cell cycle. Furthermore, the interaction between ferutinin's estrogenic and ionophoric activity reduces side effects from conventional estrogen therapy. In vitro and in vivo studies have demonstrated that ferutinin exhibits antiproliferative effects, affecting both cytotoxicity and cell proliferation. Its bioactivity is dependent on dose and varies across different cell types, with a notable preference for tumor cell lines. Specifically, evidence from in vivo experiments indicates Ferula L. extract (30–60 mg) in ovariectomized rats leads to better sexual behaviour. The effect appears to be connected to the phytoestrogenic properties of ferutinin, the main bioactive compounds found in the extract. The presence of this effect qualifies this molecule as a potential treatment for gynecological pathologies. The purpose of this study is to assess the clinical impact of Ferula communis L. (titrated at 20% ferutinin; 100 mg /die) extract in the quality of life of 64 menopausal women.

Who can participate?

The criteria for inclusion were: postmenopausal women, with a minimum of 12 months of amenorrhea and a follicle-stimulating hormone level above 30 mIU/mL. The criteria involved

women with a sexually active life, a stable partner, and postmenopausal sexual dysfunction. The study excluded women with hormonal therapy, diabetes, cognitive disorders, hormone-dependent tumors, psychiatric disease, liver diseases (except prior cholecystectomy), renal disease, cardiovascular disease, and those who used drugs that decrease sexual desire.

What does the study involve?
After randomization, participants were divided into two groups: the placebo group (n = 32) received placebo in a tablet identical in appearance to that used for the second group, once a day for 90 days, while the treatment group for received Ferula L. extract (n = 32), as an oral tablet (100 mg/die) , once a day for 90 days.
The questionnaires used were the Sexual Quotient—female version (SQ-F) and the Female Intervention Efficacy Index (FIEI) questionnaire. The questionnaires were individually administered by the same researcher. The results were examined and explained using the theoretical framework of socio-historical psychology, which focuses on understanding cultural structure, social organization, and human subjectivity. The data from the initial interview and subsequent visits were compiled and frequencies were allocated to the groups (placebo and Ferula L. extract) based on the analyzed variable.

What are the possible benefits and risks of participating?
The possible benefits of subject enrolled in the study and supplemented with F. communis L. extract given at doses of 100 mg/die for 90 consecutive days, consist in the reduction of all symptoms associated to postmenopausal discomfort with a significant enhancement of sexual behaviour, reverting or mitigating menopause dysfunction.
The results obtained in different experimental wors showed an important antioxidant and phytoestrogenic regulation, exerted by ferutinin, with lack of typical side effect related to estrogenic therapy.
Furthermore, there are several evidence highlighting that about 70% of perimenopausal women displays overweight or obesity, associated with a major incidence of morbidity and mortality. Together, obesity is related to increased oxidative stress, since reactive oxygen/nitrogen species generation is caused by an imbalance between antioxidant and oxidant status, with the subsequent oxidative modification of several macromolecules, including lipids, DNA and proteins.
The results expected in the clinical study could confirm the potential protective role of ferutinin to counteract oxidative stress and weight gain in perimenopausal women, showing that F. communis L. supplementation could be able to ameliorate oxidative status and BMI, at 90 days, in the subject enrolled in the study.
Moreover, several data suggest that ROS contribute to atherosclerosis onset and progression, inducing endothelial cell (EC) dysfunction, platelet activation and vascular remodeling. ROS/RNS, produced in an unbalanced manner following hormonal changes due to menopause, could interact with platelets through the ADP receptor, triggering the same intracellular signaling cascade. In addition, nitrogen peroxide induces fibrinogen activation and fibrin clot stabilization. An interesting piece of evidence, will concern the potential ability of the extract, due to its antioxidant and phytoestrogenic property, to improve the overall dysfunctional state of perimenopausal women, without however altering the platelet aggregability.
The potential risks are minimal or nonexistent because the extract has been traditionally used in medicine to treat a range of disorders, such as infections and gastrointestinal issues. Furthermore, the safety of low doses of the ferutinin molecule, the main bioactive compound in the extract, is supported by evidence of its protective and antioxidant properties.

