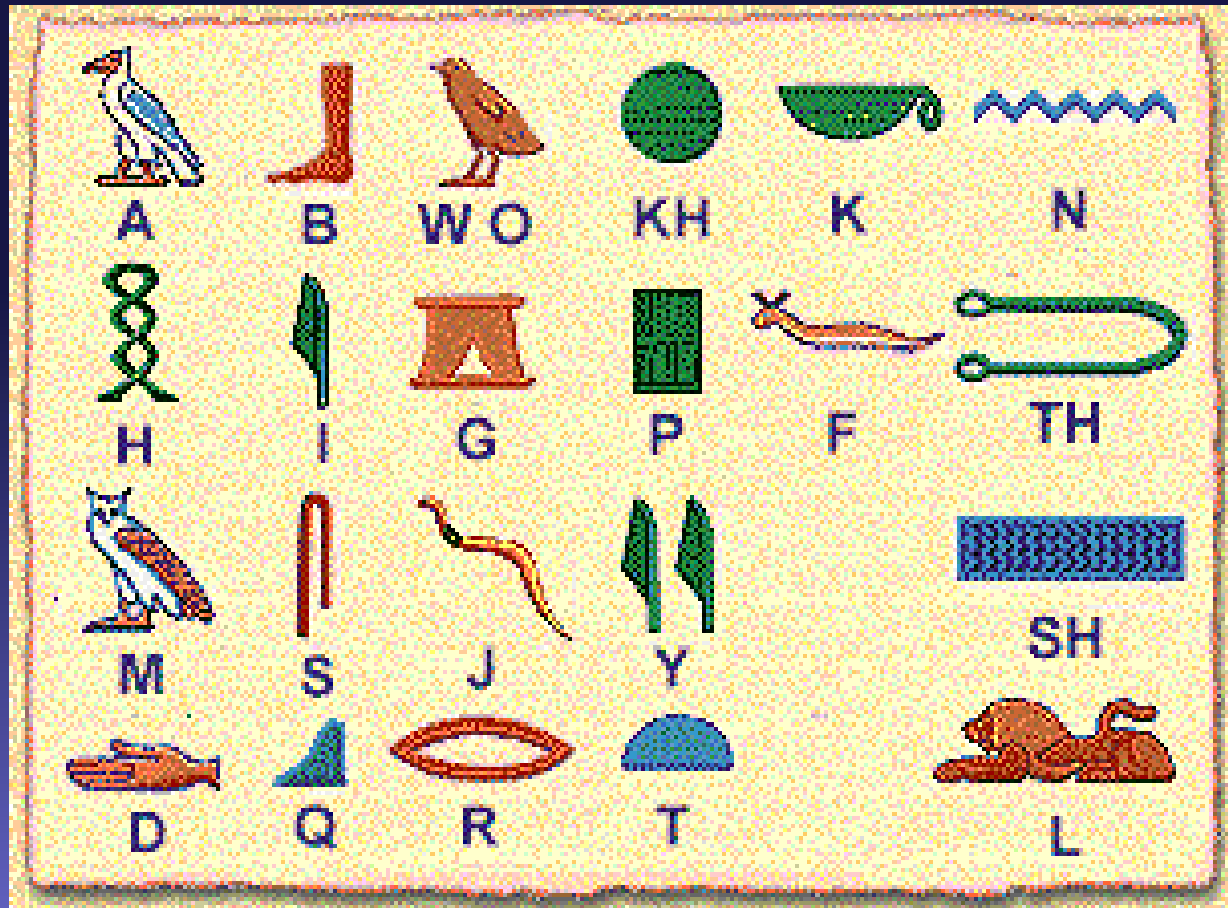


# Beyond dose-response: concentration responses and food

Dr. Jaap C. Hanekamp  
Roosevelt Academy Middelburg, The Netherlands  
Univ. of Massachusetts, Amherst, MA

Prof. dr. Aalt Bast  
Department of Toxicology, Maastricht University  
The Netherlands

# Food taster: a risky occupation





He restored the  
chief cupbearer to  
his position,  
so that he once  
again put the cup  
into Pharaoh's  
hand, but he  
hanged the chief  
baker.

