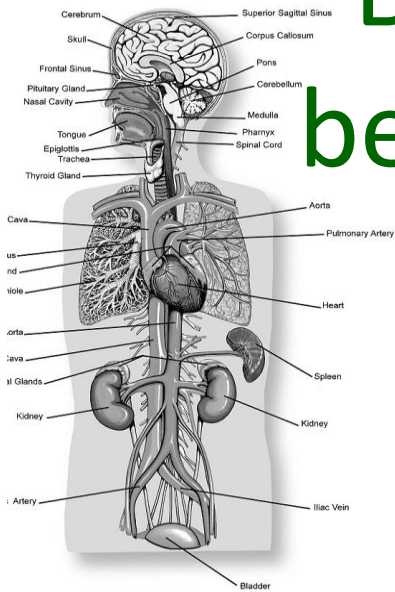




Bioactive components from berries: Human Health Effects



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Berry research at JHI

We breed market-leading varieties

- *Blackcurrants – the “Ben” series*
- *Raspberries – the “Glen” series*
- *Strawberry – “Symphony, Rhapsody....”*
- Research into Health Benefits of Berries
- Feedback and direct breeding of new varieties



Scheme of talk

Background

Biological activities of berry components

- MODEL SYSTEMS
- Cardiovascular Health
- Cancer
- Control of nutrient availability

Diabetes & Obesity

Analytical studies

- Correlate bioactivity with polyphenol composition





■ “Insufficient intake of fruit and vegetables increases the chances of developing cancers, cardiovascular disease and strokes” - World Health Organisation (2003)

■ The 3 main causes of premature death in Scotland

Led to the “5 a day” programme -

Government led intervention to alter our diet

How do FAV affect health?

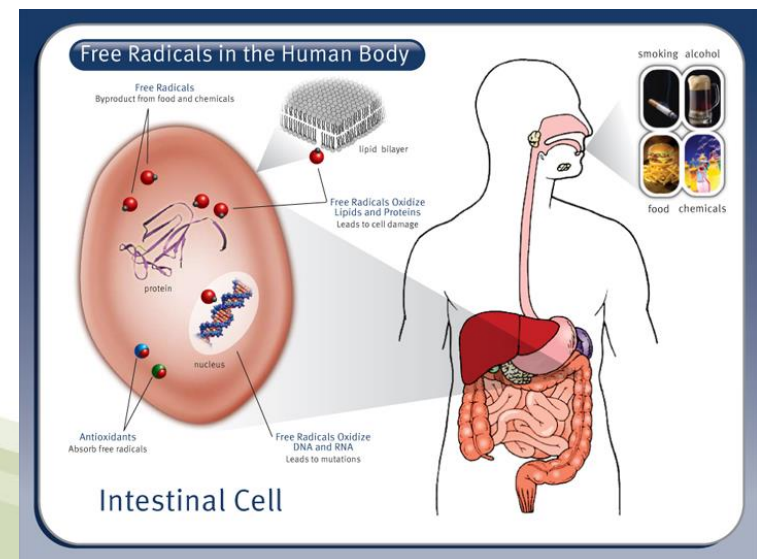
Minerals (Zinc)? Vitamins (C and E)?
Fibre? Displacement? Lower Fat?

Antioxidants? **Phytochemicals?**



Living with oxygen & free radicals

- We “burn” our food with Oxygen to release energy
- By-products include free radicals which are **VERY** reactive. They can damage the body and cause disease.
- Our bodies work hard to remove these radicals and prevent damage
- Dietary antioxidants are proposed to “top-up” protection



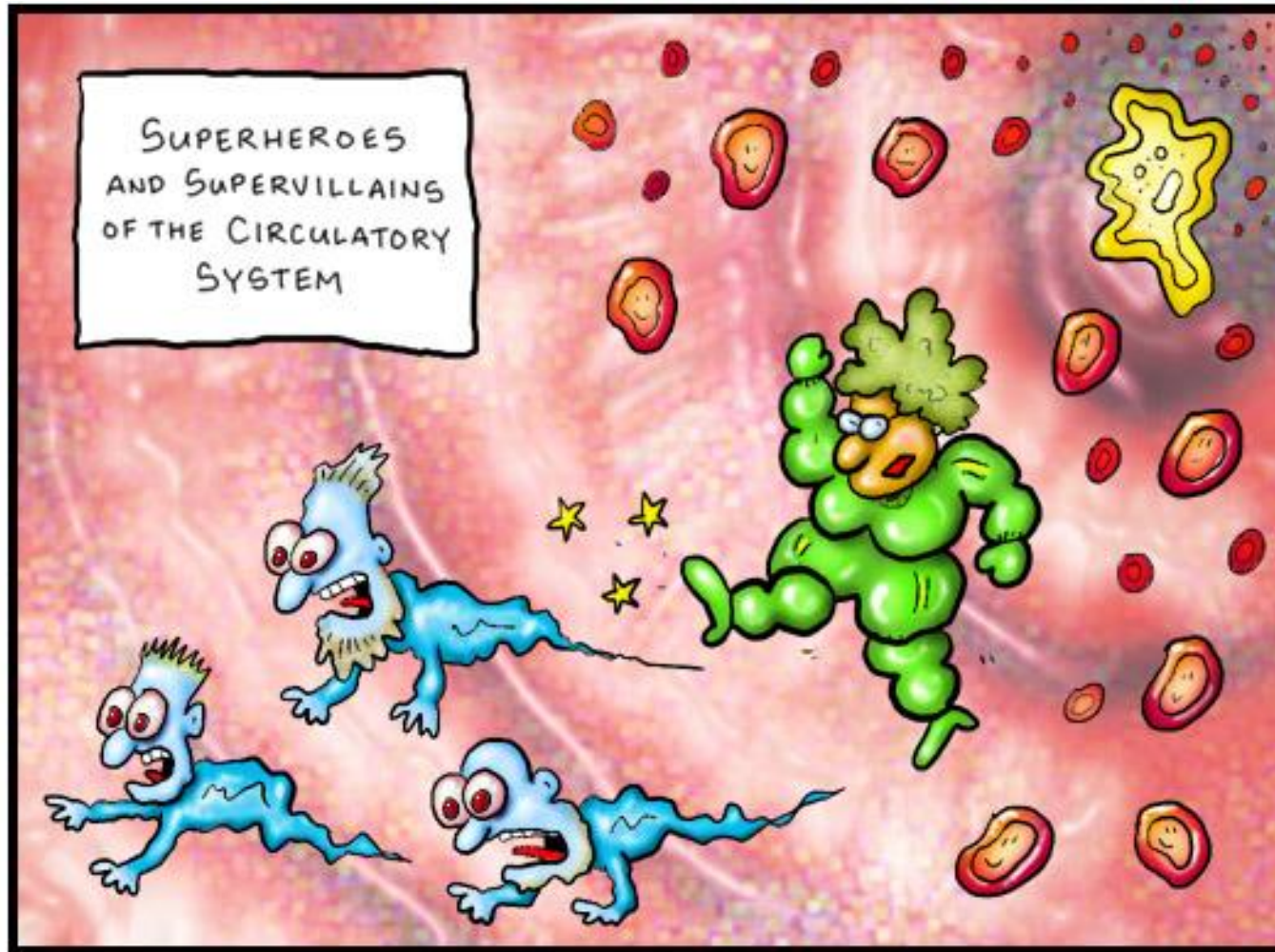
A simplified version?

Polyphenols as antioxidants

23 May 2000



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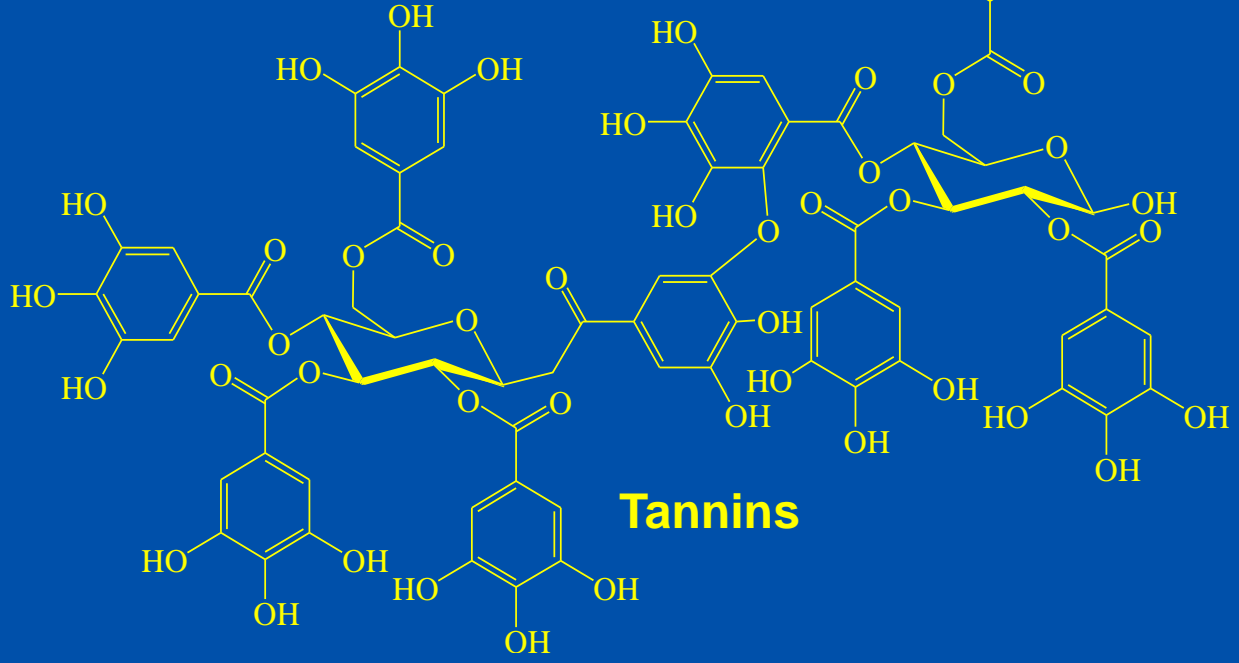
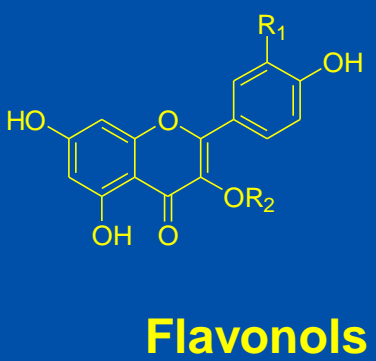
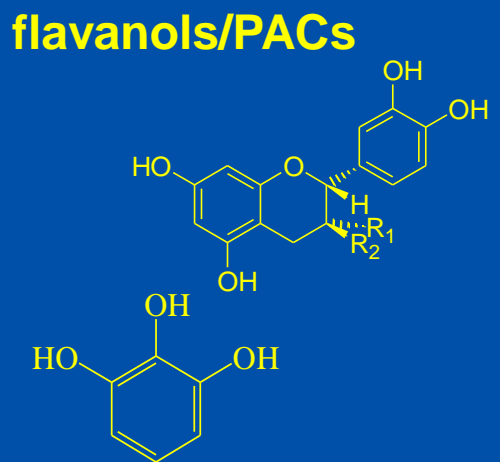
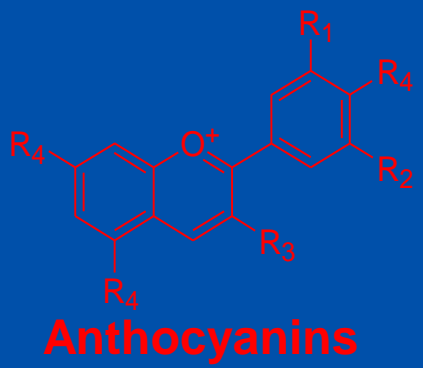
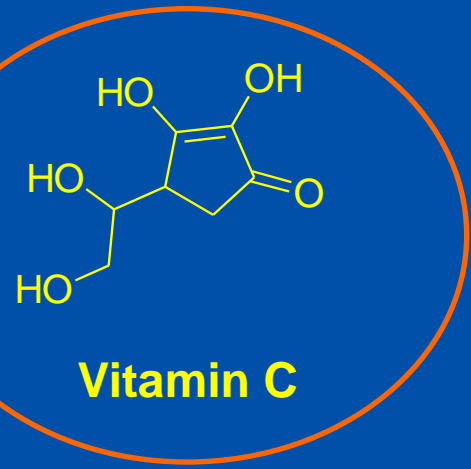


