

Détendez-vous grâce au cassis

Derek Stewart

Plant Products and Food Quality Programme
Scottish Crop Research Institute



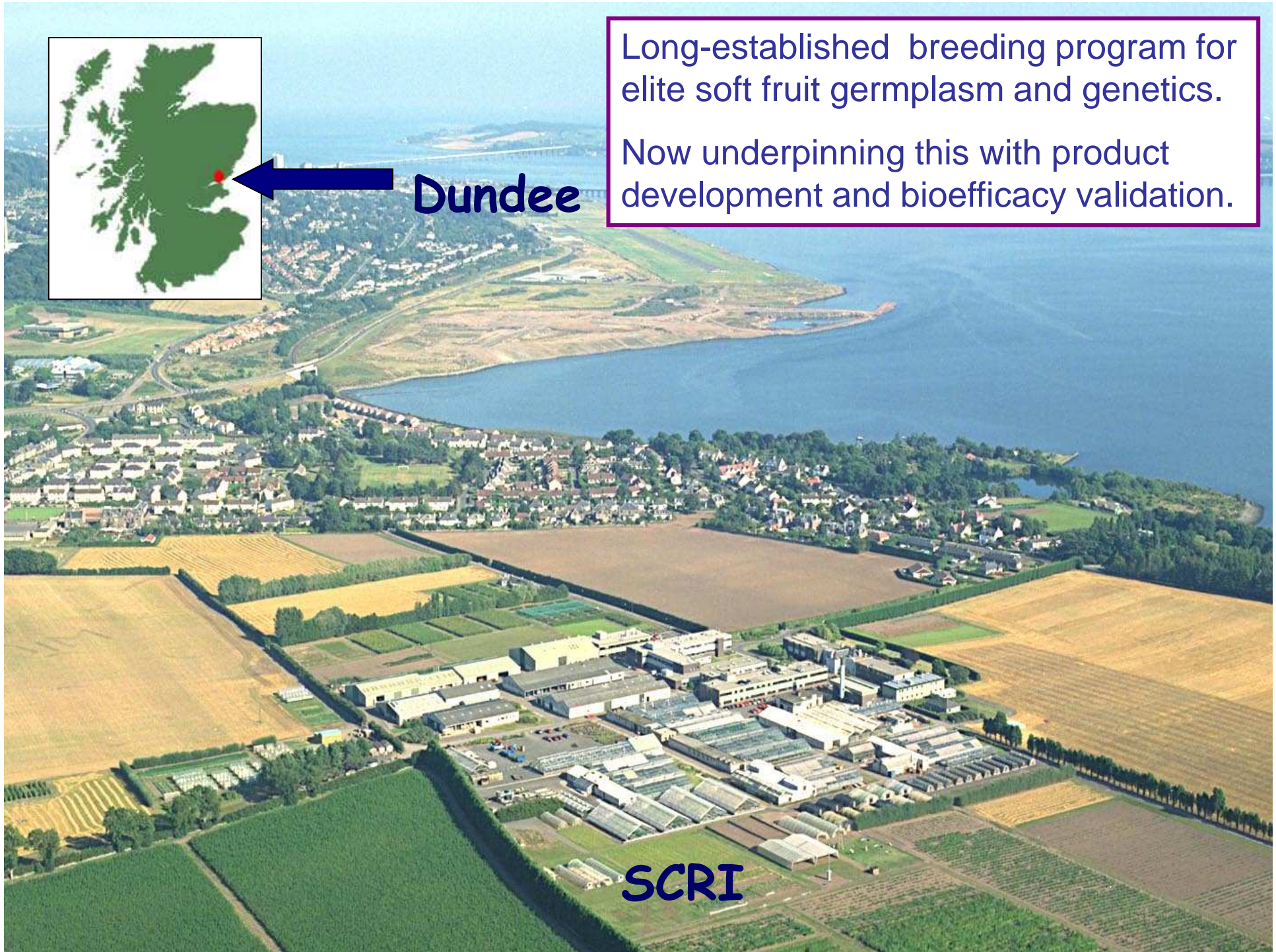


Dundee

Long-established breeding program for elite soft fruit germplasm and genetics.

Now underpinning this with product development and bioefficacy validation.