Genesis 40: 21



**Ukraine president (candidate) Viktor Yushchenko in  
2004  
before (L) dioxin poisoning and after (R)**

**Aalt,**

**Apparently for pharaohs and presidents, food  
can be rather unsafe and they protect themselves.**

**But how does the consumer ensure that his food is safe?**

# Organic farming?





**Jaap,**

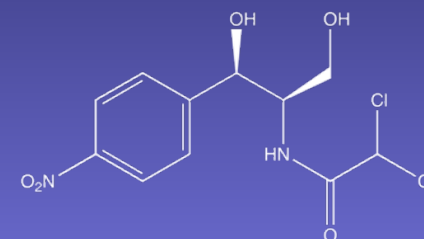
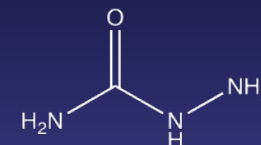
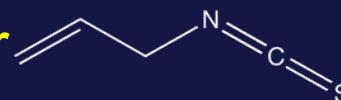
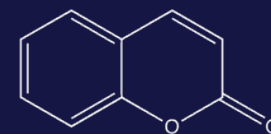
**The consumer has a skewed perspective on food safety.**

**But food, obviously, has to be safe, right, that is without harmful chemicals?**



**Natural Toxins:  
Name  
your Poison**

- *Coumarin*, one of the compounds in cinnamon, is moderately toxic to liver and kidneys.
- *Benzo[a]pyrene* is found in coffee and is a well-known carcinogen.
- *Allyl isothiocyanate* causes the pungent taste of mustard and wasabi and is a strong lachrymator and moderately toxic.
- *Semicarbazide*, once regarded as a marker for the antibiotic nitrofurazone, is a natural metabolite in crustaceans.
- *Chloramphenicol*, a broad-spectrum antibiotic and a suspected carcinogen, is found in nature and food.



Of all chemicals we are exposed to, 99.9% are of natural origin.

Of all dietary pesticides we consume, 99.99% are of a natural origin.

This amounts to daily intake of 1500 mg of natural pesticides and their breakdown products.

Human exposure to synthetic pesticide residues amounts to about 0.09 mg per day.

**Aalt,**

**Pharmacology also uses the toxicity of compounds to the benefit of the patient, right?**

ADRIEN ALBERT

# Selective Toxicity

*The physico-chemical basis of therapy*

SEVENTH EDITION



Pharmacology  
of drugs is a  
form of selective  
toxicity

**But Jaap,**

**If food contains so many 'toxic' ingredients,  
couldn't we use food as medicine?**

*Functional foods:*

foods that support human health and wellbeing, providing health benefit beyond basic nutrition.

*Food supplement (nutraceutical):*

A product isolated or purified from food, (and generally sold in medicinal forms not usually associated with food) and demonstrated to have a physiological benefit or provide protection against chronic disease.



Pharaohs regarded food to be the bearer of both divinity and vital strength. Current interest in the positive health effects of functional foods, nutraceuticals and herbal medicines seems to be a return to the philosophy of ancient Egypt.

