

GUEST SPEAKER: (David Archibald)

Mr Archibald's address is titled "Anticancer Garden". He was introduced by Kevin Jackson David advised that his talk will be broken down into these elements

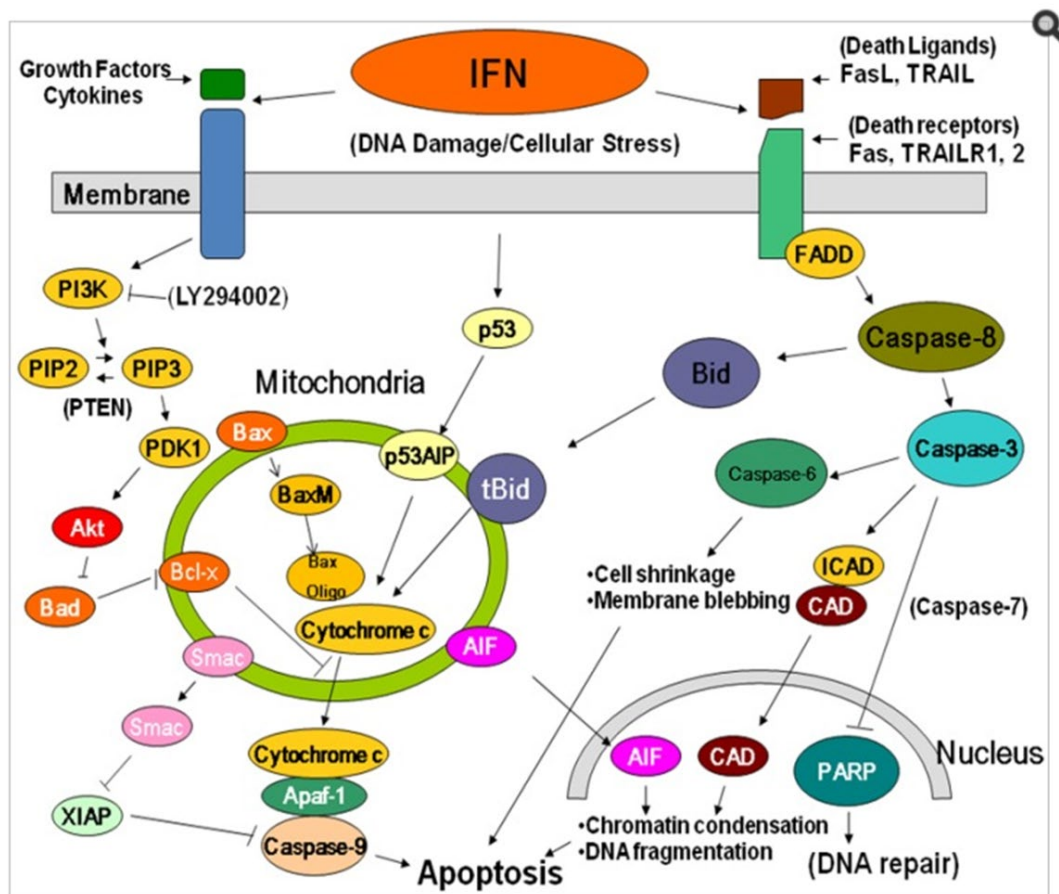
1. **How we evolved to stop cancer.**
2. **How we know it is the plants.**
3. **Getting plant molecules into the bloodstream and keeping them there**
4. **Prostate cancer in particular.**
5. **Plants and the prostate**
6. **Good plants to have.**

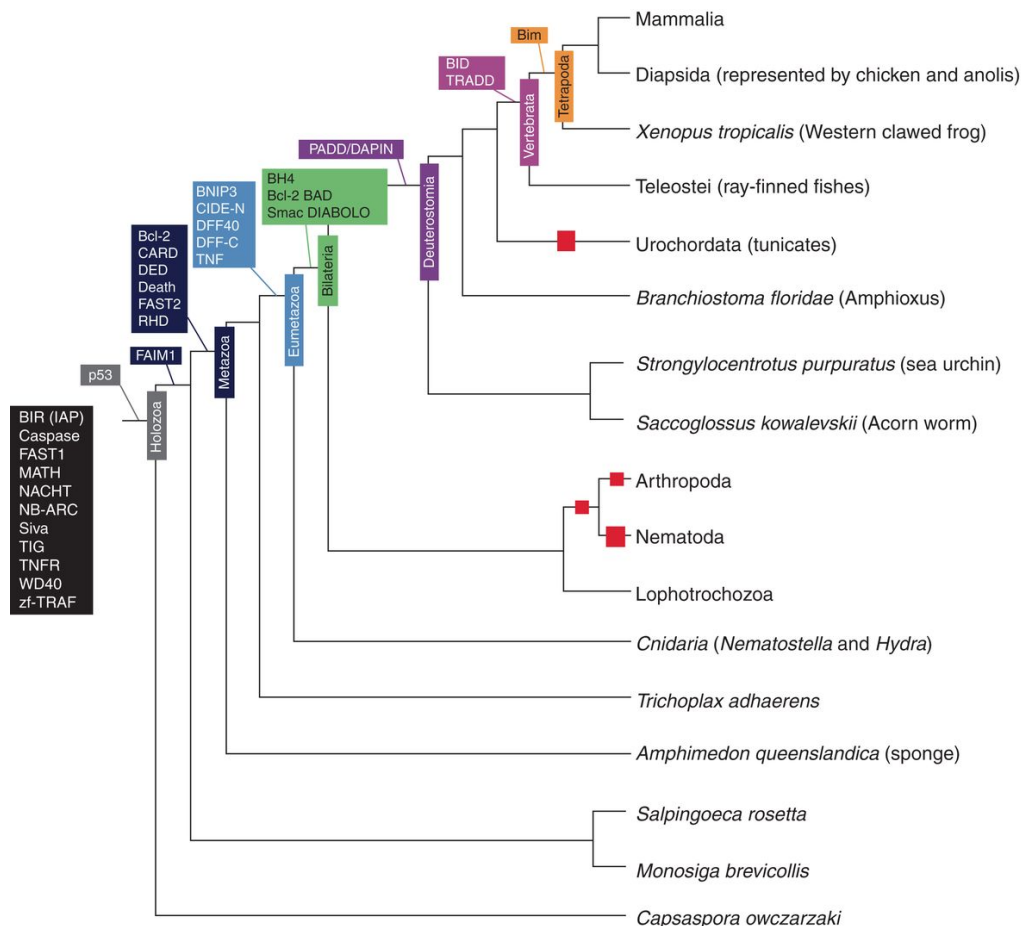
1. **2,000 million years of life on this planet before the first animal appeared.**

First Planets – 1.547 Billion Years leads to Animals – 1.538 Million Years leads to Fungi

Cellular mechanisms to deal with mutation were fully developed when the animals split from the plants because both use the same pathways.

