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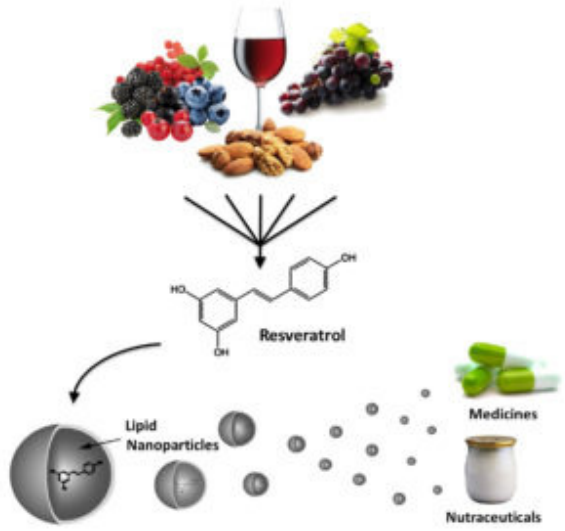
# Design of supplements and nutraceuticals enriched in resveratrol: a promising natural compound

Resveratrol is a polyphenol compound found in grapes, red wine, berry fruits and nuts. Given the favorable prophylactic and therapeutic effects of resveratrol, nanocarriers have been developed for enhancing its bioavailability for further application as supplements or nutraceuticals with health benefits similar to the ones attributed exclusively to fruits and red wine consumption.

In the last decades, great attention has been paid to resveratrol due to its ability to promote benefits for human health, providing protection against some neurodegenerative diseases, reducing the risk factors of cardiovascular diseases, and promoting cancer prevention. However, this polyphenol compound present poor bioavailability, low water solubility, and chemical instability, being rapidly eliminated from the human body. Lipid-based nanoparticles have been developed since lipids are known to promote oral absorption of drugs or vitamins, providing physical stability and compatibility, conferring protection from degradation and controlling the transport of resveratrol in the bloodstream after oral administration. Moreover, nanoparticles surface has been coated with polyethylene glycol (PEG) in order to reduce the hepatic clearance and prolong blood circulation time.




Spherical and uniform nanoparticles with smooth surfaces have been produced. A very high resveratrol entrapment efficiency of 70%, size range between 160 and 190 nm, and highly negative zeta potential of −30 mV suggest a good physical stability over at least 3 months. Nanoencapsulation effectively protected resveratrol from photodegradation and the release studies showed a neglectable resveratrol release at storage conditions. The *in vitro* simulation of gastrointestinal transit showed that resveratrol remained mostly associated to the lipid nanoparticles after their incubation in digestive fluids. MTT assays demonstrated that neither resveratrol nor lipid nanoparticles adversely affected cell viability and integrity of Caco-2 cell monolayers, the most commonly used model of the human intestinal membrane barrier. The intestinal permeability of resveratrol was significantly improved by nanoparticles and they were able to cross the intestinal barrier by a preferential transcellular route, mainly through a clathrin-mediated endocytosis mechanism, although caveolae-mediated endocytosis was also involved in the uptake. Moreover, resveratrol oral absorption can be enhanced during meals, since the intestinal permeability was increased in the presence of fed-state intestinal juices.

In conclusion, this work contributed to enhance the therapeutic effects of resveratrol through the development of effective lipid-based nanoparticles that minimize the instability of resveratrol, allowing a

controlled release after uptake. These nanodelivery systems seem to be suitable carriers for resveratrol oral administration, for further use as supplements or nutraceuticals.

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## Publications

Nanoscale Delivery of Resveratrol towards Enhancement of Supplements and Nutraceuticals.
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Neves AR, Reis S, Segundo MA
*J Agric Food Chem. 2015 Apr 1*