Veri-te™ RESVERATROL

Bioavailability

What is the "resveratrol paradox"?

Although it is thought that resveratrol has low bioavailability, the evidence of its bio-activity with more than 200 published clinical studies seems unquestionable. Additionally, numerous systematic reviews and meta-analysis have reported positive associations. Therefore, it is clear that the low levels of resveratrol found in blood plasma are not telling us the whole story, and resveratrol is considered to have high bio-efficacy.[2, 3]

Rethinking bioavailability for resveratrol

Bioavailability is classically defined as "the rate and extent to which the active substance or active moiety is absorbed from a pharmaceutical form and becomes available at the site of action."[1]

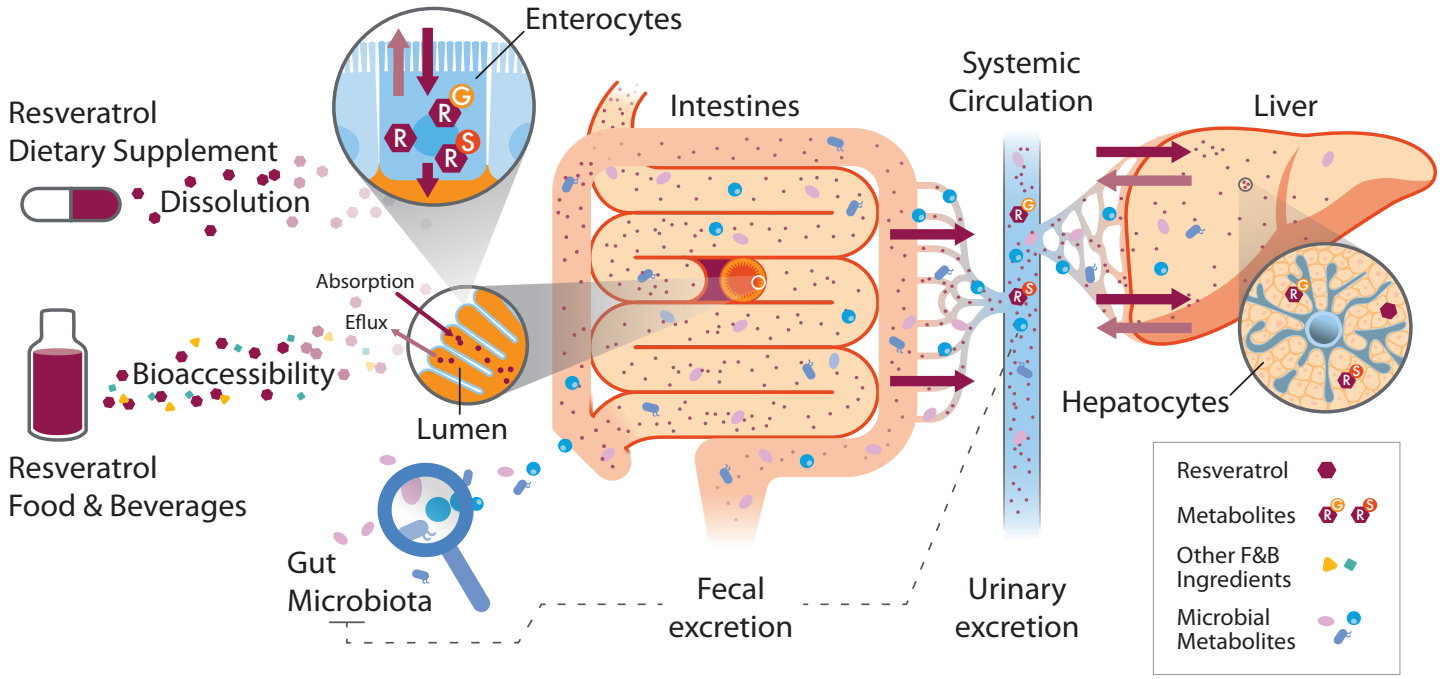
Although monitoring the circulating levels of a compound in the blood may be informative, it is important to consider that many compounds undergo *in situ* activation. Due to this activity, many compounds can be transformed into one or more active metabolites and potentially contribute to the observed clinical response. Another critical point to consider is the definition of "site of action." The site of action or target can be an organ, tissue, or impact humans and animals on a cellular level; this is a critical factor when considering bio-efficacy.[1] This broadened understanding is key, particularly with dietary supplements containing bio-active compounds such as resveratrol, since resveratrol metabolites should be considered as part of the answer to bio-efficacy.

How bioavailable is resveratrol?

Resveratrol has been reported as being highly absorbed orally (~70%) in humans, yet has low systemic bioavailability (~0.5%), meaning that only low levels are found in the blood plasma.[4] Figure 1 summarizes the metabolic fate and bio-transformation of resveratrol in the human gastrointestinal tract and metabolism in different organs.