Animals have the receptors to use plant molecules.





How Chemotherapy and Radiotherapy Work

Most cancers are immortal due to the over-production of anti-apoptotic proteins

Chemotherapy and radiotherapy cause cell cycle arrest.

The nucleus sends signals to the cell surface to express more death receptors.

That overwhelms the anti-apoptotic proteins and allows the apoptotic cascade to continue to completion.

Death Receptors

Anti-apoptotic Proteins

A1
 Bcl-2
 Bcl-XL
 CED-9
 cIAP1
 C-IAP2
 Cp-IAP
 FAIM3
 FLIP
 Livin
 Mcl-1
 NAIP
 Op-IAP

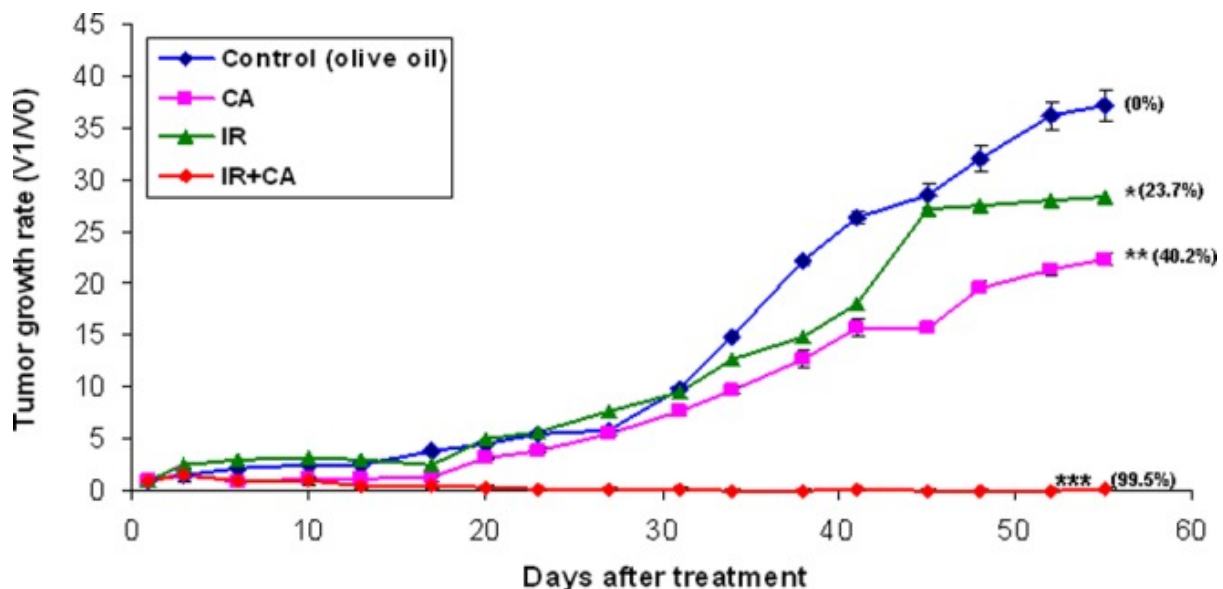
The problem of overproduction of anti-apoptotic proteins

Nature's solution relies upon plant molecules arriving in the diet and binding to receptors which reduce the production of anti-apoptotic proteins and/or increase production of pro-apoptotic proteins.

The chemotherapy/radiotherapy solution is to overwhelm the anti-apoptotic proteins with signalling from more death receptors due to mitotic arrest.

Theoretically there would be synergy between these two approaches. Maximum efficacy results from reducing the overproduction of anti-apoptotic proteins at least 48 hours before chemotherapy/radiotherapy.

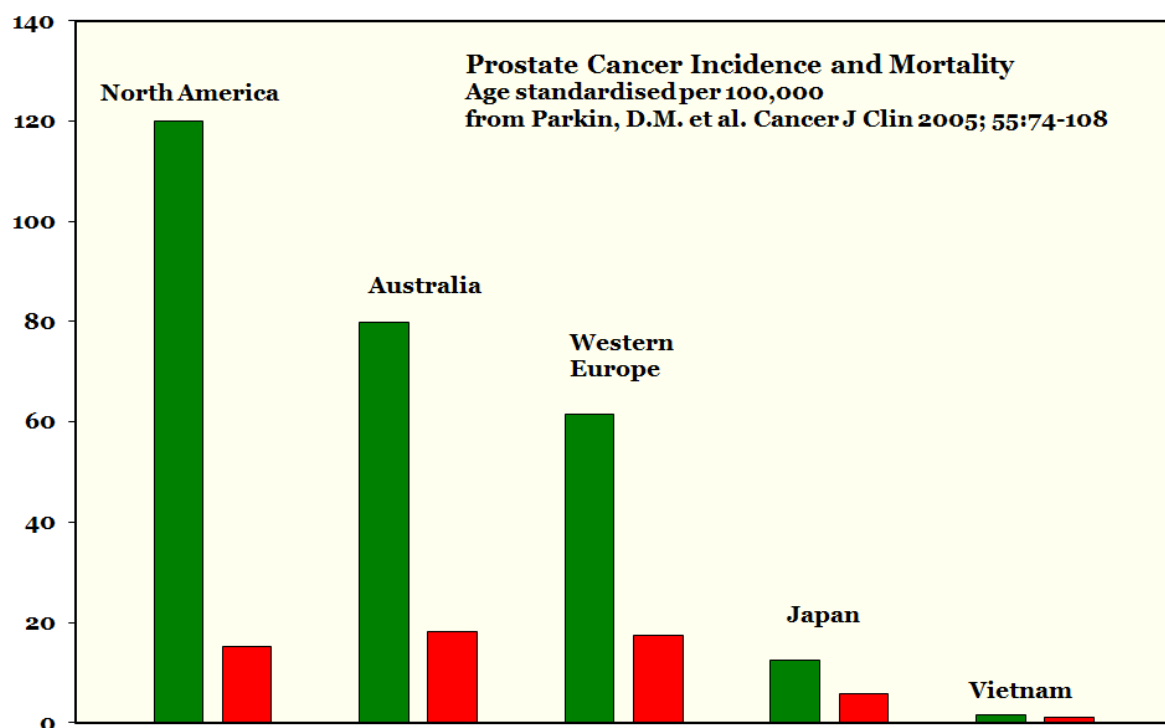
And so there is.



