



1st International Symposium for TCM and Integrative Medicine

Stip, 06.12.2017



Plant (Food) Bioactives: from Total Antioxidant Capacity to Gene Expression and Beyond

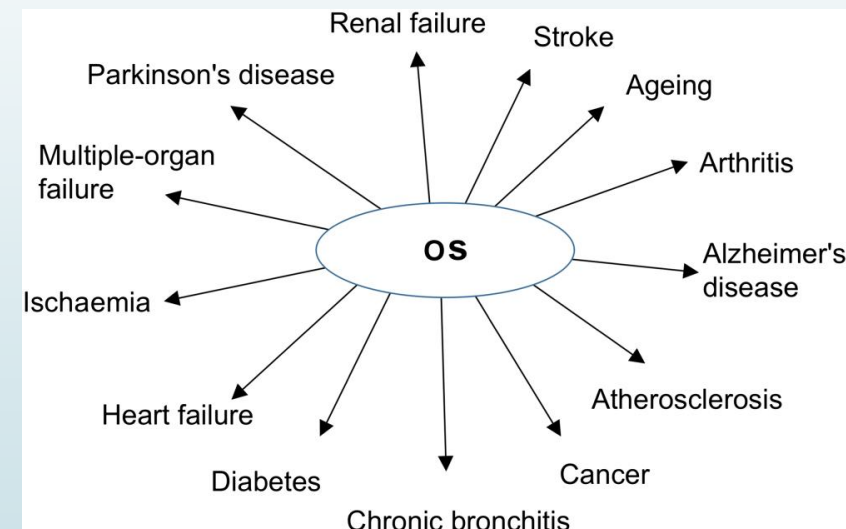
Prof. Dr. Tatjana Ruskovska

Faculty of Medical Sciences

Goce Delcev University - Stip

Oxidative Stress and Human Diseases

➡ Search term “oxidative stress” ≈175 000 papers on PubMed only, since 1970.



Antioxidant Supplements

► Translation of knowledge to clinical practice.

Free radicals are bad. Antioxidants are good.

Antioxidants, by scavenging ROS, will be beneficial in all the diseases...



The screenshot shows the PubMed.gov website interface. At the top, there is a navigation bar with 'NCBI', 'Resources', and 'How To'. Below this is the 'PubMed.gov' logo and the text 'US National Library of Medicine National Institutes of Health'. A search bar contains the text 'PubMed' and a dropdown menu. To the right of the search bar is a button labeled 'Advanced'. Below the search bar, there is a section for 'Format: Abstract' and a 'Send to' button. The main content area displays a search result for 'Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases.' The result includes the journal 'Cochrane Database Syst Rev', the date '2008 Apr 16;(2):CD007176', and the DOI '10.1002/14651858.CD007176'. The authors listed are 'Bjelakovic G¹, Nikolova D, Gluud LL, Simonetti RG, Gluud C.' Below the authors, there is a section for 'Author information' and a section for 'Update in' which mentions 'Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. [Cochrane Database Syst Rev. 2012]'.

NCBI Resources How To

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Cochrane Database Syst Rev. 2008 Apr 16;(2):CD007176. doi: 10.1002/14651858.CD007176.

Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases.

Bjelakovic G¹, Nikolova D, Gluud LL, Simonetti RG, Gluud C.

⊕ Author information

Update in
Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. [Cochrane Database Syst Rev. 2012]



Antioxidant Supplements

- There is no evidence to support antioxidant supplements for primary or secondary prevention.
- Vitamin A, beta-carotene, and vitamin E may increase mortality.
- Future randomized trials could evaluate the potential effects of vitamin C and selenium for primary and secondary prevention.
Such trials should be closely monitored for potential harmful effects.
- Antioxidant supplements need to be considered medicinal products and should undergo sufficient evaluation before marketing.

