P011 Phytonutrient activation of the Nrf2 pathway

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Abstract

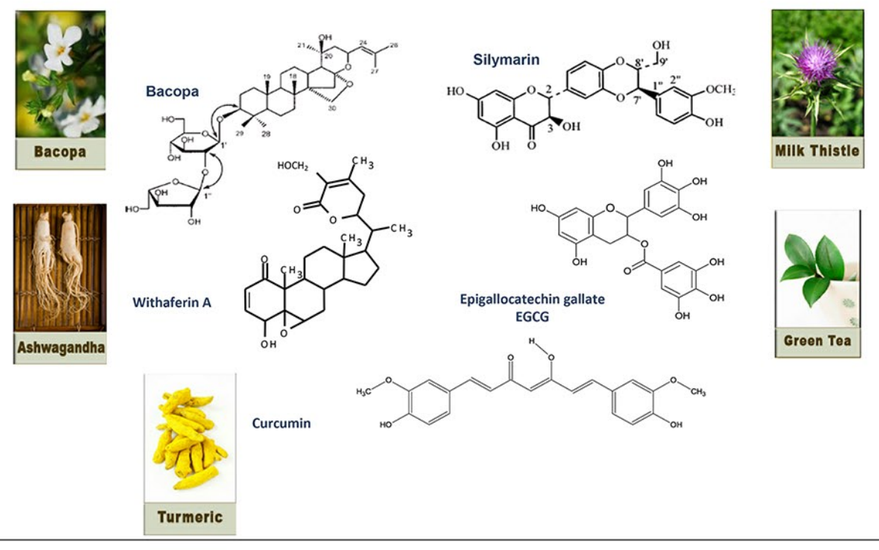
A number of natural dietary compounds have been shown to modulate expression of hundreds of genes associated with superior health of the heart, colon, brain, and other tissues – suggesting that our cells possess all the genetic resources required to maintain proper oxidative balance, promote health, and slow the aging process at the genetic level by triggering the Nrf2 pathway.

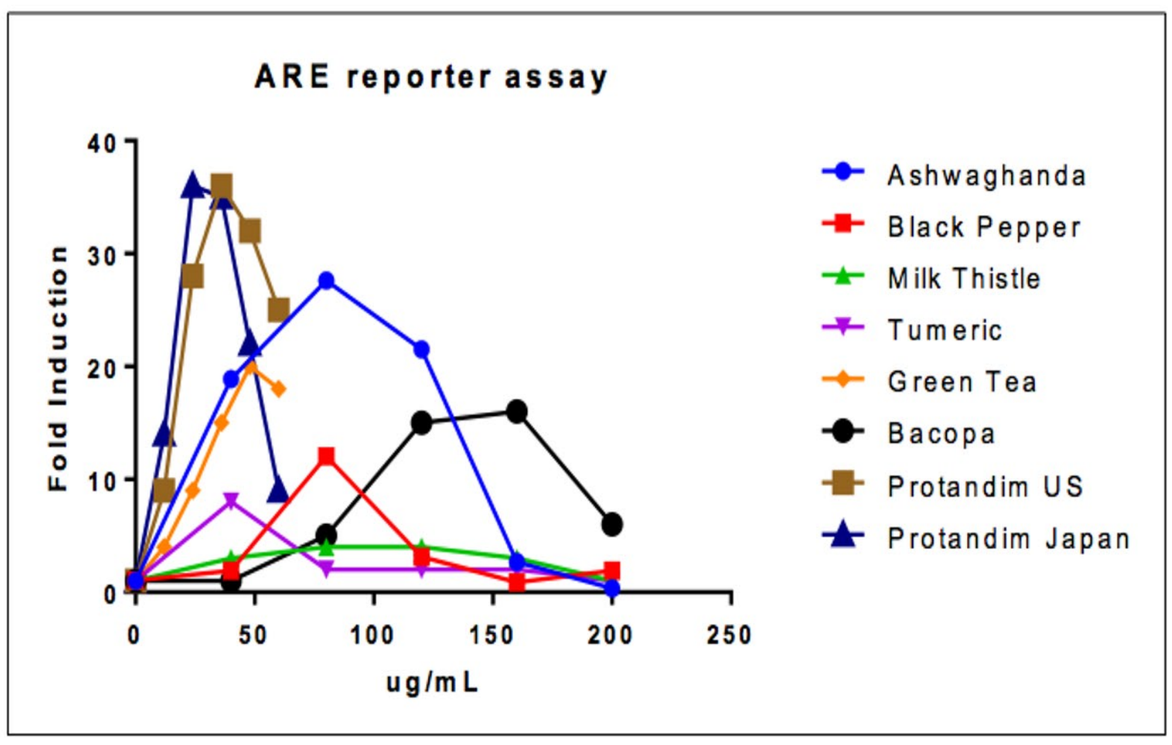
Interestingly, many "healthy" foods may actually owe many of their health-promoting benefits to the induction of Nrf2 pathways by naturally-occurring bioactive compounds. For example, sulforaphane from broccoli, curcumin from turmeric, resveratrol from red grapes/wine, quercetin from apples/onions, catechins from tea, and many others.

