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Selenium-enriched functional foods for cancer prevention

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What are “functional foods”?

US Institute of Medicine's Food and Nutrition Board (IOM/FNB, 1994) definition:

“Any food or food ingredient that may provide a health benefit beyond the traditional nutrients it contains”

Historical perspective

- Chinese recorded use of medicinal foods ~1000 BC.
- Hippocrates stated ~ 2,500 years ago:
“Let food be thy medicine and medicine be thy food”

Birth of FF

- The term “functional foods” was first introduced in Japan in the mid-1980s.
- Japan has a specific regulatory approval process for FF known as Foods for Specified Health Use (FOSHU).

Functional foods in US

- **The FF terminology is relatively new to the United States.**
- **30-50 billion \$ markets per year.**

An excerpt from *Nutrition Action*, April 1999

“Millions of Americans already eat functional foods. They routinely start their day with **folate-enriched toast** (to prevent birth defects and protect their hearts) washed down with **calcium-fortified orange juice** (to strengthen their bones). Sometime soon, they’ll be able to slather that toast with a **margarine that lowers cholesterol.**

For lunch, some may have a bowl of **pea soup spiked with St. John’s wort** (hoping to prevent depression) and a glass of **apple juice with echinacea** (hoping to ward off the sniffles). In between, they may chew on a **gum made with phosphatidyl serine** (hoping to slow memory loss).

Eat at your own risk

“What’s wrong with adding vitamins, fiber, herbs, and extracts to foods that ordinarily don’t contain them?”

Maybe nothing...if research shows that they’re safe and that they work.

Unfortunately, there’s no guarantee of either.”

Regulatory Issues

- **FF exist at the interface between food and drugs.**
- **There is no provision in existing food regulations for foods intended to be consumed to prevent disease.**
- **Structure/function (health promoting) claims without mentioning specific diseases are allowed without FDA approval.**

Opportunities and challenges

- **CAN benefit health**
- **Huge global markets**

- **Efficacy/health promoting effects**
- **Safety/side effects**

Selenium functional foods?

What is selenium?

- Trace mineral nutrient essential for healthy heart, muscle and joints.
- Recommended daily value for adult: 55 μg .
- Present in foods and crops in varying amount, depending on the soil Se level
- Toxic when intake is excessive

Issues

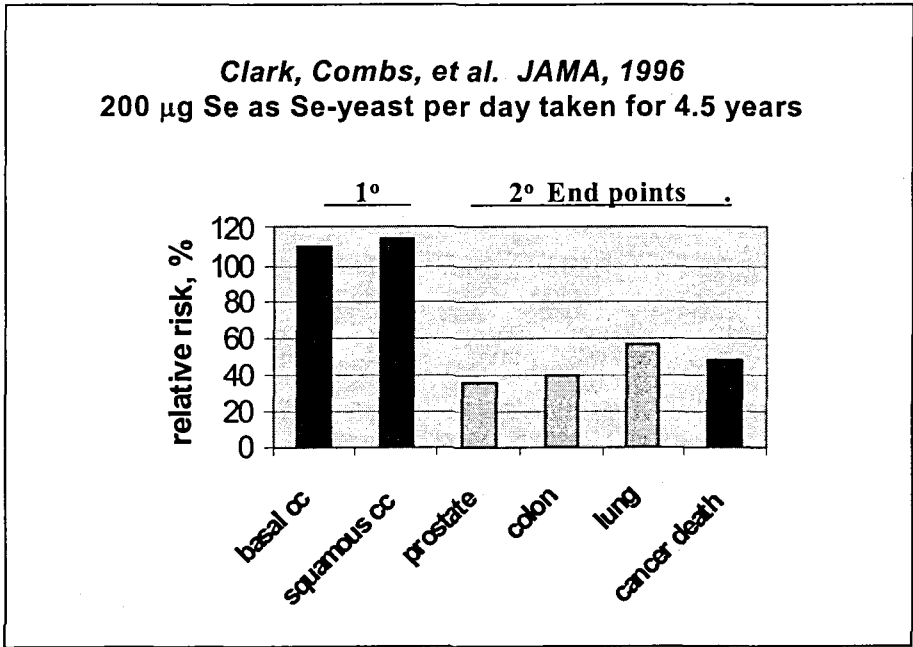
- What functions to promote?
- What Se forms?
- What dose/level?
- What organ sites?
- What target populations?
- What side effects?