Copyright © 2000 David Farley, d-farley@metablab.unc.edu
<http://metablab.unc.edu/Dave/drfun.html>

This cartoon is made available on the Internet for personal viewing only. Opinions expressed herein are solely those of the author.

Auntie Oxidant kicks out the Free Radicals.

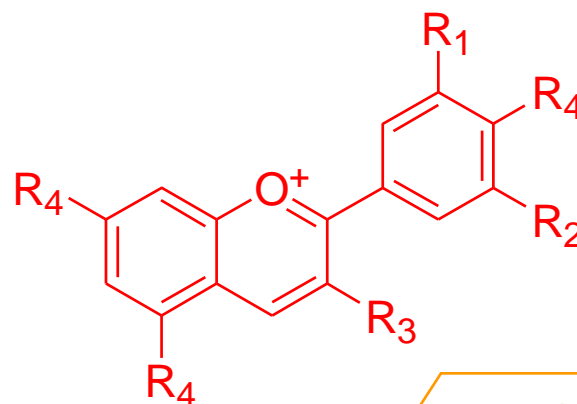
Berries contain a diverse and species specific mixture of antioxidants – the two main types are Polyphenols and **Vitamin C**





Cardiovascular disease (CVD)

- Protection of vasodilatory responses of rat aorta against inflicted oxidative damage
- Protective effect of polyphenols
not predicted by *in vitro* antioxidant activity
- Anthocyanins particularly effective

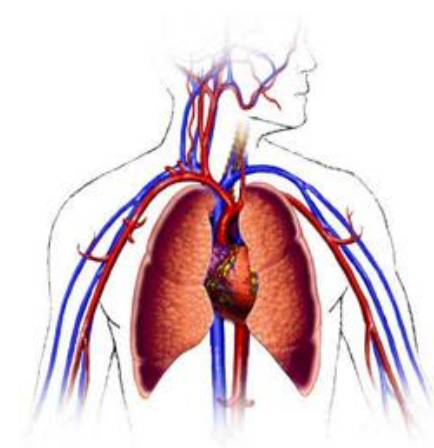


Prof. Ian Megson, Univ. Highland and Islands

Cardiovascular function and intake of soft fruit: Effects of qualitative and quantitative variation in berry antioxidant status

Intervention trial – assess effects of six week ingestion of

- blackcurrant berries with low vitamin C content
- blackcurrant berries with high vitamin C content
- blueberries (No vitamin C)
- coloured flavoured water (control)



Effects on cardiovascular function

Positive effects on blood vessel flexibility (intima media thickness) and *in vivo* markers for endothelial cell function and oxidative stress



Effect on Alzheimers?

Oxidative stress, Alzheimer's and the Brain

Brain = 2 % adult body mass but uses 20 % oxygen inhaled

Poorer antioxidant mechanisms

High levels of PUFAs, minerals and neurotransmitters – good targets for free radicals

Brain cells don't renew by cell division - accumulate FR-induced damage with age & FR damage implicated in AD

- *EU project*
BrainHealthFood
- **Bioactive compounds from blackcurrant processing waste for brain health**

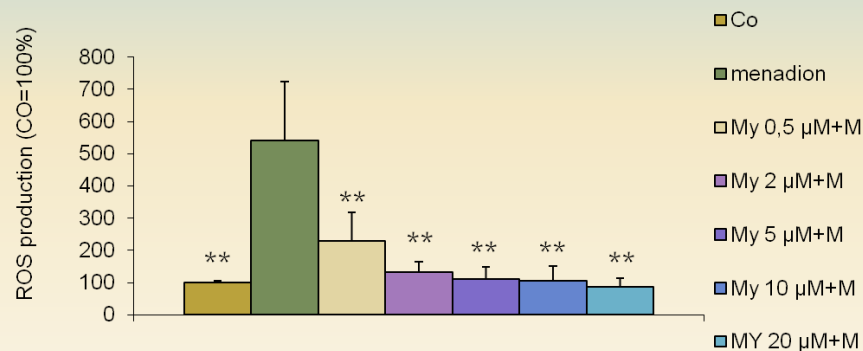
MTT Agrifood

JHI

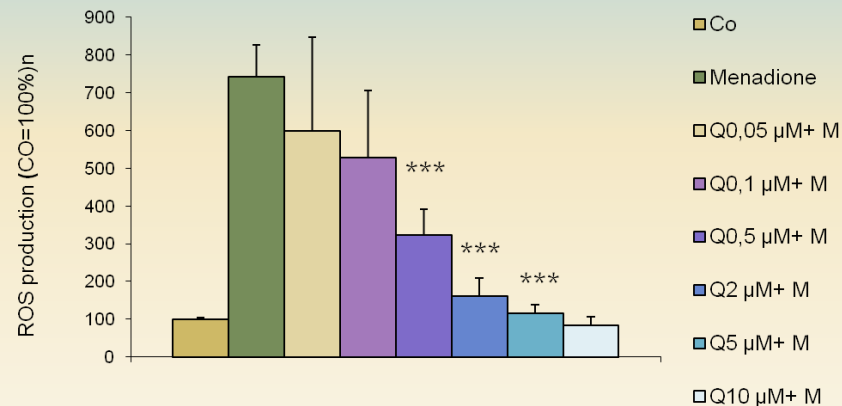
TTZ

**Univ. Kuopio
& SME partners**

ROS production in SH-SY5Y-APP751 cells
when treated 60 minutes with Myricetin
and/or 50 μ M menadion, n=6 ,SD

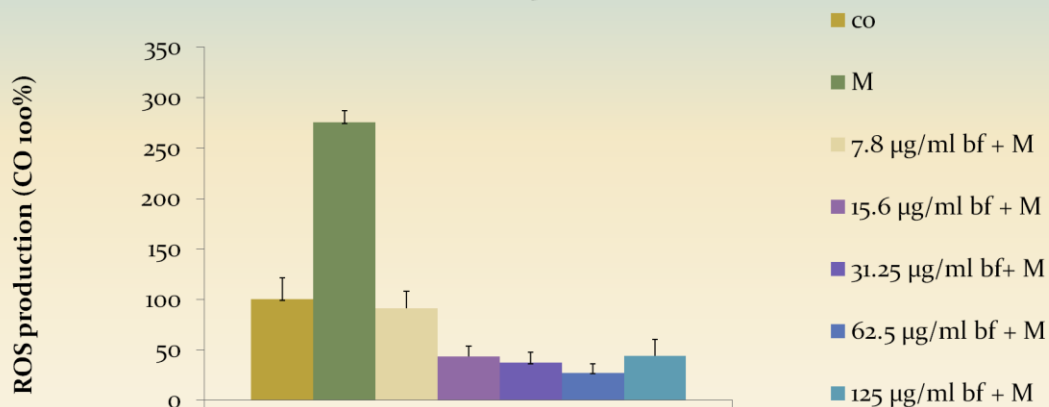


ROS production in SH-SY5Y-APP751 cells
when treated with 50 μ M menadion and/or
Quercetin (Q), n=2-6, SD