SCRI

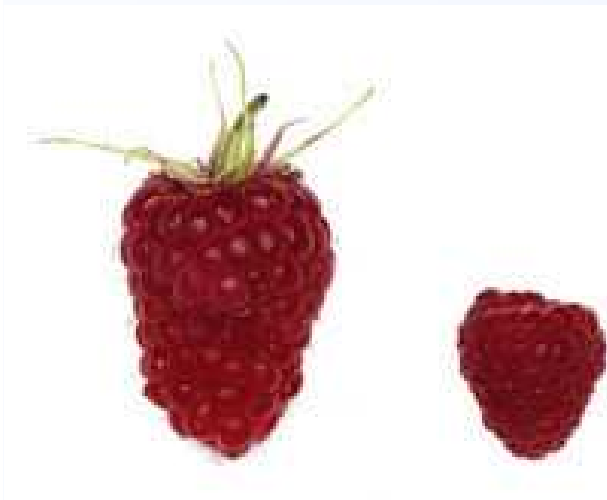


Traditional fruit breeding

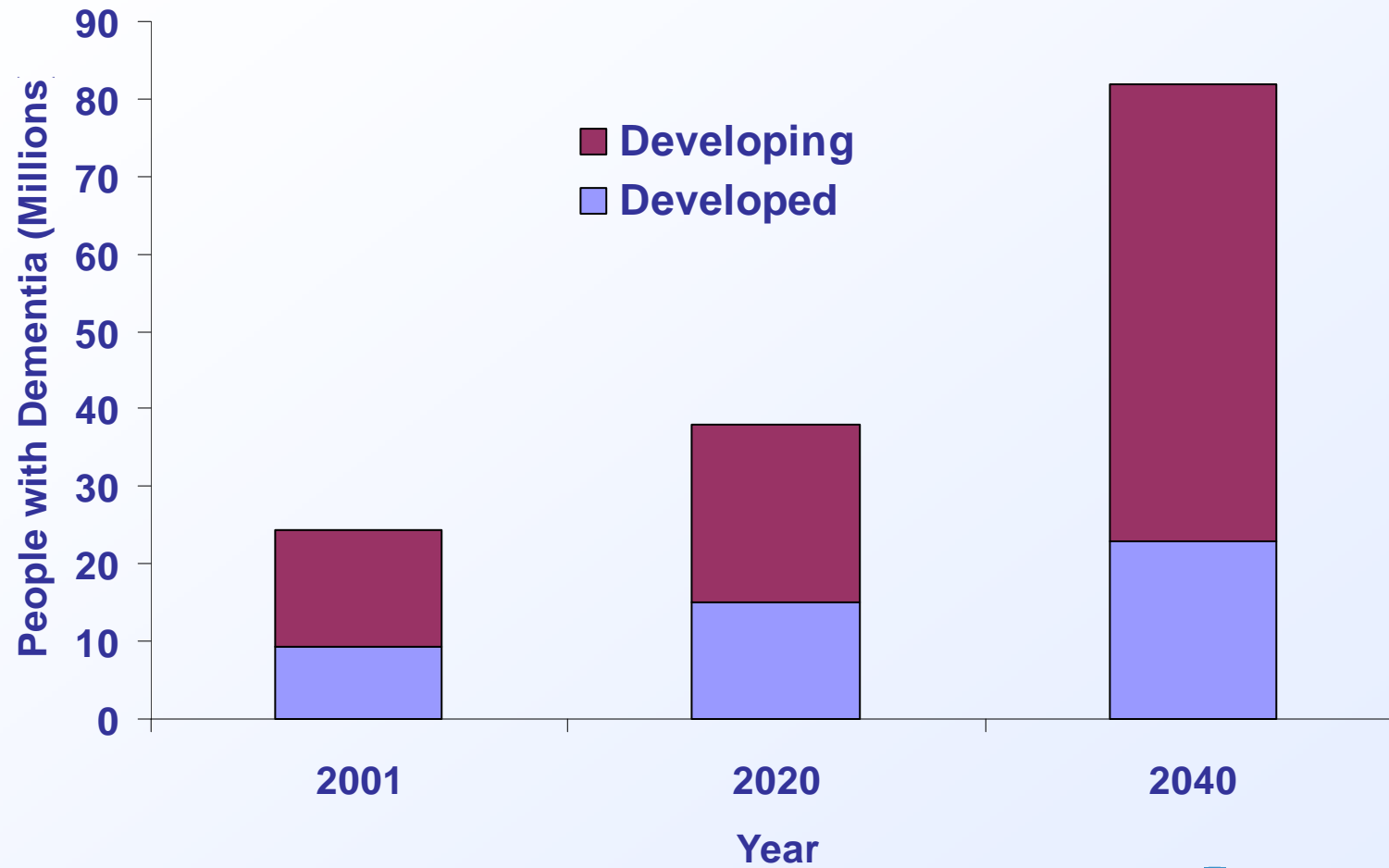


Health

Heart disease, Atherosclerosis, Cancer, Alzheimer's/Dementia, Ageing, Diabetes, Inflammation, Gut health, Obesity. "Well being".



The problem: Neurodegeneration Alzheimer's, Parkinson's, Huntington's etc



Statistics concerning major neurodegenerative diseases

Disease	Total prevalence in top seven market (US, Japan, Germany, France, UK, Spain & Italy)		
	2002	2012 (predicted)	Age-Dependence
Alzheimer's	5.2 x 10 ⁶	6.7 x 10 ⁶	1 in 10 at age 65 1 in 2 at age 85
Parkinson's	2.8 x 10 ⁶	3.4 x 10 ⁶	1 in 10 at age 65 1 in 10 at age 65
ALS*	8.7 x 10 ⁵	11 x 10 ⁵	Risk increase with age up to 74
Huntingdon's	3-5 x 10 ⁶	Unavailable	Unavailable

Sources

EPI database 2003; DR DB7,2003, DR Cognos 2002

Estimated from indications on several websites of Huntington's disease organizations

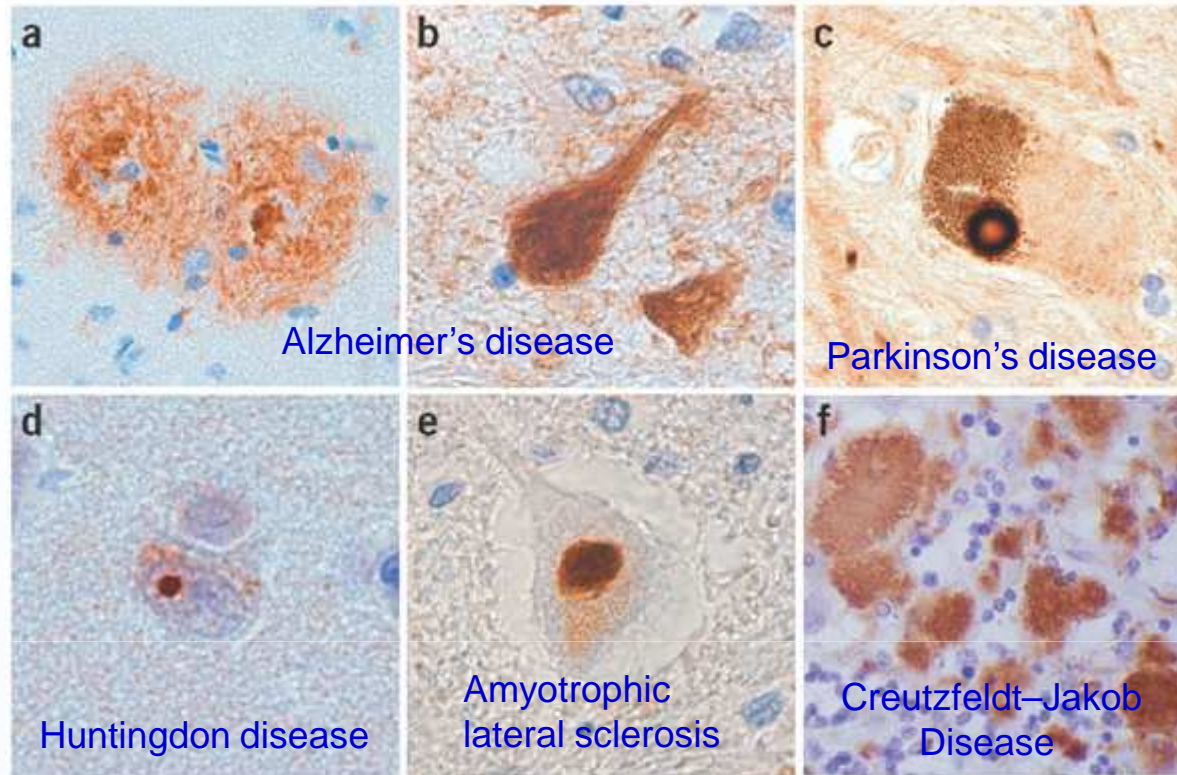
<http://www.alz.org/ResourceCenter/FactSheets/FSAlzheimerStats.pdf>