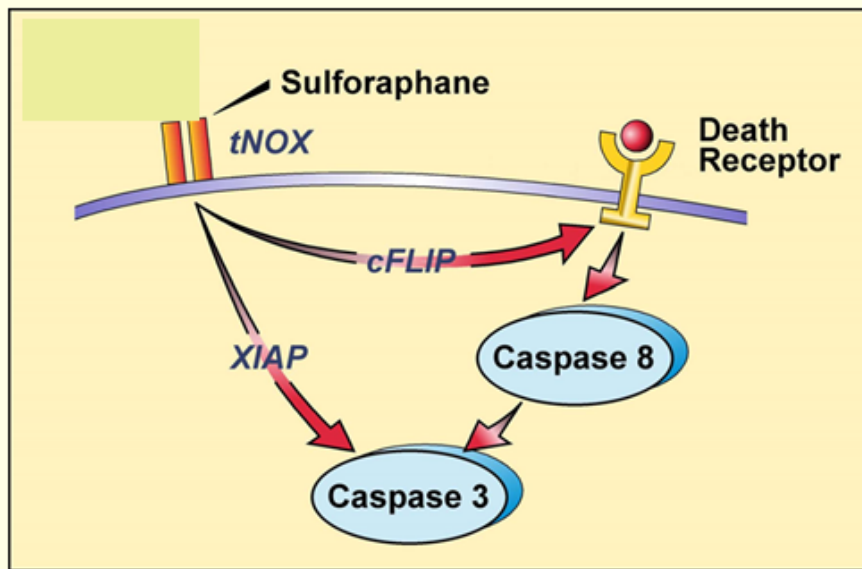
Human glioblastoma treated with ginger extract (CA), irinotecin (IR), control and the combination of ginger extract with irinotecin (IR and CA). Irinotecin is a chemo drug from the bark of *Camptotheca acuminata*.

Zero tumour growth rate with the combination.

- 2. How we know it is the plants -1.**
- **As with lung cancer, prostate and breast cancer are largely self-inflicted in Western countries.**



How we know it is the plants -2. - the tNOX receptors



The NOX molecule on the external membrane supplies the energy for making the anti-apoptotic molecules cFLIP and XIAP.

Upon a cell becoming a cancer cell, 40% of NOX molecules will switch to the tumour variant, tNOX.

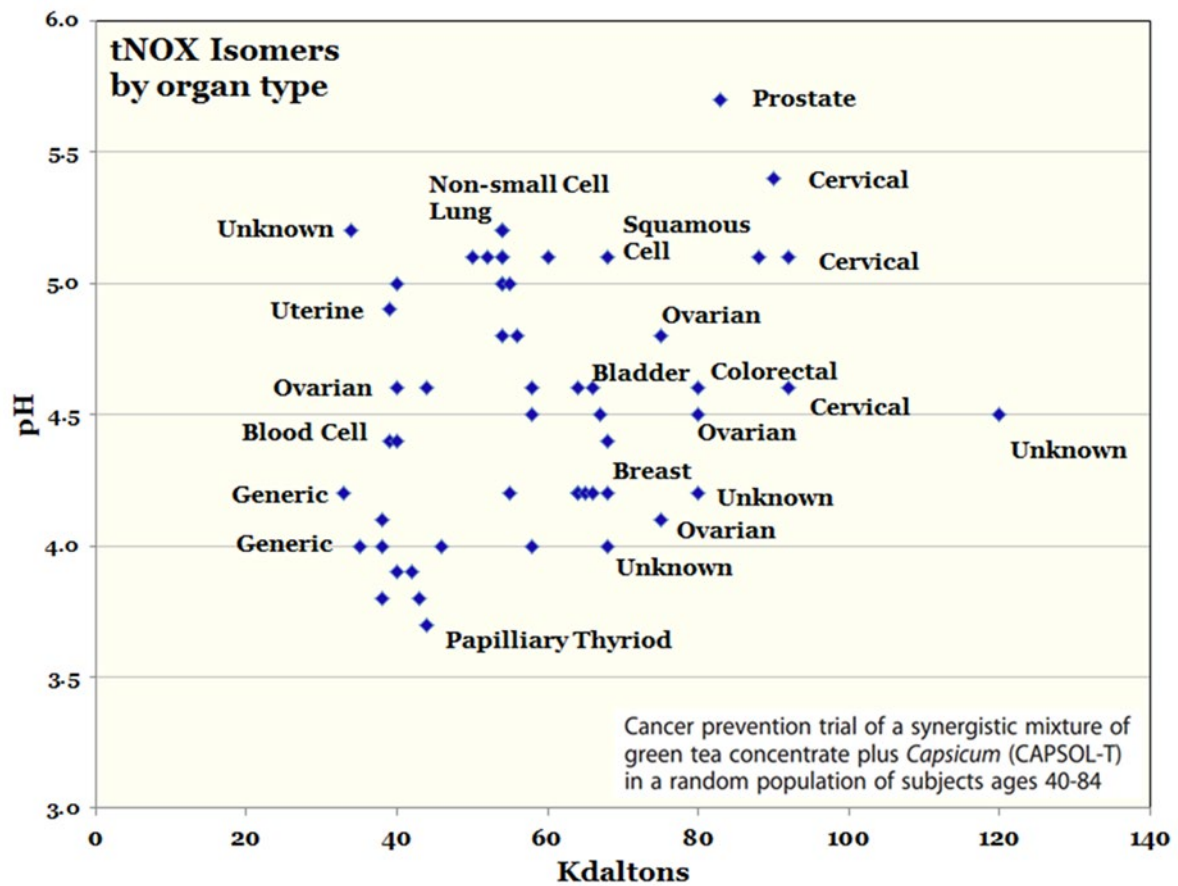
No molecules bind to ordinary NOX but a number of plant molecules bind to tNOX, reducing the production of anti-apoptotic proteins.

