

The anticancer effects of plants we can grow.

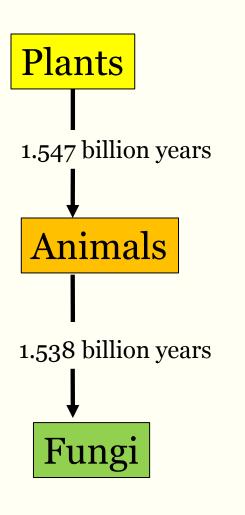
#### <sup>THE</sup>Anticancer Garden ™Australia



David Archibald

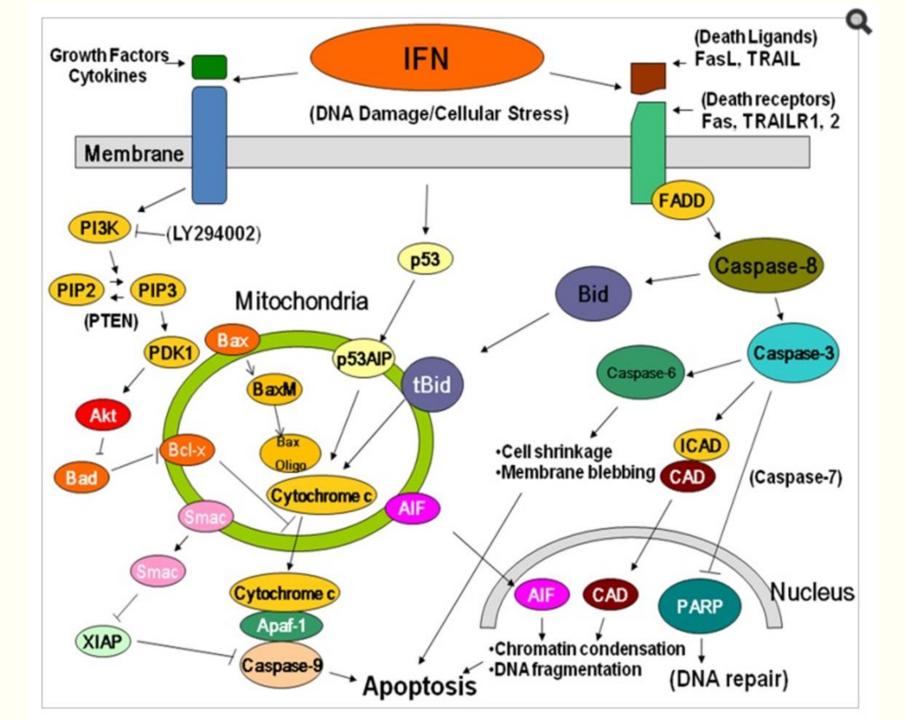
- 1. How we evolved to stop cancer.
- 2. How we know it is the plants.
- 3. Prostate cancer in particular.
- 4. Good plants to have.

2,000 million years of life on this planet before the problem of mutation was largely overcome.



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

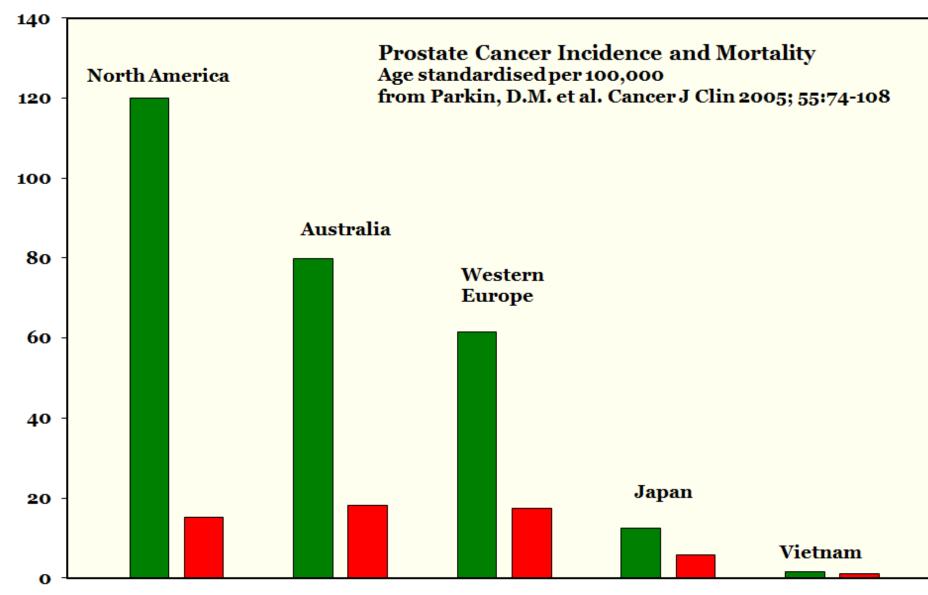
Animals can't make plant molecules but we have the receptors to use them.