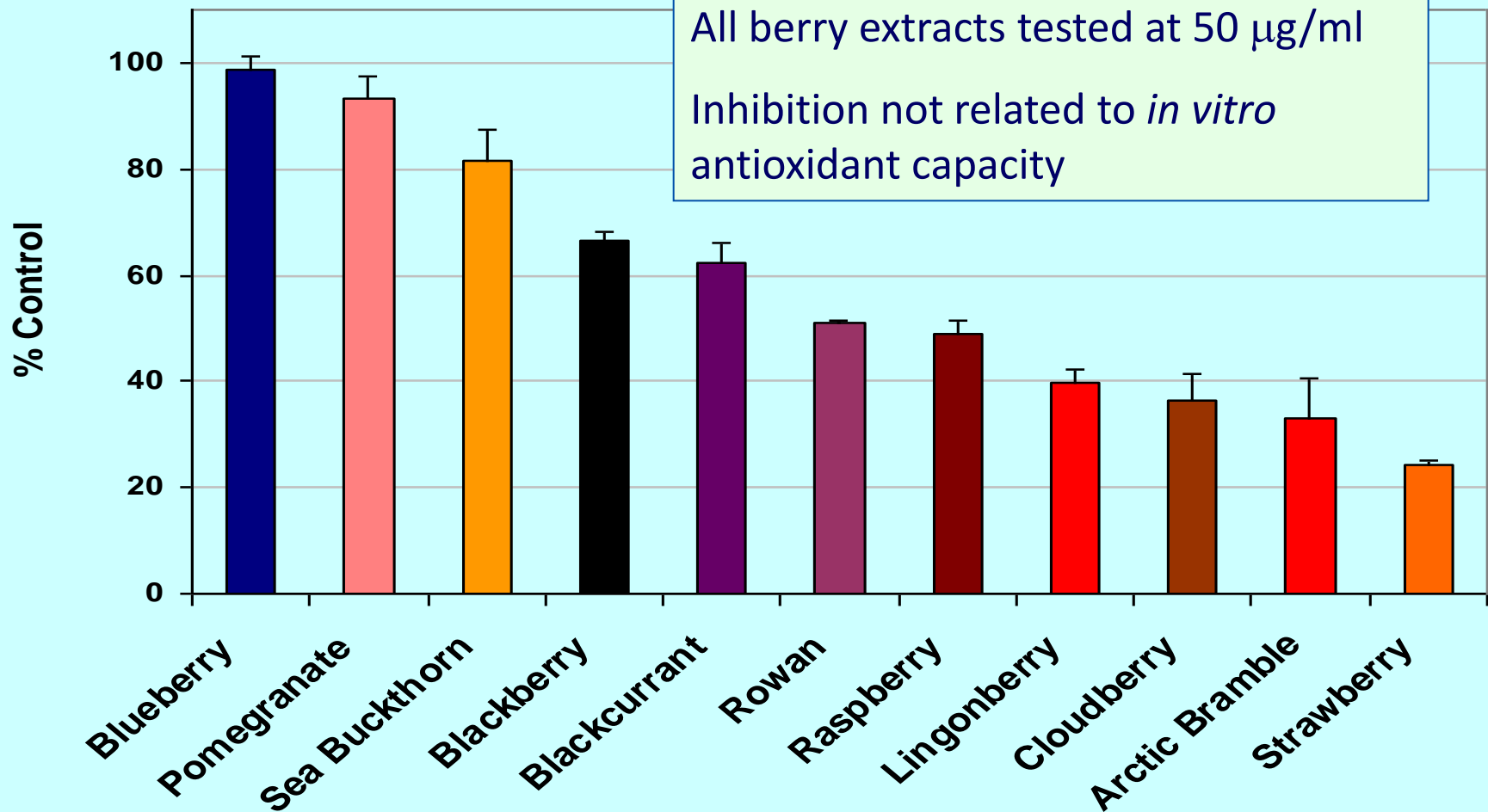


Protective effect of anthocyanins in Alzheimer's model system

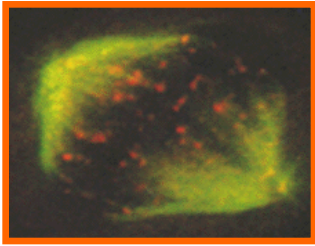
New studies confirm effects in mice models



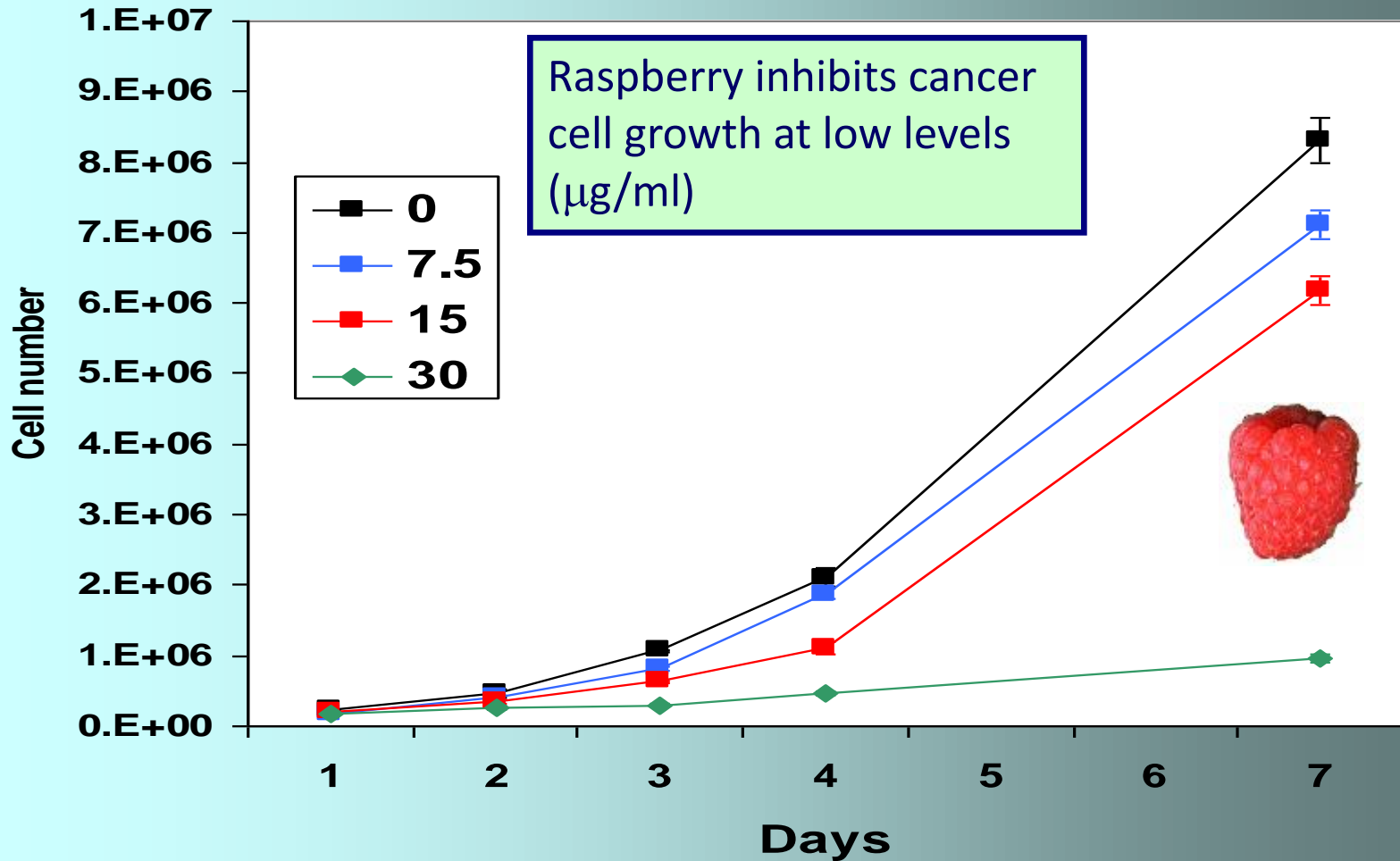
Effects on cancer cells



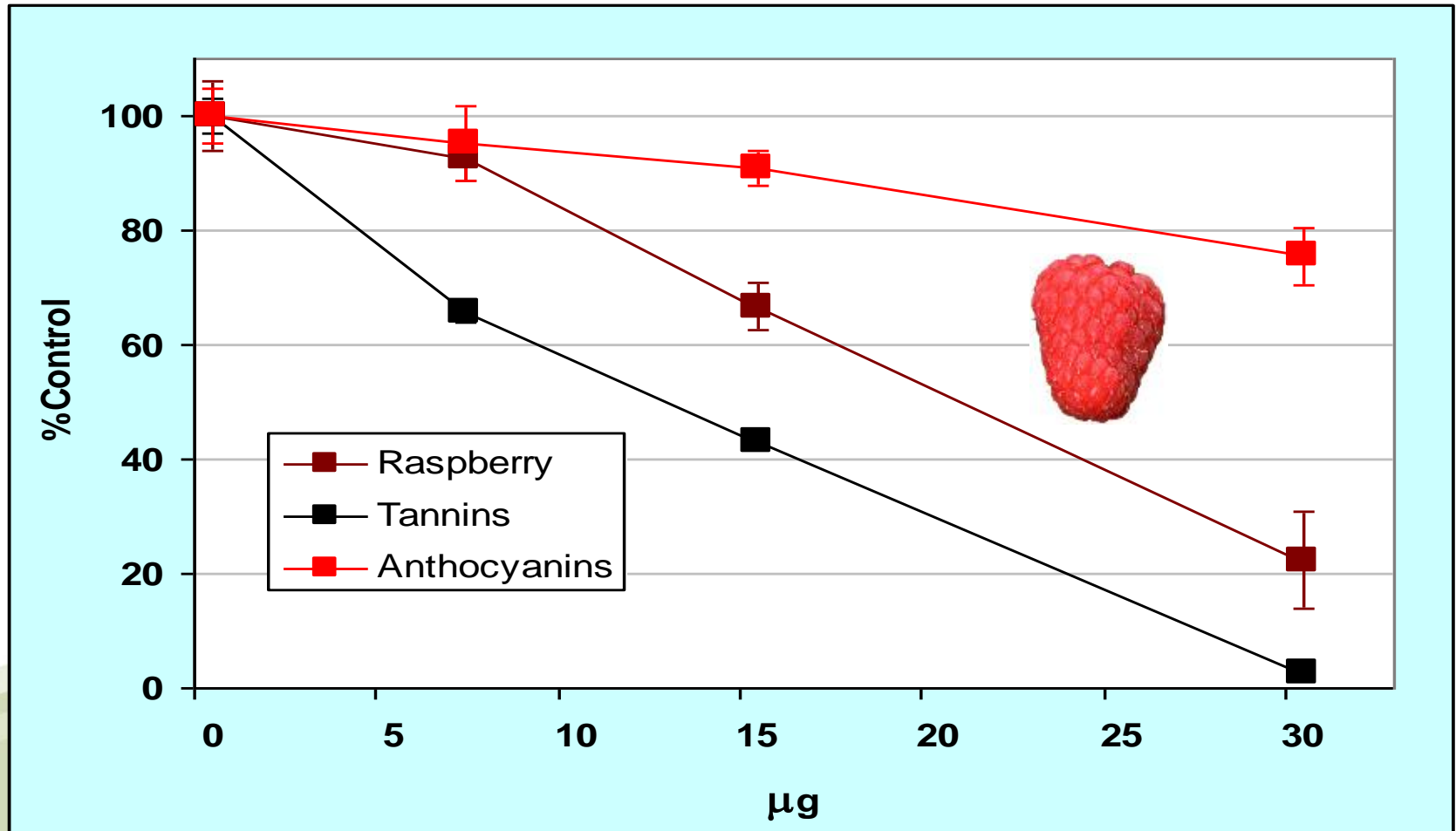
McDougall et al. (2008) JAFC 56; 3016-3023