Discussions, Issues and New Perspectives in Redox Biology

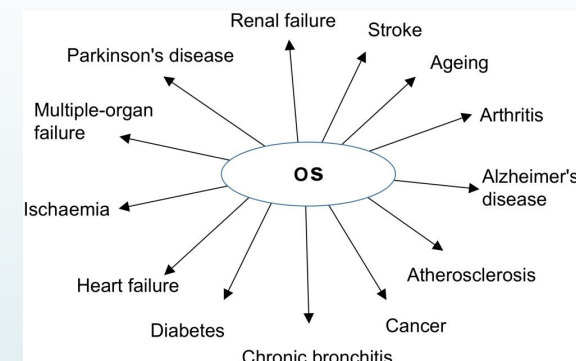
► Causality

- an association does not necessarily mean causation
- look for specific mechanisms, instead of scavenging all ROS

► The role of ROS and free radicals in cellular signaling

► Oversimplification that led to translational shortcut (an easy solution for a complex problem)

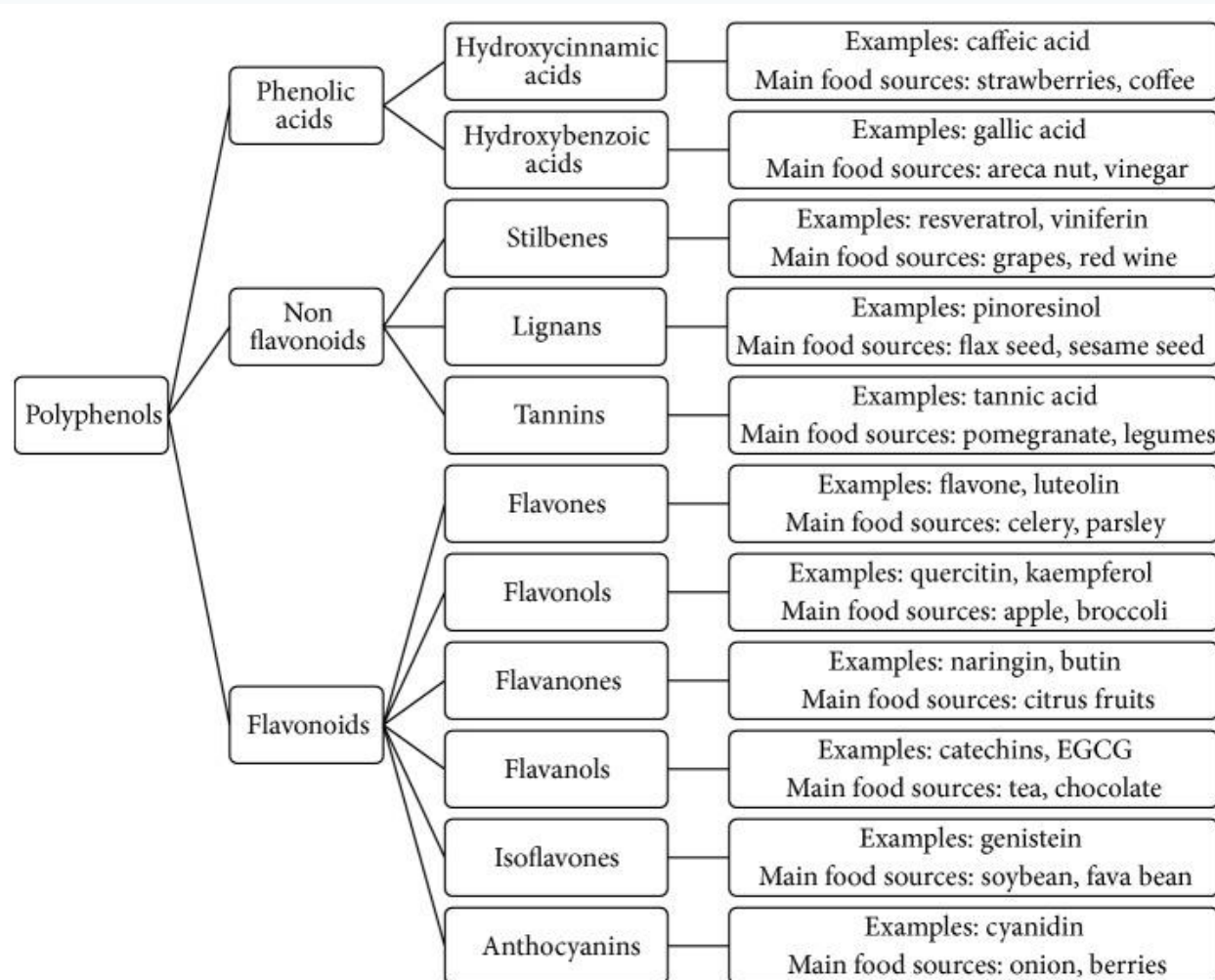
- add complexity, integrate the current knowledge, with help of bioinformatics