**Aalt,**

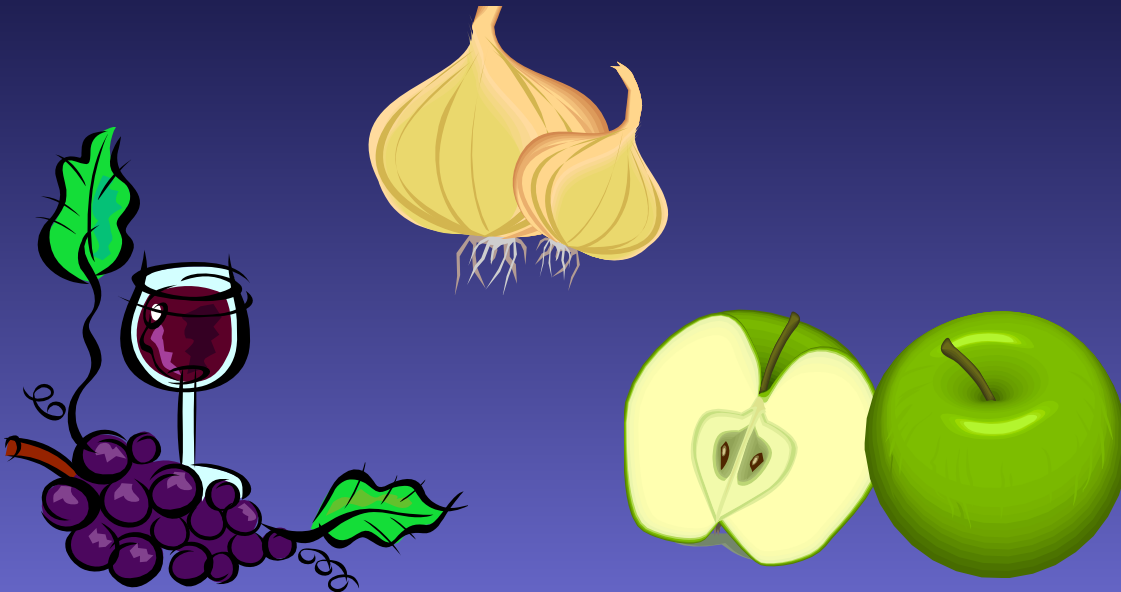
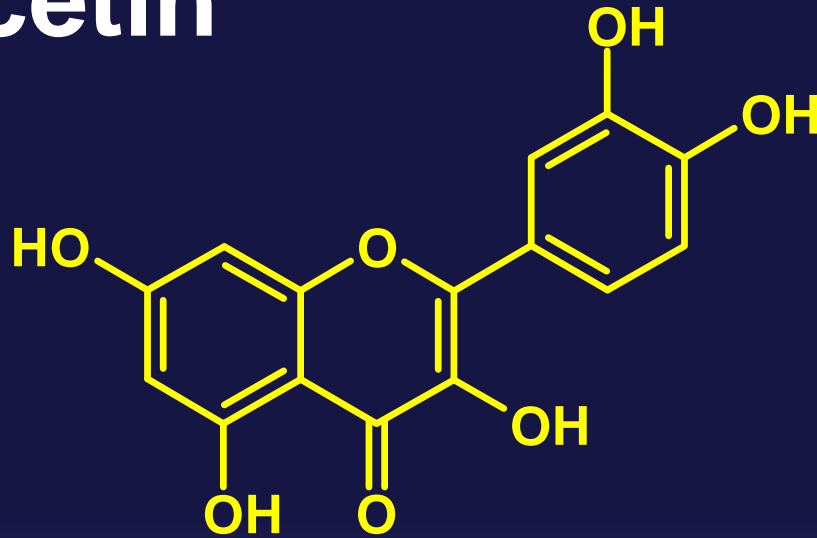
**Could we not introduce more specificity in the action of food?**



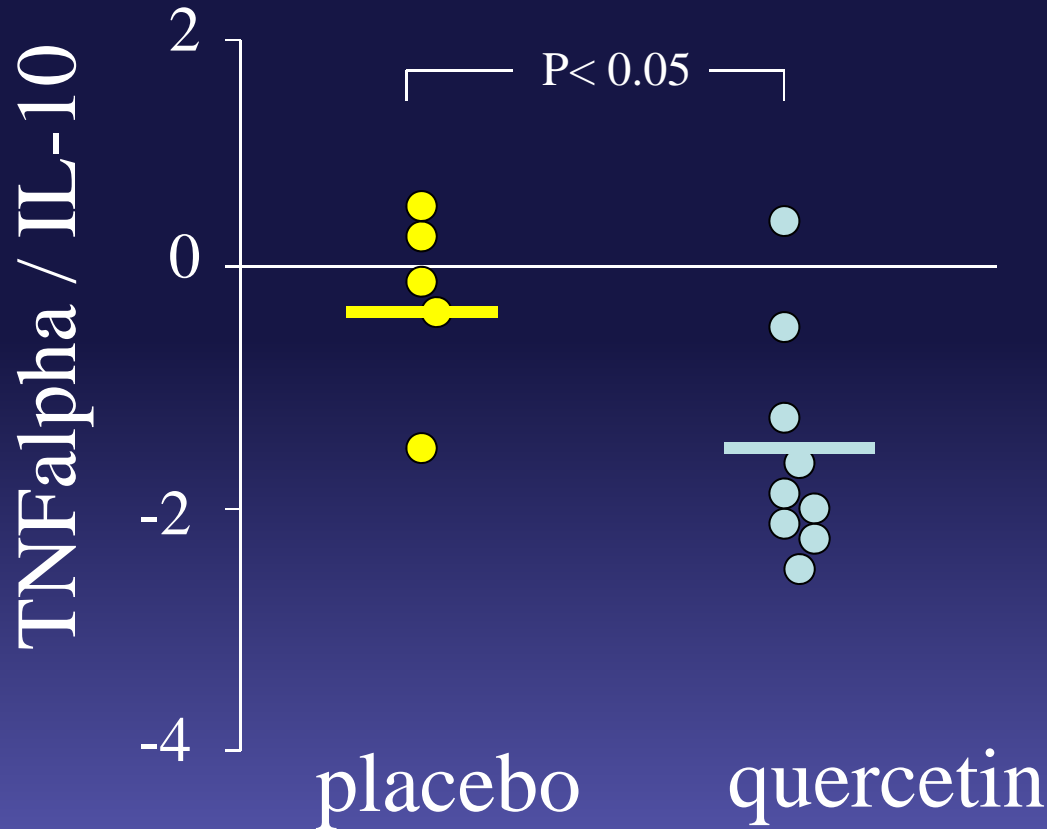
**Natural Toxins:  
Name  
your Poison**