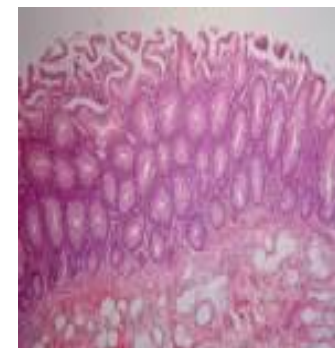
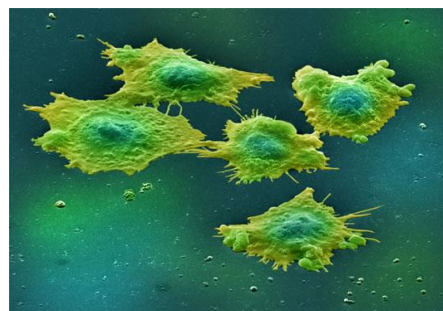
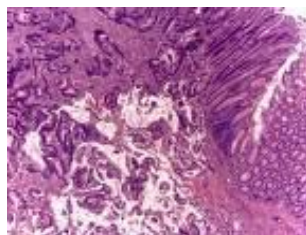
Anti-cancer effects



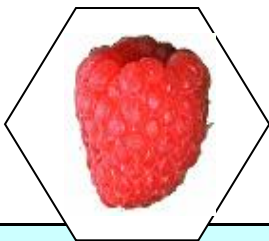
Most effective components are tannins



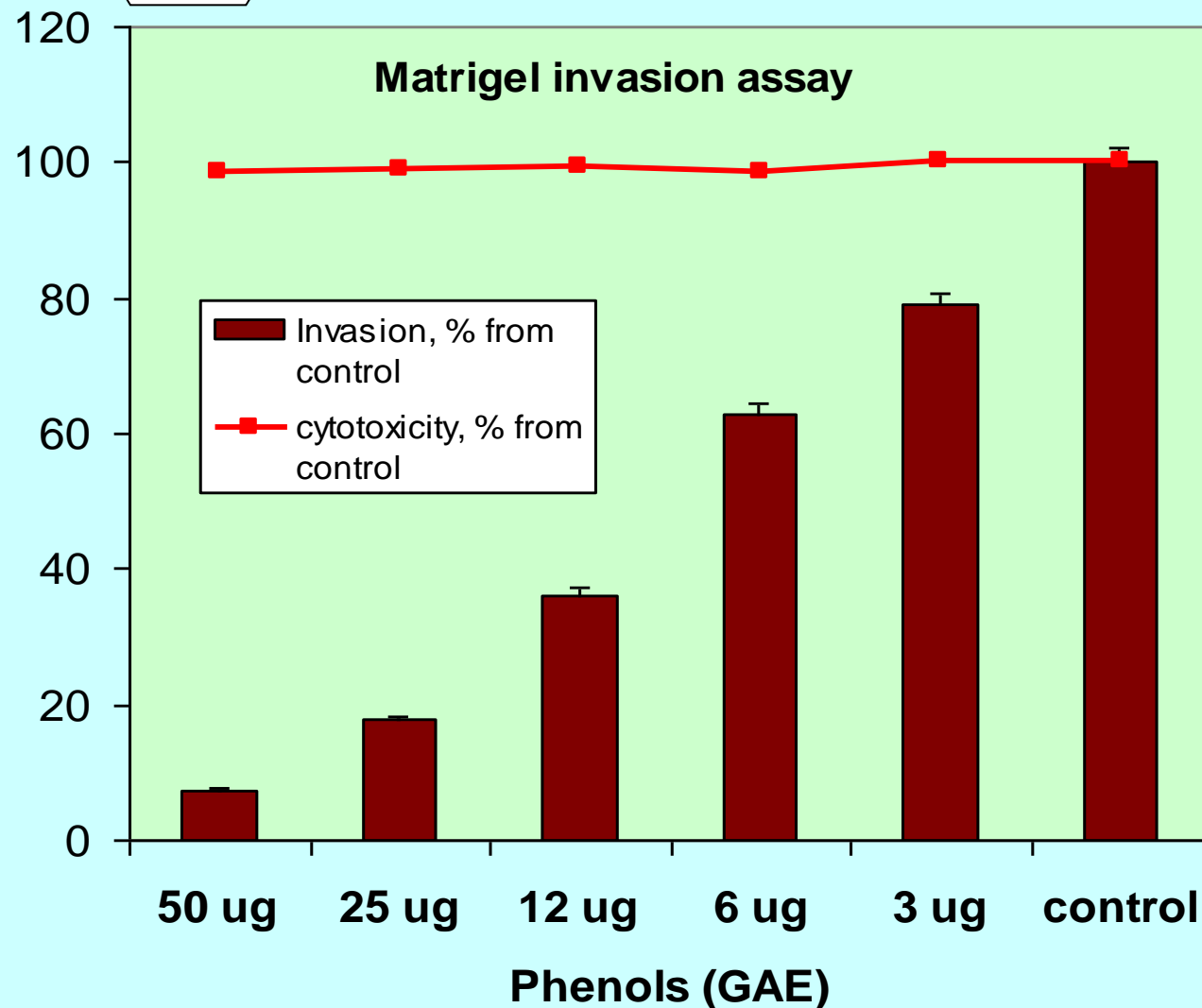
Joint projects on berry polyphenols & colon cancer



Emma Brown and Dr Chris Gill, School of Biomedical Sciences, University of Ulster, Coleraine



Colon cancer and polyphenols



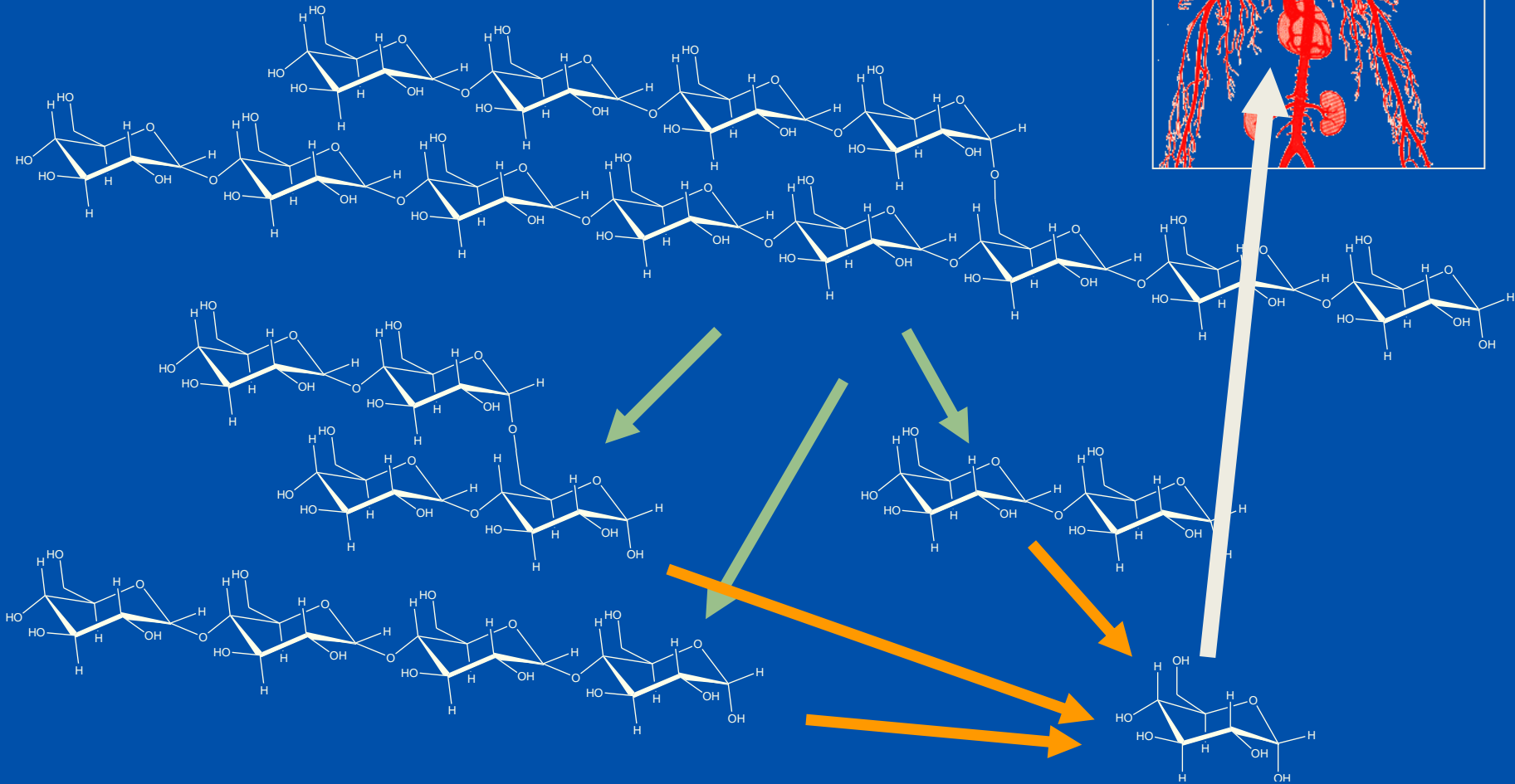
Invasion by HT115 colon cancer cells was inhibited by raspberry polyphenols in the μg range