Existing Se products

- **Inorganic salts such as selenite, selenate**
- **Seleno amino acids**
- **Se-yeast**
- **Se-garlic, Se-onion, Se-broccoli**
- **Se-fungi/spore**
- **Se-crops/nuts/tea/malt**
- **Se-eggs, Se-milk**

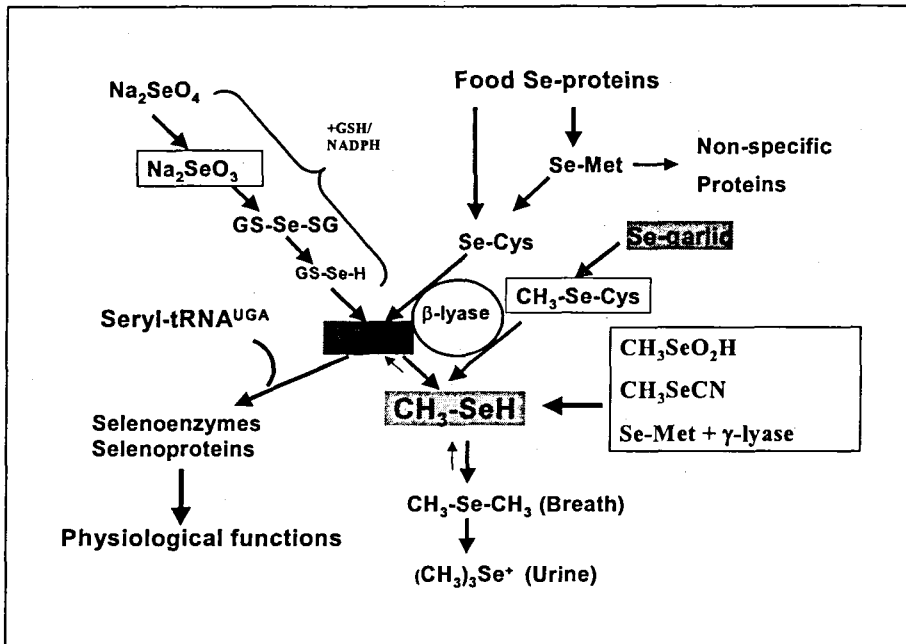
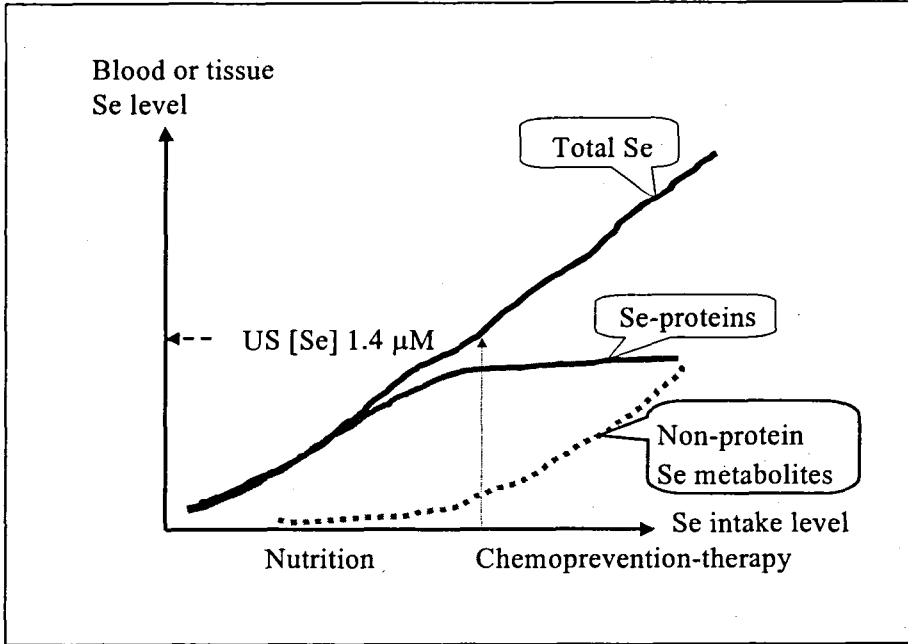
What functions to promote?

