

Soft fruit Health Benefits; Hype or Hope?

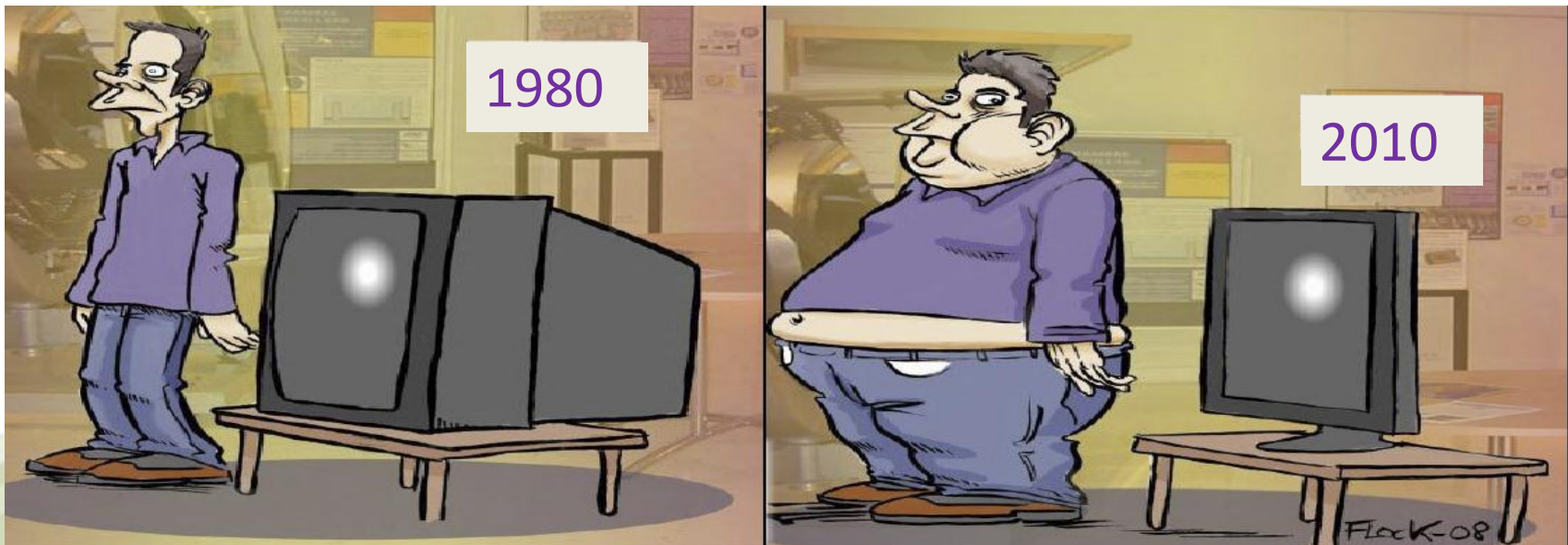
Derek Stewart

Enhancing Crop Productivity and Utilisation



The problem is not abating

- Mortality ↓ : Morbidity ↑
- Western population is living longer but is sicker.
- CVD, Diabetes, (some) cancers, neuro-degeneration and inflammation associated disorders



Berries...

- Good nutritional value
- Excellent source of bioactive compounds called polyphenols; Health beneficial effects
- Good source of antioxidants, compounds that *in vitro* are able to scavenge free radicals cause of cell aging and death... However....!!
- Is this what happens in vivo??



