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Occurrence of urolithins, gut microbiota ellagic acid metabolites and proliferation markers expression response in the human prostate gland upon consumption of walnuts and pomegranate juice.

<u>GonzÃ;lez-SarrÃas A, Giménez-Bastida JA, GarcÃa-Conesa MT, GÃ³mez-SÃ;nchez MB,</u> <u>GarcÃa-Talavera NV, Gil-Izquierdo A, SÃ;nchez-Alvarez C, Fontana-Compiano LO, Morga-Egea JP, Pastor-Quirante FA, MartÃnez-DÃaz F, TomÃ;s-BarberÃ;n FA, EspÃn JC</u>.

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Abstract

Epidemiology supports the important role of nutrition in prostate cancer (PCa) prevention. Pomegranate juice (PJ) exerts protective effects against PCa, mainly attributed to PJ ellagitannins (ETs). Our aim was to assess whether ETs or their metabolites ellagic acid and urolithins reach the human prostate upon consumption of ET-rich foods and to evaluate the effect on the expression of three proliferation biomarkers. Sixty-three patients with BPH or PCa were divided into controls and consumers of walnuts (35 g walnuts/day) or pomegranate (200 mL PJ/day) for 3 days before surgery. Independently of the ETs source, the main metabolite detected was urolithin A glucuronide, (3,8-dihydroxy-6H-dibenzo[b,d]pyran-6-one glucuronide) (up to 2 ng/g) together with the traces of urolithin B glucuronide, (3-hydroxy-6H-dibenzo[b,d]pyran-6-one glucuronide) and dimethyl ellagic acid. The small number of prostates containing metabolites was likely caused by clearance of the compounds during the fasting. This was corroborated in a parallel rat study and thus the presence of higher quantities of metabolites at earlier time points cannot be discarded. No apparent changes in the expression of CDKN1A, MKi-67 or c-Myc were found after consumption of the walnuts or PJ. Our results suggest that urolithin glucuronides and dimethyl ellagic acid may be the molecules responsible for the beneficial effects of PJ against PCa.

PMID: 19885850 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

Substances:

- <u>CDKN1A protein, human</u>
- <u>Coumarins</u>
- <u>Cyclin-Dependent Kinase Inhibitor p21</u>

- <u>Hydrolyzable Tannins</u>
- Intracellular Signaling Peptides and Proteins
- <u>MKI67IP protein, human</u>
- <u>MYC protein, human</u>
- <u>Nuclear Proteins</u>
- <u>Plant Extracts</u>
- <u>Proto-Oncogene Proteins c-myc</u>
- <u>RNA, Messenger</u>
- <u>Tumor Markers, Biological</u>
- <u>3,8-dihydroxy-6H-dibenzo(b,d)pyran-6-one</u>
- <u>Ellagic Acid</u>

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Medical:

• <u>Prostate Cancer - MedlinePlus Health Information</u>

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• <u>Pomegranate ellagitannin-derived metabolites inhibit prostate cancer growth and</u> localize to the mouse prostate gland. [J Agric Food Chem. 2007]

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Seeram NP, Aronson WJ, Zhang Y, Henning SM, Moro A, Lee RP, Sartippour M, Harris DM, Rettig M, Suchard MA, et al. J Agric Food Chem. 2007 Sep 19; 55(19):7732-7. Epub 2007 Aug 28.

• <u>Pomegranate juice and extracts provide similar levels of plasma and urinary</u> <u>ellagitannin metabolites in human subjects.</u> [J Med Food. 2008]

Pomegranate juice and extracts provide similar levels of plasma and urinary ellagitannin metabolites in human subjects.

Seeram NP, Zhang Y, McKeever R, Henning SM, Lee RP, Suchard MA, Li Z, Chen S, Thames G, Zerlin A, et al. J Med Food. 2008 Jun; 11(2):390-4.

• <u>Pomegranate juice ellagitannin metabolites are present in human plasma and some</u> persist in urine for up to 48 hours. [J Nutr. 2006]

Pomegranate juice ellagitannin metabolites are present in human plasma and some persist in urine for up to 48 hours.

Seeram NP, Henning SM, Zhang Y, Suchard M, Li Z, Heber D. J Nutr. 2006 Oct; 136(10):2481-5.

• <u>Review Ellagic acid, pomegranate and prostate cancer -- a mini review.</u> [J Pharm Pharmacol. 2008]

Review Ellagic acid, pomegranate and prostate cancer -- a mini review. *Bell C, Hawthorne S. J Pharm Pharmacol.* 2008 *Feb;* 60(2):139-44.

• Review Multitargeted therapy of cancer by ellagitannins. [Cancer Lett. 2008] Review Multitargeted therapy of cancer by ellagitannins. *Heber D. Cancer Lett. 2008 Oct 8; 269(2):262-8. Epub 2008 May 12.*

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