Optimization of trans-Resveratrol bioavailability for human therapy.


University Aix Marseille, INRA UMR 1260, 13385 Marseille, France; University Aix Marseille, INSERM UMR 1062, 13385 Marseille, France; University Aix Marseille, Faculte de Medecine La Timone, Marseille F-13385, France.

Abstract

We have developed an innovative soluble galenic form to overcome the low absorption of trans-Resveratrol (t-Res) as a dry powder. We present here data on pharmacokinetics, bioavailability, and toxicity of t-Res in human volunteers treated with this soluble form, plus additional data on biological effects in rodents. Fifteen healthy volunteers of both sexes received 40 mg of t-Res in two forms, the soluble formulation (caplets) and the original powder (capsules), in a crossover design. Blood samples were collected at 15 min, 30 min, and every hour for 5 h. Plasma concentrations of t-Res and its metabolites were analyzed by liquid chromatography and mass spectrometry. The single dose (40 mg) of the soluble t-Res was well absorbed and elicited biologically efficient blood levels (0.1-6 μM) for several hours, despite metabolism into glucuronide and sulfate conjugates coupled to renal elimination. In contrast, t-Res administered as a dry powder barely elicited efficient blood levels for a short duration. The new formulation led to 8.8-fold higher t-Res levels in plasma versus the powder. t-Res metabolism was not modified and neither intolerance nor toxicity were observed during the study and the following week. The soluble formulation elicited a robust anti-inflammatory effect in various tissues of mice fed a high-fat diet, while dry powder t-Res was almost inactive. Our data suggest that significant improvements in t-Res bioavailability and efficiency can be obtained by this soluble galenic form, also allowing lower doses. The use of t-Res in human therapy is thus greatly facilitated and the toxicity risk is reduced.