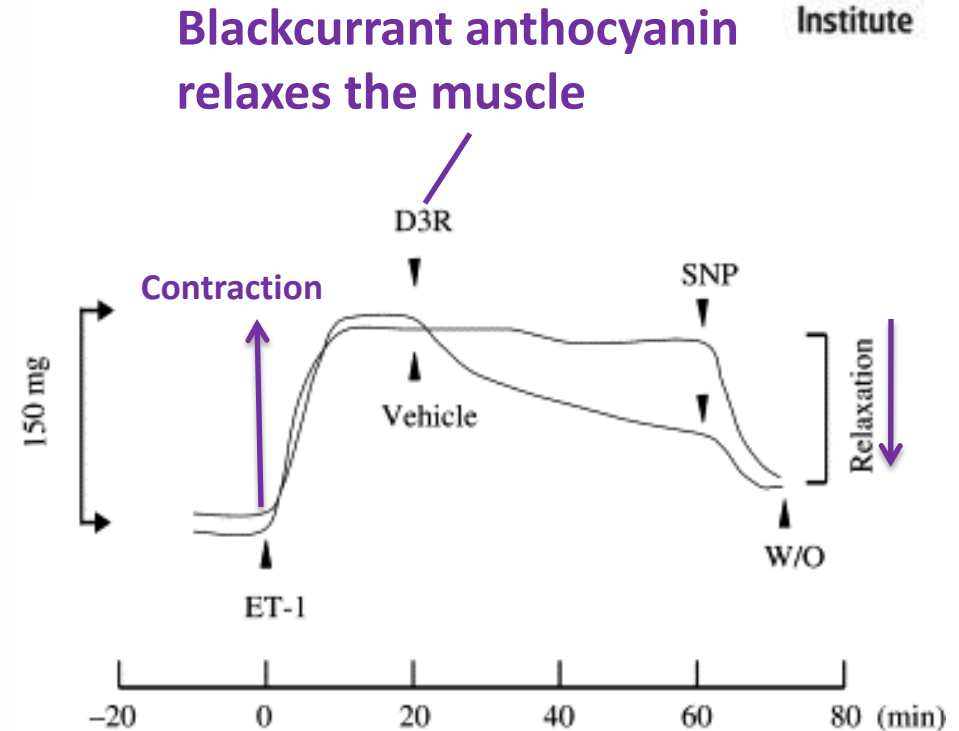
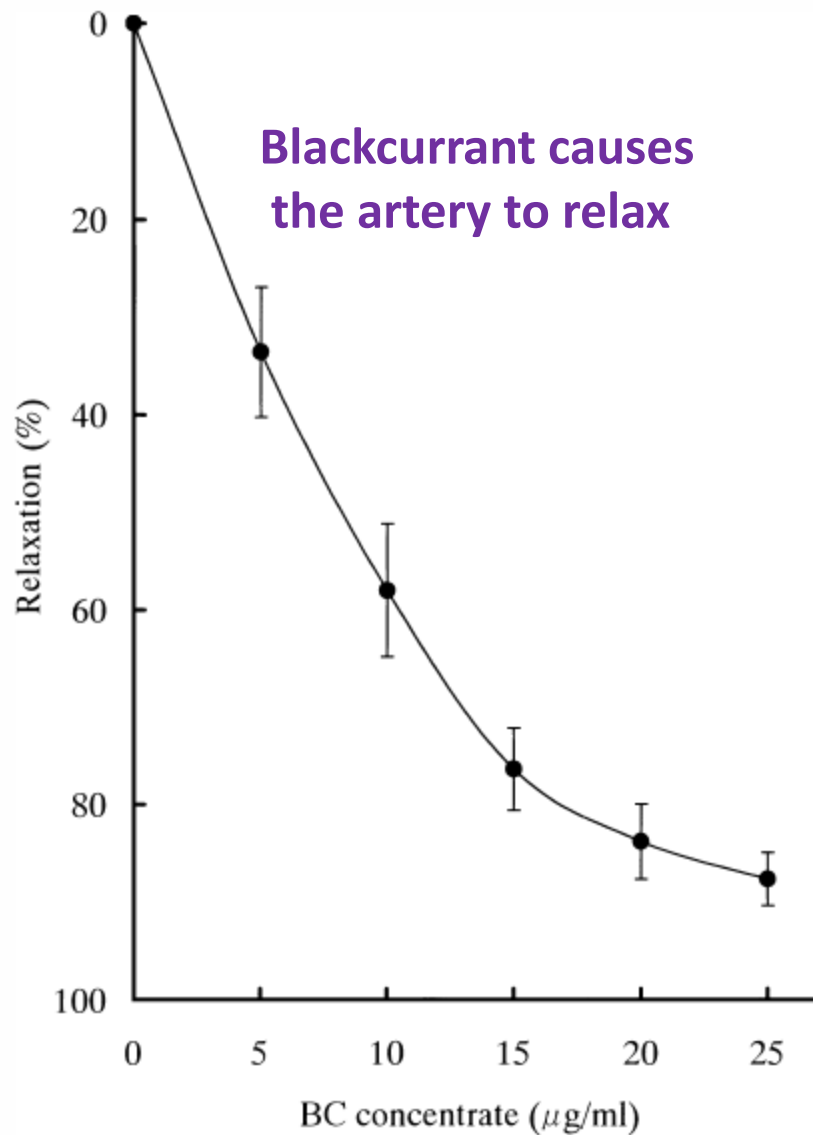
In Vitro (Cell) Systems

No
account of
digestion!