Invasion related to ability to spread from initial site

Control of nutrient availability

- Polyphenols can inhibit digestive processes and slow or modulate nutrient release from food
- Inhibition of starch digestion – blood glucose control and type 2 diabetes
- Inhibition of lipid digestion – control of hyperlipidemia, CVD and obesity

Inhibition of starch digestion



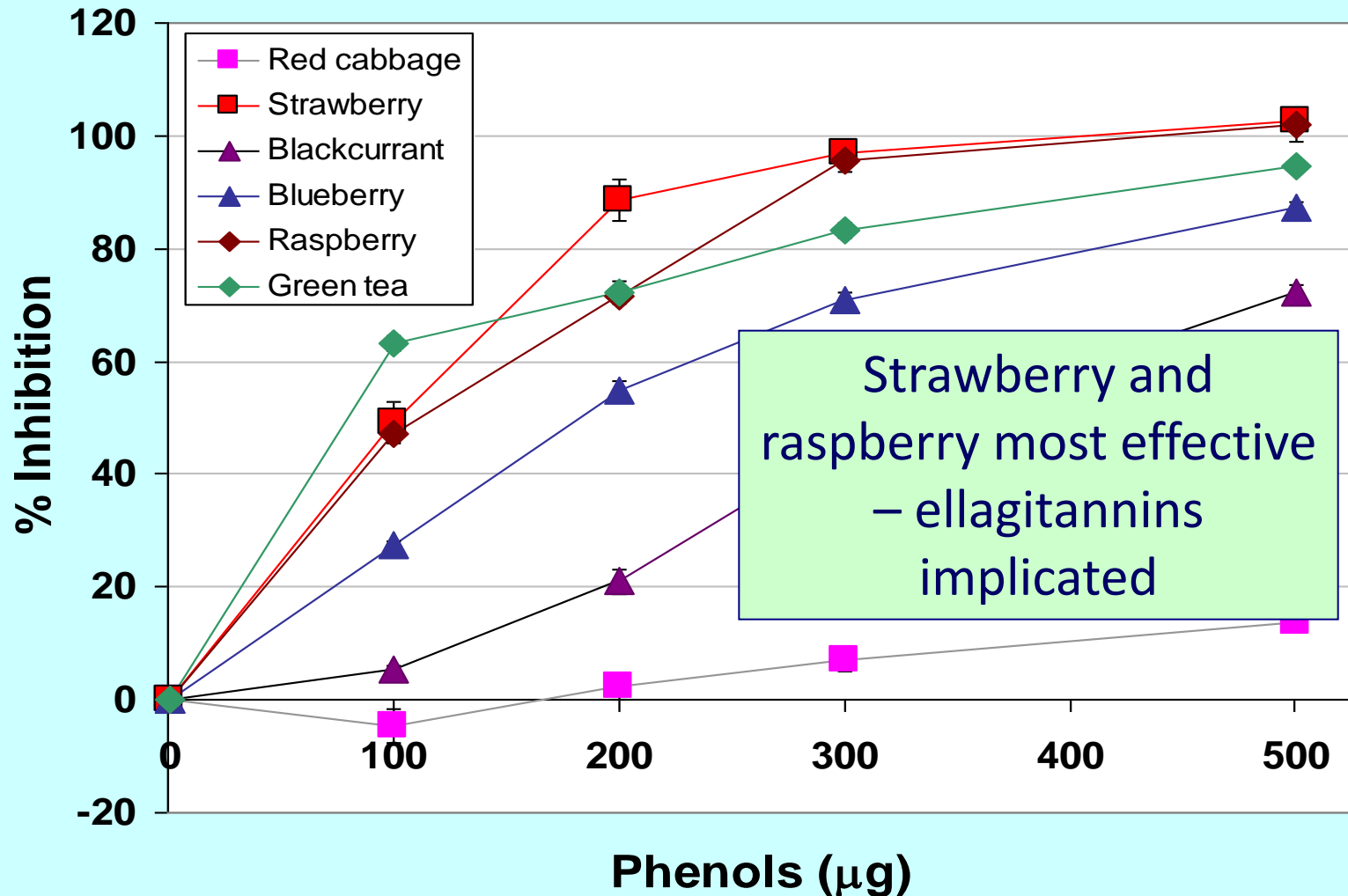
Amylase chops into fragments

Glucosidase nibbles off glucose

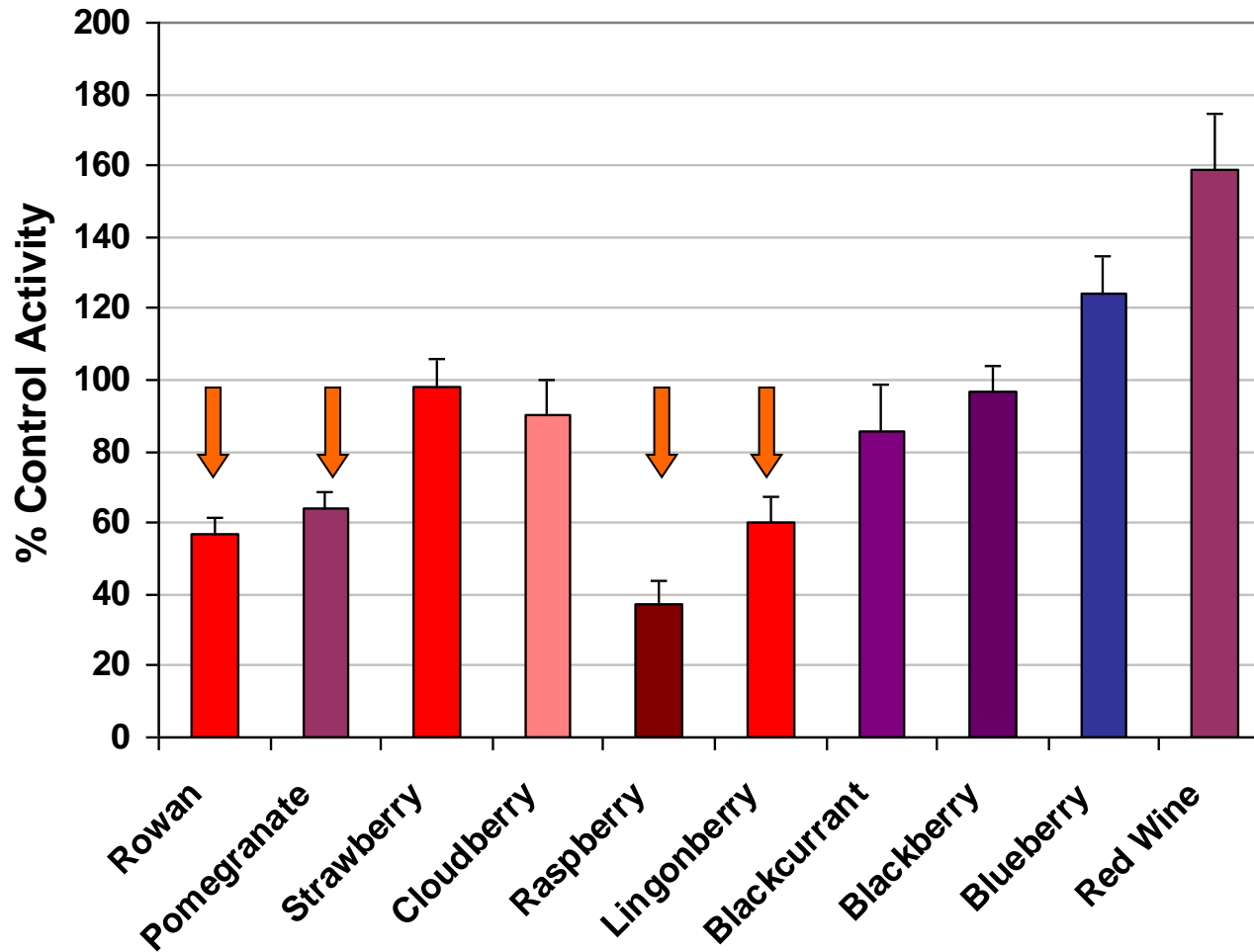
α -amylase inhibition



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α -glucosidase inhibition by berries