Br J Pharmacol. 2017 Jun;174(12):1784-1796.

Plant (Food) Bioactives

-they can have influence on health



-Highly abundant in our diet.
-Well studied and classified.

Epidemiological study

➡ FLAVONOID INTAKE IS INVERSELY ASSOCIATED WITH MORTALITY FROM CORONARY HEART DISEASE.

[Lancet](#). 1993 Oct 23;342(8878):1007-11.

Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study.

[Hertog MG¹](#), [Feskens EJ](#), [Hollman PC](#), [Katan MB](#), [Kromhout D](#).

⊕ Author information

Abstract

Flavonoids are polyphenolic antioxidants naturally present in vegetables, fruits, and beverages such as tea and wine. In vitro, flavonoids inhibit oxidation of low-density lipoprotein and reduce thrombotic tendency, but their effects on atherosclerotic complications in human beings are unknown. We measured the content in various foods of the flavonoids quercetin, kaempferol, myricetin, apigenin, and luteolin. We then assessed the flavonoid intake of 805 men aged 65-84 years in 1985 by a cross-check dietary history; the men were then followed up for 5 years. Mean baseline flavonoid intake was 25.9 mg daily. The major sources of intake were tea (61%), onions (13%), and apples (10%). Between 1985 and 1990, 43 men died of coronary heart disease. Fatal or non-fatal myocardial infarction occurred in 38 of 693 men with no history of myocardial infarction at baseline. Flavonoid intake (analysed in tertiles) was significantly inversely associated with mortality from coronary heart disease (p for trend = 0.015) and showed an inverse relation with incidence of myocardial infarction, which was of borderline significance (p for trend = 0.08). The relative risk of coronary heart disease mortality in the highest versus the lowest tertile of flavonoid intake was 0.42 (95% CI 0.20-0.88). After adjustment for age, body-mass index, smoking, serum total and high-density-lipoprotein cholesterol, blood pressure, physical activity, coffee consumption, and intake of energy, vitamin C, vitamin E, beta-carotene, and dietary fibre, the risk was still significant (0.32 [0.15-0.71]). Intakes of tea, onions, and apples were also inversely related to coronary heart disease mortality, but these associations were weaker. Flavonoids in regularly consumed foods may reduce the risk of death from coronary heart disease in elderly men.

PMID: 8105262

[Indexed for MEDLINE]



Full text links



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Similar articles

Dietary flavonoids and cancer risk in the Zutphen Elderly Study. [Nutr Cancer. 1994]

Inverse association of tea and flavonoid intakes with incident myocardial inf [Am J Clin Nutr. 2002]

Flavonol and flavone intakes in US health professionals. [J Am Diet Assoc. 2002]

Review Mechanisms of action of antioxidants as exemplified in vegetal [Food Chem Toxicol. 1999]

Review Flavonoids for reduction of atherosclerotic risk. [Curr Atheroscler Rep. 2004]

See reviews...

See all...