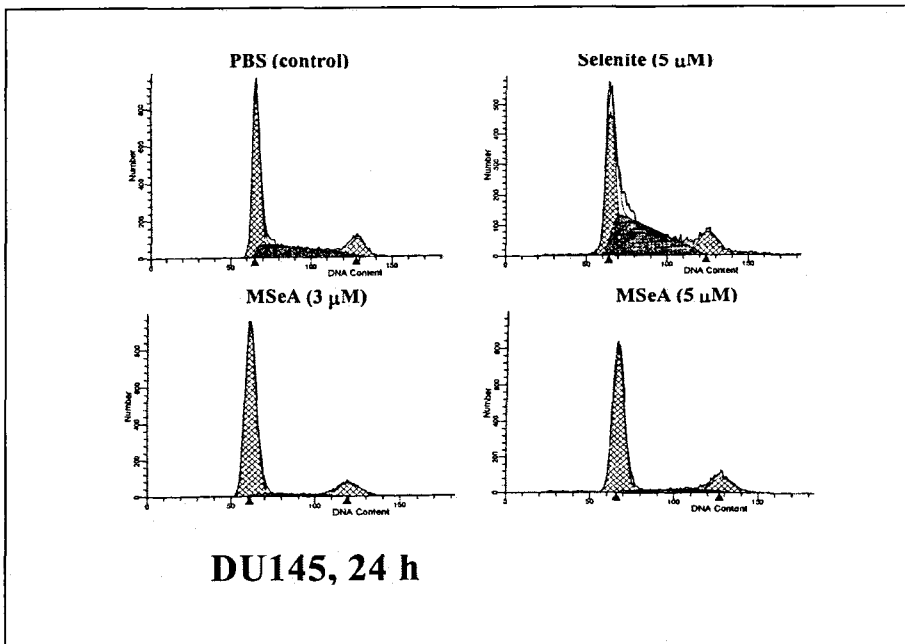
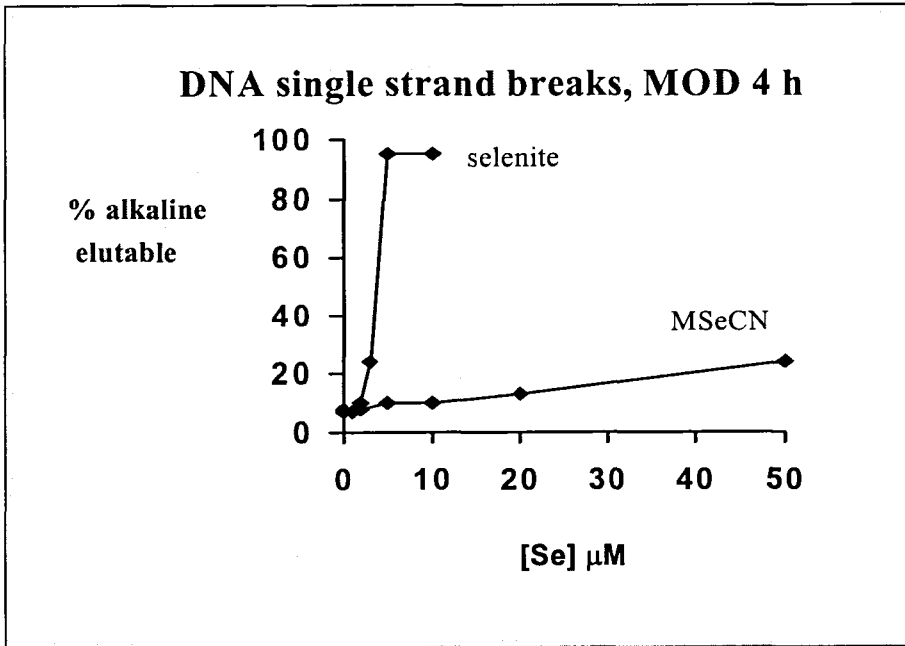
- **Correcting nutritional selenium deficiency (anti-oxidant, energy metabolism, redox regulation etc.)**
 - **Supporting selenoprotein synthesis**
- **Cancer prevention and Rx**
 - **Enriching critical desirable metabolites**