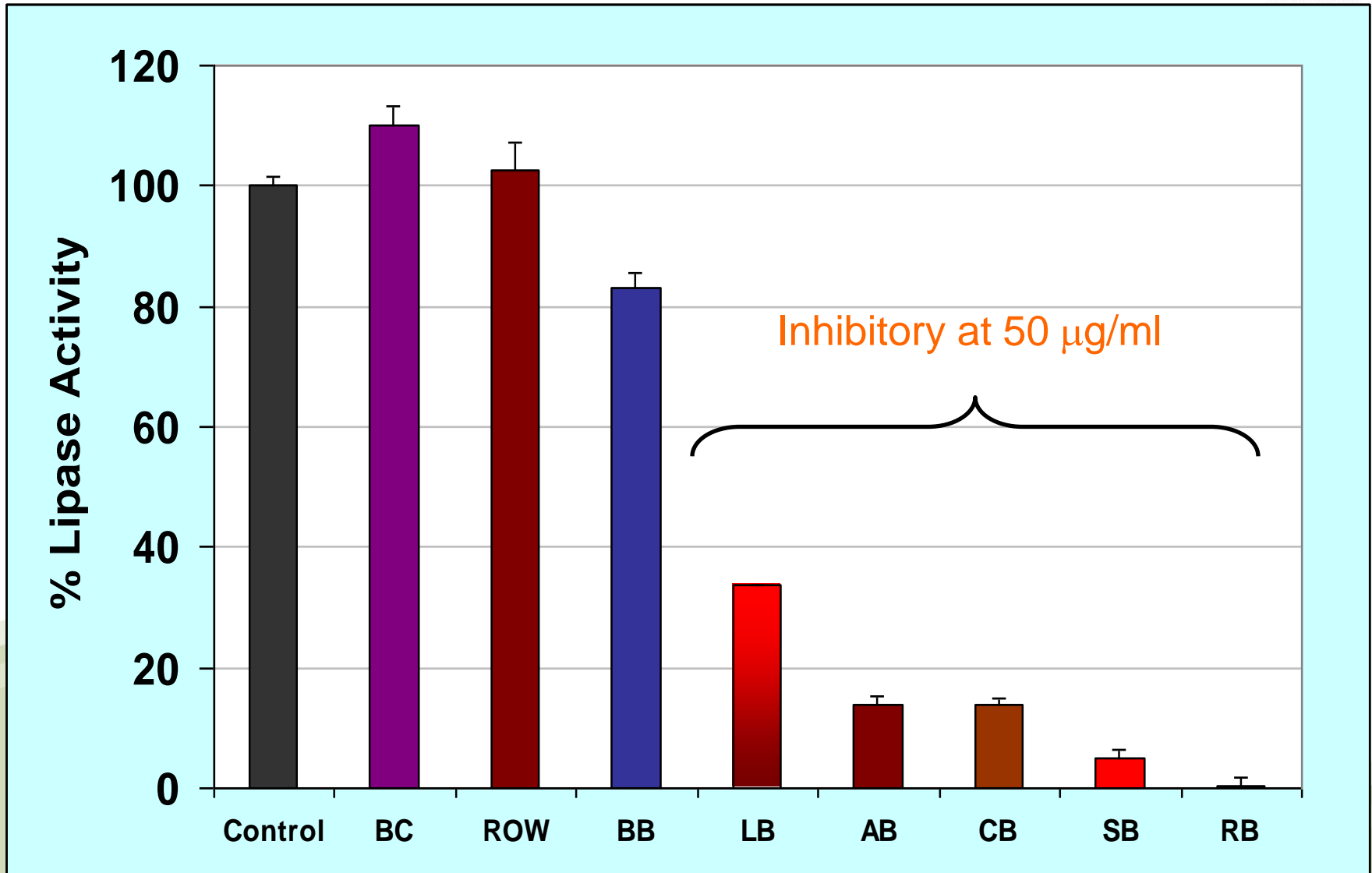


Pharmaceutical
inhibition with
acarbose ?

Not obvious which
polyphenols
involved?

Human studies
show promise

Lipid digestion and lipase



Summary

- Berry polyphenols have bioactivities that may influence human health
- Their mechanisms of action are not well defined
- Efficacy not always related to antioxidant capacity
- Their stability and bioavailability *in vivo* is not fully understood

Acknowledgements



All staff in CPU, JHI

Universities of Dundee, St Andrews and Abertay

Dundee for B.Sc and M.Sc students

Questions?



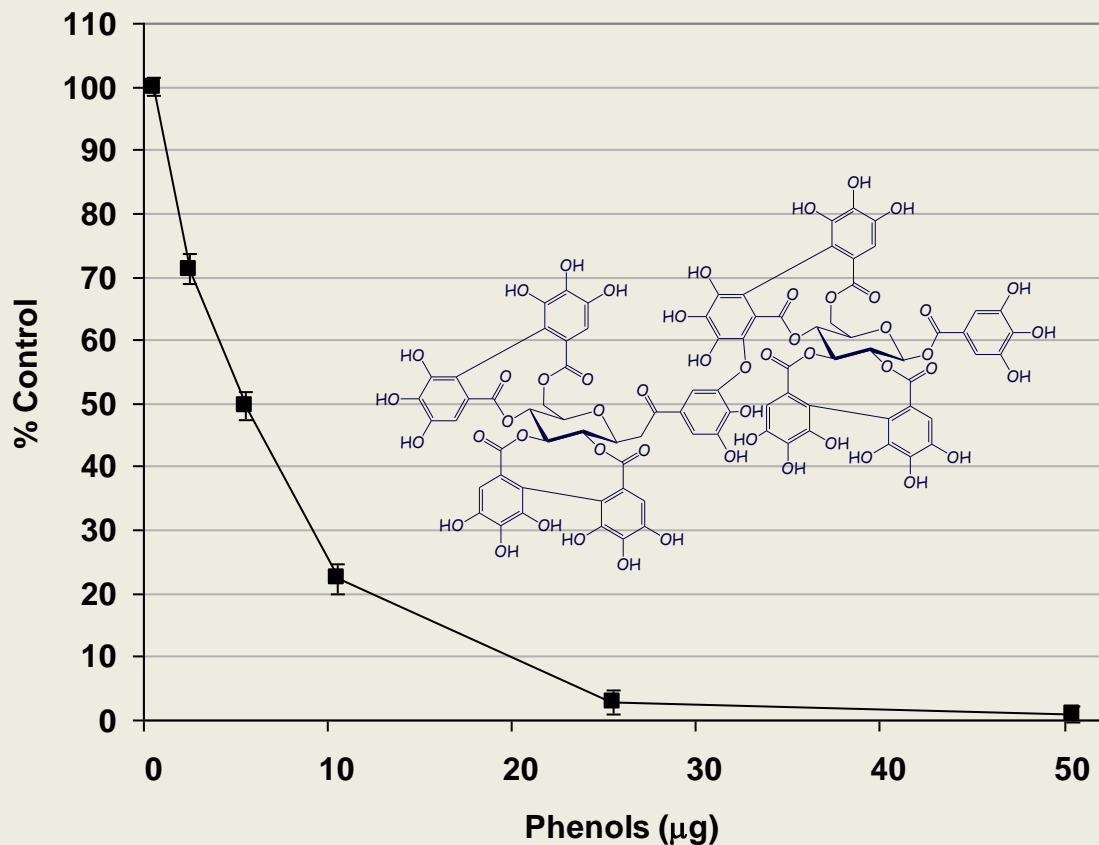
Visit <http://www.hutton.ac.uk>



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Lipase inhibition



Inhibition by cloudberry extracts is saturable

Due to ellagitannins (ETs) in cloudberry, arctic bramble and raspberry and

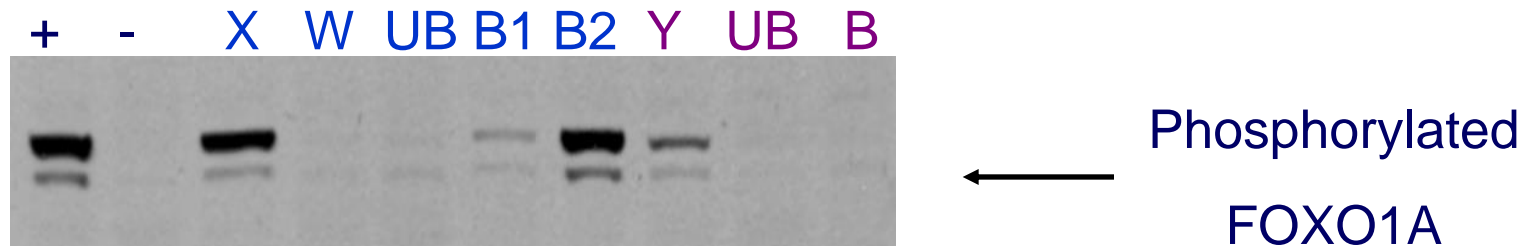
procyanidins and ETs in strawberry

Mainly procyanidins in lingonberry

Ties in with animal studies on obesity

Insulin mimicking

Various polyphenols stimulate the phosphorylation and activation of FOXO1A, a transcription factor involved in regulating insulin responses and controlling glucose mobilization.



Two different berry extracts stimulate phosphorylation of FOXO1A but the active ingredients fractionate differently on SPE.

About JHI



Dundee

**Long-established
breeding program for
berries**

JHI

Developing high-through-put methods for assessing inheritance of polyphenols

- Link to genetic maps and markers to speed up selection
- Improve on traditional means of assessing polyphenol levels slow
- Develop and validate new methods
- Use power of mass spectroscopic and metabolic profiling methods

Stewart et al (2007) Mol.Nutr.Food Res. 51, 645–651

McDougall et al (2008) J. Chromatog. B 871, 362–369



X

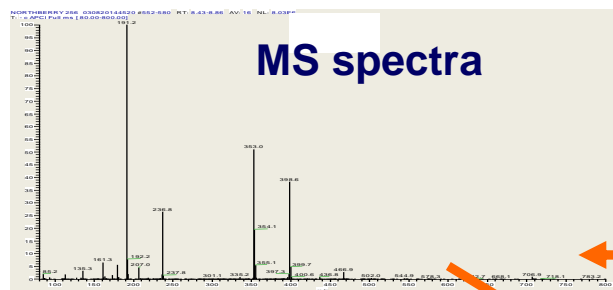
Targeted analysis

Yield, flavour, aroma taste, texture, disease resistance, bioactivities, antioxidant capacity, polyphenol content, ascorbate, anthocyanins



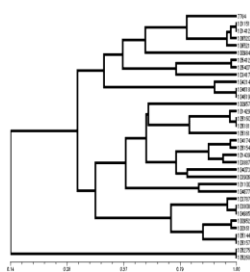
Untargeted analysis Hi-throughput metabolic profiling

Two environments, 5 seasons

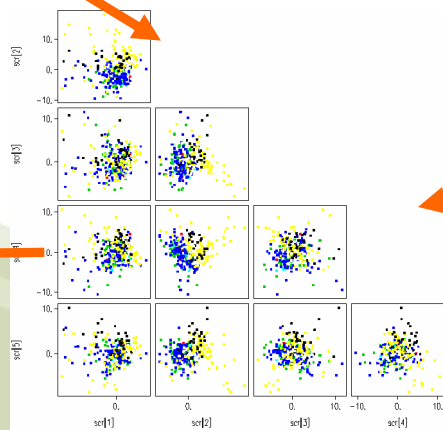


MS spectra

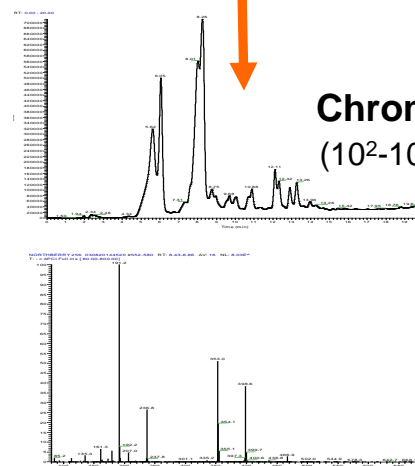
Direct Infusion MS No chromatography



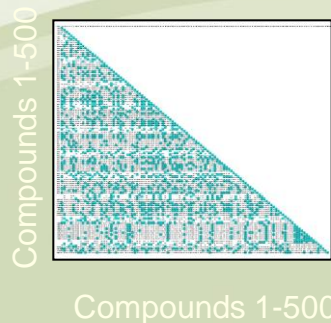
Hierarchical cluster analysis: Measure of (phytochemical) biodiversity - link to genetic map



Principal component analysis of MS data



Chromatogram (10²-10³ compounds)



Correlation Network: Interrelate metabolite changes.

