

COMPLEMENTARY AND ALTERNATIVE MEDICINE

Is it **safe** in cancer patients ?

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คุณพ่อ สัมฤทธิ์ คำหงษ์ บ้านละว้า หมู่ 6 อ.บ้านไผ่ จ.ขอนแก่น
ไปรักษาที่โรงพยาบาล หมอบอกเป็นโรคมะเร็งลำไส้ ระยะสุดท้าย ให้ทำใจรักษาไม่ได้แล้ว
ได้เอาลำไส้ออกมาข้างนอก เพื่อเจาะรูถ่ายเนื่องจากระบบขับถ่ายเสียหมด มีน้ำเลือด น้ำเหลือง
ไหลออกมามากจากแผล ร่างกายไม่มีแรง เจ็บปวดมาก มีคนแนะนำให้กิน คอลดาต้า ครั้งแรกไม่เชื่อว่าดี
เพราะกินมาหลายยี่ห้อแล้ว ได้เอาคอลดาต้า ไปถามหมอ หมอบอกว่าให้กินได้ เลยลองกินดู
ปรากฏว่า อาการดีขึ้น ร่างกายมีแรงมากขึ้น น้ำเลือด น้ำหนอง หายไป เดินรอบหมู่บ้านได้ ขับจกัรยานได้
เหมือนคนปกติ วันนี้มีความเชื่อว่าอาการดีขึ้น เพราะ คอลดาต้า นี้แน่นอน

ยาของหมอพิภพชัย ภูมิปัญญาชาวบ้านของบรรพบุรุษ เภสัชกร ชอชชงษ์ ภาเภสัชกร
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อีสา หมอทวด!!

ชาวบ้านแห่รักษา มะเร็ง



ศูนย์ธรรมชาติบำบัด

BALAVI NATURAL HEALTH CENTER

ประสบการณ์ 3 ทศวรรษ บำบัดโดยแพทย์

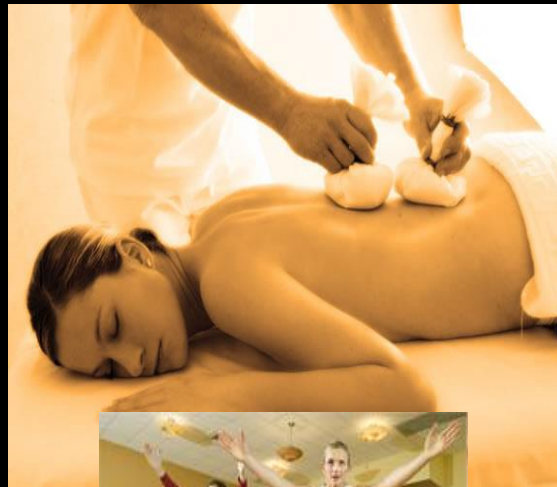


SCOPE

- Definition of Complementary and Alternative Medicine (CAM)
- Cancer prevention and CAM
- Popular CAM
- CAM and toxicity