Natural Nrf2 activators have been studied in a variety of scenarios, including *in vitro, in vivo*, and gene expression microarray analysis. Because Nrf2 regulates the gene expression of a wide variety of antioxidant enzymes and cytoprotective proteins, it is logical for natural Nrf2 triggering to play a pivotal role in the cellular defense against environmental stresses, particularly against diseases related to immune and inflammatory responses, tissue remodeling and fibrosis, carcinogenesis and metastasis, and neurological and cognitive dysfunction.

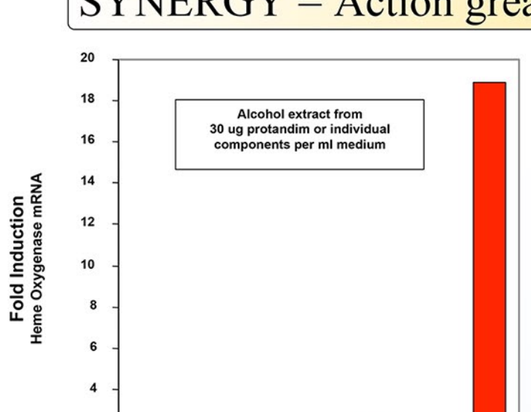
This presentation will examine a range of experiments on phytonutrient activators of the Nrf2 pathway and induction of endogenous antioxidant enzymes (catalase, heme-oxygenase, superoxide dismutase, glutathione peroxidase, and others) to elucidate the potential of natural Nrf2 triggering not only for specific disease prevention, but also for general health promotion.

Protandim = a synergistic combination of 5 phytonutrient Nrf2 activators





SYNERGY = Action greater than the sum of the parts



All five ingredients together produced an **18-fold increase** in the expression of this antioxidant gene.

Protandim works ***18 times more effectively than the sum of its parts***.

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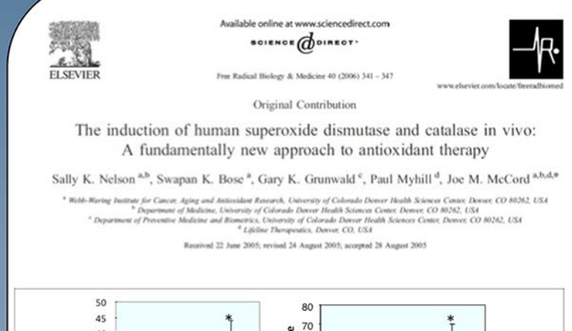
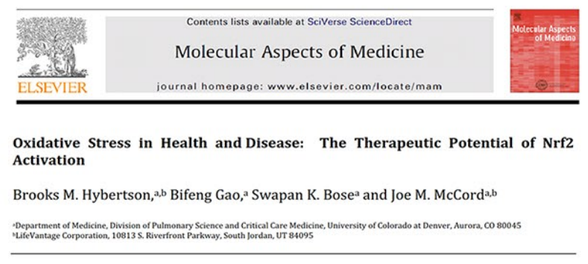
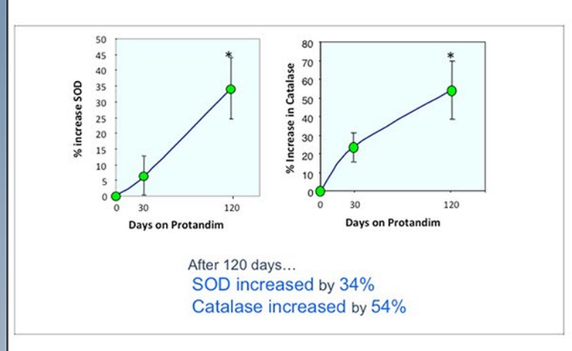


