



# **Glucosinolates from Brassica vegetables: risks and benefits**

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# Glucosinolates

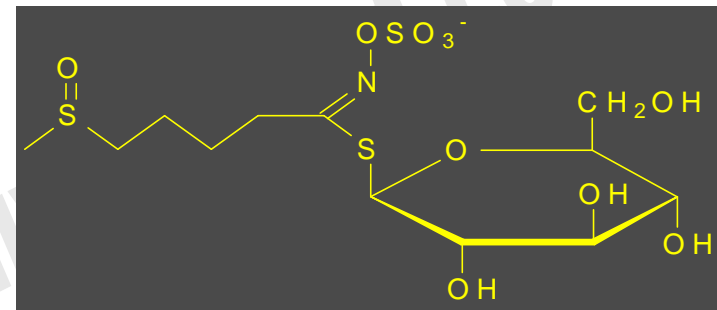
- Glucosinolates occur in Cruciferous plants.
- On damage to the plant, including food processing, chewing, cooking, etc., the glucosinolates breakdown into a variety of highly bioactive products.
- The breakdown products are isothiocyanates, nitriles, epithionitriles and thiocyanates.

# Glucosinolate breakdown

glucosinolates e.g.  
glucoraphanin

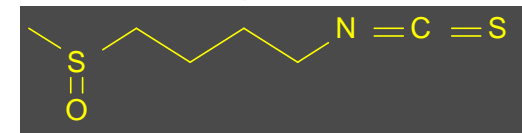
phytochemical

sugar



Myrosinase in the plant or colon bacteria

myrosinase



sulforaphane

Compound	Source	Flavour/taste, quality
2-Propenyl isothiocyanate	Horseradish, mustard	Pungency, lachrymatory, bitter
2-Propenyl thiocyanate	Horseradish	Horseradish, garlic-like, lacking in pungency and lachrymatory quality
3-Butenyl isothiocyanate	Brown mustard	Pungency, aroma
4-Pentenyl isothiocyanate	Horseradish	Acrid, fragrant leaf
3-Methylpropyl isothiocyanate	Horseradish	Acrid, leaf green aroma
2-Phenylethyl isothiocyanate	Horseradish, watercress, turnip	Strong aroma of watercress, tingling sensation
2-Phenylethyl nitrile	Watercress	Very weak watercress, almost odourless
<i>p</i> -Hydroxybenzyl isothiocyanate	Radish	Pungency, no aroma
4-Methylthiobutyl isothiocyanate	Rutabaga	Pungency, sulfury aroma
Benzes thiocyanate	Cress	Radish-like
5-vinyloxazolidine-2-thione	Cabbage, Brussels sprouts	Garlic-like
Methyl isothiocyanate	Horseradish	Bitter
Ethyl isothiocyanate		Powerful lachrymator, horseradish-like
<i>iso</i> -Propyl isothiocyanate		Extremely pungent, garlic-like
		Pungent

## Several decades ago:

- Glucosinolate breakdown products were considered only as natural toxicants.
- Oil seed rape contained a high level of progoitrin, a glucosinolate which exhibited some toxic properties when given in high amounts to farm animals.
- This led to the development of varieties of oil seed rape low in glucosinolates (and also erucic acid).

# Isothiocyanate-protein interactions

## **XLIII. A NOTE ON THE COMBINATION OF CYSTEINE WITH ALLYL ISOTHIOCYANATE**

BY ARCHIBALD TODRICK AND ERNEST WALKER

*From the Department of Biochemistry, Oxford*

*(Received 29 December 1936)*

IN an earlier paper [Walker, 1925] it is recorded that the sulphhydryl group of tissues and muscle protein disappears on treatment with allyl isothiocyanate. The

hydantoins of cystine and cysteine [Nicolet, 1930] have been described. Aschan [1884] reported failure of reaction between amino-acids and alkyl isothiocyanate;

# 50mg benzyl isothiocyanate/g protein reduced protein intake and weight gain in growing rats

Protein intake and growth response of rats fed for 9 days with egg white proteins and its BITC derivatives (50mg/g protein)

Group/diet <sup>2</sup>	Protein intake (g)	Weight gain (g)	Weight gain/ g protein consumed
Casein + Met (I)	7.37 ± 0.03 <sup>AB</sup>	23.1 ± 1.2 <sup>A</sup>	3.13 ± 0.16 <sup>A</sup>
Egg white (II)	7.38 ± 0.03 <sup>A</sup>	23.1 ± 0.9 <sup>A</sup>	3.13 ± 0.13 <sup>A</sup>
Egg white + BITC (III)	6.14 ± 0.24 <sup>C</sup>	9.4 ± 1.5 <sup>B</sup>	1.51 ± 0.21 <sup>B</sup>
Egg white + BITC + Lys (IV)	6.95 ± 0.19 <sup>B</sup>	19.6 ± 1.9 <sup>A</sup>	2.81 ± 0.25 <sup>A</sup>

<sup>1</sup>Values are means ± SEM ( $n = 6$ ). Means in each column having different superscript letters are significantly different ( $P < 0.05$ ).