The pro-apoptotic proteins prevail and the cell enters apoptosis.

This is like vitamin C – we evolved to expect it to arrive in our diet.

The tNOX molecule evolved in the expectation that we would be eating certain plant molecules.

How we know it is the plants -2. - the tNOX receptors

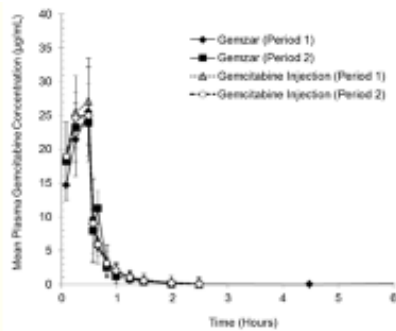


The older an organ, the lower the cancer incidence.

Organs	Most primitive vertebrate class to have them	Time of appearance
mouth, ovary pharynx, testis thyroid	Chordates, the immediate ancestors of the vertebrates	600 million years
bile duct, gall bladder, oesophagus	agnatha (jawless fish)	564 million years
lips, pancreas, stomach, rectum	chondrichthyes (cartilaginous fish)	528 million years
colon, larynx	amphibians	360 million years
alveolar lung, bladder, metanephric kidney, ureter	amniotes	310 million years
mammary gland	monotremes	170 million years
prostate gland, uterus	marsupials	150 million years

How we know it is the plants -3. - β -glucuronidase

1. Foreign molecules are removed from the bloodstream by the liver attaching a sugar molecule to them in a process called glucuronidation. The kidneys excrete the conjugated molecule.
2. An enzyme called β -glucuronidase cleaves the sugar molecule off the foreign molecule which regains its original functionality.
3. Cancer cells over-express β -glucuronidase relative to normal tissue.
4. For pancreatic cancer it is 1.6 fold, for prostate cancer it is 3.6 fold higher normal tissue.
5. So cancer cells want plant molecules to hang around longer.
6. Which plant molecules would that be?

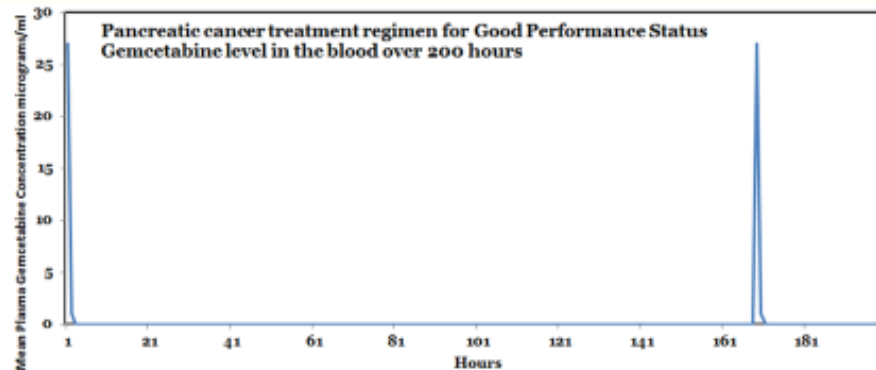


The crudity of traditional chemotherapy

Gemcitabine + Capecitabine¹

Days 1, 8, and 15: Gemcitabine 1,000mg/m² IV
 Days 1-21: Capecitabine 1,660mg/m² orally daily (830mg/m² twice daily).
 Repeat cycle every 4 weeks until disease progression.

Gemcitabine IC50: 0.13 µg/ml
 Capecitabine IC50: 1.17 µg/ml



3. Getting plant molecules into the blood stream.

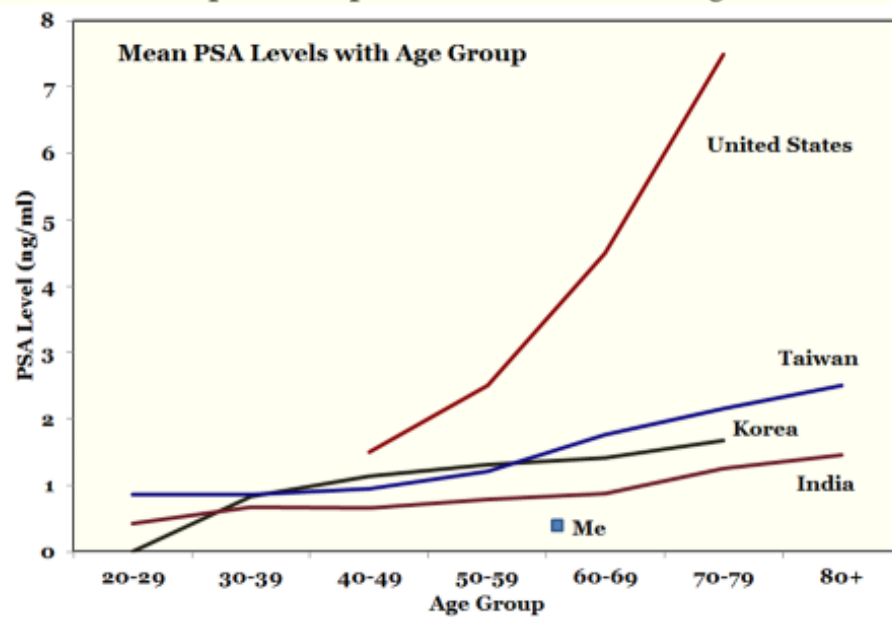
1. Most anti-cancer molecules are either only weakly soluble in water or insoluble.
2. Taking molecules with a fatty meal can increase bioavailability by up to four-fold.
3. Thus in ayurvedic medicine plant extracts are incorporated into ghee.

And keeping them there.