ORAC – Oxygen Radical Absorbance

- ORAC
- TEAC
- DPPH
- FRAP

USDA Database for the Oxygen Radical Absorbance Capacity (ORAC) of Selected Foods, Release 2



Prepared by
David B. Haytowitz and Seema Bhagwat

Nutrient Data Laboratory
Beltsville Human Nutrition Research Center (BHNRC)
Agricultural Research Service (ARS)
U.S. Department of Agriculture (USDA)

May 2010

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NATURE PROTOCOLS | PROTOCOL



Rapid measurement of total antioxidant capacity in plants

Kelly M Gillespie, June M Chae & Elizabeth A Ainsworth

[Affiliations](#) | [Corresponding author](#)

Nature Protocols **2**, 867–870 (2007) | doi:10.1038/nprot.2007.100

Published online 12 April 2007



How Do Nutritional Antioxidants Really Work?

- The ORAC list was withdrawn – *in vitro* TAOC is not a direct determinant of *in vivo* effects.
 - Low bioavailability – low concentrations in systemic circulation and tissues.
 - Extensive metabolism, which diminishes their free radical scavenging activity.


Cellular and Molecular Targets

- In vitro studies
- Animal studies
- Human studies



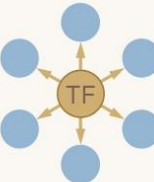
Analysis of transcription factors






TRRUST version 2

Transcriptional Regulatory Relationships
Unraveled by Sentence-based Text mining



[About TRRUST](#)
[Search](#)
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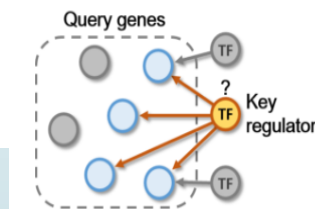
1. Search a gene in TRRUST database

Submit a query gene below.

Tables for human genes and mouse genes included in TRRUST.

Species: ☒ Human ☐ Mouse

****Examples****



2. Find key regulators for query genes

Submit a set of genes for a function/pathway/phenotype. (Min=5, Max=500)

Each gene name must be separated by comma, tab, white space or new line.
Input format: Entrez Gene ID (79923) or Gene Symbol (NANOG)

Species: ☒ Human ☐ Mouse

****Examples****

Example gene sets

#1: 33 DEGs perturbed by ESR1 knockdown in human breast tumors.
Muthukaruppan et al., Clin Breast Cancer, 2017

Pathways analysis



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Statistical analysis of molecular signatures

Transcriptomics

Upload **gene expression** data and perform enrichment analysis based on gene sets derived from popular databases like GO, KEGG and Reactome.

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Proteomics

Upload **protein** data and perform enrichment analysis based on protein datasets like SMPDB, or map proteins to corresponding genes and perform a gene set analysis.

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Upload **miRNA** data and perform enrichment analysis based on miRNA categories like miRDB or miRtarBase, or map miRNAs to gene targets from popular databases and perform a gene set analysis.

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Upload **SNP** data and perform enrichment analysis based on popular GWAS and P catalogs. This will identify variants associated with your up

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Statistical analysis of molecular signatures

Upload Data

Select your data source:

- ☐ a **GSE file** containing data of both, the sample and the reference group
- ☐ **two GDS files** for the sample and the reference group
- ☐ a **text file** containing a list of identifier with or without scores in a tabular format
- ☒ a **list of scores** in a tabular format

Help

Your options:

- a **GSE file** enter a valid GSE identifier (e.g., **GSE10072**). The corresponding GEO Series .soft file is then downloaded to the *GeneTrail 2* server automatically. In a next step, you may specify the sample and the reference group.
- two GDS files** enter valid GDS identifiers (e.g., **GDS2161** and **GDS2162**) for the sample and reference group, respectively. The corresponding GEO Data Set .soft files are then downloaded to the *GeneTrail 2* server automatically.
- a **text file** upload a plain text file containing identifier with or without pre-computed scores. The values have to be whitespace separated. (identifier list, score list, matrix)
- a **list** paste a pre-computed list of scores. The values have to be whitespace separated.

Functional links between proteins

- Differentially expressed genes were mapped via the STRING database.
- The STRING database takes a meta-analysis approach and identifies:
 - Protein-protein interactions and
 - Functional links between proteins.