<sup>2</sup>For composition of the diets see Methods and materials.

# Toxicities of various dietary compounds

	LD50	NOAEL
	(mg/kg rat)	(mg/kg/day)
allyl isothiocyanate	112	
allyl nitrile	115	
phenethyl isothiocyanate	700	
quercetin	159	
vitamin D	42	
vitamin C	11900	
vitamin K	500	
proanthocyanidins	>5000	1400
green tea flavanols		1000



# Toxicity at high doses of pure compounds

- Thyroid gland, liver, kidney, and pancreas are the main targets.
- In rats, toxicity at daily doses  $> 10 - 50$  mg/kg body weight. At such high concentrations, certain isothiocyanates and nitriles may initiate mutagenic, cytotoxic, and carcinogenic processes.
- Promoter post-initiation effects of phenethyl isothiocyanate and butyl isothiocyanate on liver and bladder carcinogenesis in rats pre-treated with nitrosamines.
- Thyroid-toxicity in animal experiments: certain isothiocyanates interfere with the synthesis of thyroid hormones, whereas thiocyanates compete with iodine and inhibit iodine uptake by the thyroid gland.

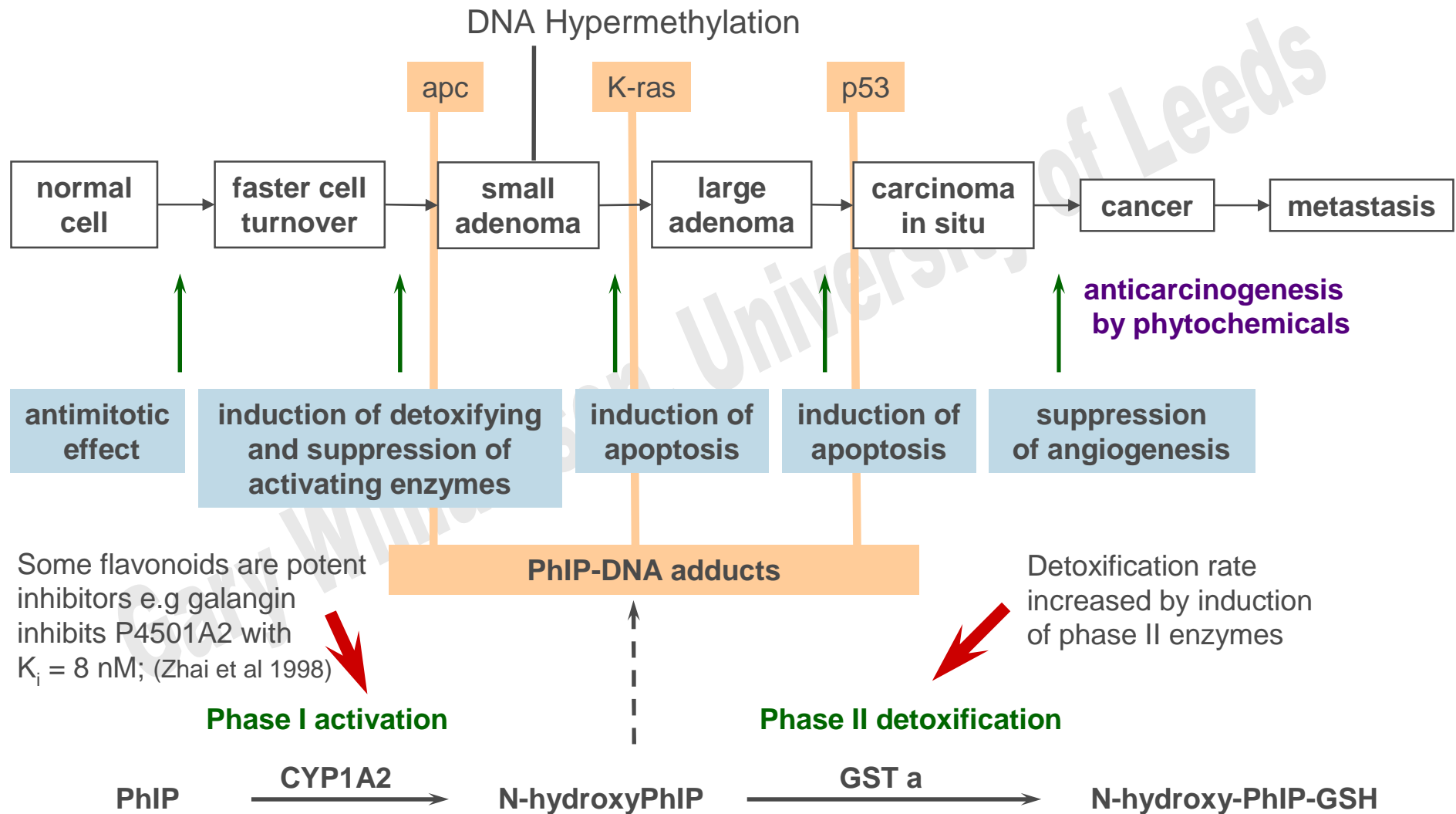
## However...