In food  
pharmacology,  
general  
'toxicity' is the  
basis for a  
multitude of  
beneficial  
physiological  
effects

# Quercetin



# Effect of quercetin (p.o. 2x 500mg) on inflammation in sarcoidosis

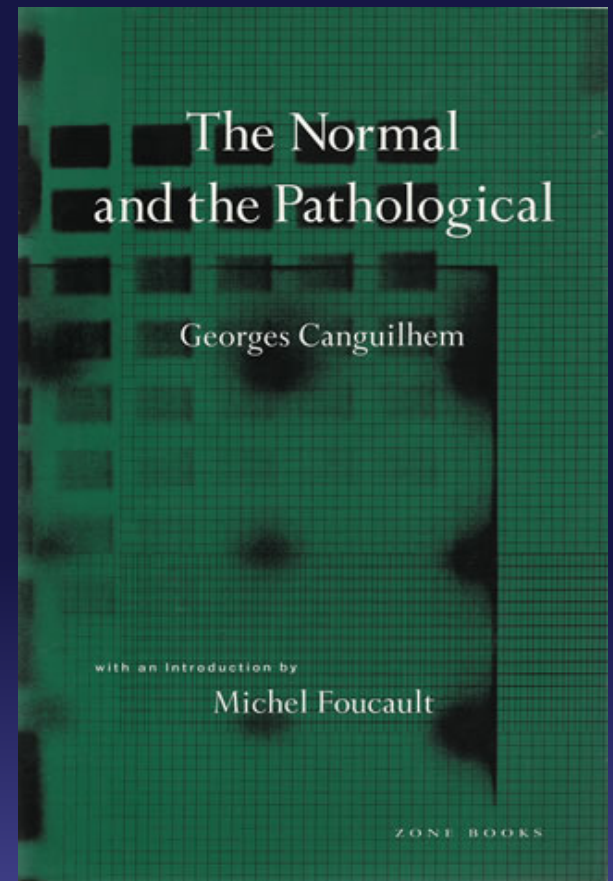


**Jaap,**

**Could this pleiotropic action of food not be a basis  
for research?**

## Definition of Health

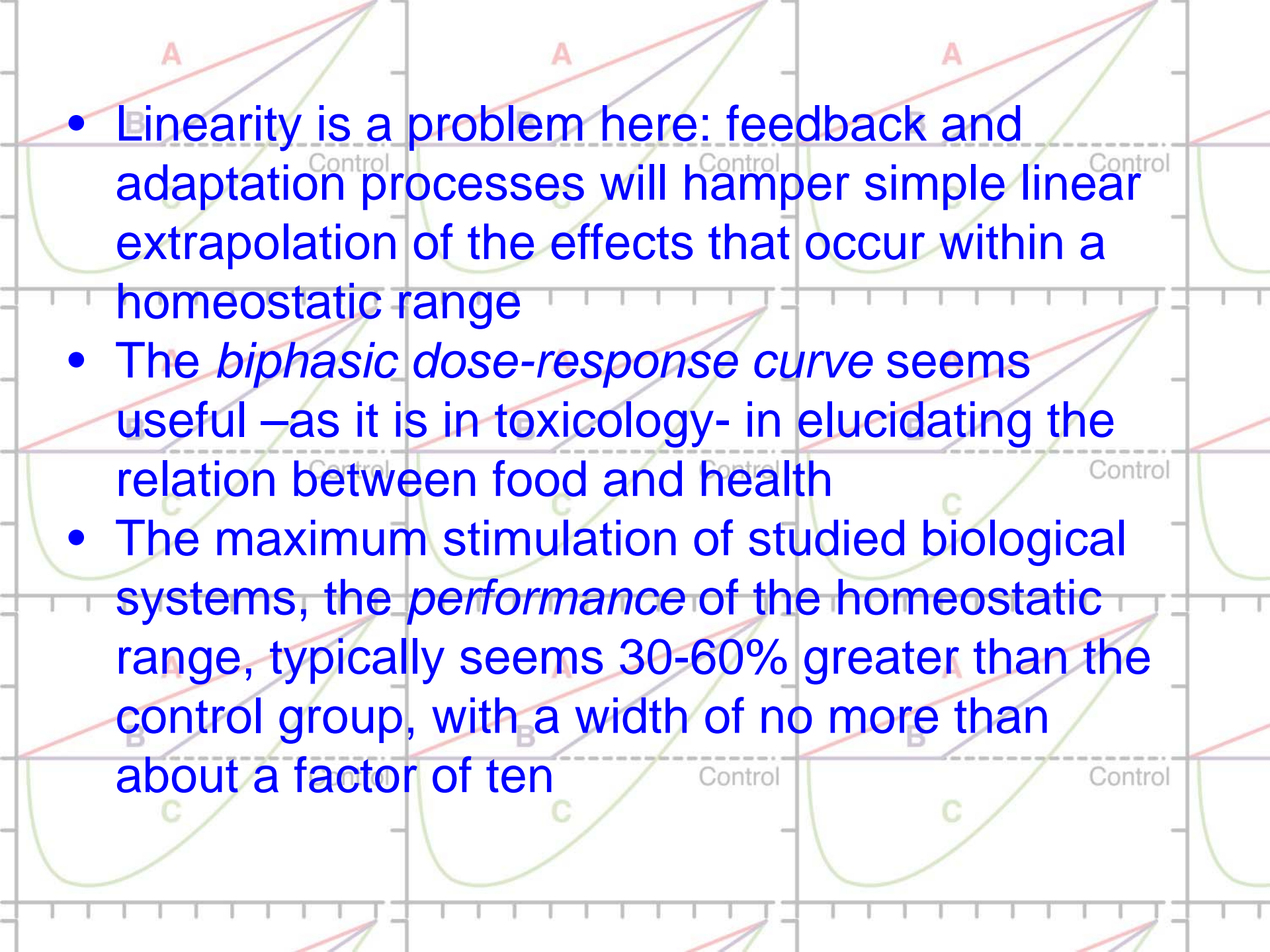
Health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.



**‘Health is the ability to adapt.’**

G. Canguilhem, ‘The normal and the pathological’, 1943.

- Nutritional effects are both pleiotropic and relatively small (and fortunately so)
- Adding the small multiple effects of dietary components –comparable to combi-toxicology- could correspondingly be employed to define a 'beneficial capacity'
- Current scientific methodology does not take account thereof: studies defining health aspects of foodstuffs tend to focus on separate, isolated compounds and isolated 'cause-effect'-related identifiable phenomena

- 
- Linearity is a problem here: feedback and adaptation processes will hamper simple linear extrapolation of the effects that occur within a homeostatic range
  - The *biphasic dose-response curve* seems useful –as it is in toxicology- in elucidating the relation between food and health
  - The maximum stimulation of studied biological systems, the *performance* of the homeostatic range, typically seems 30-60% greater than the control group, with a width of no more than about a factor of ten