The Rhubarb story

Food Chemistry 119 (2010) 758–764



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Food Chemistry

journal homepage: www.elsevier.com/locate/foodchem



Effect of different cooking regimes on rhubarb polyphenols

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ABSTRACT

Polyphenolic components, such as anthraquinones and stilbenes, from species of the genus *Rheum* have been shown to have a range of bioactivities relevant to human health. This paper outlines the polyphenolic composition of edible petioles of garden rhubarb (*Rheum rhabarbarum*) and describes the effects of common cooking methods on total polyphenolic content, anthocyanin content and total antioxidant capacity.

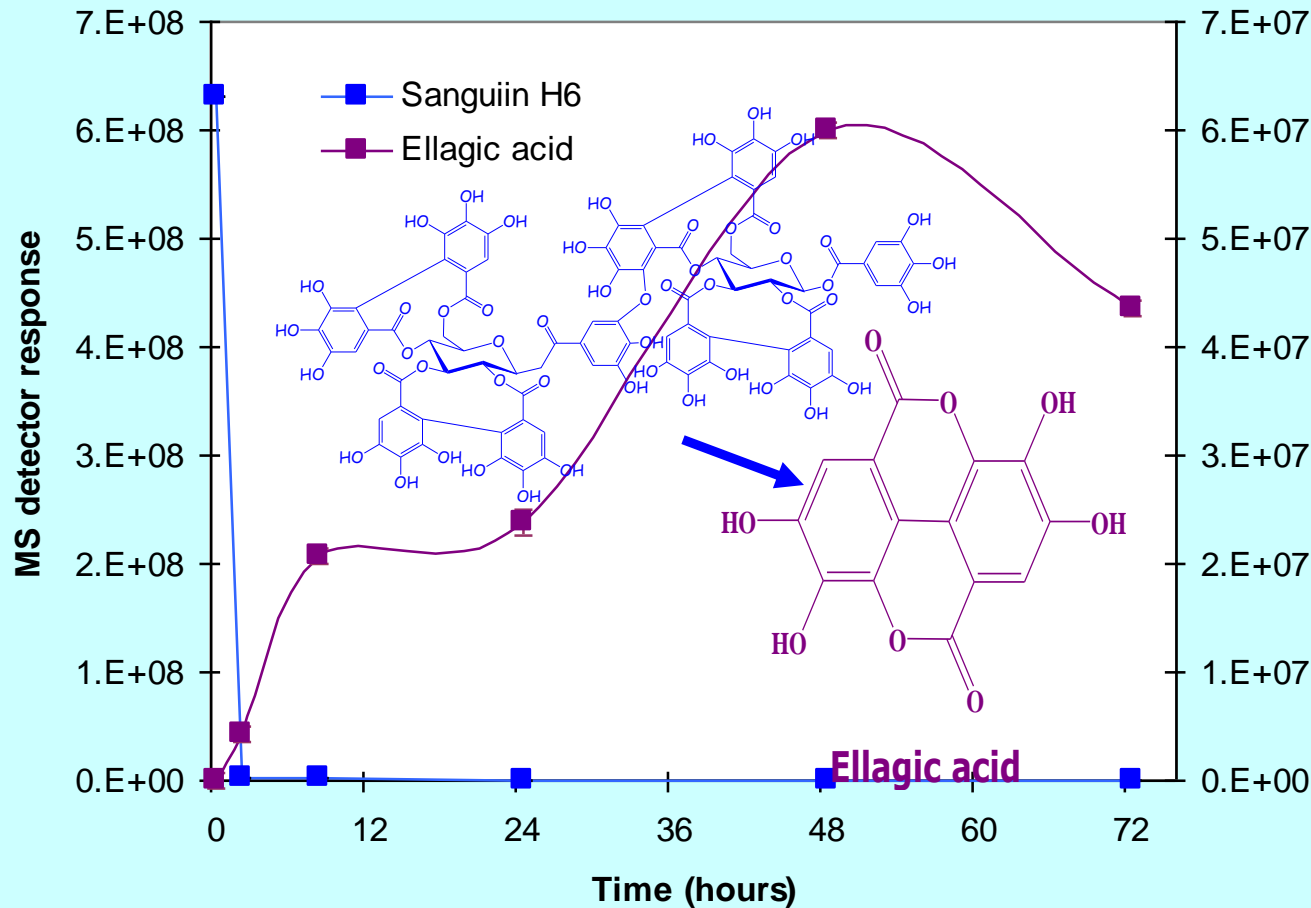
Most cooking regimes (fast stewing, slow stewing and baking) except blanching increased total polyphenol content and overall antioxidant capacity, compared to the raw material. The patterns of anthocyanin content and total polyphenol content between the different cooking regimes suggested a balance between two processes; cooking facilitated the release of polyphenol compounds from the rhubarb but also caused breakdown of the released compounds.

Baking and slow stewing offered the best maintenance of colour through preservation of anthocyanin and the highest antioxidant capacity. Baking for 20 min provided well-cooked rhubarb with the highest antioxidant capacity and the highest anthocyanin content, which is important for the aesthetic quality of the dish.

Liquid chromatography–mass spectrometric (LC–MS) analysis putatively identified over 40 polyphenol components in raw rhubarb, including anthraquinone, stilbene, anthocyanin and flavonol derivatives. Baking caused selective effects on the stability of the different polyphenol components. Initially, the yield of all components increased but there was a drastic decline in the relative stability of anthraquinone aglycones with increasing cooking time and initial evidence for the turnover of other anthraquinone derivatives was obtained.



Stability and Bioavailability



Raspberry
ellagitannins inhibit
cancer cell growth

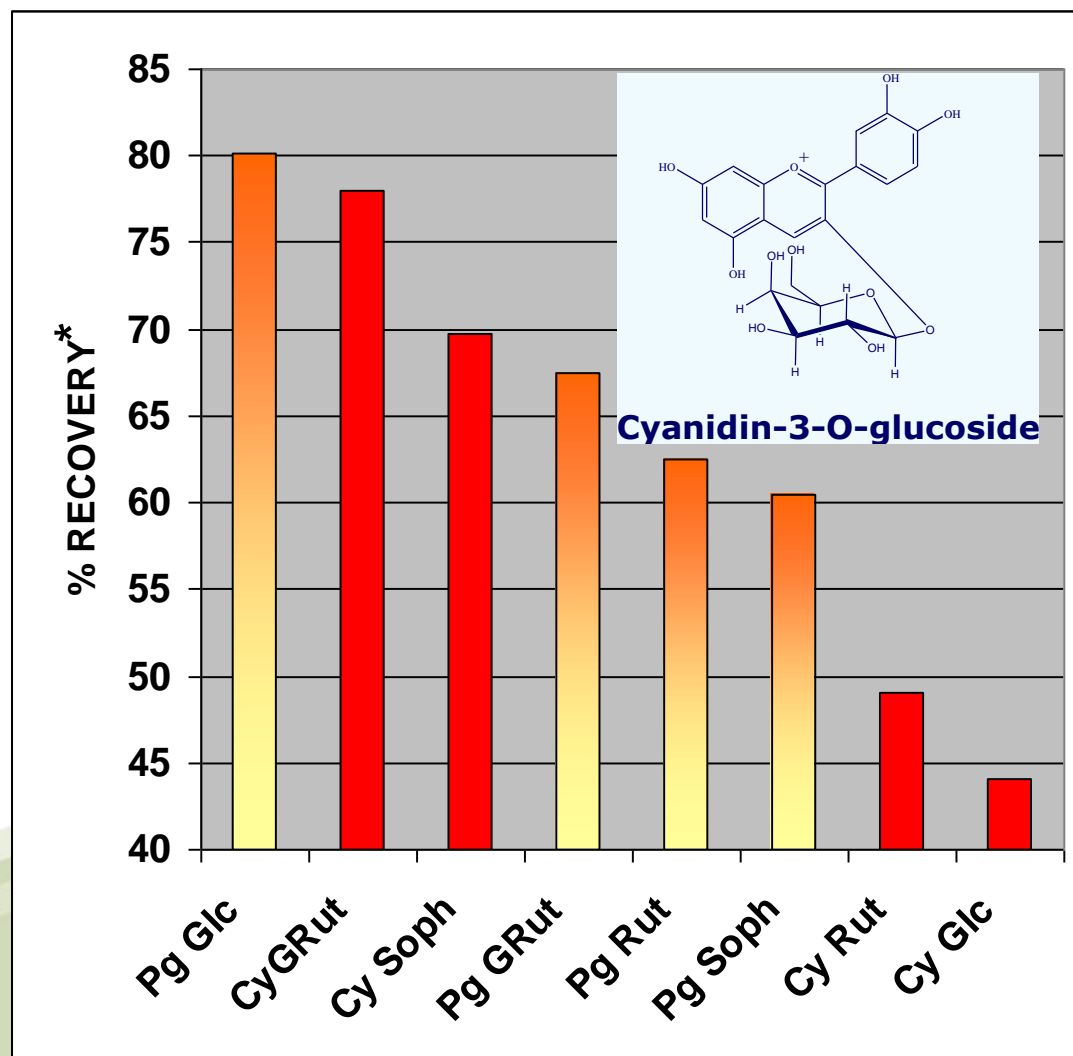
Ellagitannins bind to
proteins in media

Not taken up by cells!

