Effects of dietary supplements in young and aged rats

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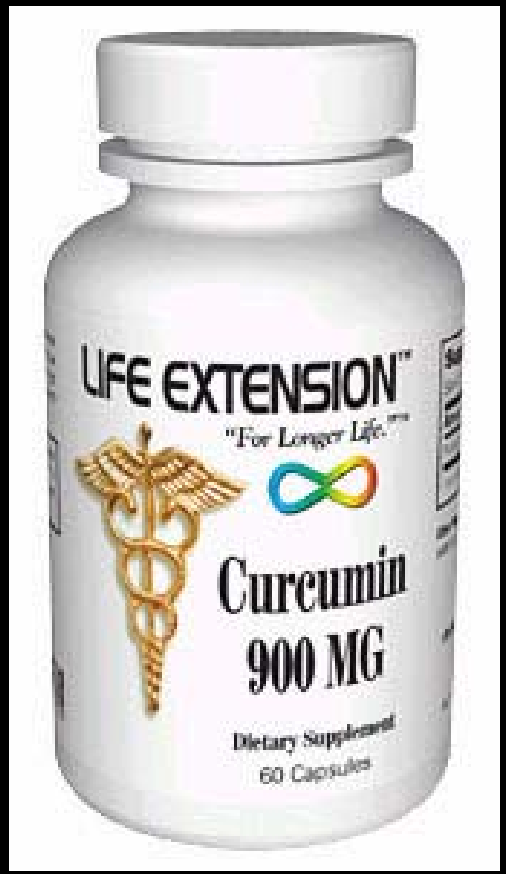
Background

- Estimated that 40% of US population uses dietary supplements often
- Over 80% have tried at least 1 of 29,000 supplements on the market
- Safety concerns for special populations
  - Children, elderly
  - Pregnant women, health compromised
- Evaluated curcumin and soy isoflavones

Curcumin



- Claims include:
- Anti-inflammatory
- Antioxidant
- Anticarcinogenic
- Anti-aging

Curcumin

- Colorectal cancer prevention in rodent studies with young rats
- Phase 1 Clinical trials in humans
  - no toxic effect in humans consuming 8 gm/d for 3 mo
  - 5 other studies lower doses

Project Objectives

- What effect does curcumin have on the development of age-related pathological changes in rats?
- Does age affect prevention of early stage colorectal cancer by curcumin?

Experimental Design

- F344 male rats:
  - 6 week-, 12 month-, and 22 month-old
- Six rats of each age group
  - randomly assigned to either 0.6% curcumin or control diet.
- One week after starting experiment diet, all the rats were treated with a colon carcinogen
- Rats were fed experimental diets for 12 wks
- Tissues were obtained and evaluated.

Common age-related changes in rats were not affected by curcumin

- Kidney damage
  - chronic progressive nephropathy
  - degree of severity **increased with age**
  - dietary curcumin did not affect
- Heart damage
  - chronic cardiomyopathy
  - the degree of severity **increased with age**
  - dietary Curcumin effect was not observed.