Death Receptors	How Chemotherapy and Radiotherapy Work		
	Cell Surface		
A1 Bcl-2 Bcl-XL CED-9 cIAP1 C-IAP2 Cp-IAP FAIM3 FLIP Livin Mcl-1 NAIP Op-IAP Survivin	Anti-apoptotic Proteins	Most cancers are immortal due to the over-production of anti-apoptotic proteins	
XIAP Nucleus	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.		

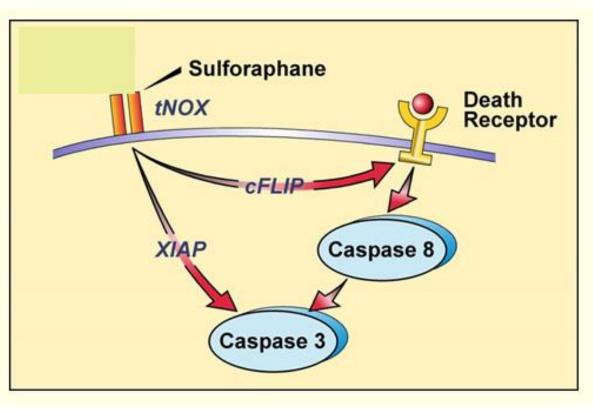
How we know it is the plants -1.

- As with lung cancer, prostate and breast cancer are largely self-inflicted.



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.

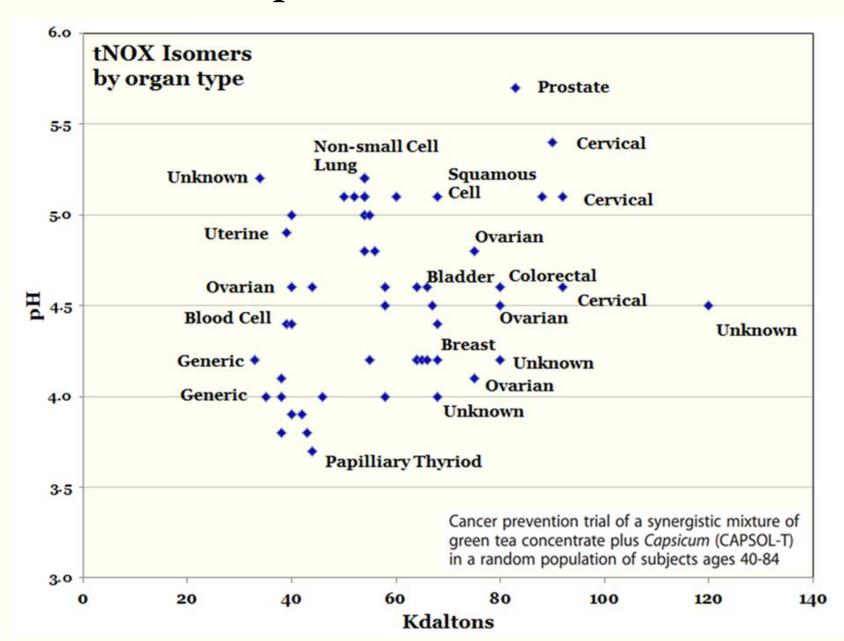


Upon a cell becoming a cancer cell, 40% of NOX molecules will switch to the tumour variant, tNOX.