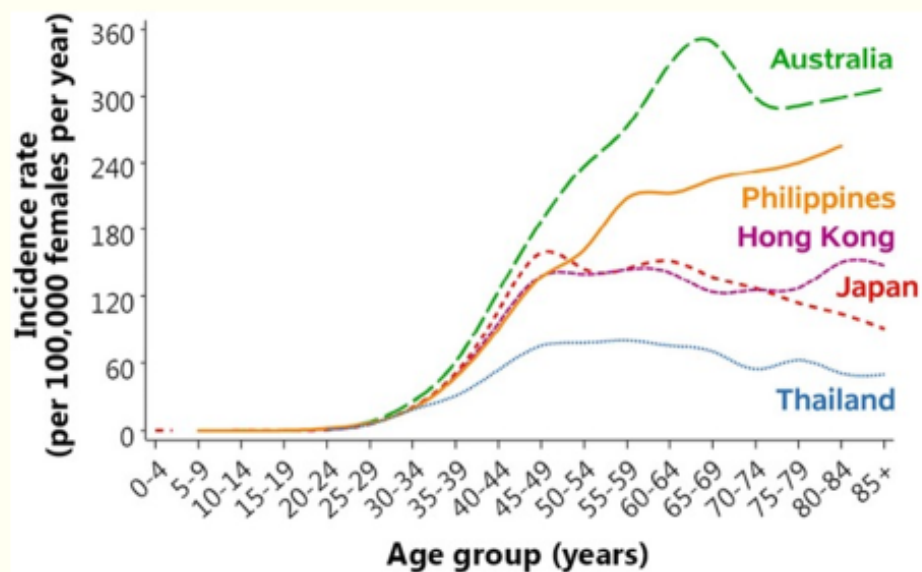
1. Piperine inhibits both the drug transporter P-glycoprotein and the major drug-metabolizing enzyme *CYP3A4*.
2. Almost no curcumin, from turmeric, gets into the bloodstream without piperine from black pepper.
3. Bergamottin, from grapefruit, is a powerful *CYP3A4* inhibitor.

4. Prostate Cancer

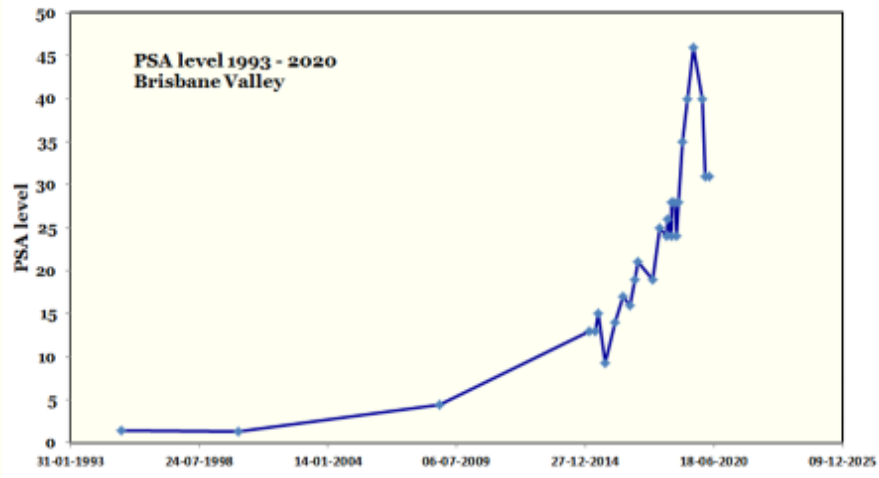
Asians keep their neoplasias under control through their diet.



Why isn't there more interest in the difference between Australian and Thai breast cancer rates?



Prostate Cancer: The large unmet need



The break in uptrend in early 2020 likely caused by boswellia, ashwagandha, andrographis, schisandra and milk thistle.

The prostate is a zinc hog.

Human prostate zinc levels	(nmol/g)
Peripheral zone- normal	3,000–4,500
Peripheral zone- cancer	400–800
Prostatic fluid- normal	8,000–10,000
Prostatic fluid- cancer	800–2000
Other soft tissues	200-500
Blood plasma	150

Prostatic fluid contains 60x the zinc level of blood plasma.

Quercetin is a zinc ionophore.

Evidence that Human Prostate Cancer is a ZIP1-Deficient Malignancy that could be Effectively Treated with a Zinc Ionophore (Clioquinol) Approach

Similar story with selenium.

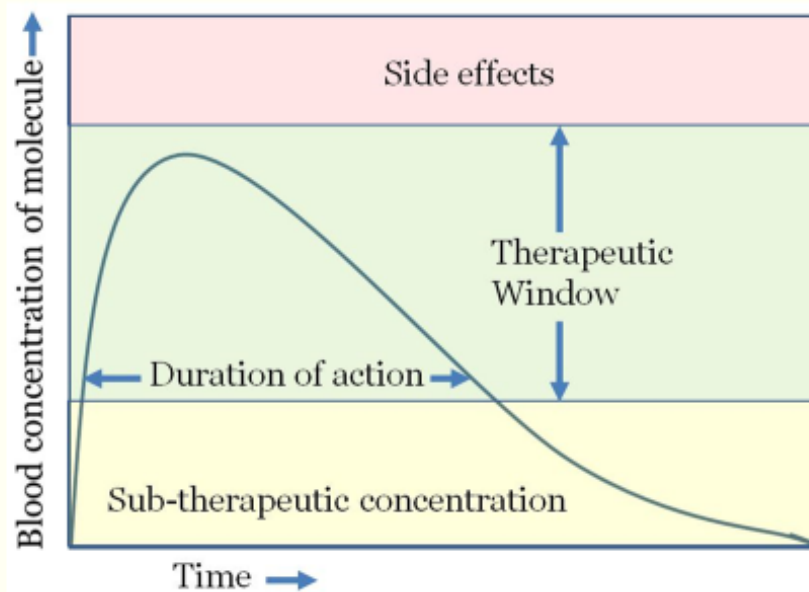
Dosing with Sodium Selenite Cell Type	IC ₅₀ μg/ml
Normal Prostate Epithelial	4.67
LNCaP	0.03
PC-3	0.64
DU145	0.67

Na_2SeO_3 (sodium selenite) is the more potent inducer of apoptosis in normal and cancer prostate cells than *l*-selenomethionine.