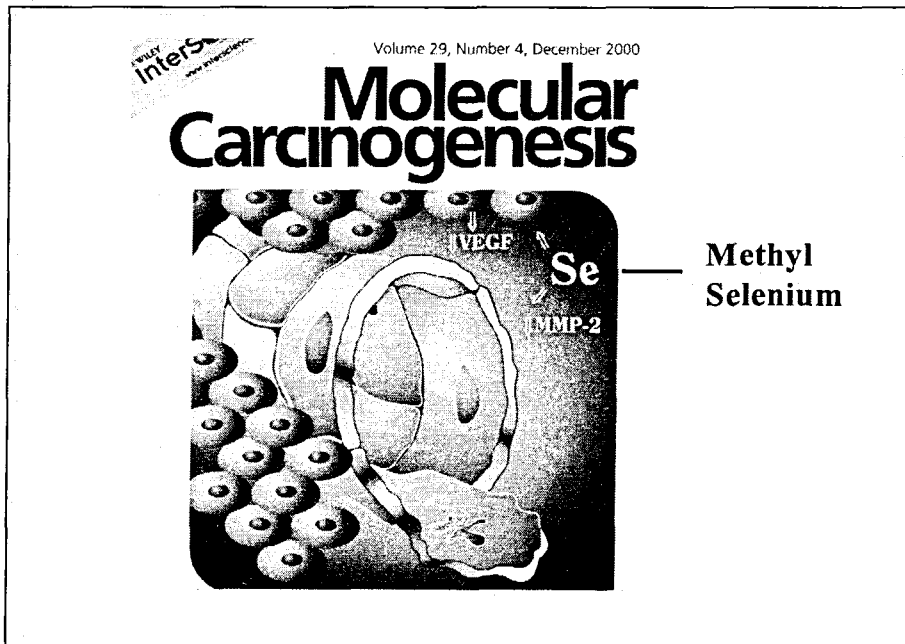
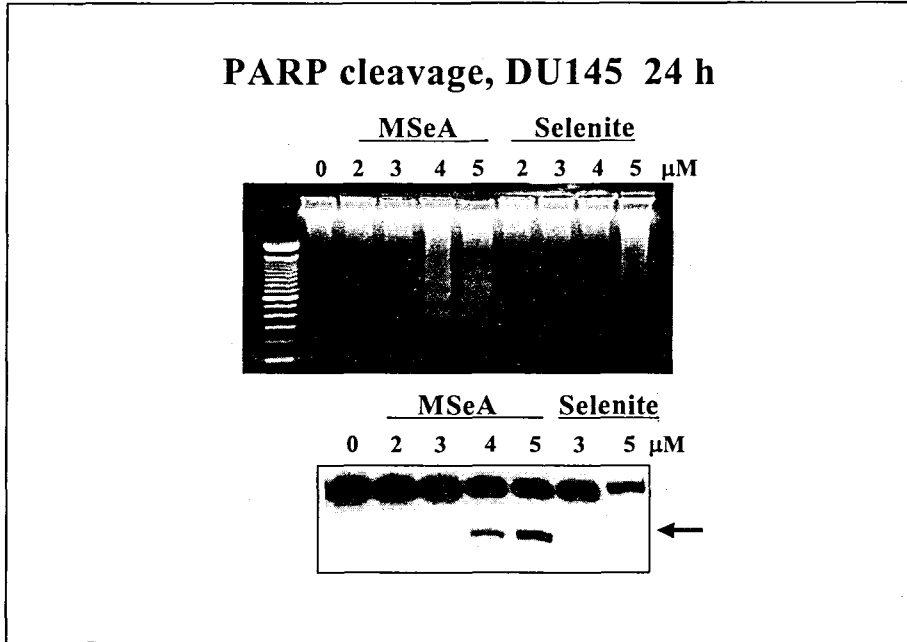