Black currant fraction	Cell line	Pharmacological effect	Reference
CARDIOVASCULAR SYSTEM			
Juice	J774A.1 macrophage cell line	Increased paraoxanase 1 expression, improving macrophage cholesterol attenuation	Rosenblat <i>et al.</i> , 2010 ⁶²
Extract	Human umbilical vein endothelial cells	Increased activation of endothelial NO synthase and dilation of blood vessels	Edirisinghe <i>et al.</i> , 2011 ⁶³
NERVOUS SYSTEM			
Extract	M1 transfected COS-7 cells	Increased recovery of calcium flux in type-1 muscarinic R's	Joseph <i>et al.</i> , 2004 ⁷⁰
PULMONARY SYSTEM			
Extract (proanthocyanidin)	A549 alveolar epithelial cell line	Induced CCL26 secretion and amplified interferon-gamma	Hurst <i>et al.</i> , 2010 ⁷¹
TUMORS			
Whole fruit extract	HT29 colon cancer; MCF-7 breast cancer	Decreased the proliferation of cancer cells	Olsson <i>et al.</i> , 2004 ⁷²
Whole fruit extract	HT29 colon cancer	Inhibited cancer cell growth	Wu <i>et al.</i> , 2007 ⁷³
Whole fruit extract	HeLa cervical cancer	Reduced cell viability	McDougall <i>et al.</i> , 2008 ⁷⁴
Juice	Caco-2 colorectal adenocarcinoma; MCF-7 and MDA-MB-231 breast cancer; AGS stomach adenocarcinoma; PC-3 prostate cancer	Suppressed cancer cell proliferation	Boivin <i>et al.</i> , 2007 ⁷⁵
CAPS	Ehrlich ascites tumor	Exhibited cytotoxicity	Takata <i>et al.</i> , 2005 ⁷⁶
Press residue extracts	Caco-2, HCT 116 and HT-29 colon cancer	Inhibited cell proliferation	Holtung <i>et al.</i> , 2011 ⁷⁷
Skin extract	HepG2 liver cancer	Displayed antiproliferative effect	Bishayee <i>et al.</i> , 2010 ⁷⁸

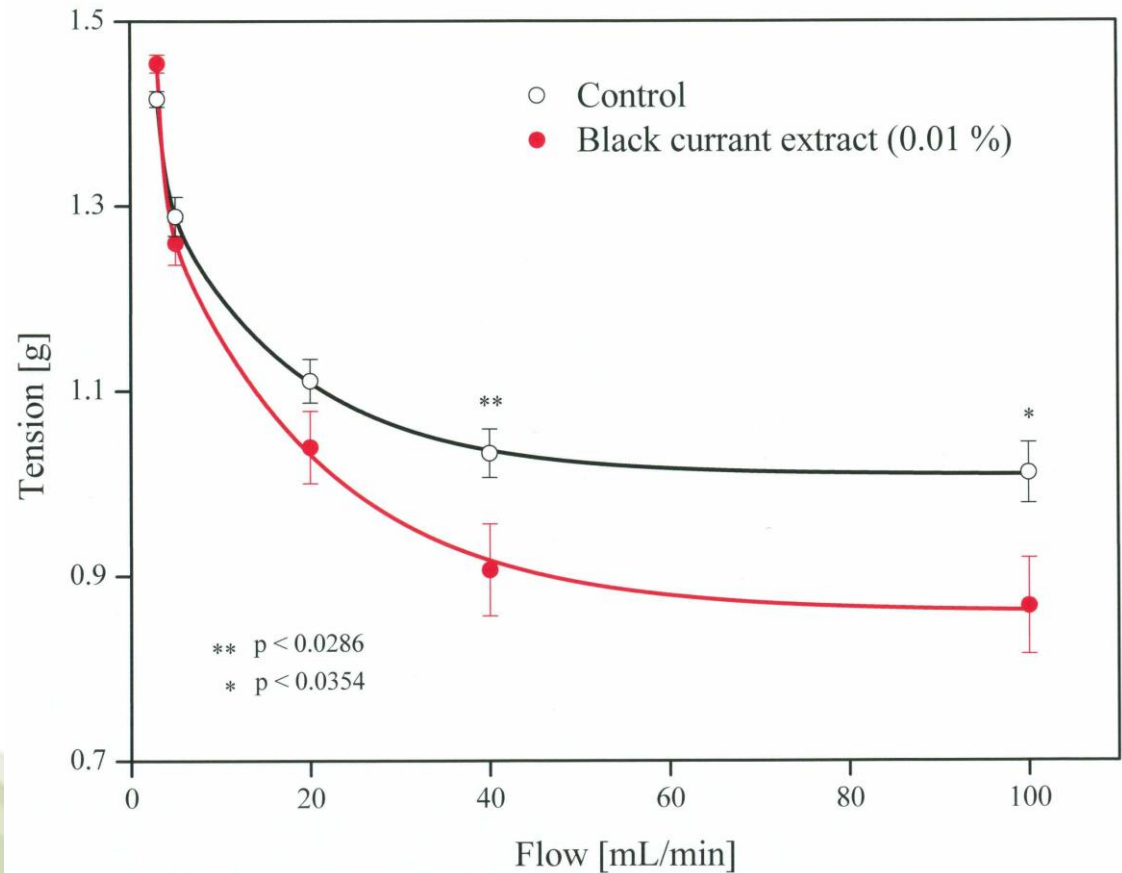
Black currant fraction	Animal model In Vivo: Model	Pharmacological effect	Reference
CARDIOVASCULAR SYSTEM			
Oil (GLA)	Spontaneously hypertensive rats	Decreased blood pressure values	Engler, 1993 ⁷⁹
Olive-blackcurrant-fish oil mixture	Wistar rats	Decreased serum TXA-B2 prothrombotic factor	Pregnotato, 1996 ⁸⁰
Anthocyanin fraction	Sprague-Dawley rats	Decreased relative amount of hepatic saturated fatty acids and increased plasma tocopherol levels	Frank <i>et al.</i> , 2002 ⁸¹
Black currant concentrate	Norepinephrine-precontracted thoracic aortas of rats	Induced vasodilation via H1 receptors to increase NO levels	Nakamura <i>et al.</i> , 2002 ⁸²
Oil	Wistar rats	Inhibited accumulation of n-3 PUFA in liver and significantly decreased plasma GSH	Vecera <i>et al.</i> , 2003 ⁸³
Seed oil	Wistar female rat blood samples	Decreased plasma GSH and <i>t</i> -butyl hydroperoxide-induced lipoperoxidation; did not effect hepatic GSH levels	Breinholt <i>et al.</i> , 2003 ⁸⁴
Anthocyanin fraction	Watanabe heritable hyperlipidemic rabbits	Increased LDL and cholesterol and decreased VLDL content	Nielsen <i>et al.</i> , 2005 ⁵⁶
Anthocyanin component (delphinidin-3-O-rutinoside)	rod outer-segment membranes in frogs	Inhibited endogenous NO and cGMP release	Matsumoto <i>et al.</i> , 2005 ⁸⁵
Concentrate (delphinidin)	Sprague-Dawley rats	Decreased peripheral vascular resistance	Iwasaki-Kurashige <i>et al.</i> , 2006 ⁸⁶