*Curcumin-fed rats had **higher** incidence of some lesions*

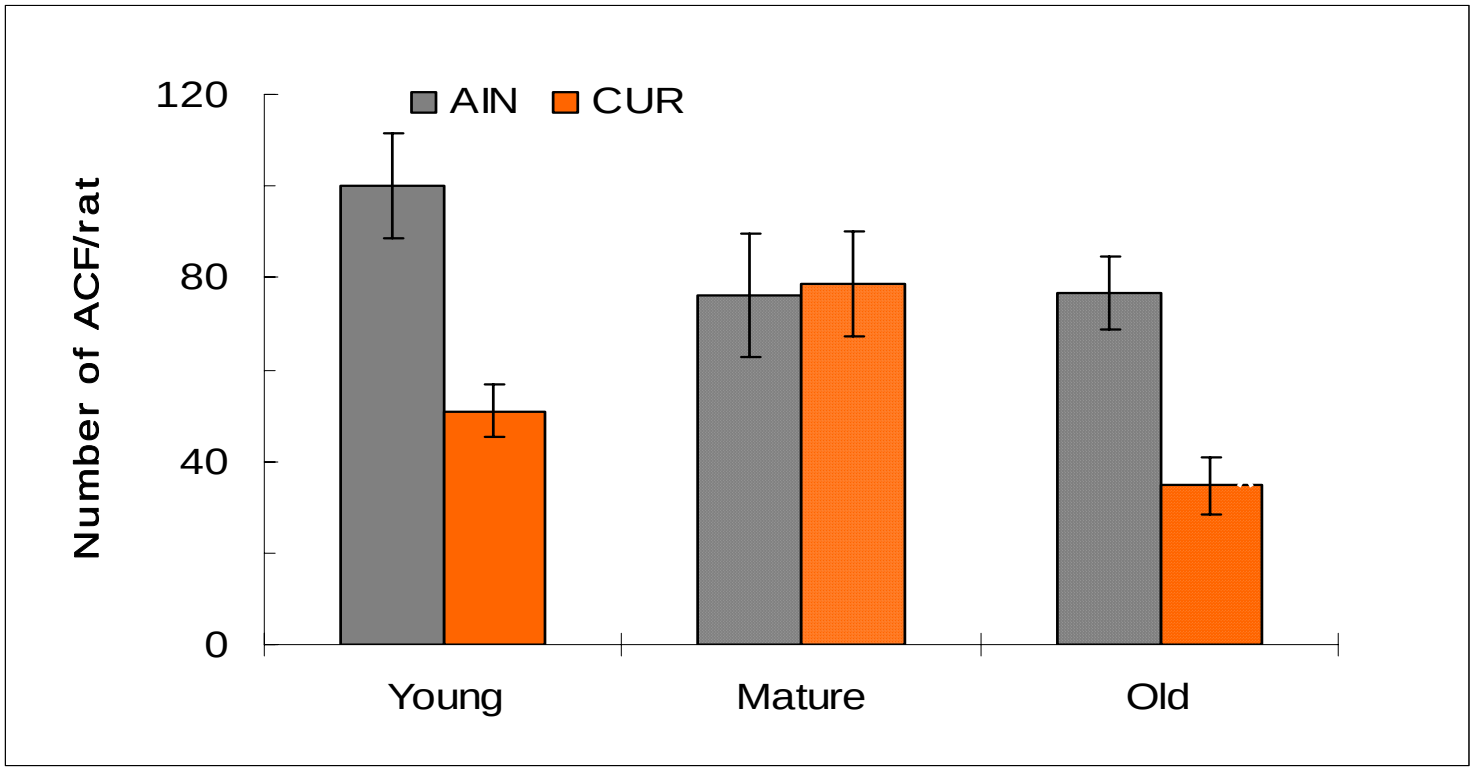
- Lung, heart and liver lesions
  - Pulmonary microgranulomas
  - Myxomatous degeneration of heart valves
  - Liver microgranulomas
- Gastrointestinal tract
  - Lymphoplasmocytic infiltrates in stomach, duodenum and colon

At this time, the significance of these finding is not clear due to the small number of animals

Old *Curcumin-fed had* ***<u>lower</u>*** *incidence of all neoplastic lesions*

- Malignant (aggressive) lesions found only in control diet rats
  - Lung carcinoma, histiocytic sarcoma of spleen, C-cell carcinoma in thyroid, tumors in adrenals
  - Pancreatic islet cell adenoma, testicular adenoma, pituitary adenoma, skin fibroadenoma

Curcumin reduces early stage colon cancer in young & old, but not Mature rats



(mean ± SE, n=6 rats/group).

Curcumin Study Conclusions

- No support for anti-aging claims
- Support for anti-cancer claims in old group

- Lack of effect in middle-aged group raises questions about testing in only young for preclinical testing

Soy Isoflavones

- Prevention of
  - breast cancer
  - Heart disease
  - prostate cancer
  - symptoms of menopause

-also colon cancer, but only done in males

Project Objectives

- Is soy isoflavone effective in females?
- Does age affect prevention of early stage colorectal cancer by soy isoflavones?