http://www.departmentofmedicine.ualberta.ca/pdf/halfday/ahd_01-23-03-2.pdf

<http://www.neuro.wustl.edu/neuromuscular/spinal/als.htm>

Waldmeier and Tatton (2004) Drug Discovery Today, 9, 210-218: *Amyotrophic lateral sclerosis

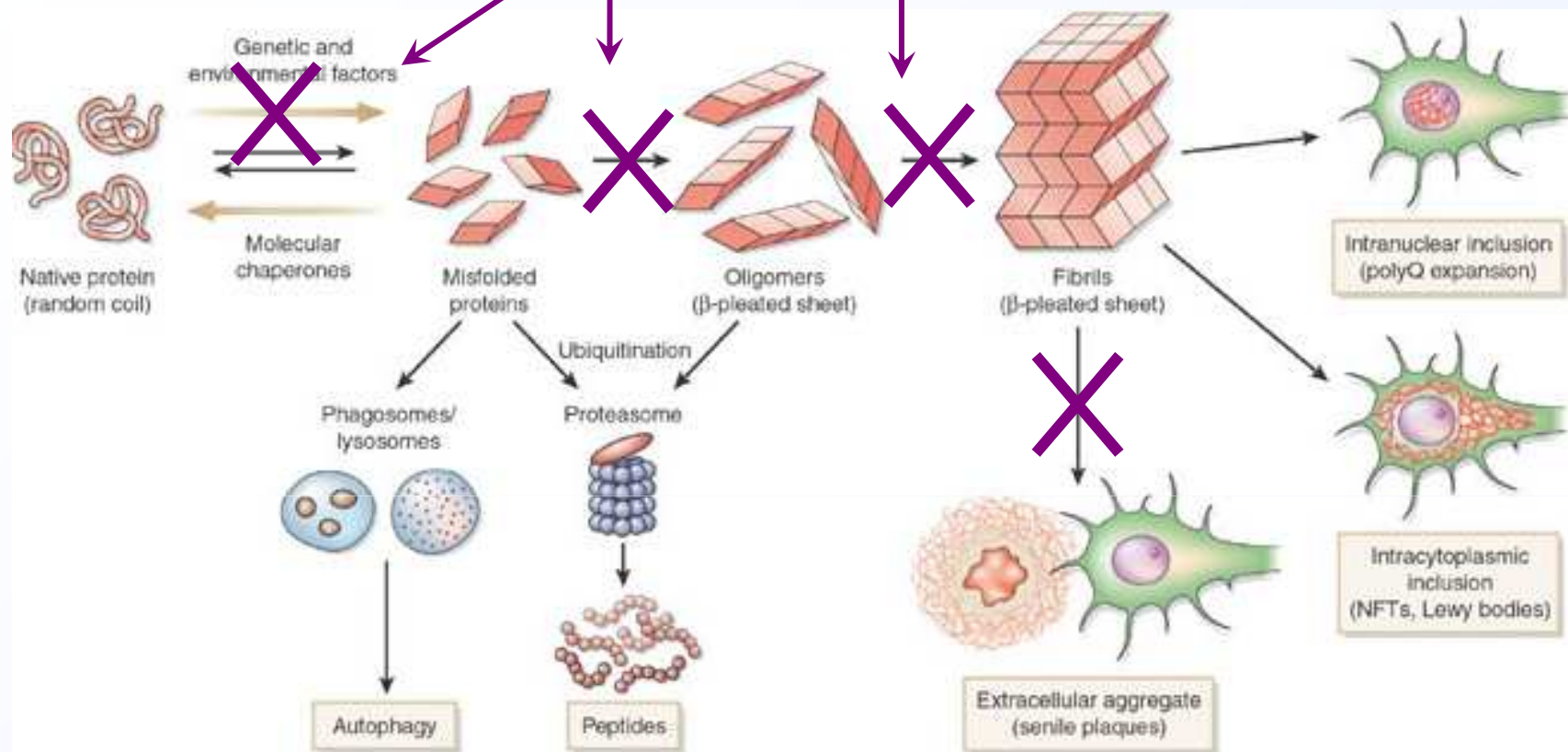




- (a) Senile plaques in neocortex of Alzheimer disease.
- (b) NFTs in hippocampus of FTDP-17 (R406W mutation).
- (c) Lewy body in substantia nigra of Parkinson disease.
- (d) Intranuclear polyglutamine inclusion in neocortex of Huntington disease.
- (e) Ubiquitinated inclusion in spinal cord motor neuron of ALS.
- (f) Protease-resistant PrP in cerebellum of CJD (panel f courtesy of Nigel Cairns).

Foreman et al Nature Medicine **10**, 1055 - 1063 (2004)

Blackcurrant polyphenols



Model of protein misfolding and fibrillization, leading to the deposition of aggregated protein in the nucleus, cytoplasm and extracellular space.

- Genetic and environmental factors may accelerate this process
- Cellular quality-control systems limit the accumulation of misfolded proteins.