Artery and muscle model systems



Blackcurrant anthocyanins cause a flow-dependent increase in blood perfusion in isolated human intracerebral arteries

- Flow-dependent isometric tension was measured in segments of isolated human intracerebral arteries from consciousness areas: derived from brain surgery.
- The anthocyanin driven vasodilatation may have a beneficial effect on the cognitive functions in dementia of the Alzheimer type, in the prevention of TIA and stroke
- Flow-dependent relaxation is almost identical to fluvistatin.



NERVOUS SYSTEM			
Oil (GLA)	Streptozotocin-induced diabetes in mature Sprague-Dawley rats	Modulated TXA2 and increased motor nerve conduction velocity	Dines <i>et al.</i> , 1996 ⁸⁷
OCULAR SYSTEM			
Juice extract (cyanidin)	Wistar rats and Japan White rabbits	Improved rhodopsin regeneration and dark adaptation by enhancing rhodopsin precursor formation	Matsumoto <i>et al.</i> , 2006 ⁸⁸
Extract	1 day old white Leghorn chicks	Inhibited enlargement of the globe component dimensions in artificially induced myopia	Iida <i>et al.</i> , 2010 ⁸⁹
PULMONARY SYSTEM			
Leaf extract (proanthocyanidin)	Saline-induced pleurisy and carrageenin-induced right hind limb edema in male Wistar rats	Decreased inflammation and inhibited neutrophilic cellular infiltration	Garbacki <i>et al.</i> , 2004 ⁴⁸
SKELETAL SYSTEM			
Seed oil	Monosodium urate crystal-induced inflammation in subcutaneous air pouches formed in Sprague-Dawley rats	Inhibited formation of monosodium urate crystal formation	Tate <i>et al.</i> , 1994 ⁹⁰
TUMORS			
Oil (GLA)	Metastatic 13762MAT:B breast tumor in the lungs of Fischer rats	Reduced the number of foci and tumor burden	Karmali <i>et al.</i> , 2004 ⁹¹
Juice	Xenografted Ehrlich ascites tumor in ICR mice	Inhibited tumor growth	Takata <i>et al.</i> , 2005 ⁷⁶
Modified CAPS	Xenografted Ehrlich ascities tumor in ICR Mice	Reduced tumor weight	Takata <i>et al.</i> , 2007 ⁹²
Skin extract	DENA-initiated and PB-promoted hepatocarcinogenesis in Sprague-Dawley rats	Suppressed the number, size, and volume of hepatocyte nodules	Bishayee <i>et al.</i> , 2011 ⁹³
		Lowered the number and area of GGT-positive foci; reduced the expression of HSP70, HSP90, COX-2 and NF-κB	Bishayee <i>et al.</i> , 2012 ⁹⁴
		Diminished lipid and protein oxidation; reduced the expression of iNOS, 3-NT, antioxidant enzymes and Nrf2	Thoppil <i>et al.</i> , 2012 ⁹⁵

Cancer

Reduced cancer levels in oxidant induced animal systems.