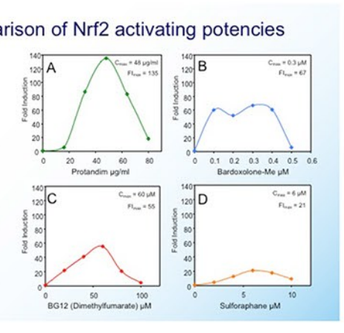


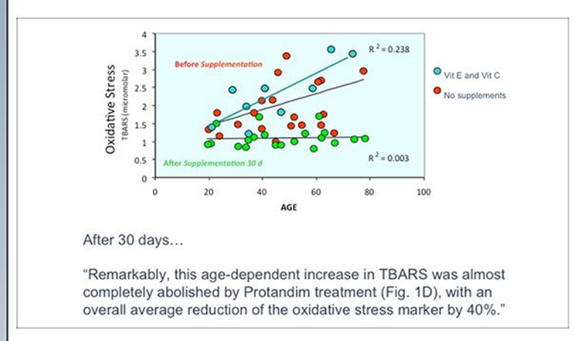


After 120 days…
SOD increased by 34%
Catalase increased by 54%

A side-by-side comparison of Nrf2 activating potencies

Agent	Fold Induction
Protandim	135
Bardoxolone Me	67
Dimethylfumarate	55
Sulforaphane	21





After 30 days…

"Remarkably, this age-dependent increase in TBARS was almost completely abolished by Protandim treatment (Fig. 1D), with an overall average reduction of the oxidative stress marker by 40%."

19 genes associated with atherosclerosis are regulated by Protandim

Gene symbol	Gene title	Disease process	Protandim	Fold-change
Atherosclerosis (19 genes)				
CTNNB1	catenin (cadherin-associated protein), beta 1, 88kDa	↑	↓	-2.34
* **DHFR**	dihydrofolate reductase	↑	↓	-1.94
* **EDN1**	endothelin 1	↑	↓	-2.00
ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	↑	↓	-2.69
MKI67	antigen identified by monoclonal antibody Ki-67	↑	↓	-5.05
MMP11	matrix metallopeptidase 11 (stromelysin 3)	↑	↓	-2.75
MMP14	matrix metallopeptidase 14 (membrane-inserted)	↑	↓	-2.11
MMP2	matrix metallopeptidase 2	↑	↓	-1.75
* **PDE7A**	phosphodiesterase 7A	↑	↓	-1.52
* **PDE7B**	phosphodiesterase 7B	↑	↓	-1.62
PLAU	plasminogen activator, urokinase	↑	↓	-3.13
* **PTGS1**	prostaglandin-endoperoxide synthase 1	↑	↓	-2.80
SCARB1	scavenger receptor class B, member 1	↑	↓	-1.80
* **TUBB3**	tubulin, beta 3	↑	↓	-1.57
* **NR3C1**	nuclear receptor subfamily 3, group C, member 1	↓	↑	1.54
* **PPARA**	peroxisome proliferator-activated receptor alpha	↓	↑	2.21
EGR1	early growth response 1	↑	↑	1.66
PTGS2	prostaglandin-endoperoxide synthase 2	↑	↑	7.61
SOAT1	sterol O-acyltransferase 1	↑	↑	2.17

