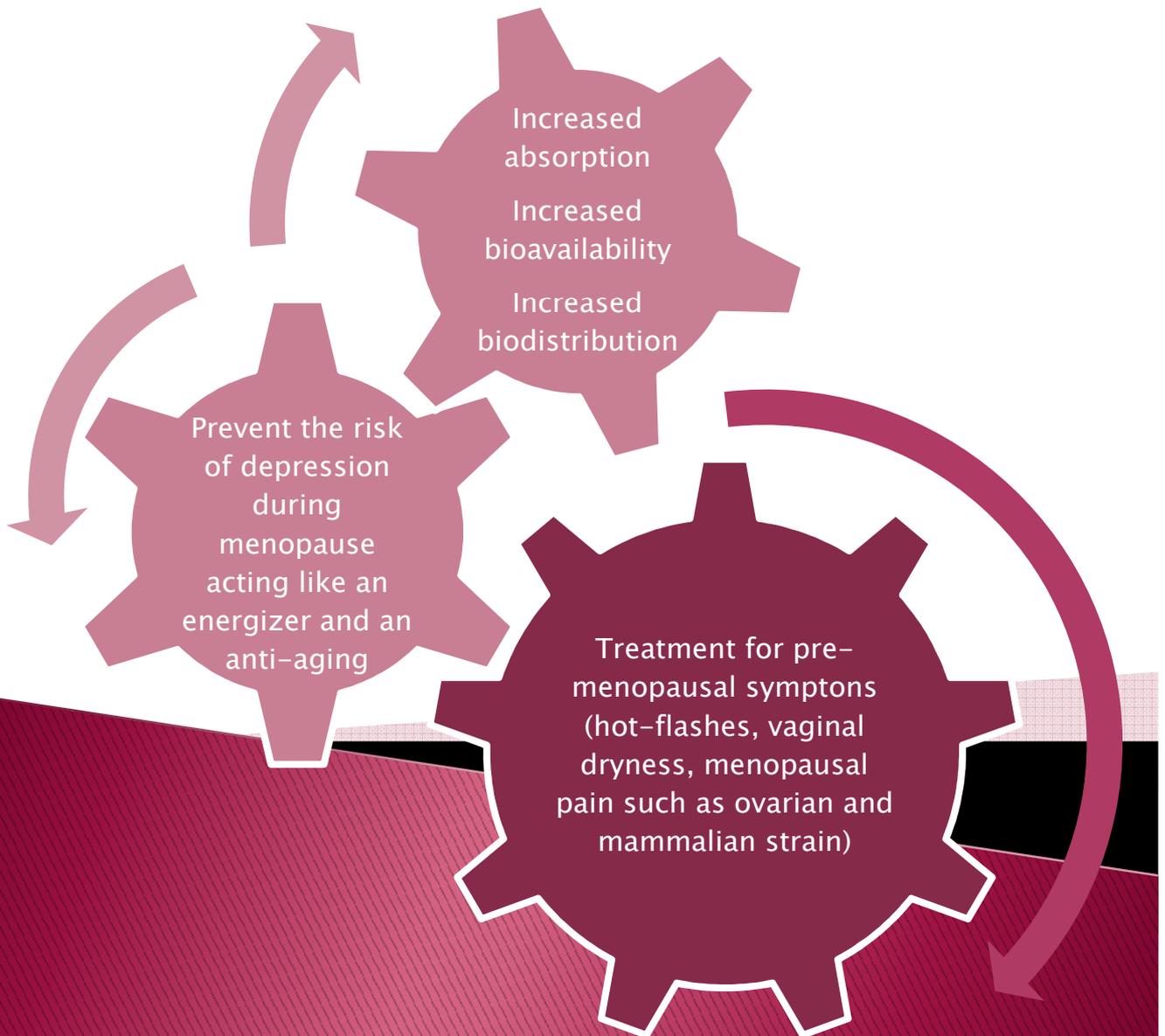


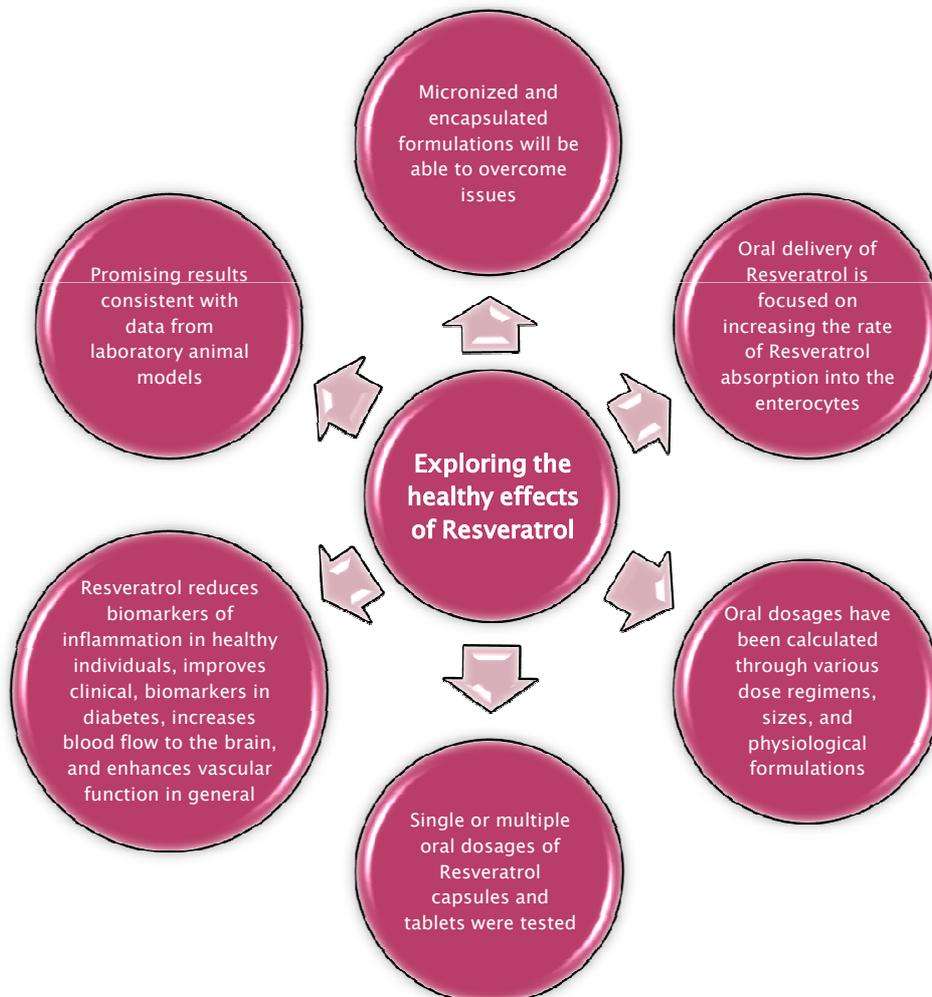