- The situation changed in 1992 after the identification and purification of sulforaphane (from glucoraphanin), which showed anticarcinogenic properties.
- Substantial research effort has now confirmed this, at least in vitro and in animal models.
- This highlights the dual nature of many naturally occurring compounds in plants, but the concept is not new to nutrition.

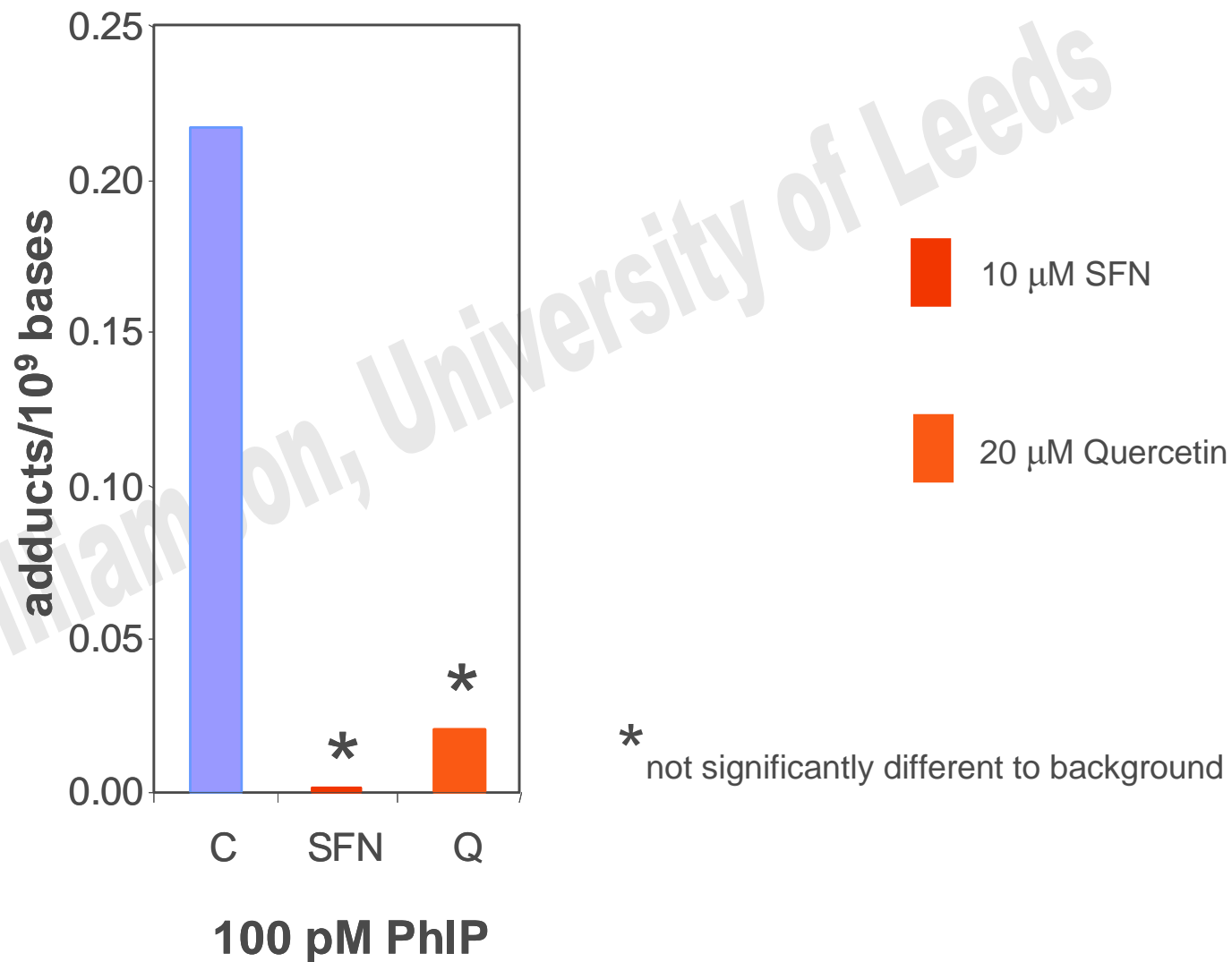
## Beneficial effect of Cruciferous vegetables:

- Isothiocyanates are potent inducers of Phase II detoxification enzymes, and increase the metabolism and detoxification of chemical carcinogens *in vitro* and in animal models.
- Some inhibit mitosis and stimulate apoptosis in tumour cells by blocking DNA damage, thus inhibiting the growth of tumour cells after initiation by chemical carcinogens.

# Synergistic effects may occur with other compounds of the diet at all stages of carcinogenesis



# <sup>14</sup>C-PhIP DNA adducts formed in human cultures HepG2 cells after 24h treatment with PhIP– modification of dose response by sulforaphane or quercetin



# Epidemiology: most studies support a protective effects of Brassicas

6 cohort studies: inverse associations between brassica consumption and risk of lung cancer, stomach cancer, all cancers taken together.

64% of 74 case-control studies: inverse association between consumption of one or more brassica vegetables and risk of cancer at various sites.

Comparison of the diets of 2,832 postmenopausal women diagnosed with invasive breast cancer, to the diet of 2,650 healthy women of the same age. Result: no correlation between total fruit and vegetable consumption and breast cancer risk but women consuming 1 to 2 servings of Brassica vegetables daily had a 20 to 40 % decreased risk of breast cancer

'Health Professionals' study followed over 47,000 men for 6.3 years and compiled food intake data for 8 years. Brassica vegetable consumption was related to a 51 % reduction in the risk of bladder cancer

No effect of brassica consumption

e.g.

'pooled analysis of cohort studies' conducted by Smith-Warner et al.

# U shaped curve

- The U shaped dose-response curve is now a commonly accepted concept in nutrition and toxicity
- Paracelsus said, more than 400 years ago, that the dose makes the poison.
- This implies that all substances which are biologically active – whether from food, drugs or other chemicals – can have possible toxicity, but this depends on the dose.

# U shaped curve

- This applies equally to vitamins, minerals, and naturally occurring plant products.
- The high amounts are generally not achievable through normal dietary means such as food, but can only be obtained from heavily fortified foods or “mega-dose” supplements.