Foreman et al Nature Medicine 10, 1055 - 1063 (2004)

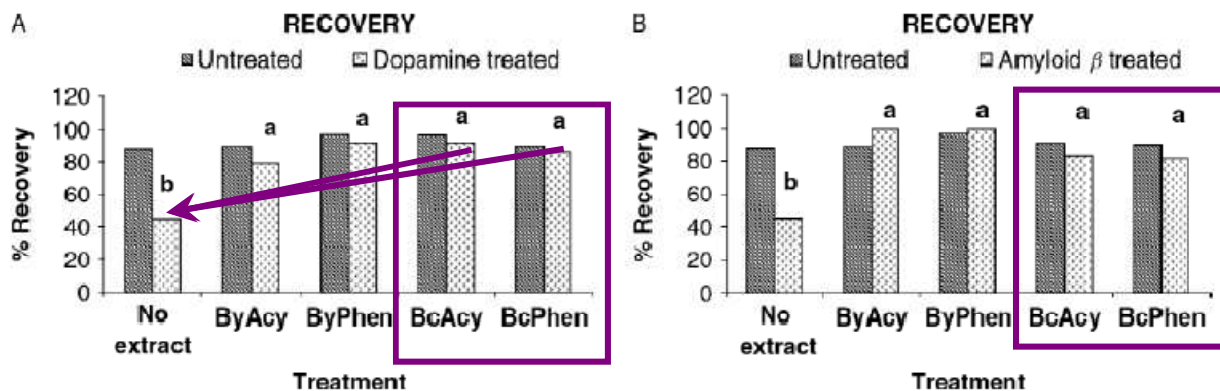
That's the problem – Do we have solutions?



Do we have solutions?

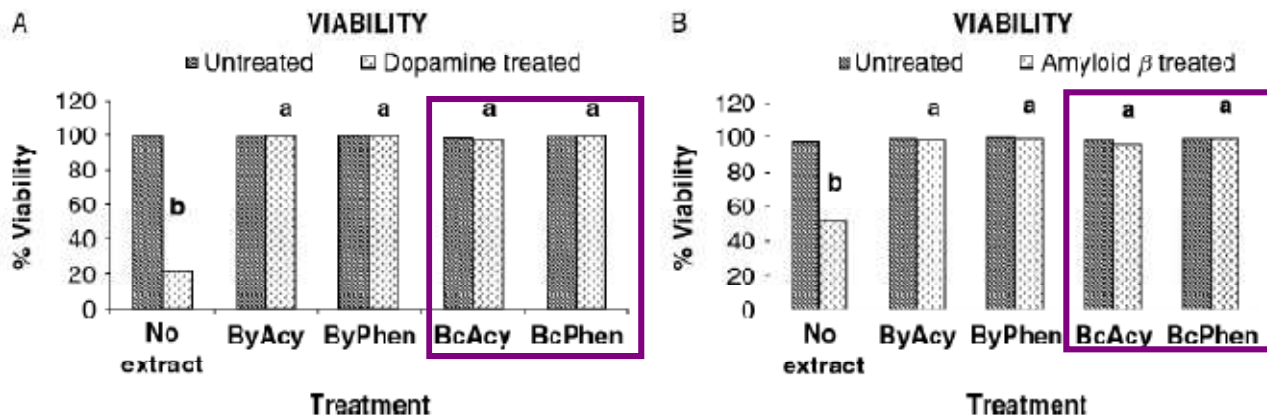
- Cell Studies - Global
- Animal Studies - Europe
- Intervention - Europe

Cytoprotective effects of anthocyanins and other phenolic fractions of blackcurrant on induced oxidative stress in mammalian cells



Recovery of cell calcium levels following oxidative stress.

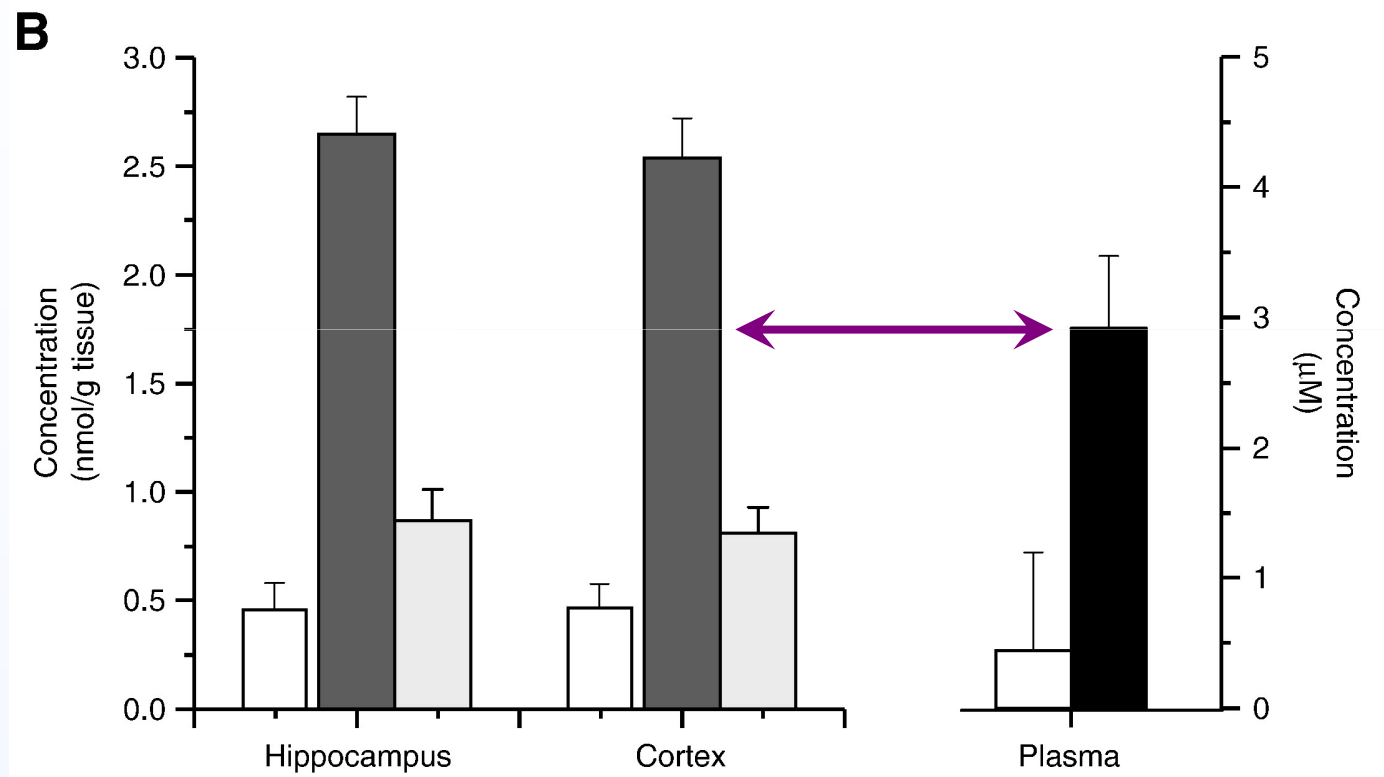
A reduced recovery increases the risk of neurodegeneration