**Aalt,**

**Did you not publish a recent paper illustrating this pleiotropic action of food in health benefit?**

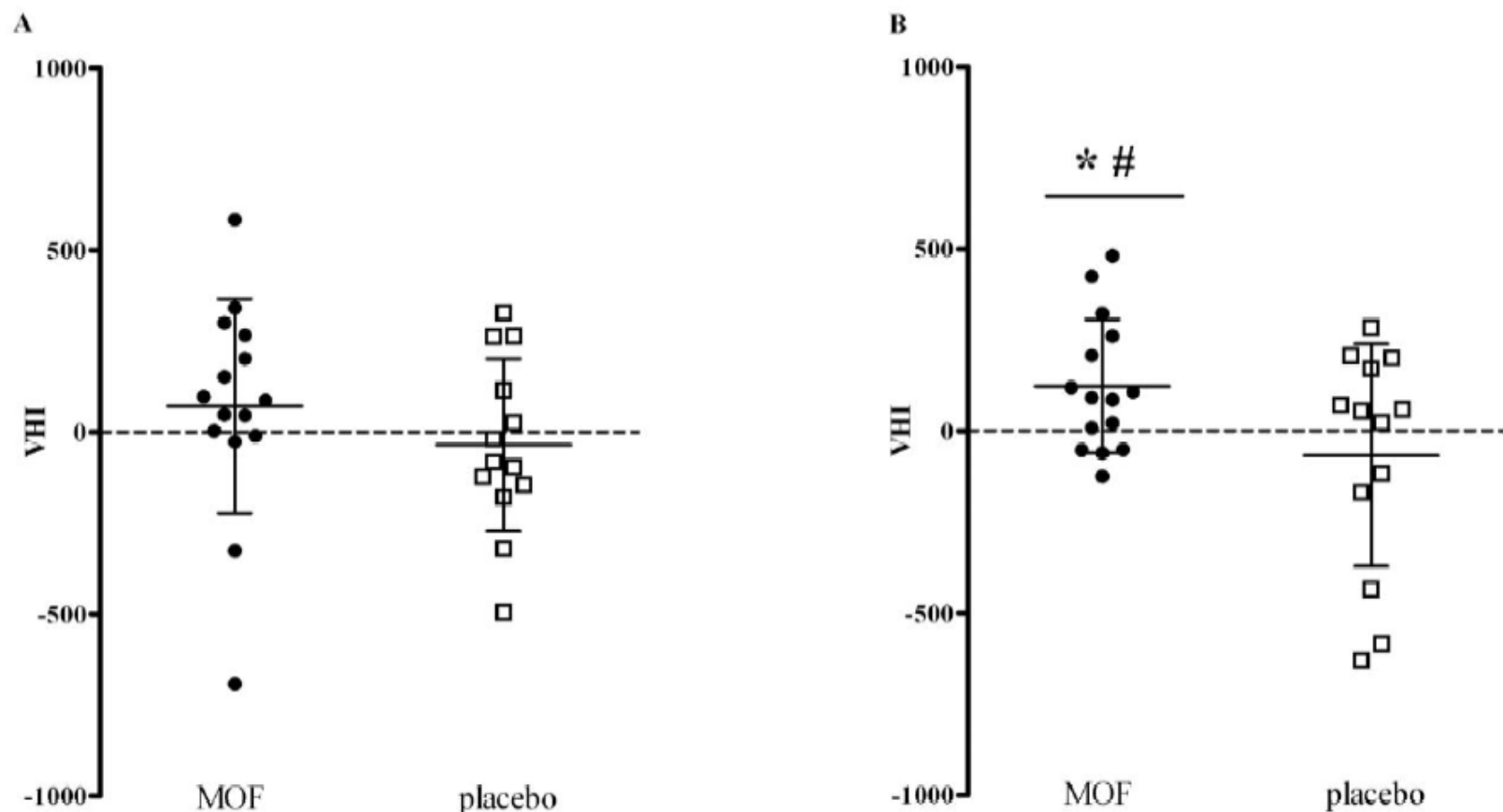
# Pleiotropic Benefit of Monomeric and Oligomeric Flavanols on Vascular Health - A Randomized Controlled Clinical Pilot Study

Antje R. Weseler<sup>1\*</sup>, Erik J. B. Ruijters<sup>1</sup>, Marie-José Drikkij-Reijnders<sup>1</sup>, Koen D. Reesink<sup>2</sup>, Guido R. M. M. Haenen<sup>1</sup>, Aalt Bast<sup>1</sup>

**Citation:** Weseler AR, Ruijters EJB, Drikkij-Reijnders M-J, Reesink KD, Haenen GRMM, et al. (2011) Pleiotropic Benefit of Monomeric and Oligomeric Flavanols on Vascular Health - A Randomized Controlled Clinical Pilot Study. PLoS ONE 6(12): e28460. doi:10.1371/journal.pone.0028460