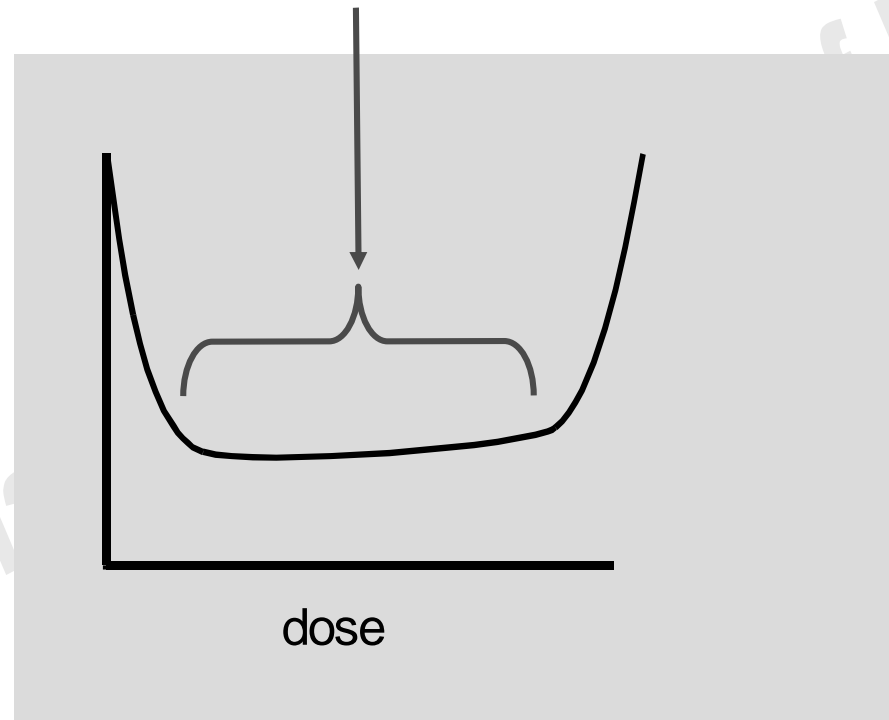
Gary Williamson, University of Leeds



# Dose-response – the key!

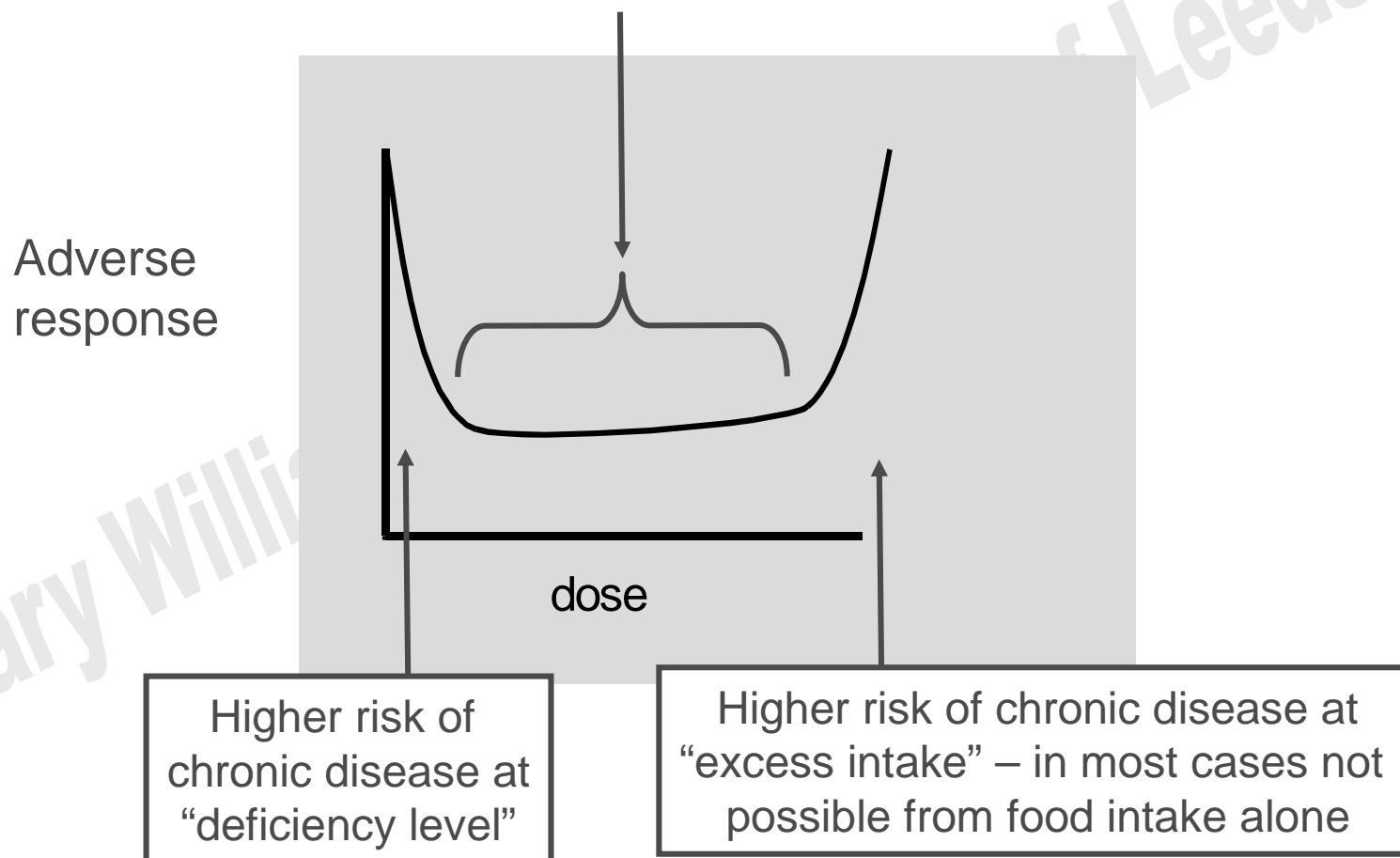