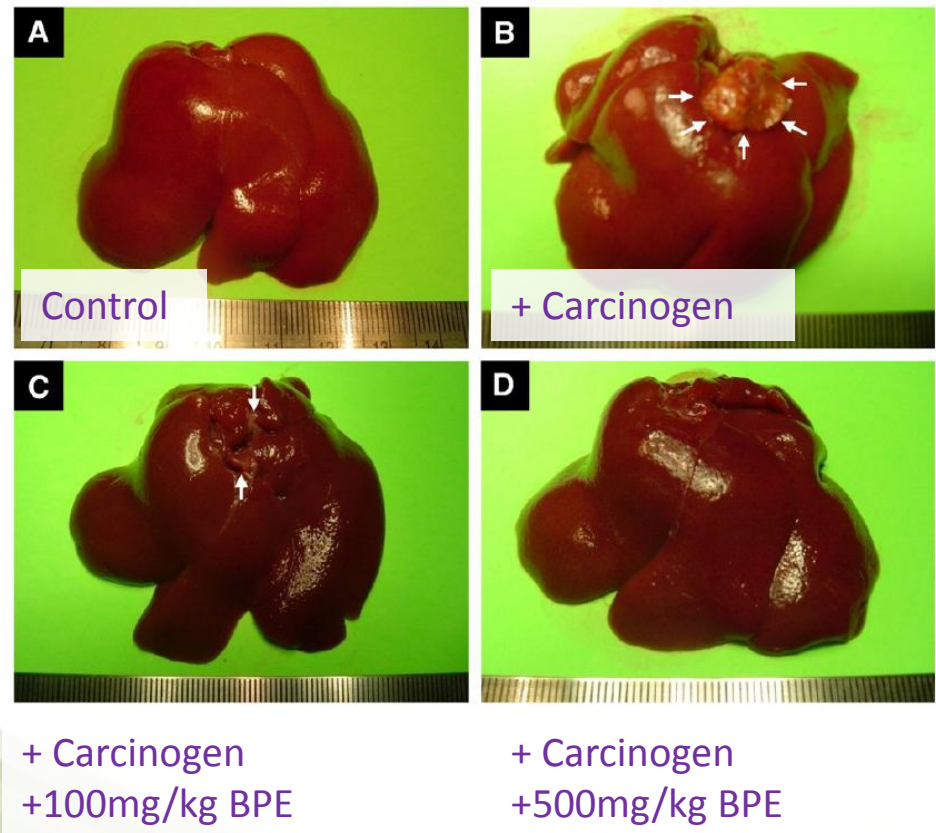


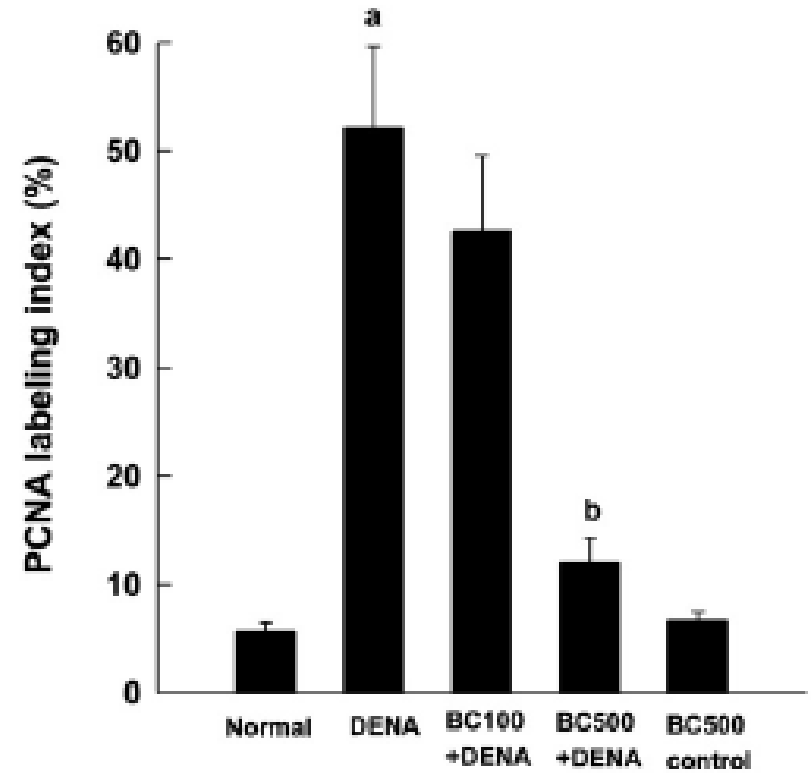
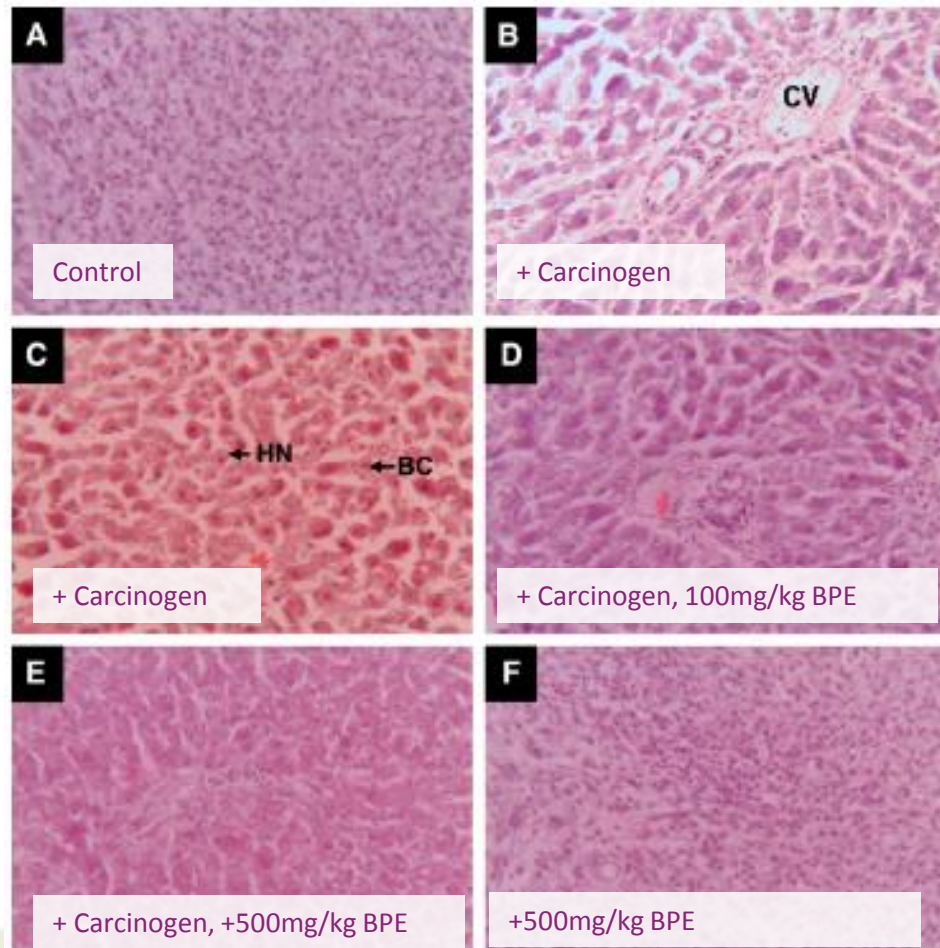
Cancer induction
& promotion



± Blackcurrant
polyphenol
extract

Reduction in macroscopic
hepatocyte nodule number, size
and proliferation.
BPE one had no deleterious
effects