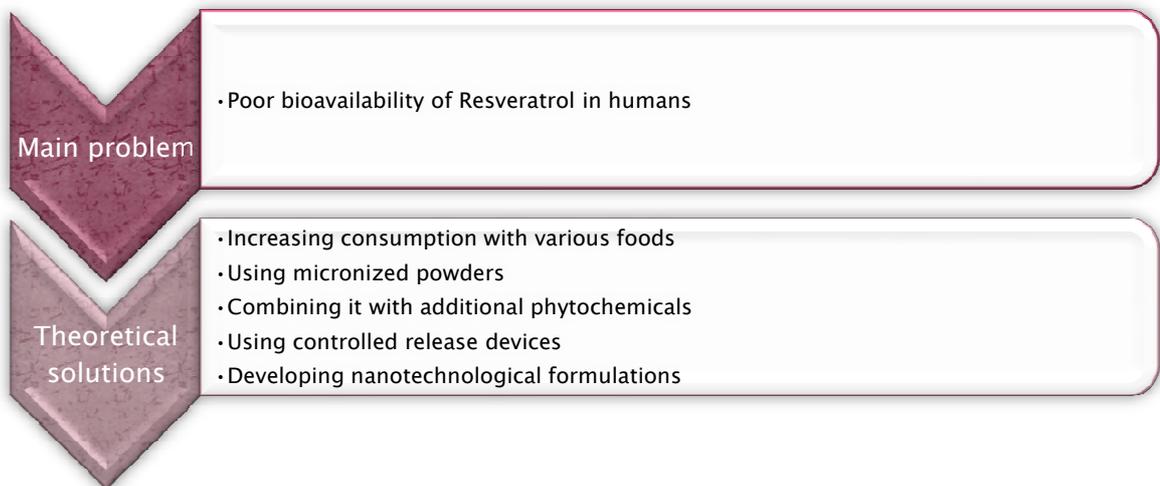
NP-RES: new Resveratrol-based supplement for gynecological disorders