Breakdown to release
ellagic acid

What is the active
anti-cancer
component?

In vitro digestion



Stability not related to aglycone or sugar moiety

For Pelargonidin

Glc > GRut > Rut > Soph

For Cyanidin

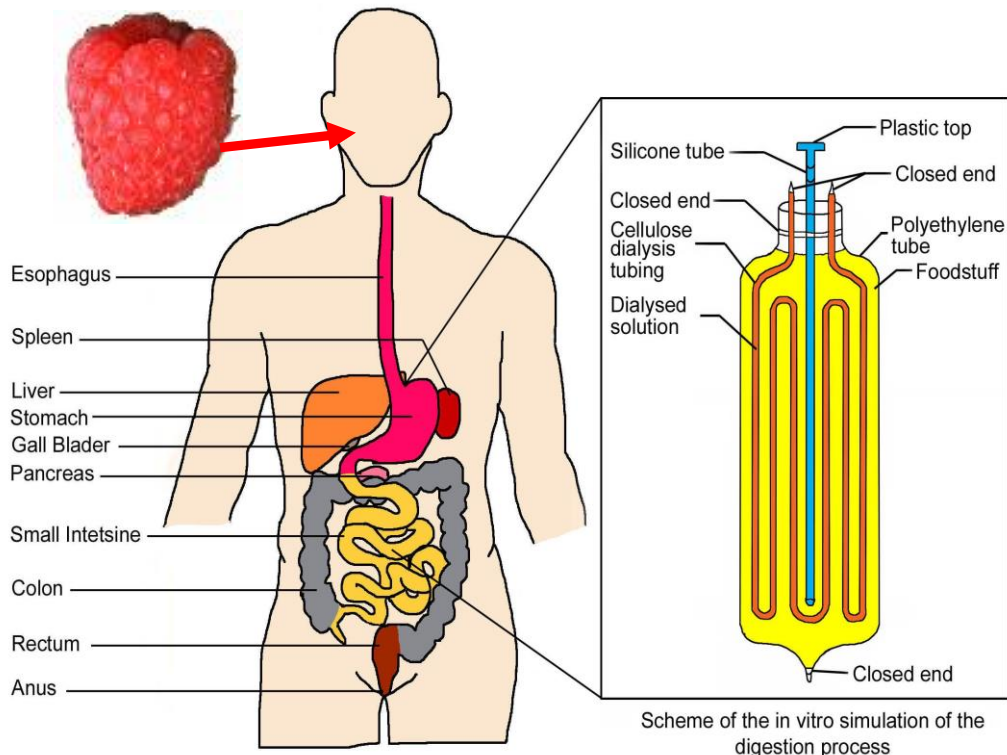
GRut > Soph > Rut > Glc

Stability dependent on components in mixture

*Total Recovery wrt gastric figures - McDougall et al. (2005) JAFC 53 5896-5904

In vitro digestion

Which components stable and bioavailable?

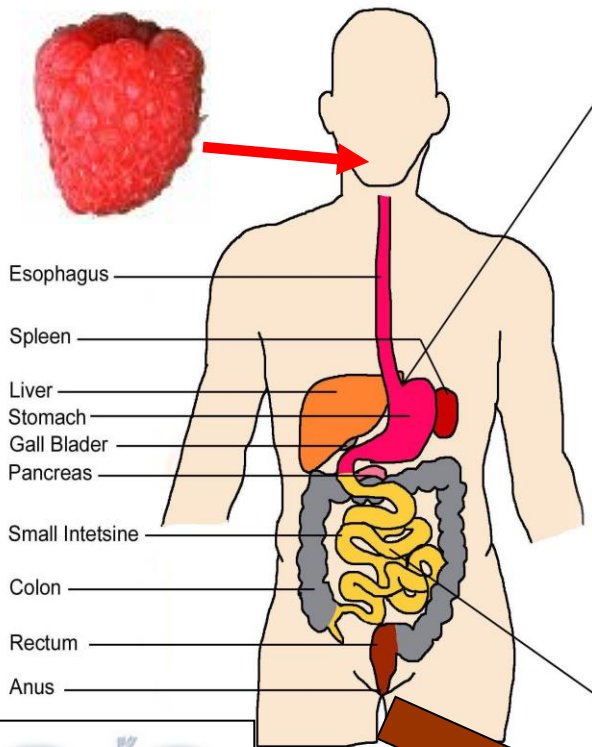


Simulation of human digestive system

1. Gastric digestion – 2 hrs at 37° C at pH 1.7 with pepsin
2. Pancreatic digestion – 2 hrs at 37° C with digestive enzymes and bile salts

Analyse recovery of components

Faecal metabolism of berry polyphenols



- Profiling of faecal water metabolites in 10 free-living students after intake of raspberry puree (200 g/d for 14 d) by gas-chromatography mass spectrometry (GC-MS)
- Substantial ingestion of anthocyanins, ellagitannins etc
- Focus on major phenolic metabolites



oted

Faecal metabolism of berry polyphenols

But not the same subjects

■ Phenylacetic acid increased in 7/10 subjects

4-hydroxy phenylacetic acid increased in 6/10 subjects

3-hydroxy phenylacetic acid increased in 5/10 subjects

3-Phenylpropionic acid increased in 6/10 subjects

3(4-hydroxy) phenylpropionic acid increased in 5/10 subjects

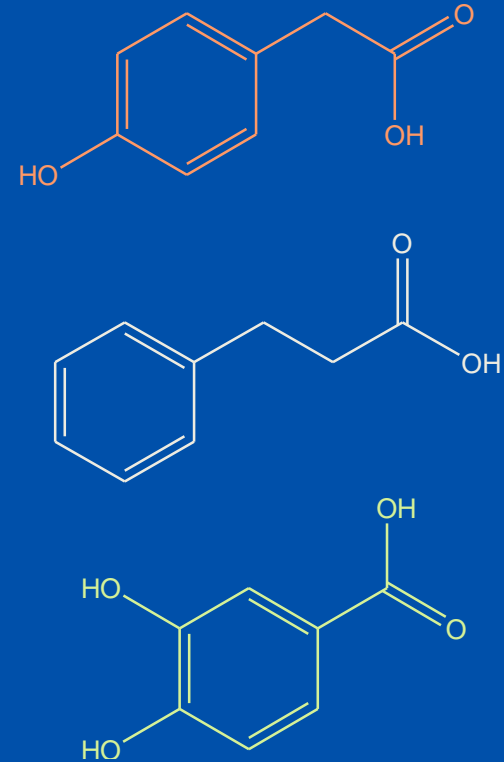
3, 4-dihydroxy benzoic acid increased in 7/10 subjects

■ 4-hydroxy benzoic acid increased in 2/10 subjects

- Fits evidence from model studies with faecal inocula but shows large inter-individual variation

- Due to differences in diet or microflora?

Gill et al, in press



Other areas

Effect of tea and coffee polyphenols on neurodegeneration and obesity models resp.

Analysis of carotenoids in sea buckthorn & carrot

Anti-parasitic effects of berry and vegetable extracts

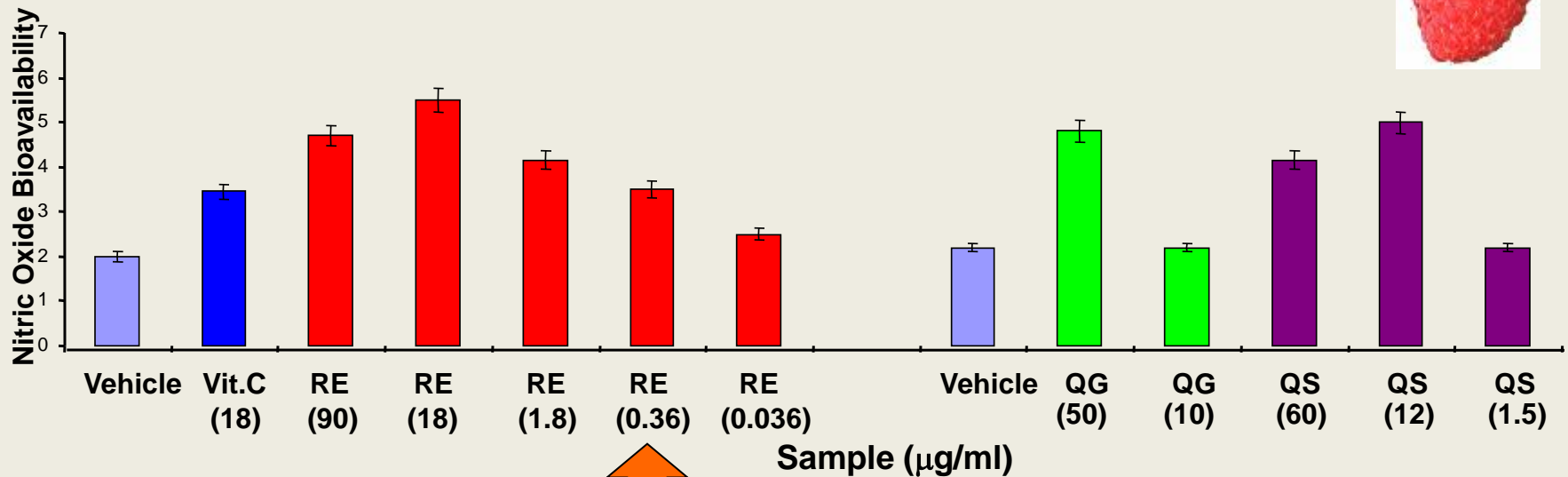
Natural products as anti-inflammatory agents





Availability of nitric oxide (NO) in *ex vitro* rat carotid arteries

Nitric oxide protection by Raspberry extracts



Raspberry extract effective at 50-fold less than Vitamin C or Quercetin derivatives – known effectors of CV performance

Protection of NO bio-availability maintains blood vessel flexibility

