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FILE: ▪ Pomegranate (*Punica granatum*)
▪ Antioxidant Effects
▪ Polyphenols
▪ Pharmacokinetics
▪ Punicalagins

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RE: Antioxidant Effects of Standardized Pomegranate (*Punica granatum*) Extract in Healthy Volunteers

Mertens-Talcott SU, Jilma-Stohlawetz P, Rios J, Hingorani L, Derendorf H. Absorption, metabolism, and antioxidant effects of pomegranate (*Punica granatum* L.) polyphenols after ingestion of a standardized extract in healthy human volunteers. *J Agric Food Chem*. 2006 Nov 15;54(23):8956-8961.

The results of many case-control and cohort studies indicate that polyphenol intake may be inversely correlated with the incidence of many types of cancer and cardiovascular disease. The mechanism for this effect is thought to be related to the antioxidant, immunomodulatory, and anti-inflammatory activities of polyphenols. Several studies have shown the potential health benefits of pomegranate (*Punica granatum*), a rich source of polyphenols—particularly its ellagitannins of which punicalagins are the primary antioxidant components found in the whole fruit. Commercial pomegranate juice (PJ) has been shown to have a higher antioxidant activity than tea (*Camellia sinensis*), red wine (*Vitis vinifera*), and other fruit juices. However, due to processing and storage techniques, the ellagitannin and antioxidant content of PJ can vary widely, and there may be limitations to using PJ to benefit health due to excess sugar and calorie intake.

The objective of this study was to evaluate the pharmacokinetic properties and immunomodulatory and antioxidant effects of intake of commercial pomegranate extract standardized to punicalagins and containing no more than 5% ellagic acid.

Thirteen healthy men and women aged 37.6 ± 3.6 years underwent a 3-day washout period during which time they were asked to abstain from eating polyphenol-containing foods and large amounts of alcohol or antioxidant supplements. Two subjects withdrew from the study, so that only 11 subjects completed the study. On the study day, the subjects consumed 2 capsules with water; each capsule provided 400 mg pomegranate extract

(POMELLA®, Verdure Sciences, Inc.; Noblesville, IN) containing 165.2 mg of punicalagin isomers and 10.8 mg of free ellagic acid. Blood samples were drawn at baseline and 30 minutes and 1, 2, 4, 6, 8, and 24 hours after capsule consumption for the measurement of ellagic acid, metabolites of ellagic acid, antioxidant capacity of blood (plasma), reactive oxygen species (ROS), and interleukin-6. The study was conducted at the University of Florida.

Metabolite concentrations were consistent with previous in vitro research on the hydrolysis of punicalagin into ellagic acid, and pharmacokinetic research on PJ concentrate standardized to punicalagins. In this study, punicalagins were not detected; however, ellagic acid and its metabolites (urolithin A and B, hydroxyurolithin A, urolithin A-glucuronide, and dimethylellagic acidglucuronide) were found to be bioavailable in plasma after pomegranate extract intake. Ex vivo antioxidant activity in plasma was detected by oxygen radical absorbance capacity (ORAC) assay, the maximum effect observed being 32% 0.5 h after capsule consumption, falling to slightly above baseline by 4 hours post-consumption. The maximum concentration (Cmax) of ellagic acid was 33 mg/mL, and the time to reach the maximum concentration (tmax) was 1 hour, which is comparable to a Cmax of 18.5 ng/mL and tmax of 0.98 hours in a prior human study where 6 oz concentrated PJ was consumed.

The generation of ROS was not significantly affected by pomegranate extract intake, possibly because the plasma polyphenol concentration was not high enough to affect the ex vivo analysis of ROS. Interleukin-6 concentrations were not significantly changed 4 h after pomegranate consumption; an increase detected after 6 and 8 hours was attributed to factors other than polyphenol consumption.

The detection of ellagic acid in the blood supports the bioavailability of a powdered pomegranate extract taken at moderately high doses. The increase ex vivo plasma antioxidant capacity after consumption of standardized pomegranate extract suggests that it has tangible effects once in the body. "Overall, this study demonstrated the absorbablility of EA (ellagic acid) from a pomegranate extract high in elligatannin content, and its ex vivo antioxidant effects."

—Brenda Milot, ELS

The American Botanical Council has chosen not to reprint the original article.