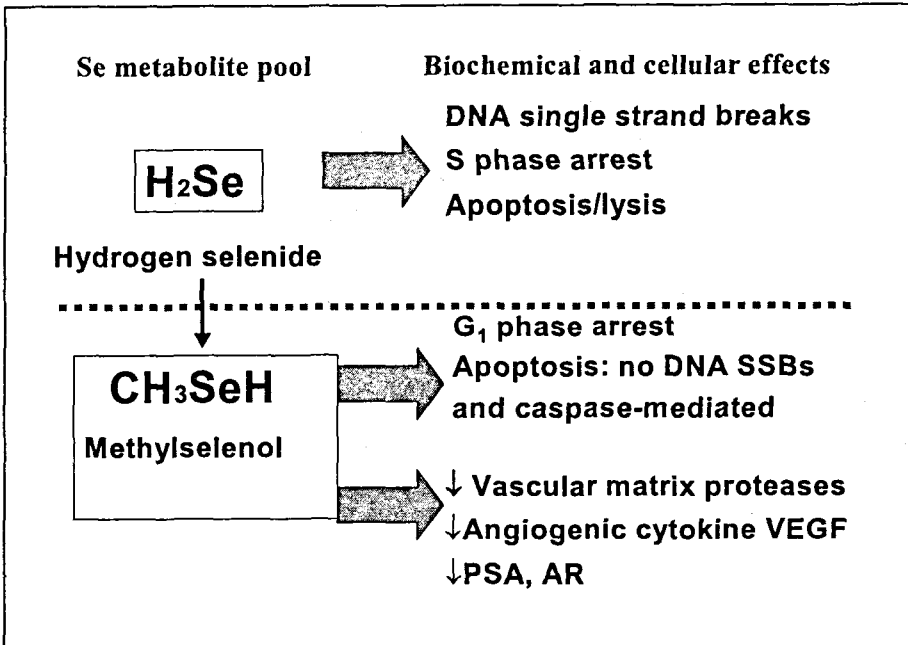
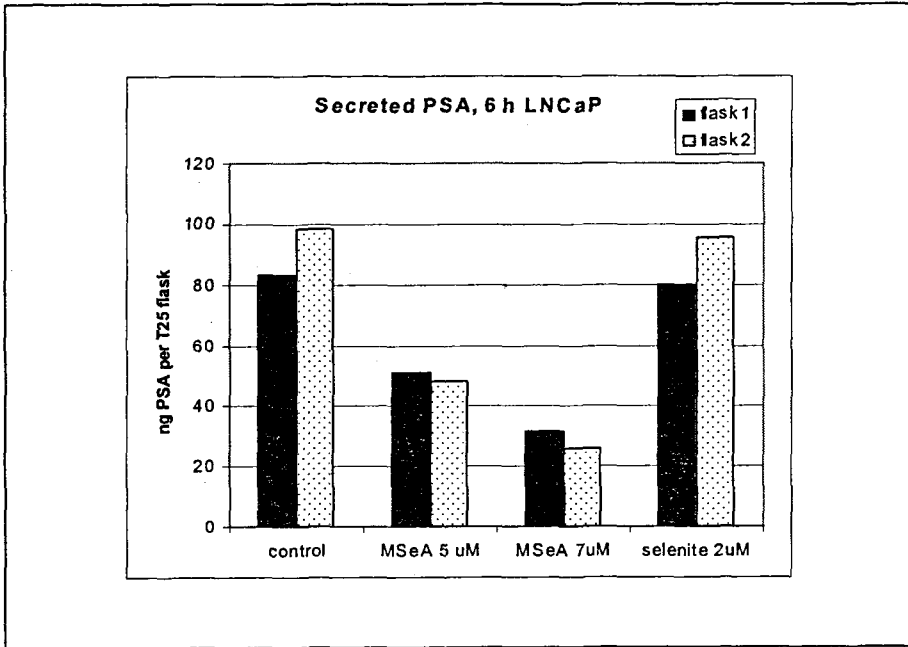
Paradigm