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.

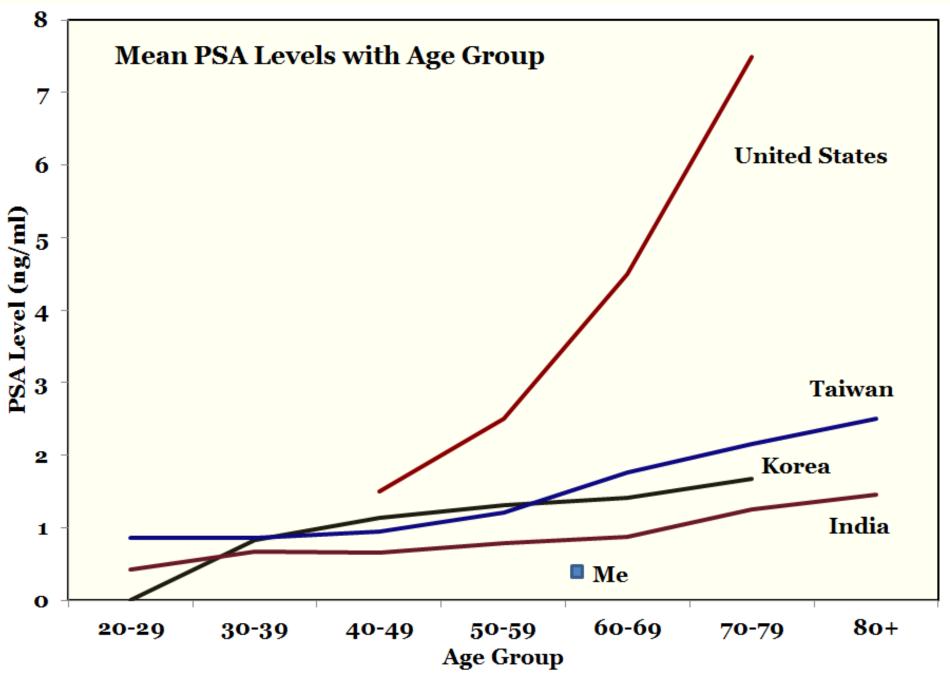
#### How we know it is the plants -2. - the tNOX receptors



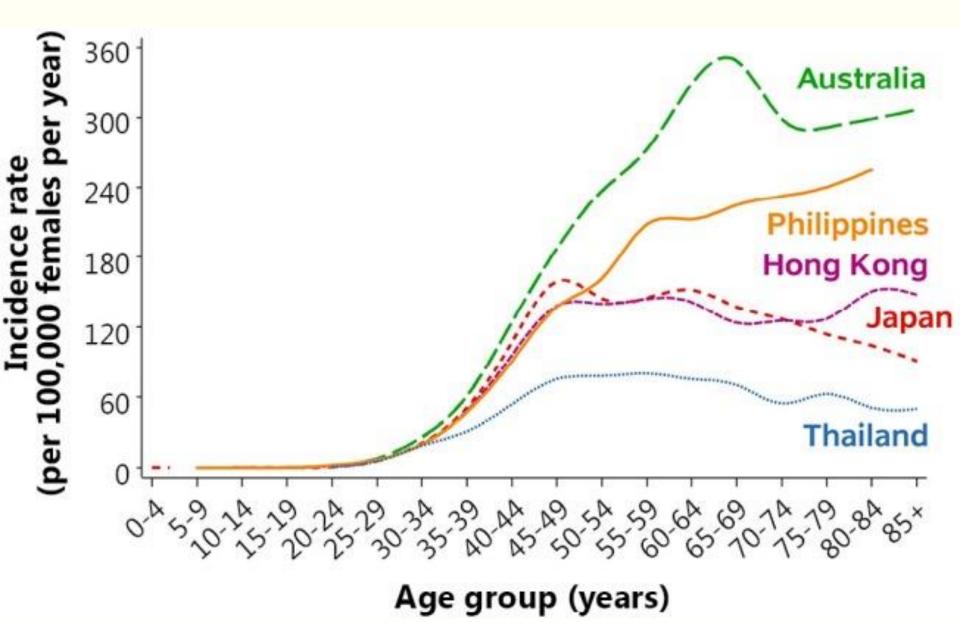
#### How we know it is the plants -3. - β-glucuronidase

- 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  $\beta$ -glucuronidase cleaves the sugar molecule off the foreign molecule which regains its original functionality.
- 3. Cancer cells over-express  $\beta$ -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?