Protection of cells from oxidative cell death by fruit extract pretreatment

Polyphenols and the impact on brain processes

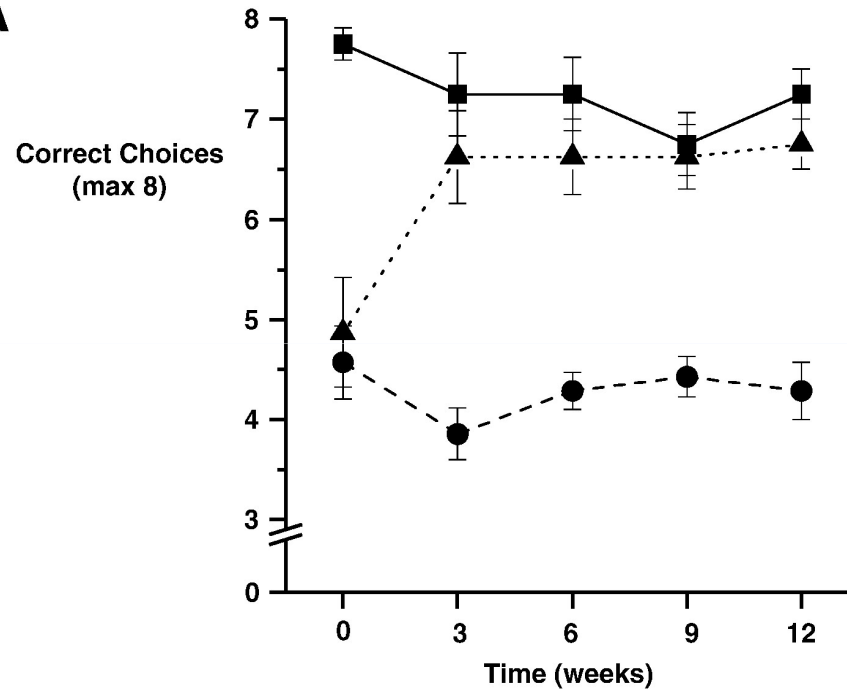
Bioavailability of selected anthocyanins and other soft fruit polyphenols



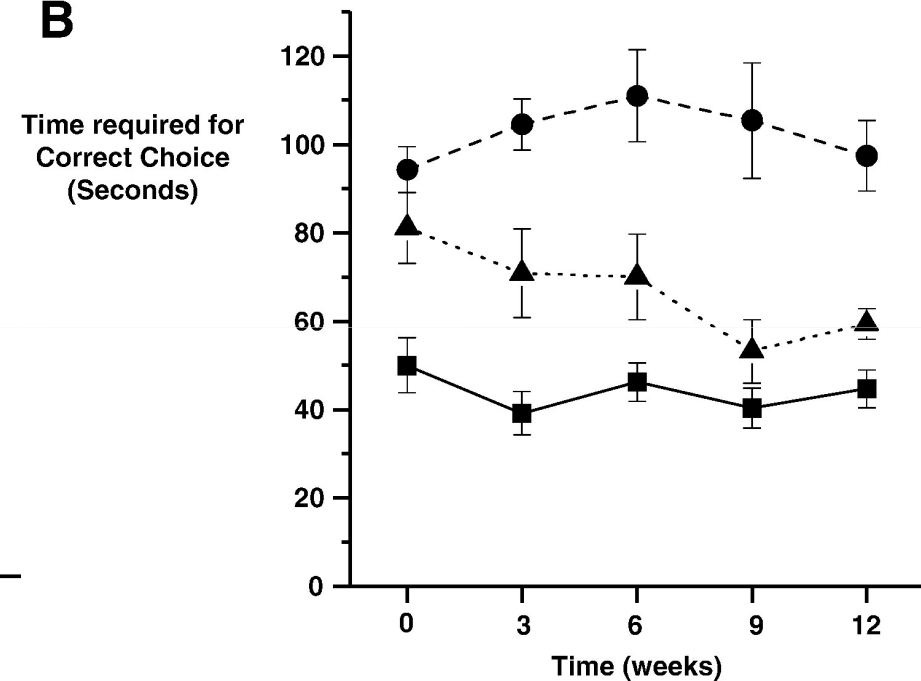
Polyphenols and the impact on brain processes