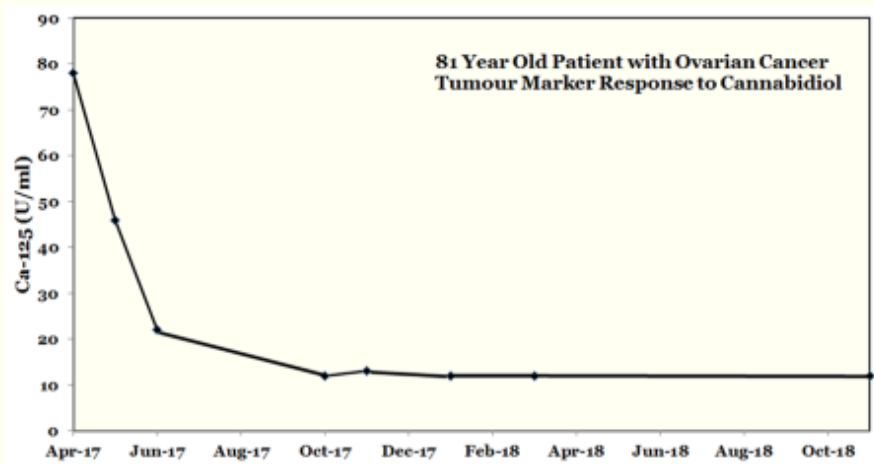
We give our sheep selenium and neglect ourselves?

David G. Menter, Anita L. Sabichi, and Scott M. Lippman, 2000, "Selenium Effects on Prostate Cell Growth"

What makes a good drug: efficacy, bioavailability, half life and therapeutic window.



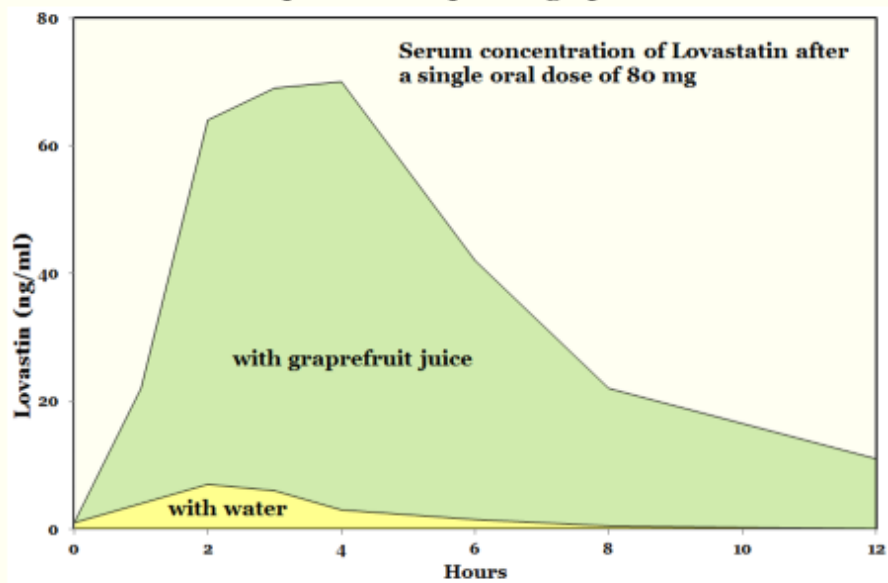
Cannabidiol



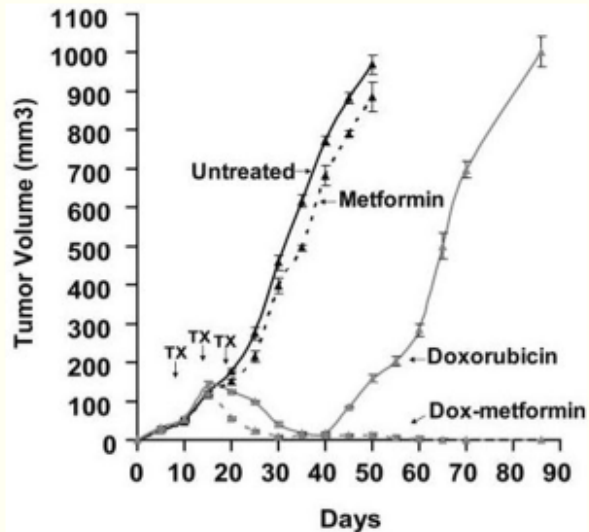
Bioavailability

Oral	6%
Oral with fats	18%
Inhalation	31%

The promise and peril of grapefruit



Bergamottin blocks the metabolising enzyme CYP3A4.



Breast cancer cell line in mice.

Synergy between the chemotherapy drug doxorubicin and diabetic drug metformin.

Cancer stem cells are virtually absent from mice treated with the drug combination, whereas they are easily detected in tumours from mice treated with doxorubicin alone.

Metformin selectively targets cancer stem cells, and acts together with chemotherapy to block tumor growth and prolong remission

Heather A. Hirsch,^{1,2} Dimitris Iliopoulos,^{1,2} Philip H. Tschida,² and Kevin Struhl^{1,4}