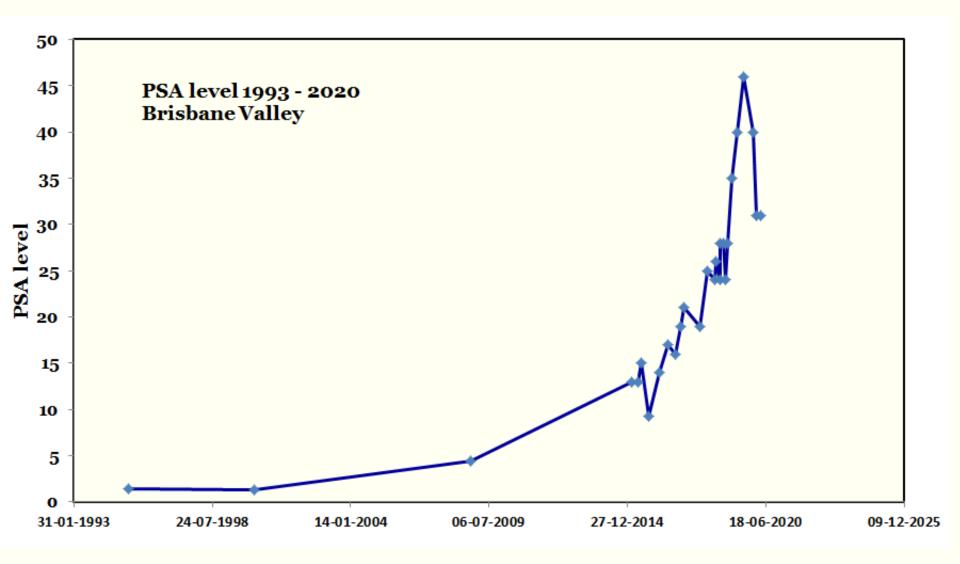
Asians keep their neoplasias under control through their diet.