Impact on choice and speed of choice

A

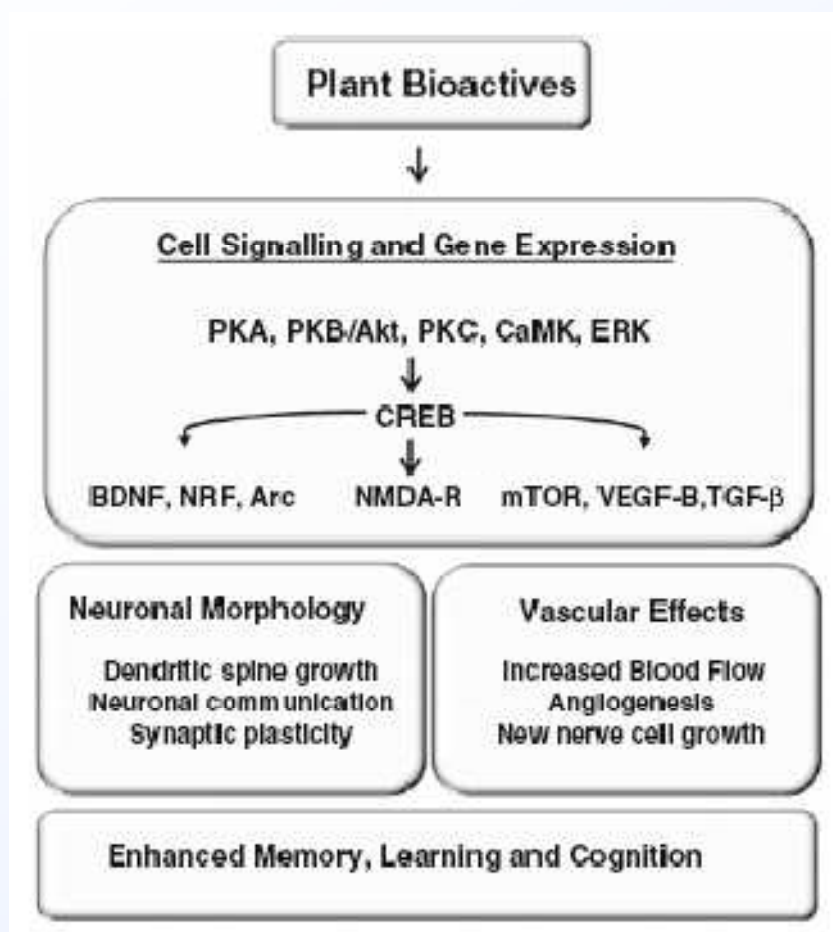


B



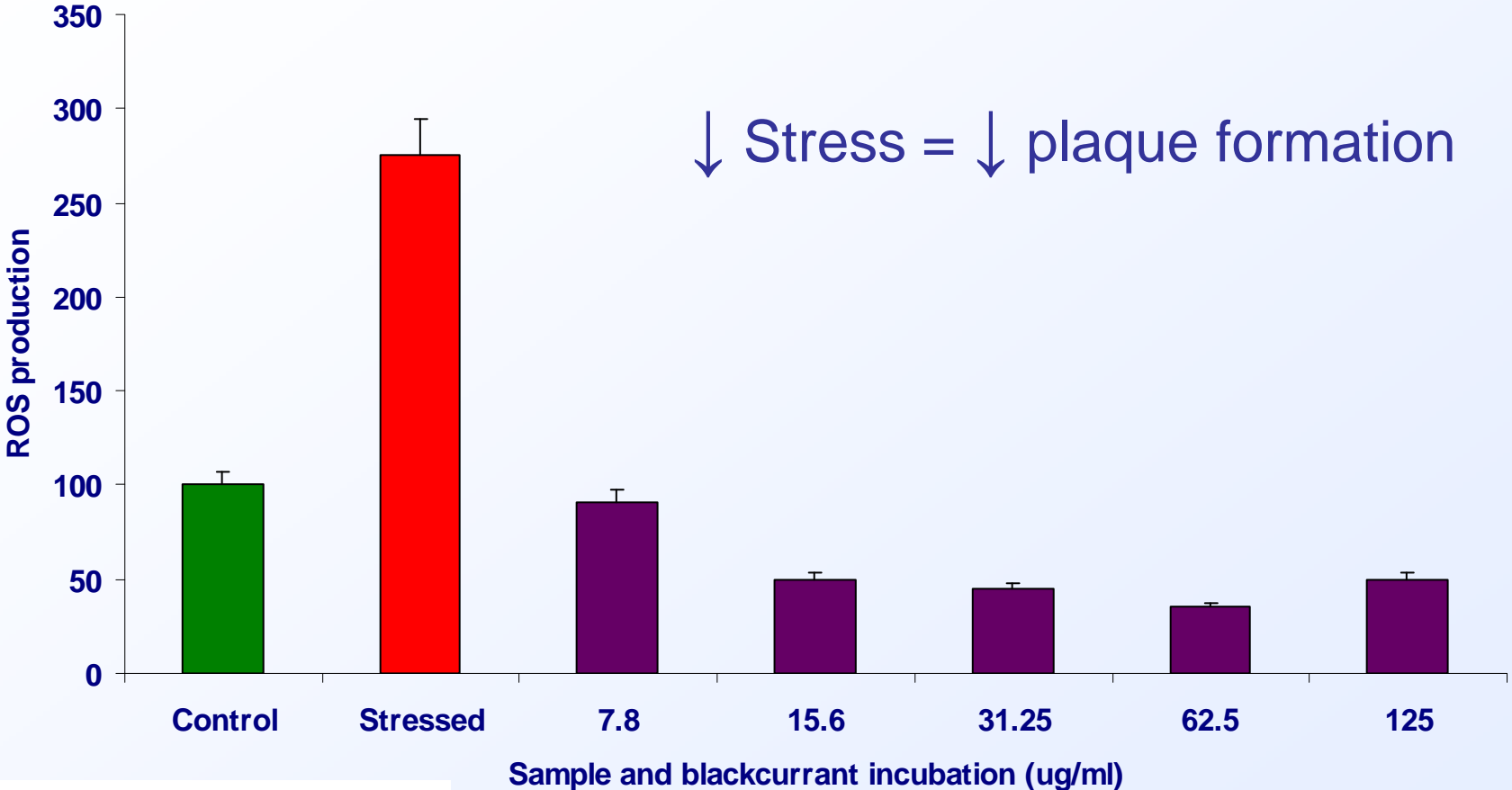
- - 9 months
- - 21 months
- ▲ - 21 months + polyphenol supplementation