5. Plants and the Prostate

Molecule/ Plant	Species Name	Cell Line	IC50 µg/ml	Notes
Ashwagandha	<i>Withania somnifera</i>	PC-3	0.7	Ethanol extract at 7% withanolides
Crepe Ginger	<i>Chelidonium speciosus</i>	PC-3	0.4	Hexane extract
Quercetin		PC-3	6.7	Zinc ionophore as well
		LNCaP	7.0	
Arctigenin	<i>Arctium lappa</i>	LNCaP	0.7	Burdock
Pomegranate	<i>Punica granatum</i>	PC-3	5.0	Peel extract
Longjack	<i>Eurycoma longifolia</i>	LNCaP	6.0	IC50 on normal prostate is ten times higher
Graviola	<i>Annona muricata</i>		~ 5.0	Also custard apple
Boswellia	<i>Boswellia serrata</i>	PC-3	8.0	Frankincense from the Bible
z-guggulsterone	<i>Commiphora myrrha</i>	PC-3	0.3	Myrrh and Frankincense are synergistic
α-Mangostin	<i>Garcinia mangostana</i>	LNCaP	2.4	Mangosteen
		DU145	9.0	
		PC-3	5.1	
Schirubisin B	<i>Schisandra chinensis</i>	PC-3	1.7	Schisandra
Hops	<i>Humulus lupulus</i>	PC-3	9.8	Hop extract is €80/kg - \$0.14 per gram
Ginger	<i>Zingiber officinale</i>	PC-3	12	Dose-limiting stomach irritation
Piperine	<i>Piper nigrum</i>	LNCaP	11.4	CYP3A4 inhibitor in Black Pepper
		PC-3	14.1	
Rottlerin	<i>Mallotus philippensis</i>	PC-3	0.4	Red Kamala
		DU145	0.9	
Cannabidiol	<i>Cannabis sativa</i>	DU145	6.6	Not psychotic - that's THC
Sulforaphane	<i>Brassica oleracea</i>		1.3	
Love Apple	<i>Paris polyphylla</i>	PC-3	4.0	
		DU145	8.0	
Sodium Selenite		LNCaP	0	
		PC-3	0.6	
		DU145	0.8	
Zinc	Zinc citrate, sulphate			

Withaferin A – The literature is confused.

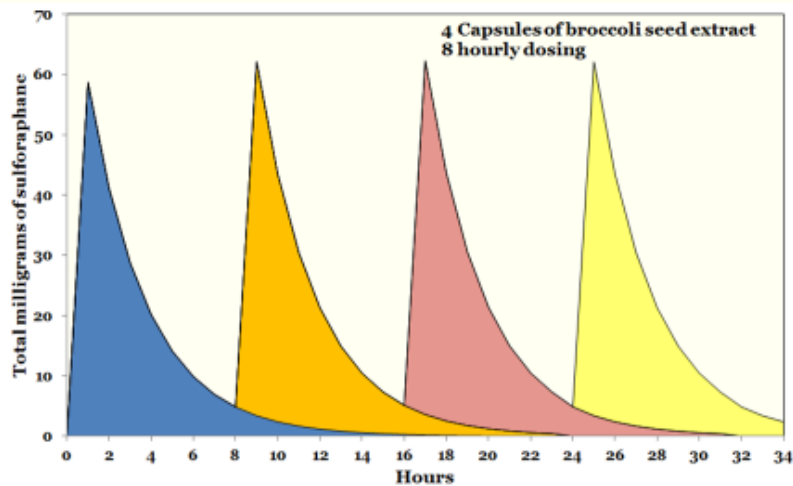
Parameters

Oral bioavailability	32.4 %	
Oral LD50	>2,000 mg/kg	Rats, <i>Withania somnifera</i> extract
Half life	1.36 hours	Sustained release might be necessary

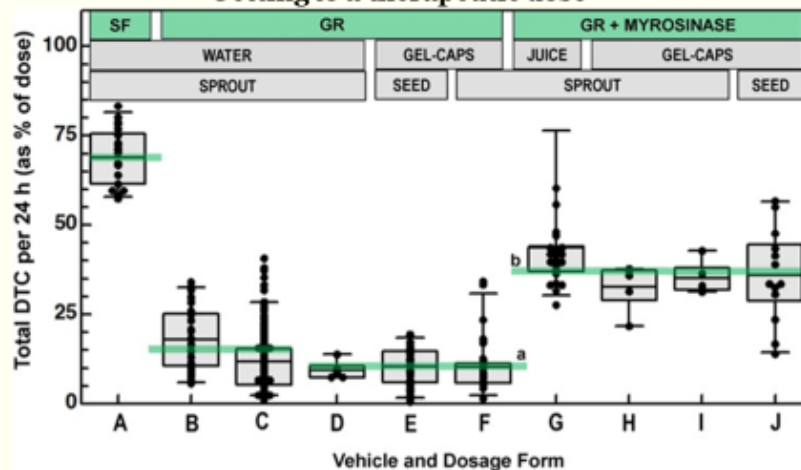
2. Withaferin A - it is important to know that not all withanolides are created equal. Withaferin A is a withanolide that is cytotoxic (toxic to living cells), and we don't want to have it in high concentrations in our ashwagandha extract. This component can be

"Cytotoxic" refers to a substance or process which results in cell damage or cell death. The prefix "cyto" refers to cell and "toxic" to poison. The term is often used to describe chemotherapy drugs that kill cancer cells.

Blood concentration of sulforaphane from broccoli seed extract



Getting to a therapeutic dose



	Price/kg US\$	Bioavailability	Cost per gram of sulforaphane in the blood
Sprout with no myrosinase - retail capsules	\$473	10%	US\$473.33
Seed extract with myrosinase added	\$300	40%	US\$7.50
Synthetic sulforaphane	\$40,000	70%	US\$57.12

42

Relative cost of treatments per cancer cell killed

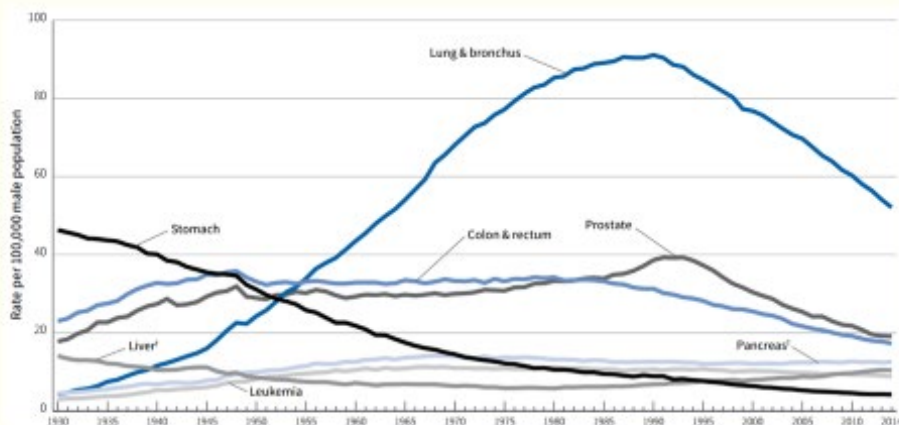
	Price per kg US\$	% Active IC50 Molecule UG/ml	IC50 Inverted	Bioavailability	Half life Hours	Therapy Value	Cost of Therapy Value Unit/US\$
Broccoli Seed Extract	\$300 Wholesale	0.1	1.3	77	0.4	2	\$ 48.75
Hop Extract	\$80 Wholesale	1	9.8	10	0.4	2	\$ 9.80
Ashwagandha	\$280 Retail	1	0.7	143	0.32	1.3	\$ 4.71
Cannabidiol - oral with fat	\$3,000 Wholesale	1	6.6	15	0.18	18	\$ 61.11
Cannabidiol - inhaled	\$3,000 Wholesale	1	6.6	15	0.31	18	\$ 35.48

43

Good plants to have.