Best effect on health at optimum levels

Adverse  
response



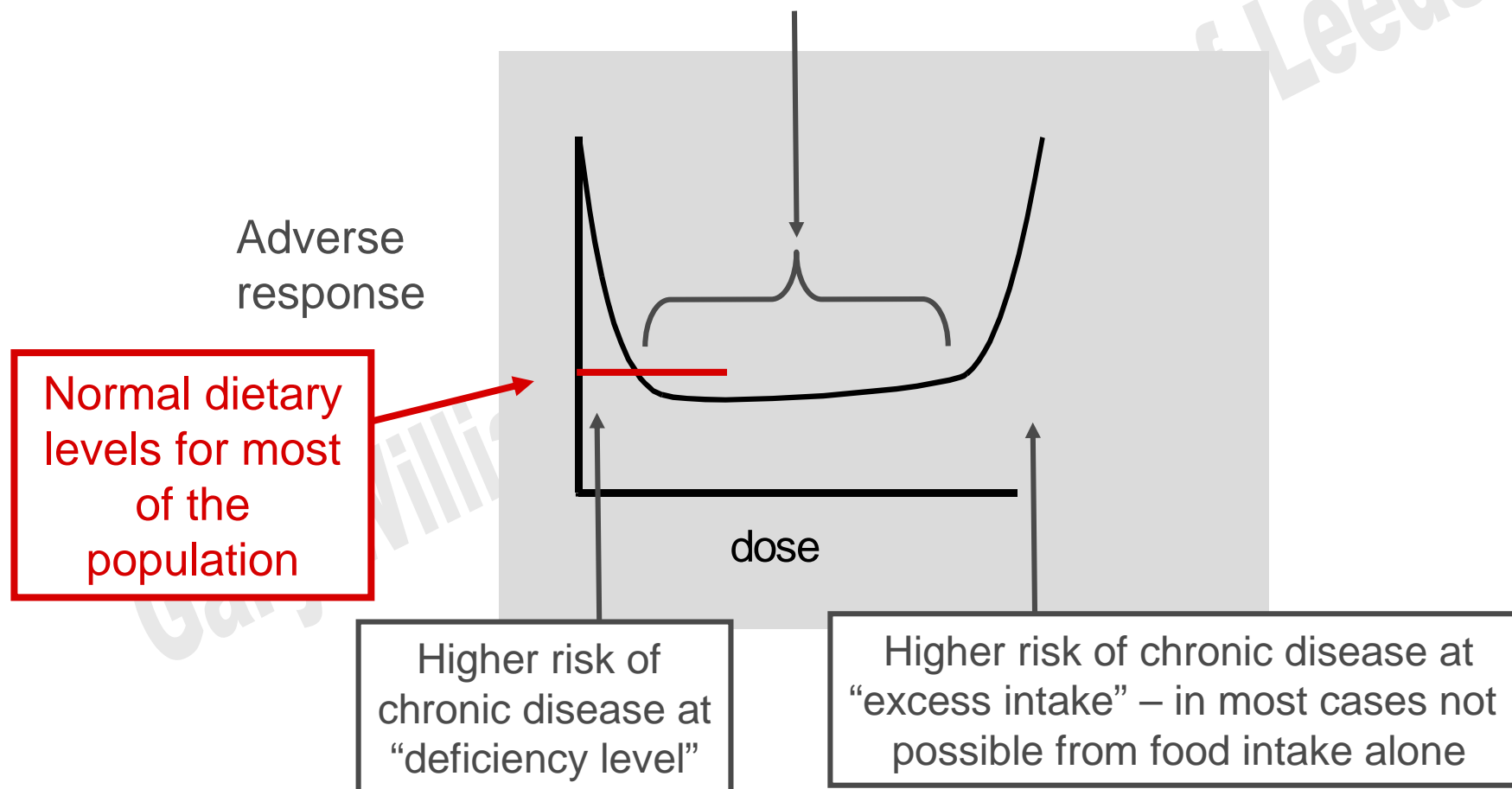
# Dose-response – the key!