Functionality must be backed by solid mechanisms









Summary 1

- Available human data support Se as a promising preventive agent for some cancers.
- Animal and cell culture data suggest methylselenol as a desirable Se metabolite pool for cancer prevention.
- Some selenium forms may possess genotoxic side effects.



Why Se-garlic?

- Garlic is rich in sulfur compounds, some of which have potential cancer preventive activity
- Selenium and sulfur share some common chemistry properties

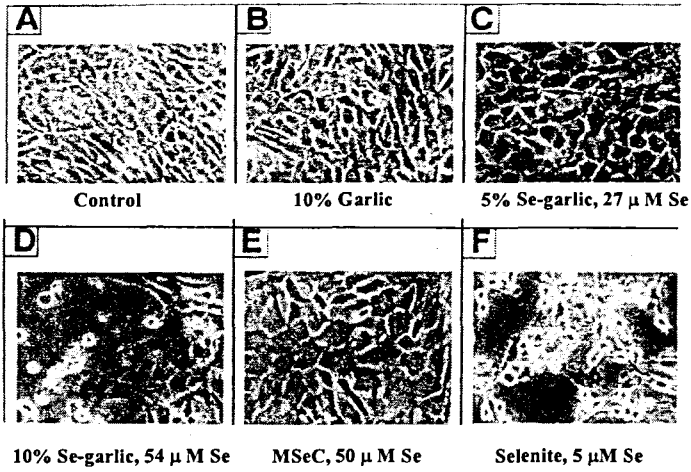
Paradigm Bio-transformation

Garlic
Selenite fertilizer → Non-genotoxic Se

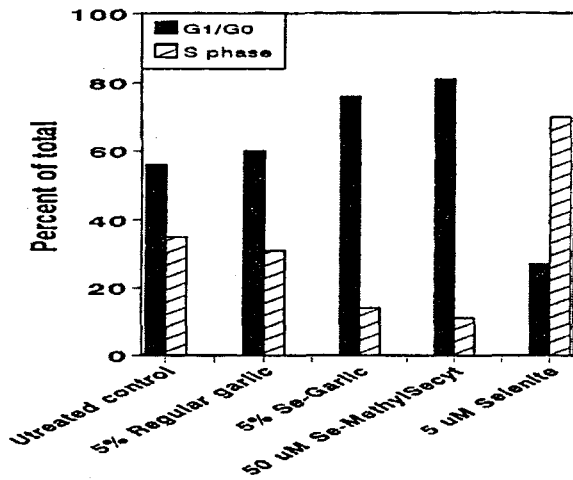
Mammary cancer prevention by Se-garlic extract given for 1 month

Group	Diet Se (ppm)	Tumor incidence	Total tumors
Control	0.1	28/30	78
Garlic extract	0.1	25/30	69
Se-garlic extract	3.0	14/30	39

Se-garlic vs. selenite and MSeC



Cell cycle distribution (TM2H cells)



DNA single strand breaks in Se exposed MOD cells

Treatment	[Se], uM	SSB
None (Control)	0	1 x
Garlic extract, 5%	0	0.8 x
Se-garlic extract, 5%	27	0.7 x
Methylselenocysteine	50	0.6 x
Selenite	5	6.5 x

Summary 2

- Selenium is mostly responsible for the cancer preventive effect of Se-garlic
- Garlic transforms inorganic selenite fertilizer into Se products with distinct modes of action and a more desirable non-genotoxicity profile

Take home messages

- Se FF should use forms appropriate for the functions to be promoted
- FF that can enrich methylselenol metabolite pool may be desirable for cancer prevention

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