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

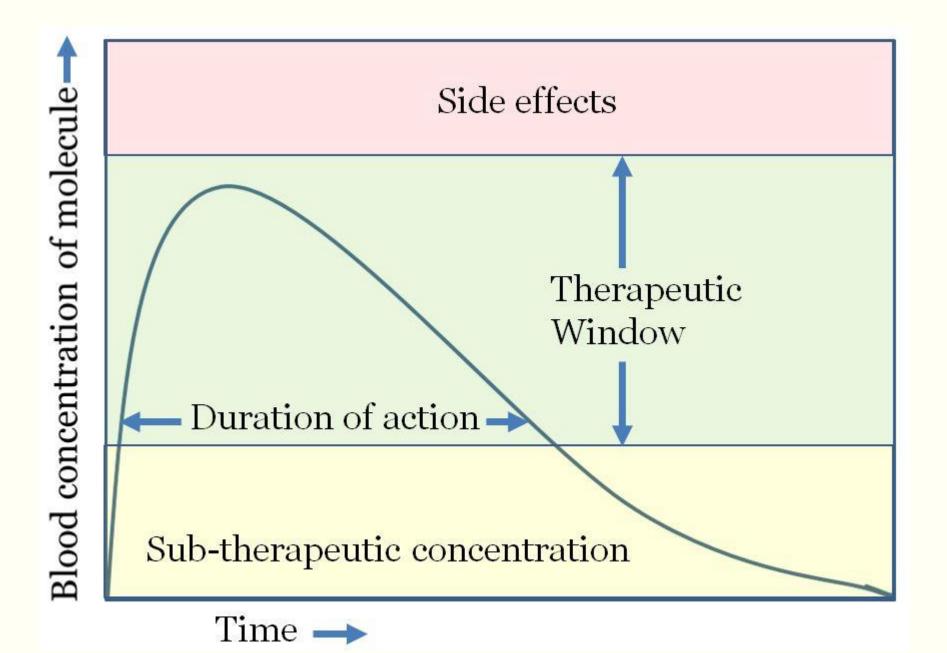


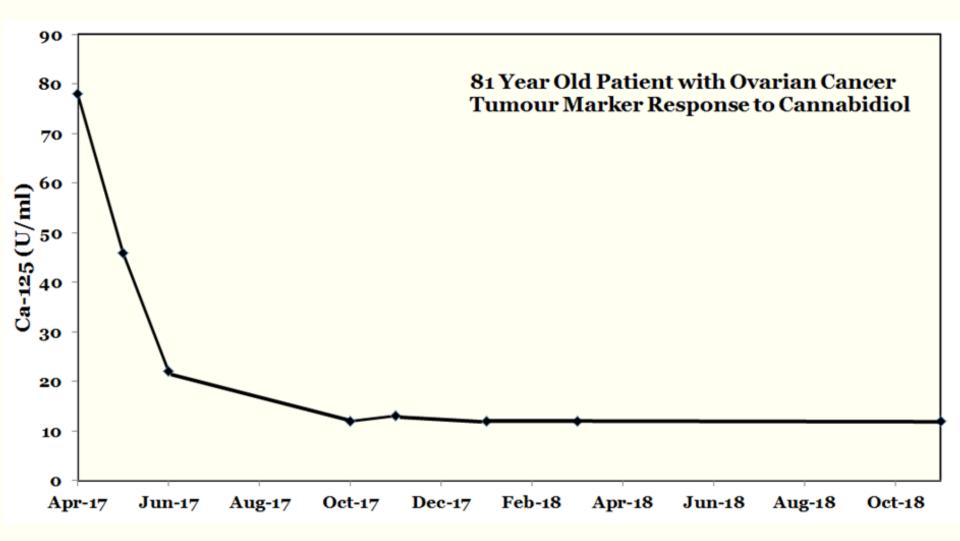
#### **Prostate Cancer: The large unmet need**



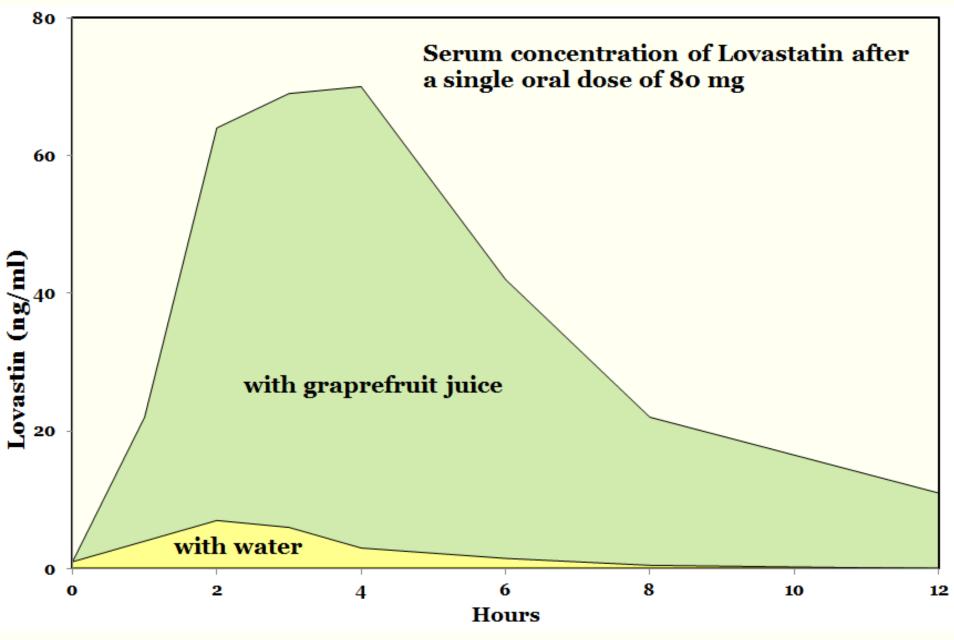
The break in uptrend in early 2020 likely caused by boswellia, ashwagandha, andrographis, schisandra and milk thistle.