Best effect on health at optimum levels



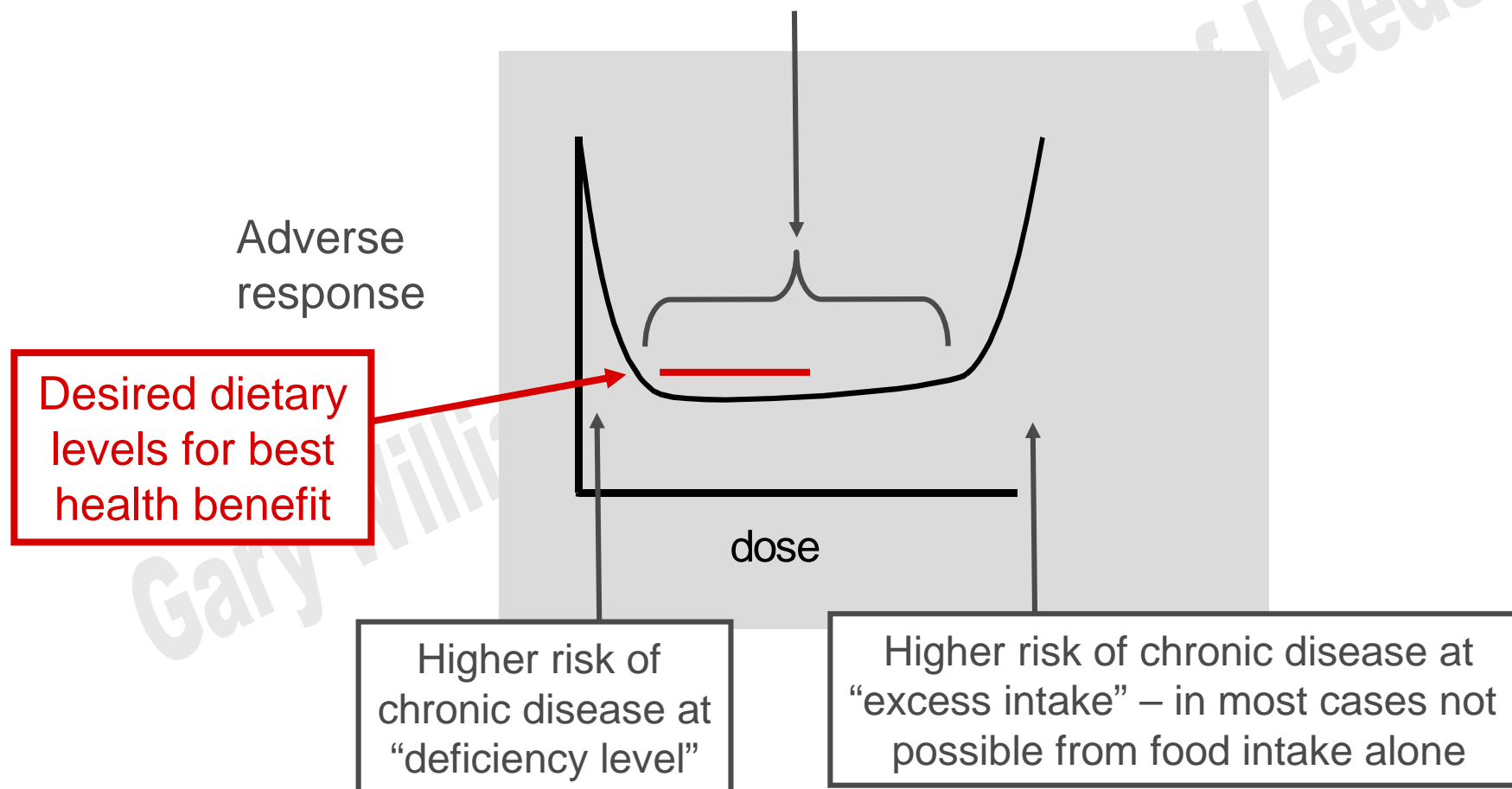
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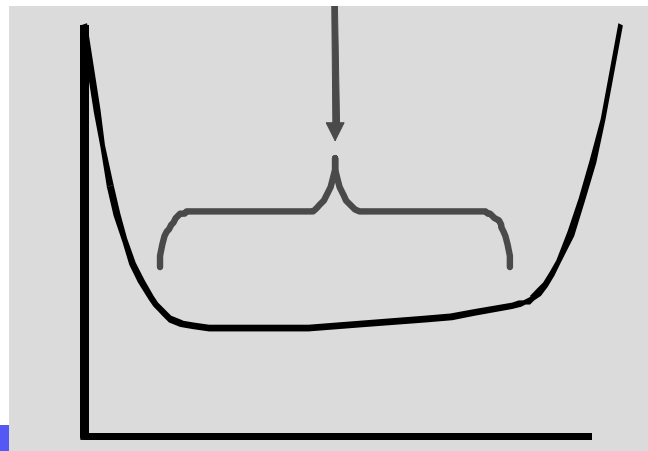
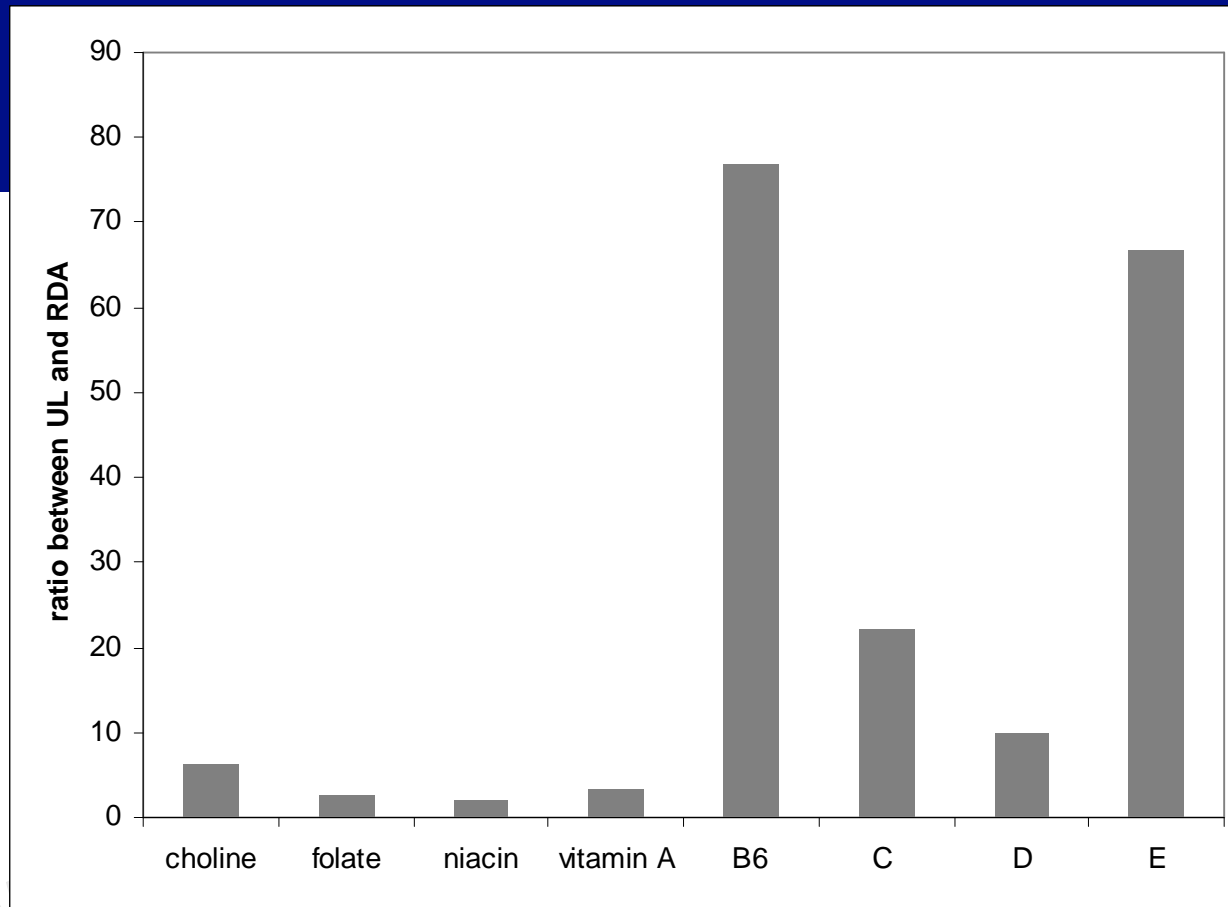
Best effect on health at optimum levels



# Dose-response – the key!

Best effect on health at optimum levels





# Intake of glucosinolates

- Daily intake of two glucosinolates, glucobrassicin and neoglucobrassicin, was 5.0 and 0.5 mg/capita/day in the Danish and 2.5 and 0.3 mg/day in the Finnish population respectively
- These average values might be very different in individuals, who like or dislike Brassicas.
- In Potsdam, Germany, the average daily cabbage consumption was 54 g/capita/day, mainly white cabbage, cauliflower and red cabbage; consumption increased with age.
- The intake was slightly higher in the winter compared to the summer.
- The uptake of progoitrin was relatively low with only 3 and 2 mg/capita/day in winter and summer, respectively.

# Conclusions

- Brassica vegetables in the diet are not toxic or dangerous in any way: in fact, increased consumption is desirable
- Supplements containing purified compounds, derived from Brassicas, should be viewed with caution
- Content-enhanced functional foods may be a way of increasing protective effects from Brassica vegetables, but should be tested for safety
- Better ways of processing could be beneficial to optimise the original and natural content of processed foods