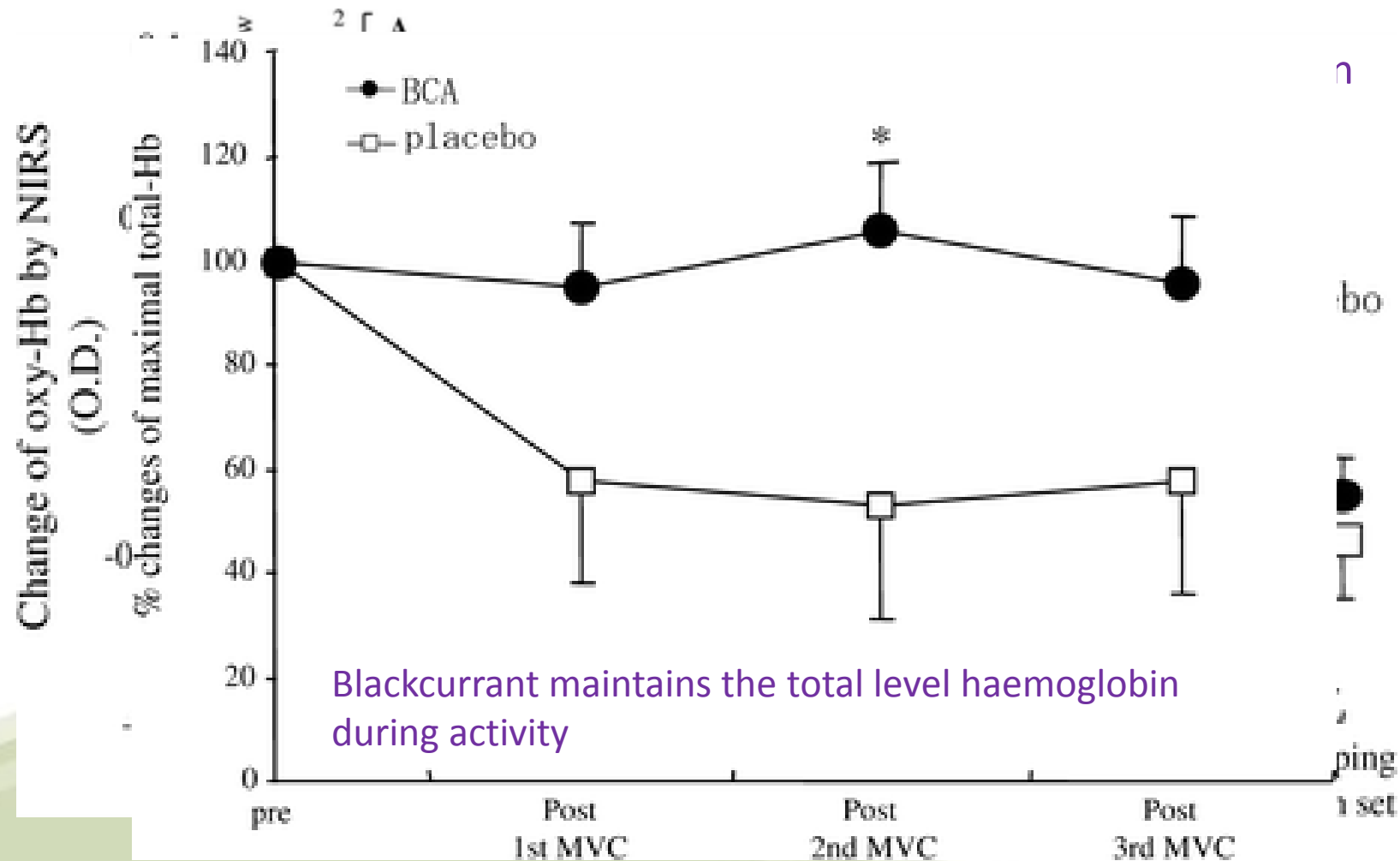




Proliferative nuclear antigen (PCNA)

Black currant fraction	Clinical study	Clinical effect	Reference
CARDIOVASCULAR SYSTEM			
Seed oil (GLA)	23 cryptogenic ischemia stroke patients undergoing transesophageal echocardiography, 26 known-cause stroke patients, 57 non stroke controls	Inhibited platelet formation, decreased fibrin formation, and increased anti-coagulant effect	Stone <i>et al.</i> , 1995 ⁹⁶
Concentrate (anthocyanin) ✓	Right trapezius muscles in 20 healthy human subjects	Induced relief of shoulder stiffness and decreased muscle fatigue via improved blood flow	Matsumoto <i>et al.</i> , 2005 ⁹⁷
Oil	Randomized, double- blind, crossover study of 15 healthy female subjects administered black currant seed oil supplements	Decreased LDL cholesterol levels when administered with fish oil	Tahvonen <i>et al.</i> , 2005 ⁹⁸
Juice ✓	Serum inflammatory markers in 48 peripheral artery disease patients	Reduced serum inflammatory markers such, e.g. C reactive protein	Dalgard <i>et al.</i> , 2009 ⁹⁹
Seed press residue	Serum and stool tocopherol concentrations in 36 healthy female subjects	Increased alpha- and gamma-tocopherol serum concentrations	Helbig <i>et al.</i> , 2009 ⁵¹
Oil (soft capsule)	Observational study of 2154 dyslipidemic patients	Increased serum HDL-C protein and lowered triglyceride and total cholesterol in low BMI patients with hyperlipidemia	Fa-Lin <i>et al.</i> , 2010 ¹⁰⁰
20% Juice (anthocyanin) ✓	Randomized, cross-over, double-blind, placebo-controlled acute meal study in 11 female and 9 male healthy volunteers	Did not have significant effect on total plasma nitrate, nitrite, ICAM, or VCAM levels	Jin <i>et al.</i> , 2011 ¹⁰¹
anthocyanin ✓	Cross-over study in 12 hypercholesterolemic patients	Increased NO-cGMP activation, improved serum lipid profile, decreased inflammatory markers	Zhu <i>et al.</i> , 2011 ¹⁰²

Blackcurrant intake increases blood and maintains the haemoglobin levels: a computer operator study





General analysis of the health studies employing blackcurrant

In vitro: CVD/Neuro/Cancer/pulmonary

Juices & Extracts (whole fruit, skins & pomace)