- Similar experiment – used Novasoy as source of isoflavones (0.4% of diet)

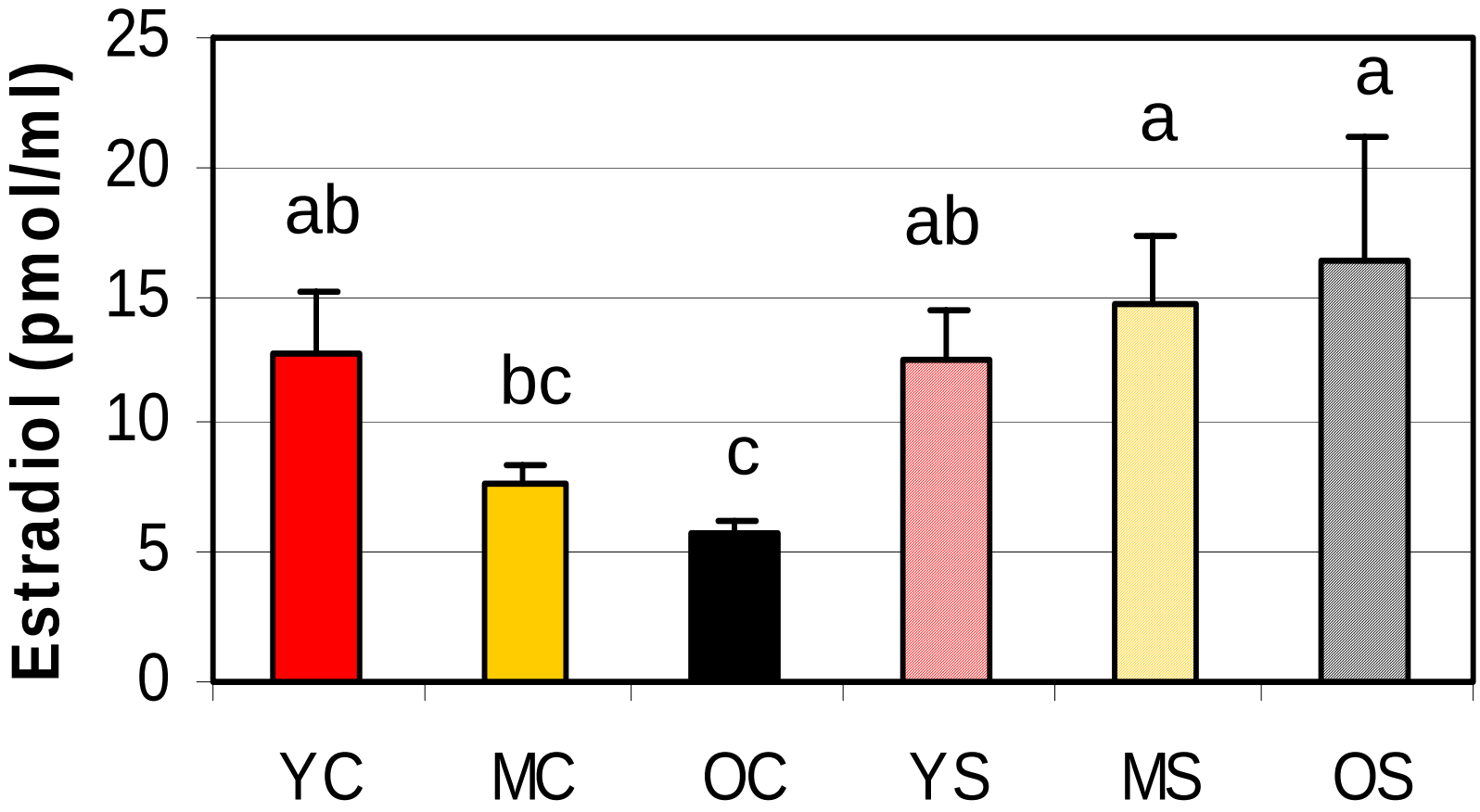
Surprising Results

- **No inhibition** of colon cancer lesions by soy

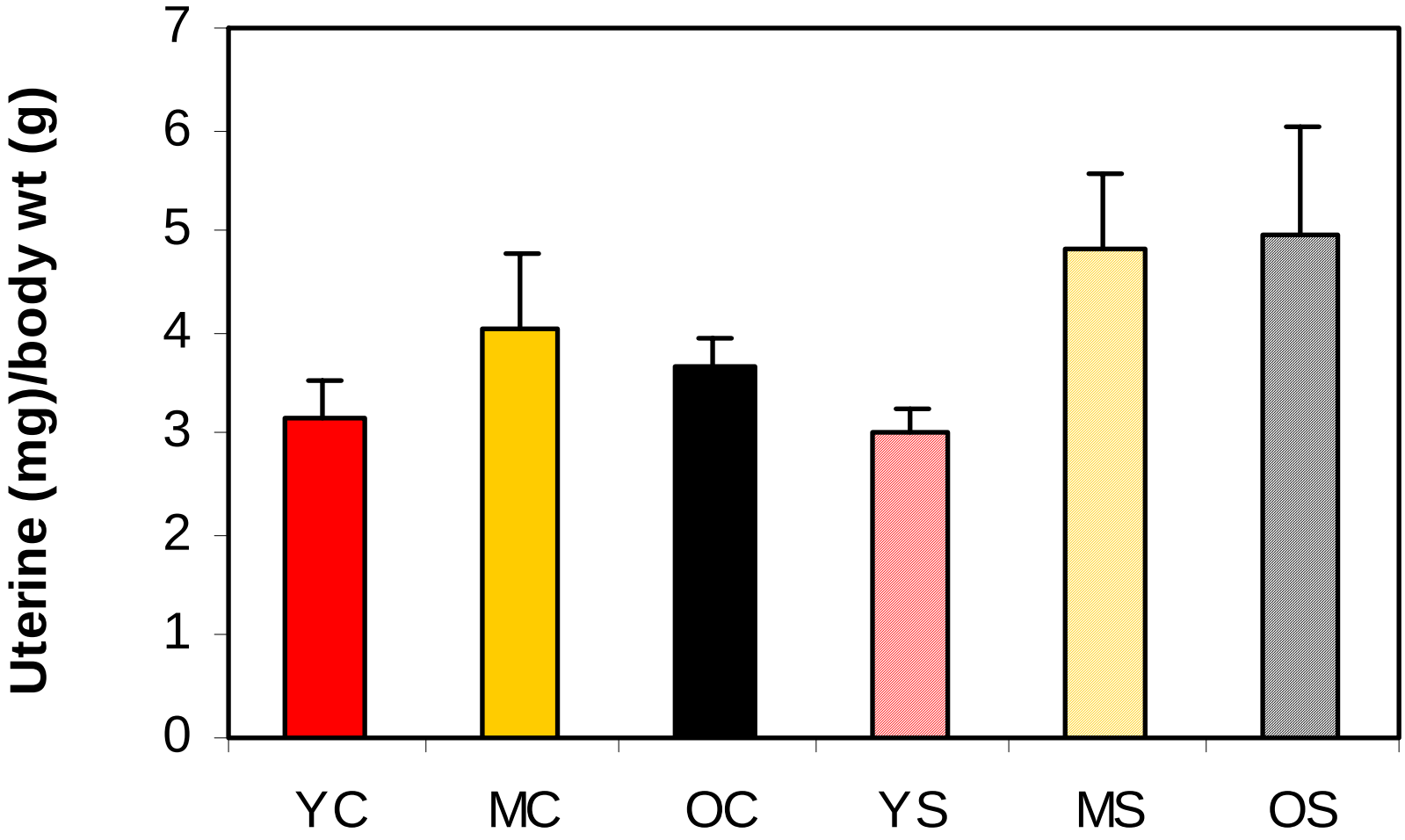
- Old female rats fed soy were VERY ill
  - 4/7 died before the end of the experiment
- Mature female rats fed soy also ill
- Young – no adverse effect

- Soy isoflavones acted like estrogen in older groups

Serum Estradiol



Uterine/Body weight



Soy Study Conclusions

- In combination with another drug, soy isoflavones were toxic to older female rats
- Is this a drug/diet interaction?
- Soy isoflavones affected estrogen and estrogen-responsive tissues in older rats
- May have adverse effects on hormone - dependent cancers

So what?

- Use of Supplements by aging consumers
  - Safety?
  - Efficacy?

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