GOAL



NP-RES

Resveratrol and clinical utility



Smoliga JM, Blanchard O. Enhancing the delivery of Resveratrol in humans: if low bioavailability is the problem, what is the solution? *Molecules*. 2014 Oct 24;19(11):17154-72

Micronized Resveratrol (micro-RES) in clinical trial

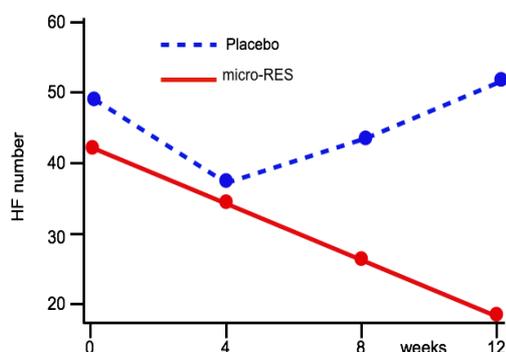
Pilot study

- Effectiveness of micronized Resveratrol orally absorbed to treat hot flushes (HF) during menopause

Randomized controlled double-blind study

- From October 2012 to July 2014 the authors considered the first 50 patients enrolled at the Center for Menopause Maggiore Hospital of Charity of Novara, with diagnosis of physiological or surgical menopause
- Each woman received a diary in which she indicated the weekly number of HF and the perceived intensity, in a 0-10 Scale (Visual Analogue Scale, VAS).
- The patients were randomized and divided into two groups and both groups were monitored for 12 months. At the first group was administrated micro-RES and at the second group a placebo drug, both following a posology of two administration/day.

- micro-RES reduces the monthly number of vasomotor episodes in woman of about 6.28 times compared to the placebo arm (95% CI: 1.61-24.49).



- micro-RES improves the intensity of symptoms and quality of life of about 4.32 times more than the placebo arm (95% CI: 1.74-10.71), with the transition from moderate/severe to mild symptoms in 78.6% of patients

Leo L, Surico D, Deambrogio F, Scatuzzi A, Marzullo P, Tinelli R, Molinari C, Surico N. Preliminary data on the effectiveness of resveratrol in a new formulation in treatment of hot flushes. *Minerva Ginecol.* 2015 Oct;67(5):475-83

NP-RES

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NP-RES activity

The effectiveness of NP-RES on climacteric syndrome is

- demonstrated by in vivo study on female rats, validated in literature using a human dosage