Where is the study run from?
IRC-FSH - University Magna Graecia of Catanzaro (Italy)

When is the study starting and how long is it expected to run for?
September 2017 to December 2024

Who is funding the study?
IRC-FSH - University Magna Graecia of Catanzaro (Italy)

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Protocol serial number
64202023

Study information

Scientific Title
Protective effects of Ferula communis L. extract supplementation in women suffering from Postmenopausal Discomfort: a randomized, double-blind, placebo-controlled clinical trial in 64 women

Acronym
BERGAFEMME

Study objectives
Given the promising preclinical evidence on the beneficial effects that ferutinin exerts in dose and cell type-dependent manner, a clinical study was performed to investigate the potential protective action of Ferula L. extract; in particular, a randomized, double blind, placebo-controlled study was conducted to verify the efficacy and safety profile of a ferutinin-rich Ferula L. extract in women with postmenopausal discomfort.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 24/09/2017, Calabria Region - Ethical Committee (Viale Europa - Cittadella Regionale - Località Germaneto, Catanzaro, 88100, Italy; +39 3343247595; palma@unicz.it), ref: Registro Protocollo n. 125 del 24 Settembre 2017

Study design
Randomized double-blind placebo-controlled clinical trial

Primary study design
Interventional

Study type(s)
Quality of life, Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied
Menopausal women suffering from post-menopausal discomfort

Interventions
A randomized, double-blind, placebo-controlled clinical trial in 64 women with postmenopausal dysfunction, was performed. The women who completed the study (n=64), after an interview, signed an informed consent form and, after randomization, were divided into two groups: the placebo group (n = 32) received placebo in a tablet identical in appearance to that used for the second group, once a day for 90 days, while the treatment group for received Ferula L. extract (n

= 32), as an oral tablet (100 mg/die) , once a day for 90 days. At day 0 and after 90 days of treatment the following parameters were evaluated: sexual behavior, other menopausal signs and symptoms, plasma free radicals, fat mass, platelet aggregation.

Intervention Type
Supplement

Primary outcome(s)
Amelioration of Sexual behavior assessed by Sexual Quotient—female version (SQ-F) and the Female Intervention Efficacy Index (FIEI) questionnaires at time 0 and at 90 days of treatment

Key secondary outcome(s))
Evaluation at time 0 and at 90 days of treatment:
1. Onset of menopause signs measured using Sexual Quotient—female version (SQ-F) and the Female Intervention Efficacy Index (FIEI) questionnaires
2. Plasma free radicals measured using blood test
3. Fat Mass (BMI assessment) measured using height (m) and weight (kg)
4. Platelet aggregation measured using platelet samples

Completion date
31/12/2024

Eligibility

Key inclusion criteria
1. Postmenopausal women, with a minimum of 12 months of amenorrhea and a follicle-stimulating hormone level above 30 mIU/mL
2. Sexually active life
3. A stable partner
4. Postmenopausal sexual dysfunction

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
48 years

Upper age limit
56 years

Sex
Female

Total final enrolment

64

Key exclusion criteria
Women with hormonal therapy, diabetes, cognitive disorders, hormone-dependent tumors, psychiatric disease, liver diseases (except prior cholecystectomy), renal disease, cardiovascular disease, and those who used drugs that decrease sexual desire

Date of first enrolment
01/01/2023

Date of final enrolment
31/05/2024

Locations

Countries of recruitment
Italy

Study participating centre
IRC-FSH clinical center at the University “Magna Graecia” of Catanzaro
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Sponsor information

Organisation
IRC-FSH -Magna Graecia University of Catanzaro

Funder(s)

Funder type
University/education

Funder Name
IRC-FSH - Magna Graecia University of Catanzaro

Results and Publications

Individual participant data (IPD) sharing plan

The data that will be shared concern the clinical status of the patient following the scheme of the inclusion and exclusion criteria, maintaining their anonymity, as explicitly stated in the documentation relating to the presentation of the ethics committee. Furthermore, the results obtained for each patient will also be made available, always anonymously. The consent from participants was obtained.
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IPD sharing plan summary

Available on request