Of the 19 genes, 16 (84%) are modulated by Protandim in the opposing direction of the disease process

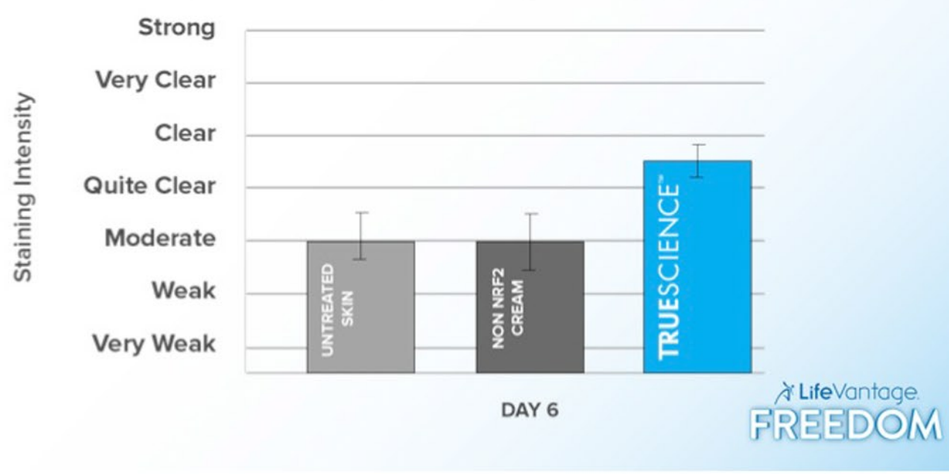
LifeVantage FREEDOM

- TrueScience™ facial cream with Advanced Nrf2 Technology applied 2 times per day for 5 days
  (Nrf2 Technology: *Bacopa, Milk Thistle, Turmeric, Green tea & Black Pepper extracts* + Brassicas extract + Plantain extract)
- Non Nrf2 cream applied 2x per day for 5 days
- Then expose the samples to UV light
- Quantify DNA damage and amount of Nrf2 Protein
- Then collect DNA, run gene expression & identify biological pathways

LifeVantage FREEDOM

Nrf2 Staining Intensity 24 hours after UV Exposure

TrueScience™ Facial Cream results in more Nrf2 in skin, thus more protection!



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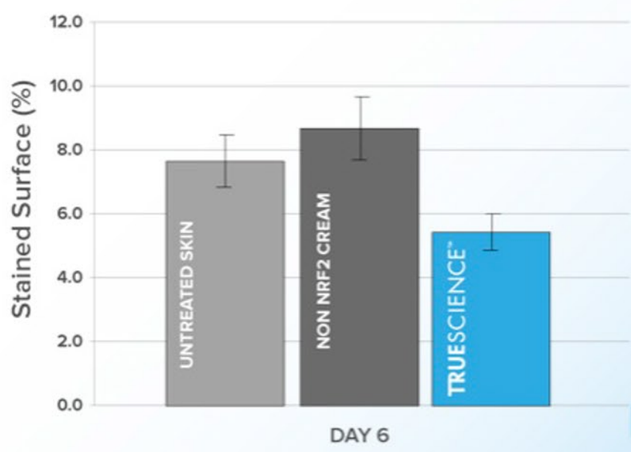
Less Thymine Dimers with TrueScience

TrueScience™ Facial Cream with Nrf2 protects the cell DNA!



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Conclusions

Synergistic phytonutrient activation of the Nrf2 pathway:

- Increases tissue Nrf2 protein levels
- Stimulates production of endogenous antioxidant enzymes
- Induces genes associated with cellular health
- Diminishes DNA damage (UV-induced)
- Reduces biochemical markers of cellular stress
- Demonstrates oral and topical efficacy

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