The effectiveness of NP-RES at molecular and biological levels is

- validated on ovarian epithelial cells (CHO-K1 cells), using a human dosage

NP-RES

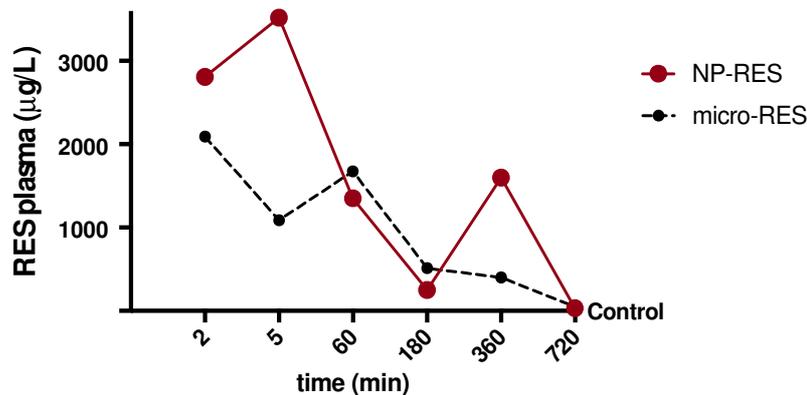


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Effectiveness of NP-RES in climacteric syndrome

Bioavailability (the absorption into blood)

Effectiveness of NP-RES on the whole body during time, evaluating the concentration of Resveratrol present into the blood after oral intake.



Female rats are treated with NP-RES or micro-RES by gavage.
All data $p < 0.05$ vs control (untreated animals).

- NP-RES demonstrates the effectiveness during time, following a biphasic curve
- NP-RES improves plasma concentration already in the first 2min (about 34% compared to micro-RES) with a maximum effects at 5min (about 220% compared to micro-RES).
- NP-RES prolongs the lifespan of Resveratrol till to 1h.
- NP-RES exerts a secondary effect at 6h. This finding about the second peak supported the hypothesis that Resveratrol can be stored in organs to explain a secondary effect in the long term.
- NP-RES maintains and supports the biological activity of Resveratrol.

NP-RES

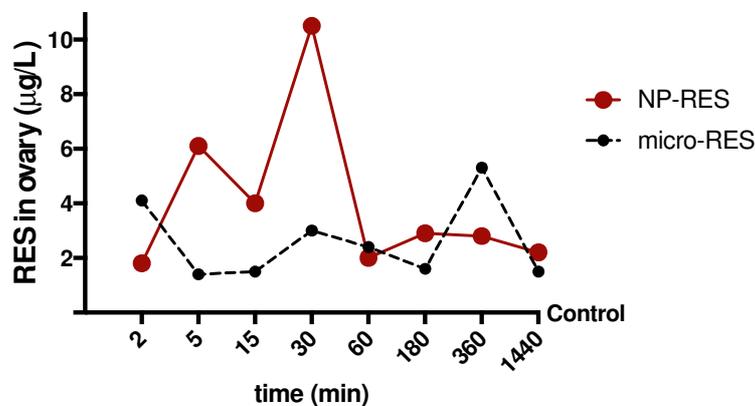
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Effectiveness of NP-RES in climacteric syndrome

Biodistribution (the absorption into different organs; particularly into ovarian tissues)

Effectiveness of NP-RES to cross the intestinal epithelium and to arrive into the organs to explain its beneficial effects during time.



Measurement of RES (µg/L) in in vivo experiments. All data $p < 0.05$ vs control (untreated animals).

- NP-RES is absorbed into the organs during time, confirming the hypothesis about the activity of NP-RES in the second peak observed in plasma samples.
- NP-RES improves a tissue deposit mainly at 360 min indicating the importance of the formulation to exert a systemic biological effect.
- NP-RES exerts beneficial effects on ovarian tissue.