Polyphenols and the impact on brain processes



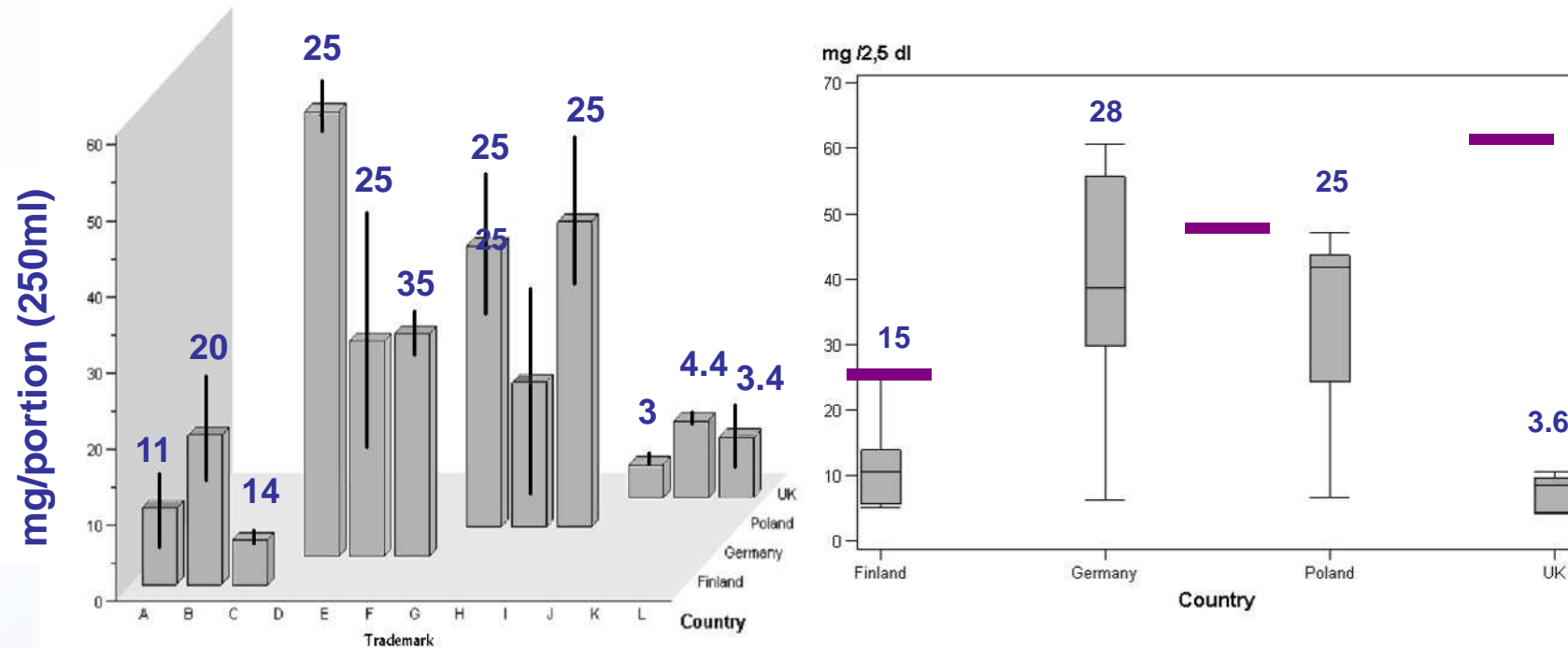
Neuroprotection via blackcurrant polyphenol pre-incubation

Human neuroblastoma cells predisposed to amyloid plaque production



Survey of concentrates juices in Finland, Germany Poland and UK Diluted according to manufactures instructions

Anthocyanins



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Animal Studies (Mice)

1. Short term study

- Group A receives a control liquid.
- Group B receives a polyphenol-rich blackcurrant juice.
- Group C receives an anthocyanin-rich blackcurrant juice.

Start feeding the juice at 4 months of age and continue until sacrificed at the age of 9 months.

At 8 months they will undergo the neurological test battery for exploratory activity, anxiety and spatial learning.

At the age of 9 months brains histology will be undertaken

2. Long term study

- Group A receives a control liquid.
- Group B receives a polyphenol-rich blackcurrant juice.

Start feeding the juice at 4 months and continue the juice until sacrificed at the age of 13 months.

At 12 months of age the mice will undergo a neurological test battery for exploratory activity, anxiety and spatial learning.

At the age of 13 months brains histology will be undertaken.



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Human Intervention Studies

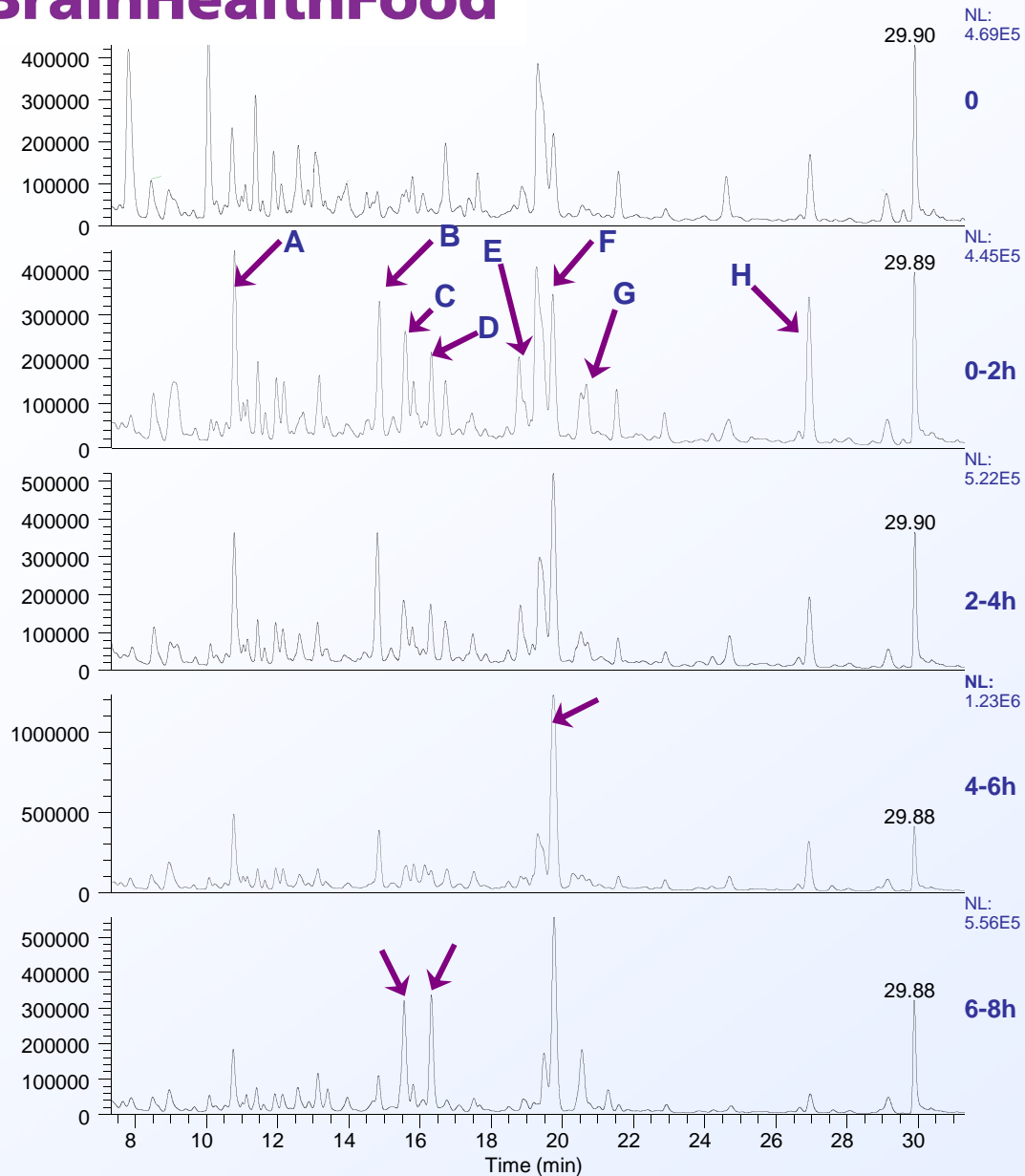
- Bioavailability of anthocyanins and other polyphenols from the two blackcurrant juices with different polyphenol contents (a control juice and a polyphenol-enriched juice)
- Randomized, controlled, double-blind cross-over study.
- Each subject in two 8-h postprandial tests, on separate days, at least 5 days apart.
- Control (pre consumption bloods taken).
- Blood taken at samples 15, 30, 45, 60, 90, 120, 150 and 180 min for plasma polyphenol, glucose and insulin measurements.
- Blood also taken at 4, 6 and 8 h for polyphenol measurements only.
- Control and trial urine taken at 0-2, 2-4, 4-6 and 6-8 hr.





