Beneficial effects of berry polyphenols in the gut: Food digestion and colon cancer

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MLURI and SCRI join forces to become The James Hutton Institute
The James Hutton Institute, Dundee

Dundee

Long-established breeding program for berries
Berry research at JHI

- Blackcurrants – the “Ben” series
- Raspberries – the “Glen” series
- Blackberries – the “Loch” series

- Strawberries – “Symphony, Rhapsody....”
- Research into Health Benefits of Berries
- Feedback to direct breeding of new varieties
Outline of talk

Berry polyphenols and the gut

- MODEL IN VITRO SYSTEMS
- Polyphenol-enriched extracts
- Effects relevant to
  - Diabetes & Obesity
  - Colon cancer

Underlying thread of understanding bioavailability
Correlate bioactivities with polyphenol composition using LC-MS techniques
How can polyphenols affect human health?

Antioxidant theory? Low serum bioavailability!

Majority of polyphenols remain in gut
Are these components inactive?

Possible roles
Modulating colonic microbiota?
In-gut antioxidants?
Benefit gut epithelia function / colon cancer
Modulate digestive processes
Control of nutrient availability

- Polyphenols can inhibit digestive processes and slow or modulate nutrient release from food

  Inhibition of lipid digestion – control of hyperlipidemia, CVD, diabetes and obesity (McDougall et al. (2009) Food Chemistry 115, 93–9)

- Inhibition of starch digestion – blood glucose control and type 2 diabetes
Inhibition of starch digestion

Amylase chops into fragments
Glucosidase nibbles off glucose

Acarbose
α-amylase inhibition

Strawberry and raspberry most effective – Ellagitannins implicated
Bind to amylase and prevent starch digestion

α-amylase inhibition

Assays at 100 µg GAE/mL
Berry extracts inhibit to different extents
Active components?

Yellow vs Red Raspberries

Re-examine inhibition by raspberry by comparing extracts of red raspberry (*Glen Ample*) with yellow raspberry (*selection 97134B1*).

These have similar polyphenol profiles but yellow raspberries effectively lack anthocyanins.
α-amylase inhibition

Yellow and red raspberry extracts are equally effective. This supports ellagitannins as active ingredients and suggests that anthocyanins are less important. However, ellagitannins are proportionally increased in yellow raspberry extracts. Possible interplay/protection from other polyphenols.
Seaweed polyphenols also effective amylase inhibitors

Phlorotannin-rich fractions from Ascophyllum nodosum are very effective amylase inhibitors (IC$_{50} \sim 0.1 \, \mu$g/mL)

Nwosu et al. (2011) Food Chem. 126, 1006–12
$\alpha$-glucosidase inhibition

Increased effectiveness with increasing anthocyanin content

Different berries inhibit to different extents

Anthocyanins implicated?


Inhibition by black currant

IC$_{50}$ = 20 µg/ml

Inhibition by rowanberry

IC$_{50}$ = 30 µg/ml
Active Polyphenol Components?

Black currant and rowanberry extracts differ greatly in their composition but both are effective inhibitors.

Black currant is rich in anthocyanins.
Rowan is rich in chlorogenic acids.
Co-incubation with acarbose

% Activity

Black currant/acarbose (µg/ml)
Co-incubation with acarbose

Berry polyphenols can potentiate, and substitute for, inhibition by acarbose

Rowanberry/Acarbose (µg/ml)
Mixing of berry extracts?

Lack of additive effect suggests that components act at same site on glucosidase?
Human trial – modified glycemic response

Patients given sucrose-loaded black currant (BC) juice and BC juice supplemented with crowberry juice. The BC + juice (*) caused a reduction in peak height of plasma glucose and extended the area under the curve

Summary

- Berry polyphenols can inhibit the main enzymes involved in starch digestion
- The inhibition occurs at concentrations easily reached in the gut
- The active polyphenols are not fully defined but different components in the same berry can inhibit different enzymes = potential synergistic effects on digestion
- Berry polyphenols can potentiate inhibition by acarbose
- Initial human studies show promise
Berry polyphenols & colon cancer

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

Professor Ian Rowland, University of Reading
Professor Alan Crozier, University of Glasgow
Effects on colon cancer cells *in vitro*

All berry extracts tested at 50 μg/ml
Inhibition not related to *in vitro* antioxidant capacity
Physiologically relevant?

In vitro digestion

Model which polyphenols survive in gut?

Simulation of human digestive system

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

Analyze recovery of polyphenol components
General effects of IVD

- Anthocyanins less stable
- Ellagitannins/PACs break down to smaller components
- Flavonols more stable
- Hydroxycinnamates stability dependent on linkages

Stability not absolute but influenced by other components

![Graph showing % recovery of different compounds](image)
IVD berry extracts and colon cancer

IVD berry extracts protect against DNA damage in colon cancer cells; $SB = BC > RB$
Colonic metabolism of berry polyphenols

Colonic bacteria degrade polyphenols

- Phenylacetic acid derivatives
- Phenylpropionic acid derivatives
- Hydroxybenzoic acid derivatives

Studies with humans fed berries show increases in similar products formed in laboratory fermentations but large inter-person variability in amounts

Use berry IVD digests as substrates for lab fermentation studies

Gill et al. (2010) J. Agric. Food Chem. 58, 10389–95
Fermentation products as effective as IVD extracts

Berry polyphenols retain effectiveness as they undergo metabolism in the colon

Berry polyphenols contribute anti-cancer activity as they pass through the colon

Equally effective but compositionally different

Colonic fermentates
Summary/Future work

- Berry polyphenols characteristic of intestinal digestion and colonic fermentation have beneficial effects on models of colon cancer.
- The differences in effectiveness between different berry samples are less apparent after fermentation to simpler components in the colon?
- Extend work on phenolic degradation products using human ileostomy studies.
- Examine effect of berry polyphenols on functional response of microbiota.
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Questions?

JHI Dundee is located in Invergowrie on the north bank of the River Tay

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Berries and Health: A review of the evidence. McDougall and Stewart