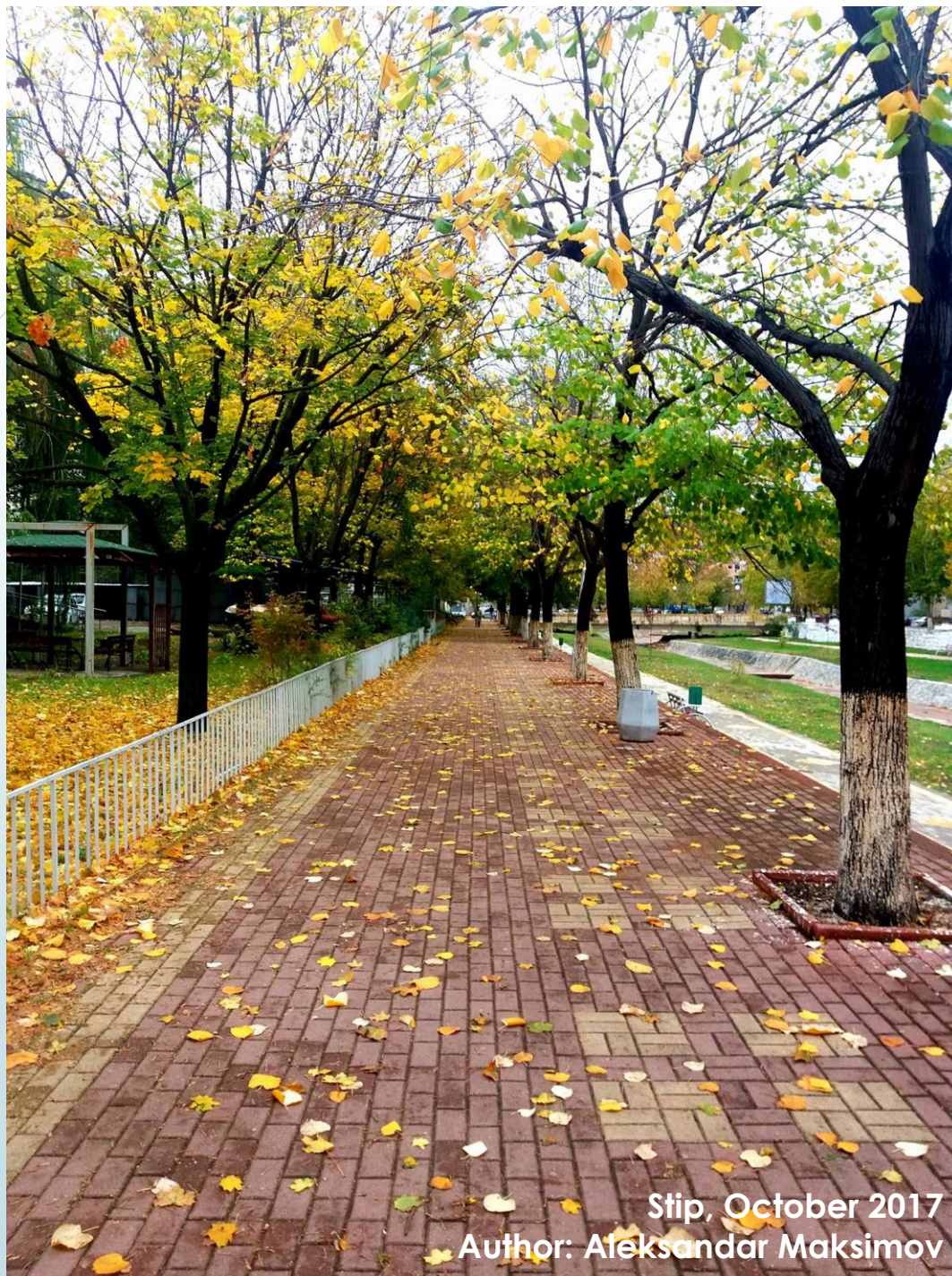




Acknowledgements



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Stip, October 2017
Author: Aleksandar Maksimov

**Thank you for
your attention!**

**Questions?
Comments?**