The reason for the referred low systemic bioavailability is that resveratrol undergoes a rapid metabolization into resveratrol sulfate and glucuronide conjugates. In addition, resveratrol can be further metabolized by the gut microbiota. All these metabolites coming from the conjugation with sulfates and glucuronides and from microbial metabolism can be further absorbed into the systemic circulation and therefore reach different organs and have an effect.

Figure 1. biotransformation of resveratrol



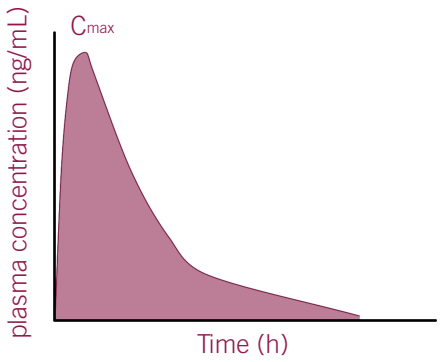
What are the key parameters?

Bioavailability of a compound is basically estimated by two key parameters, maximum plasma concentration ($\mathbf{C_{max}}$) and the area under the concentration-time curve (**AUC**). See figure 3 below.

$\mathbf{C_{max}}$ is related to the fraction of the dose that reaches the circulatory system without being metabolized. The time to reach $\mathbf{C_{max}}$ ($\mathbf{t_{max}}$) depends on the rate of absorption, distribution, and elimination.

AUC is the area under the concentration versus time curve and is expressed in (concentration) x (time), which relates to the total amount of the compound that reached the systemic circulation.

Figure 3. C_{max} and AUC



References

1. Drug Bioavailability: Estimation of Solubility, Permeability, Absorption and Bioavailability Edited by Han van de Waterbeemd and Bernard Testa Copyright 2009 WILEY-VCH *Verlag GmbH & Co. KGaA, Weiheim.*

2. Salehi B, Mishra AP, Nigam M, et al. Resveratrol: A Double-Edged Sword in Health Benefits. *Biomedicines.* 2018;6(3):91.

3. Ramírez-Garza SL, Laveriano-Santos EP, Marhenda-Muñoz M, et al. Health Effects of Resveratrol: Results from Human Intervention Trials. *Nutrients.* 2018;10(12):1892.

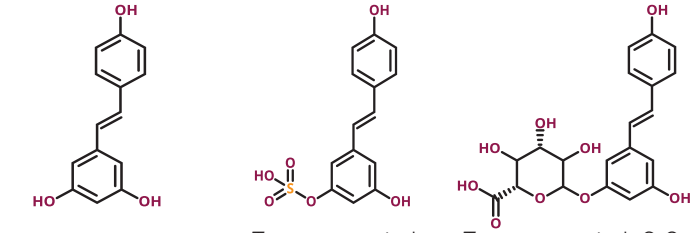
4. Springer M, Moco S. Resveratrol and Its Human Metabolites-Effects on Metabolic Health and Obesity. *Nutrients.* 2019;11(1):143.

Veri-te™ RESVERATROL

Resveratrol metabolites play an important role in bioactivity

Figure 2 summarizes the main conjugates and microbial metabolites generated by the metabolization of resveratrol. These conjugates are produced as resveratrol is processed and digested. These conjugates play an important role in resveratrol's bioactivity and can be recirculated through the blood from the liver and bowel.[4]

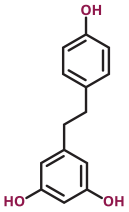
Figure 2. resveratrol metabolites



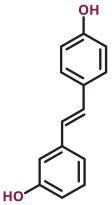
Trans-resveratrol

Trans-resveratrol -3-O-sulfate

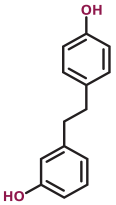
Trans-resveratrol -3-O-glucuronide



Dihydroresveratrol



3,4'-O-dihydroxy-trans-stilbene



Lunularin

About Evolva:

Veri-te resveratrol is produced by Evolva, a Swiss biotech company focused on the research, development and commercialization of products based on nature. We have leading businesses in Flavors and Fragrances, Health Ingredients and Health Protection. Evolva's employees, half of which are women, are dedicated to make the best products that can contribute to health, wellbeing and sensory enjoyment. Find out more at www.evolva.com.

For more information:

We have sales offices in the US and Europe, with distribution and regulatory approvals worldwide.* Our technical team can advise on formulations and ideal combinations. Additionally, our marketing team can help you plan your marketing strategy for Veri-te resveratrol. Contact us to order free samples for evaluation.

Evolva's website: www.evolva.com
Veri-te resveratrol website: www.veriteresveratrol.com

For general inquiries and customer service inquiries please email:
res@veriteresveratrol.com

Connect with us:
Twitter: @Veri_te
LinkedIn: www.linkedin.com/company/veri-te-resveratrol
Facebook: https://www.facebook.com/veriteresveratrol

Or phone us at:
Evolva (U.S.A./R.O.W.): +1.800.250.1032
Evolva (Europe/R.O.W.): +41.61.485.2099

evolva

*Contact Evolva for a full list of countries where approved by regulation