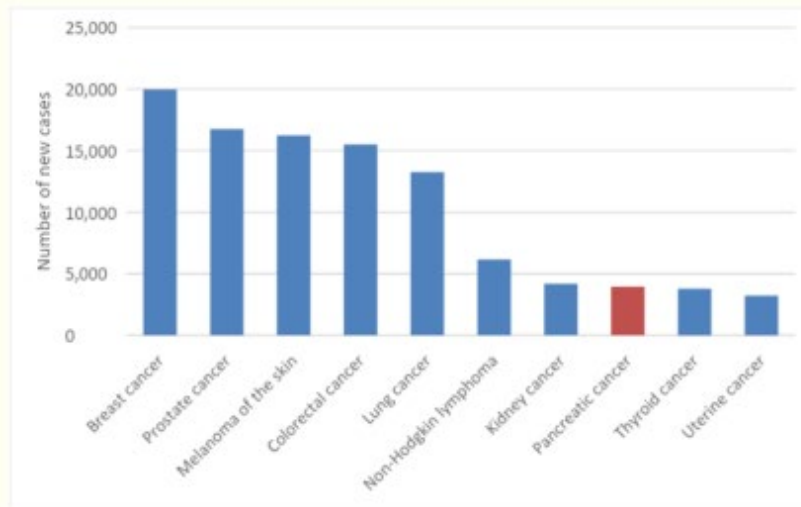
Ashwagandha	<i>Withania somnifera</i>	Hop Bush	<i>Dodonaea viscosa</i>
Barberry	<i>Berberis vulgaris</i>	Japanese Lantern	<i>Physalis alkekengi</i>
Beetroot	<i>Beta vulgaris</i>	Longjack	<i>Eurycoma longifolia</i>
Bitter Melon	<i>Momordica charantia</i>	Malabar Tamarind	<i>Garcinia gambogia</i>
Boswellia	<i>Boswellia</i> spp.	Mangosteen	<i>Garcinia mangostana</i>
Broccoli shoots	<i>Brassica oleracea</i>	Milk Thistle	<i>Silybum marianum</i>
Burdock	<i>Arcium lappa</i>	Naked Lady	<i>Euphorbia tirucalli</i>
Cape Gooseberry	<i>Physalis peruviana</i>	Pigweed	<i>Portulaca oleracea</i>
Cornelian Cherry	<i>Cornus mas</i>	Schisandra	<i>Schisandra chinensis</i>
Crepe Ginger	<i>Cheilocostus speciosus</i>	Soursop	<i>Annona muricata</i>
Custard Apple	<i>Annona cherimola</i>	Tamarillo	<i>Solanum betaceum</i>
Guacatonga	<i>Cassia sylvestris</i>	Tomatillo	<i>Physalis philadelphica</i>
Myrrh	<i>Commiphora</i> spp.		

84 years of US cancer death statistics



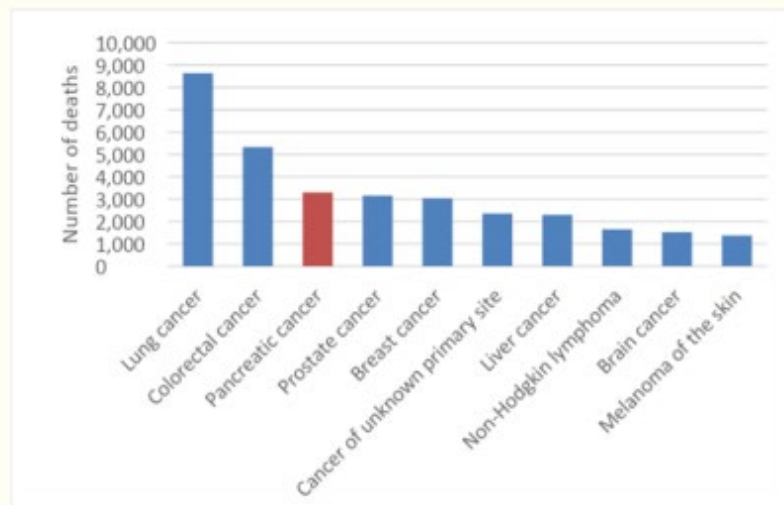
Trends in Age-adjusted Cancer Death Rates* by Site, Males, US, 1930-2014

Australian cancer incidence by organ site

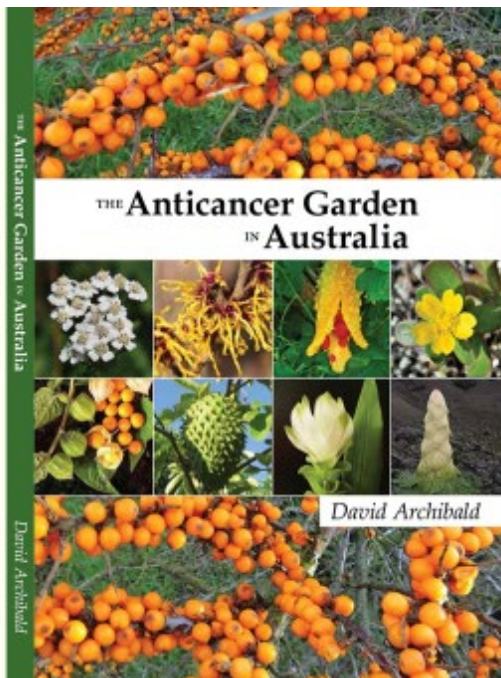


72

Australian cancer deaths by organ site



73



Available from:

www.anticancergardenaustralia.com

Boffin's Books, 88 William St, Perth

Collins Booksellers Cottesloe