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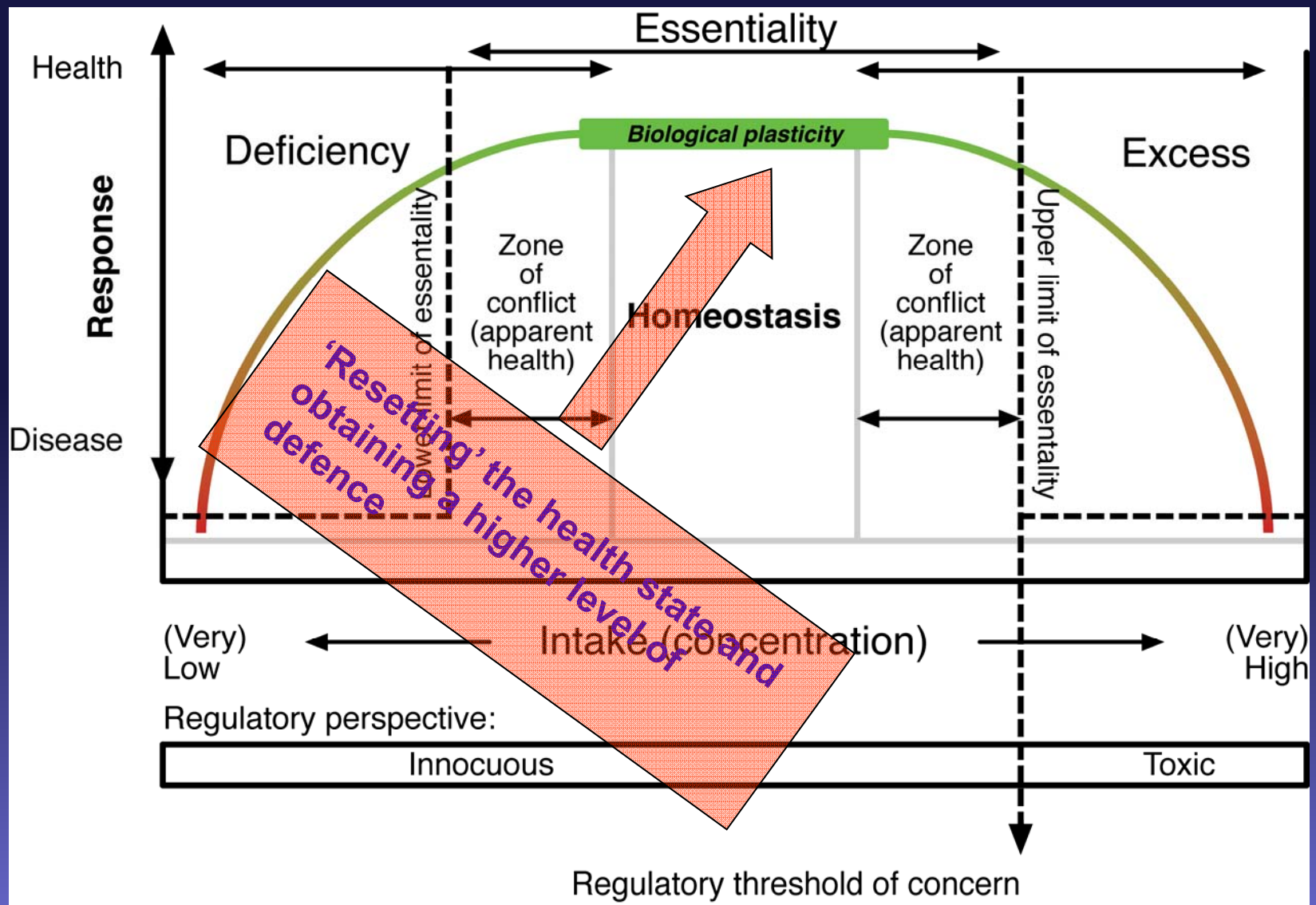
Mean  $\pm$  SD vascular health index (VHI) of individual subjects after 4 (A) and 8 wk (B) supplementation with either 200 mg/d monomeric and oligomeric flavanols (MOF,  $n=15$ ) or placebo ( $n=13$ ). Within-group changes were appraised by one-tailed paired-samples t-test, between-group changes by two-tailed independent samples t-test; \*Significantly different from baseline in the same group,  $P<0.05$ . #Significant difference between groups at the same time,  $P<0.05$ .

doi:10.1371/journal.pone.0028460.g004

**Jaap,**

**How would you now summarize this?**

# 'Toxins (read: food- and food supplements) are healthy'



# Food

- (Natural) chemicals for resetting the health state (i.e. the ability to adapt)
- Food derived compounds (toxins) are not selective
- Not a single end point, but rather a multitude of effects to illustrate the health benefit
- Increased defence against a stress response
- Regulatory efforts should incorporate these developing insights