What makes a good drug: efficacy, bioavailability and therapeuctic window.

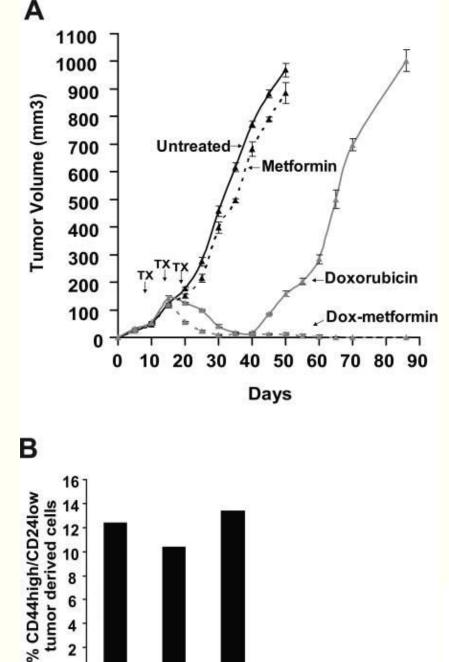




#### The promise and peril of grapefruit



Bergamottin blocks the metabolising enzyme CYP3A4.



0

Dox treated

tumors

Dox /met treated

tumors

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, 1,3 Dimitrios Iliopoulos, 1,3 Philip N. Tsichlis, 2 and Kevin Struhl 1,4

#### Good plants to have.

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

## Ashwagandha

Shrub

The main plant in Ayurvedic medicine.

Withaferin A has an IC50 of 0.27 µg/ml against the breast cancer cell line MCF-7.

Also an adaptogen.



#### Barberry

Shrub

Source of the molecule berberine.

Rich in vitamin C.

Ethanolic extract has an IC50 of 3.5 µg/ml against the breast cancer cell line MCF-7.



#### Beetroot

Anti-oxidant effect from betalain content.



#### Bitter Melon

#### Vine

A molecule isolated from bitter melon, karaviloside III, produced an IC50 result against three liver cancer cell lines as low as  $2.3 \mu g/ml$ .



### Boswellia

Desert tree.

Frankincense from the Bible.

Extract of the resin produced an IC50 against the breast cancer cell line MDA-MB-231 of  $6.0 \mu g/ml$ .



#### Broccoli

Glucoraphanin is concentrated in the seed.

Needs active myrosinase.

10%, 40%, 70% bioavailability.

Sulforphane is a powerful anticancer molecule with a wide therapeutic window but short half life.

Sulforaphane's IC50s against a range of cancer types is typically in the range of 1.0 to 2.0  $\mu$ g/ml; for example it is 1.0  $\mu$ g/ml for the bladder cancer cell line RT4.



#### Burdock

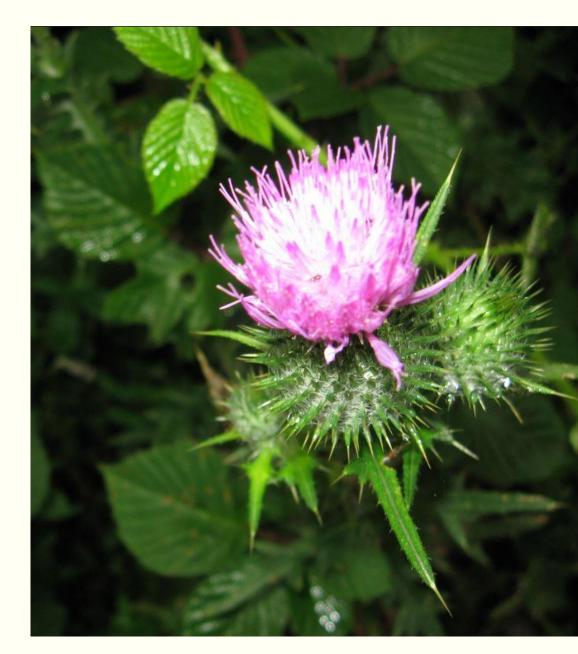
Biennial up to three metres.