NP-RES

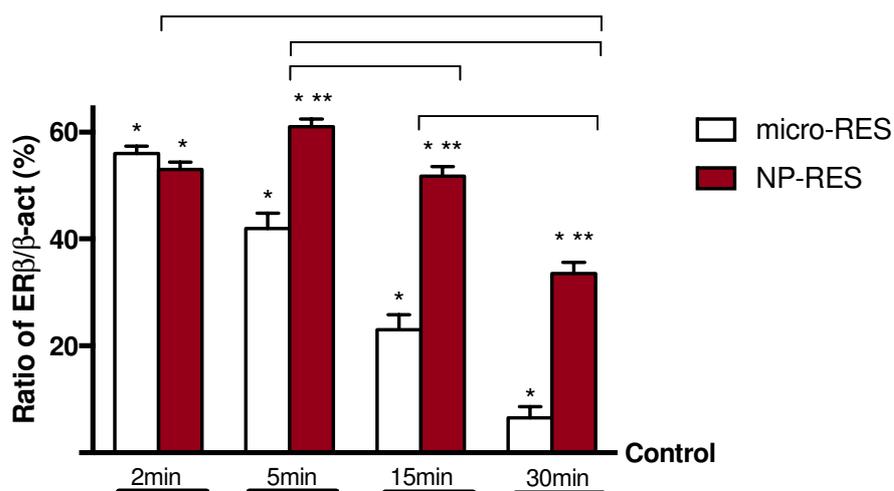
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Effectiveness of NP-RES in climacteric syndrome

Intracellular action mechanism

NP-RES exerts its beneficial effects during time through estrogenic receptor



Densitometric analysis of ER β receptor on ovarian tissue from female rats treated with NP-RES and micro-RES. * $p < 0.05$ vs control; ** $p < 0.05$ vs micro-RES; the bars $p < 0.05$ between NP-RES at different time.

- NP-RES demonstrates a better influence on ER β receptor starting from 5min ($p < 0.05$) compared to micro-RES.
- NP-RES is able to maintain this effect during all time of stimulation.
- NP-RES supports a stronger influence on ovarian tissue.

NP-RES

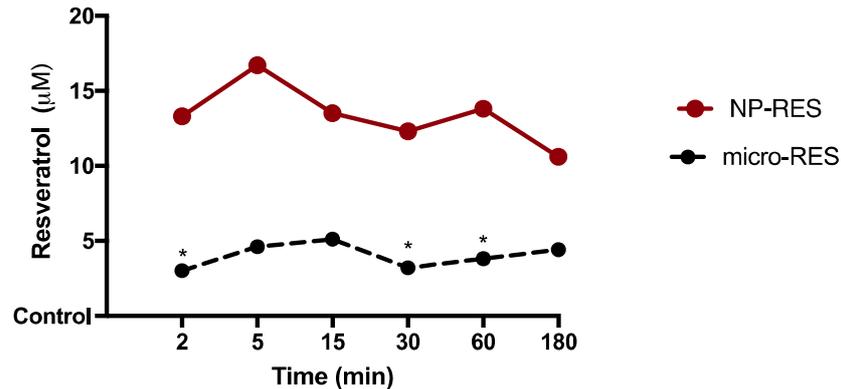
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Biological activity of NP-RES

Absorption rate (intracellular quantification of Resveratrol)

Biological and molecular activity of NP-RES on ovarian cells



Measurement of intracellular concentration of NP-RES and micro-RES in CHO-K1 cells during time.
* not significant vs control; point without symbol $p < 0.05$ vs control.

- NP-RES enhances the absorption of Resveratrol compared to micro-RES ($p < 0.05$) in the first 15min of stimulation with a maximum effect at 5min of stimulation (about 16.7 µM).
- NP-RES confirms its effectiveness and demonstrates the importance of the formulation to influence its uptake in cells and tissues

NP-RES

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NP-RES supports:

a prolonged action of Resveratrol into the bloodstream, after oral administration

a maintenance during time its beneficial effects and preserve the health of tissue

an increased bioavailability and biodistribution, ensuring a systemic effect

a significant molecular effect, acting through the involvement of ER β receptor (estrogen receptor)

a biological activity during time greater than commercial available micro-RES products