All studies report benefits - NB ALL polyphenol based



Animal Studies -

CVD/Neuro/Cancer/Ocular/Skeletal

Extracts juices bit also oils and polysaccharides

Invariable good (some very/some marginal)



Clinical - CVD/Diabetes

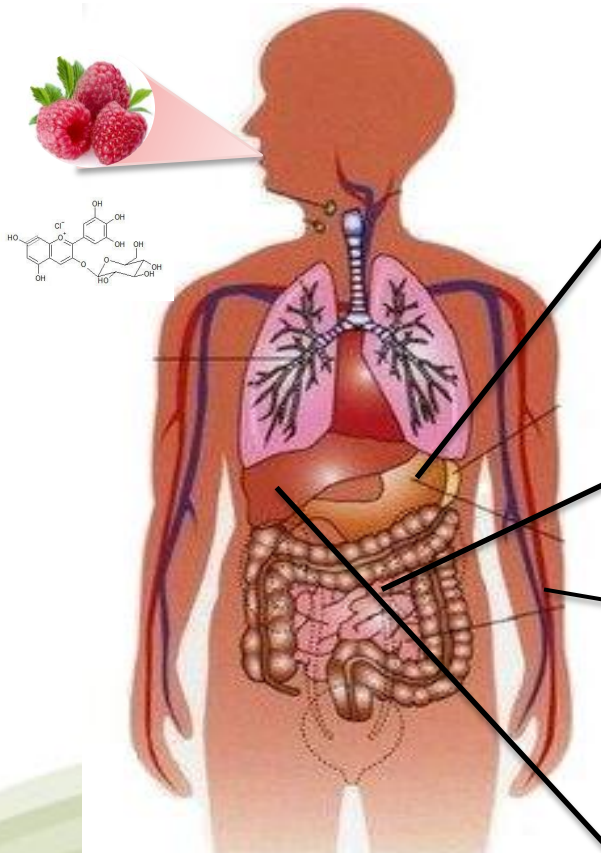
Juice (Neat and 20%/Extracts/Anthocyanins)

&

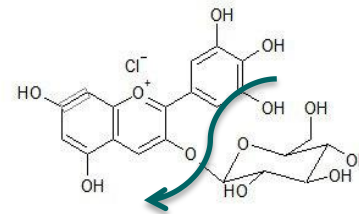
Seed oils

Conclusion
Quality
&
Relevance

Absorption and metabolism of delphinidin



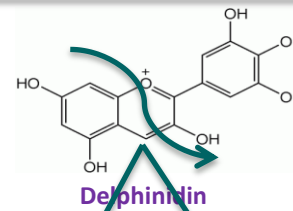
■ GUT



Delphinidin-3-O-glucoside

■ pH ~ 4

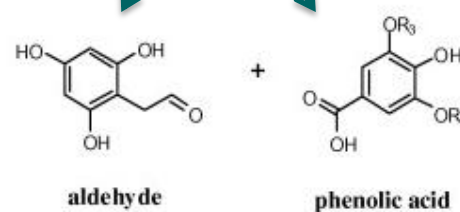
■ Small intestine



Delphinidin

■ pH ~ 7 - 8

■ Blood

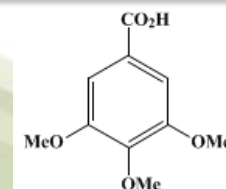


aldehyde

phenolic acid

■ pH ~ 7.4

■ Liver



- Methylation
- Sulphation
- Glucuronidation

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

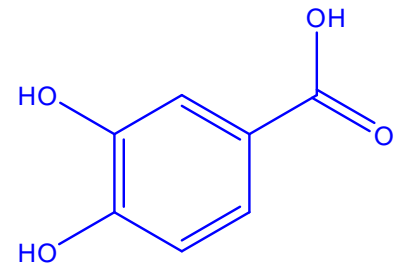
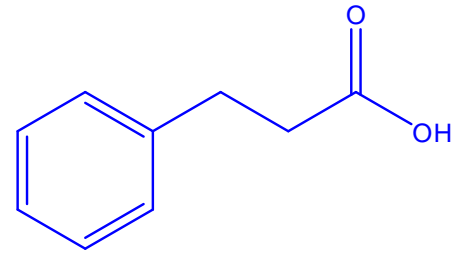
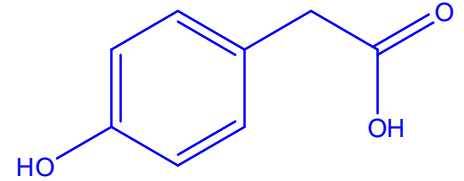
3-Hydroxy phenylacetic acid increased in 5/10 subjects

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?

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