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Human Intervention Studies: Urine analysis



As metabolism progresses BC-related compounds start to become present in the urine. These are polyphenolic & anthocyanin derived.

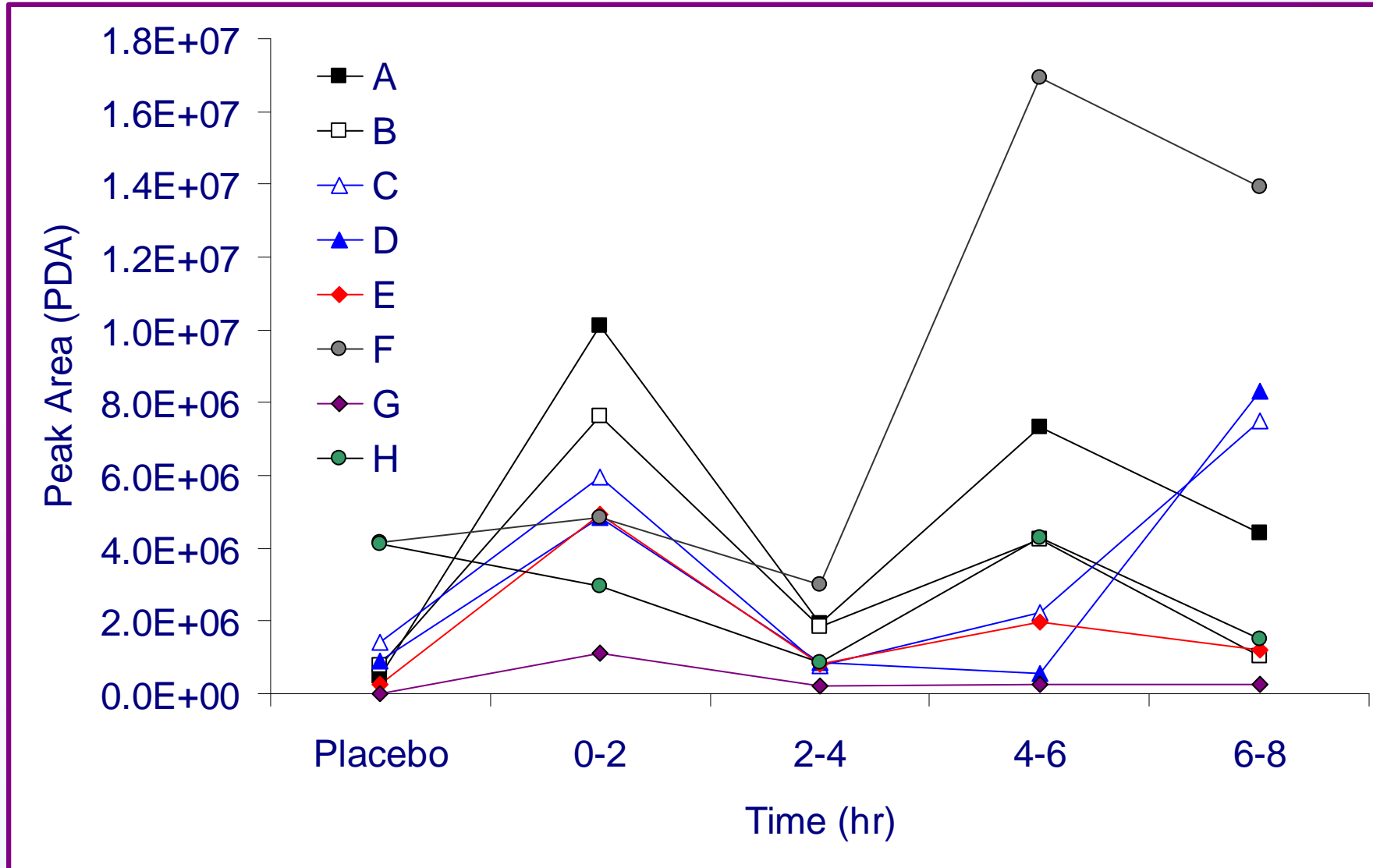
At 4-6 hrs the main peak has increased by 10-fold.

The later peaks are probably a result of colonic bacterial breakdown processes followed by reabsorption and excretion



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Human Intervention Studies: Urine analysis



Conclusions

The potential for success is good.

The cell line studies are proliferating but not just for blackcurrant.

The animal studies are increasing but mainly focussing on blueberry.

Clinical studies are sporadic but showing a trend for more fruit work.

Clinical trials currently registered

- 780 - Alzheimer's
- 650 - Parkinson's
- 190 - Fruit
- 55 - Polyphenol

Acknowledgements



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 - Pharmia Oy www.pharmia.fi
 - Vin-Kon S.A. www.vinkon.com.pl
 - Werder Frucht www.werder-frucht.com
 - Indulleida S.A. www.indulleida.com

Scottish Government Rural and Environment Research
and Analysis Directorate (RERAD)