From the forgotten European tradition.

Arctinigen is the active molecule.

Arctigenin at lower doses equating to less than 0.7µg/ml inhibited the prostate cancer cell lines LNCaP and LAPC-4 by 30 to 50 per cent at 48 hours.

Used for cancer in dogs.



#### Cape Gooseberry

Perennial to 1.6 metres.

Is "a popular folk medicine used for treating cancer, leukemia, hepatitis and other diseases."

Work on the molecule withanolide E isolated from cape gooseberry determined an IC50 for it against the lung cancer cell line H1299 at 48 hours of 0.71  $\mu$ g/ml.



## **Cornelian Cherry**

Deciduous shrub or small tree growing to five metres high.

An ethanolic extract of cornelian cherry fruit was tested against the lung non small cell cancer line A549, the breast cancer cell line MCF-7, the ovarian cancer cell line SKOV3 and the prostate cancer cell line PC3 and determined that the IC50s were all under 5  $\mu$ g/ml.



#### Crepe Ginger

Can grow to three metres in frost-free areas.

Hexane extract had results of an IC50 of 0.35  $\mu$ g/ml for the prostate cancer cell line PC-3 for 72 hours, and 48 hour IC50s of 0.6  $\mu$ g/ml for the breast cancer cell line MCF-7, 0.35  $\mu$ g/ml for the colon cancer cell line HCT-116 and 0.6  $\mu$ g/ml for the liver cancer cell line HepG2.



## Custard Apple

Can grow to ten metres.

Essential oil of custard apple was found to have IC50s of  $3.4 \ \mu\text{g/ml}$  against the breast cancer cell line MCF-7,  $3.0 \ \mu\text{g/ml}$  against the colon cancer cell line CACO and  $3.7 \ \mu\text{g/ml}$ against the liver cancer cell line HepG2.



#### Guacatonga

Shrub to three metres.

One of the most effective plants in South American traditional medicine.

Hexane extract of guacatonga bark produced IC50s of 0.1  $\mu$ g/ml for the colon cancer cell line HCT-8, 0.9  $\mu$ g/ml for the brain cancer cell line SF-295, 1.2  $\mu$ g/ml for the melanoma cell line MDA-MB-435 and 1.3  $\mu$ g/ml for the leukaemia cell line HL-60





### Myrrh

Semi-arid shrub to four metres.

From the Bible.

An IC50 against the prostate cancer cell line LNCaP equating to  $0.3 \mu g/ml z$ -guggulsterone content.

## Hop Bush

Hardy Australian native.

The ethanolic fraction of hop bush was found to have an IC50 against the ovarian cancer cell line A2780 of  $6.0 \mu g/ml$ 



#### Japanese Lantern

Perennial up to half a metre.

Very cold hardy.

Physalin B has IC50s of 0.26  $\mu$ g/ml against the cervical cancer cell line HeLa, 0.44  $\mu$ g/ml against the liver cancer cell line SMMC-7721 and 0.57  $\mu$ g/ml against the liver cancer cell line HL-60.



## Longjack

Tall, slender evergreen shrub-tree from southeast Asia.

Boosts testosterone while inhibiting prostate cancer with an IC50 of 5.9  $\mu$ g/ml.



#### Malabar Tamarind

Tree native to India, grows to 18 metres.

One of the plant's molecular components, gambogic acid, has displayed very good results in the laboratory with an IC50 over 48 hours of 1.1  $\mu$ g/ml against the melanoma cell line A375.



#### Mangosteen

Difficult to grow - picky about elevation, humidity and require annual rainfall of at least a metre with no drought.

 $\alpha$ -mangostin from the flesh of mangosteen fruit has IC50s of 2.6  $\mu$ g/ml against the squamous cell carcinoma cell line SCC-15 and 3.9  $\mu$ g/ml against the glioblastoma multiforme cell line U-118 MG.



## Milk Thistle

Common weed up to two metres.

Traditionally used to treat liver disorders.

Silymarin was found to have an IC50 of 0.7  $\mu$ g/ml against the liver cancer cell line HepG2.



## Naked Lady

Hardy, leafless ornamental shrub up to seven metres.

The milky latex is toxic and can cause blindness.

Wear eye protection gear and gloves for handling the plant.

In cancer, naked lady latex has been successfully used to treat skin cancers and ulcers.

Cut off a twig and apply the sap directly to the skin cancer or neoplasia to be treated.



## Pigweed

Annual succulent and ground cover.

Henry VIII used it for swollen prostate.

In a study of the anticancer efficacy of the methanolic extract of 13 Korean salad vegetables, pigweed extract produced an IC50 of less than  $25 \mu g/ml$  against the lung cancer cell line Calu-6.



#### Schisandra

Woody vine native to China, Korea, Japan and Russia.

Cultivation is challenging.

Schirubrisin B was found to have IC50s of  $1.7 \mu$ g/ml against the prostate cancer cell line PC-3 and  $6.9 \mu$ g/ml against the breast cancer cell line MCF-7.



#### Soursop

Native of the Caribbean to 10 metres.

Traditionally used for cancer.

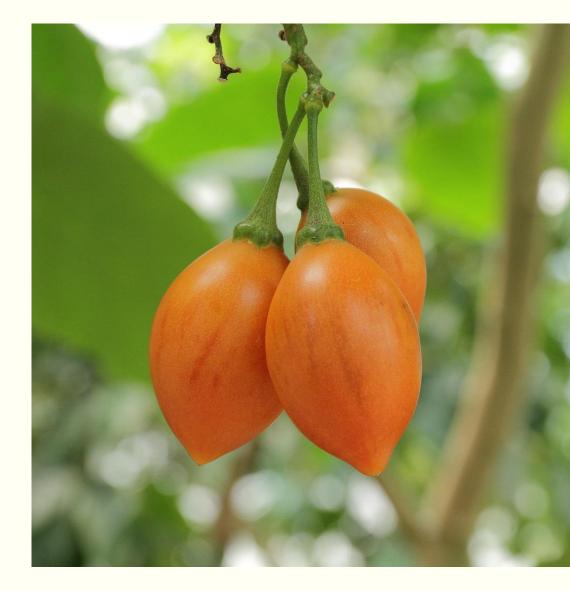
Ethyl acetate extract of soursop leaves produced IC50s of 11.4  $\mu$ g/ml against the colon cancer cell line HT-29 and 9.0  $\mu$ g/ml against the colon cancer cell line HCT-116.



## Tamarillo

Fast-growing evergreen shrub to two metres.

Ethanolic extract was found to have IC50s of 10  $\mu$ g/ml against the liver cancer cell line HepG2.





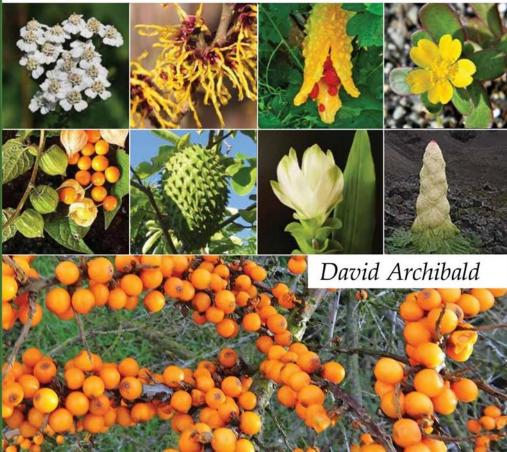
#### Tomatillo

Perennial shrub to two metres.

One of the molecules in tomatillo, a withanolide called ixocarpalactone A (IxoA), was found to have an IC50 of  $3.8 \mu g/ml$  against the mouse liver cancer cell line Hepa-1c1c7.



#### ™Anticancer Garden Australia



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