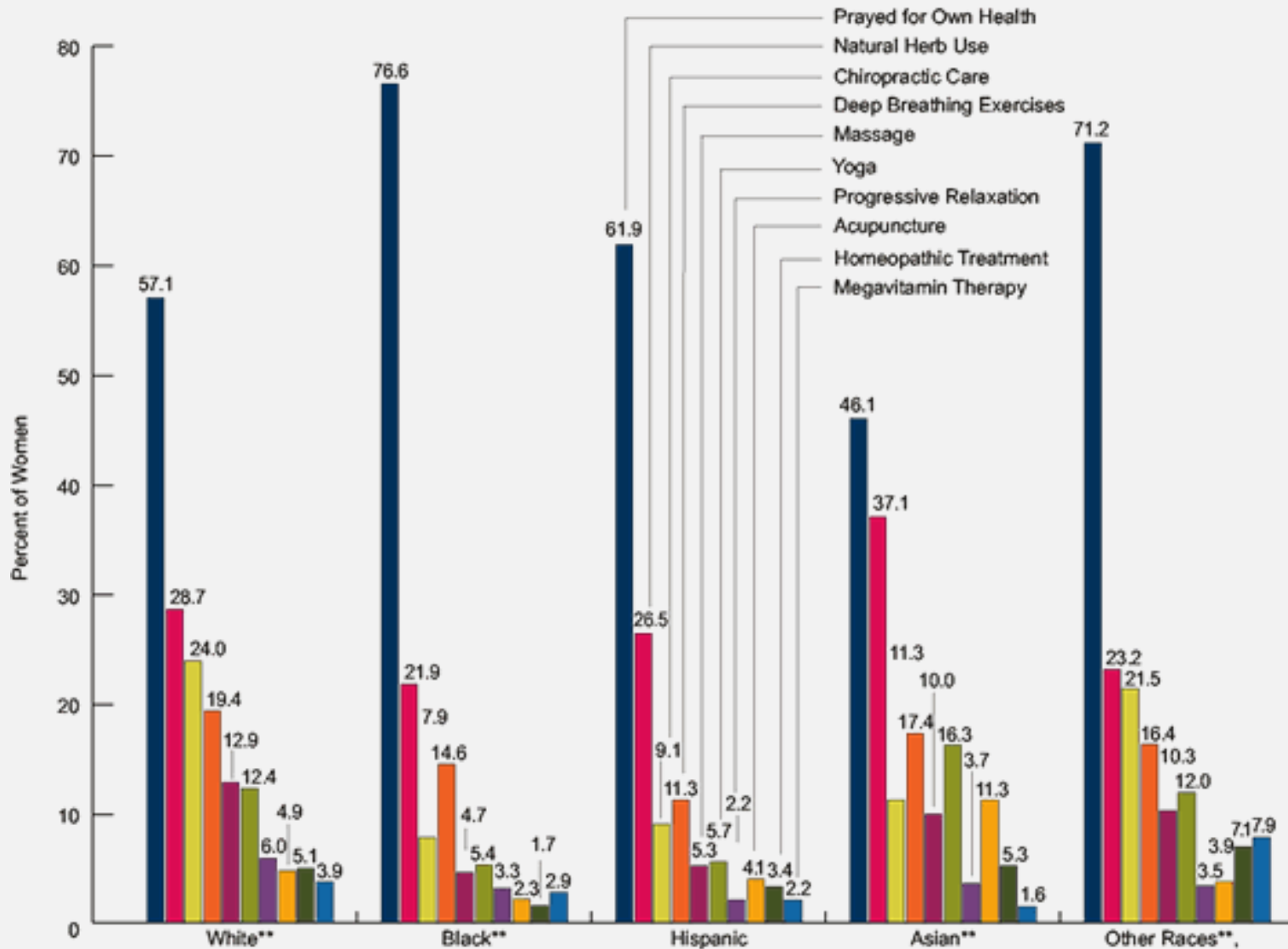


COMPLEMENTARY & ALTERNATIVE MEDICINE



Complementary and Alternative Medicine Ever Used by Women Aged 18 and Older, by Race/Ethnicity,* 2002

Source (II.1): Centers for Disease Control and Prevention, National Center for Health Statistics, National Health Interview Survey



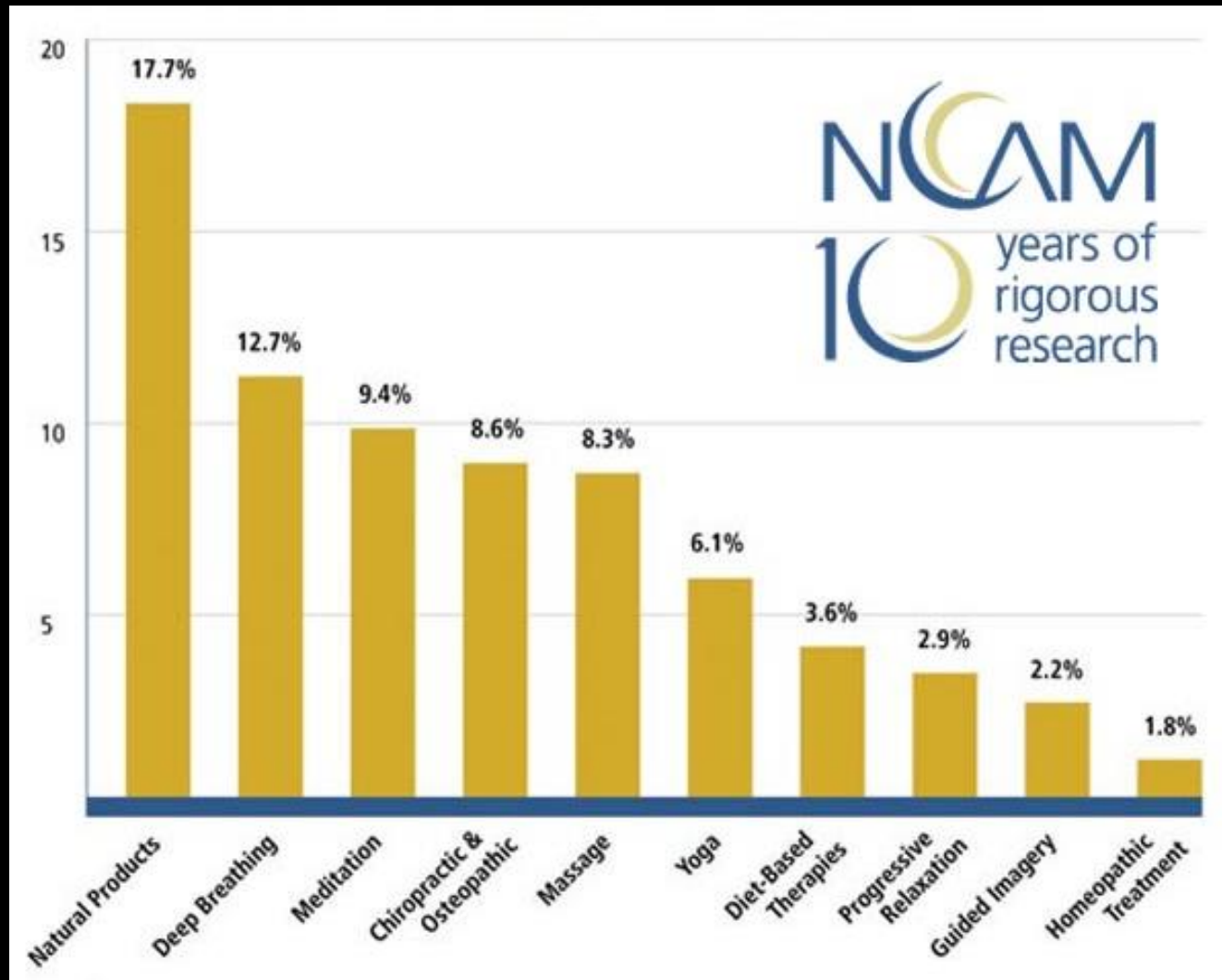
* Percents are not age-adjusted.

**Non-Hispanic

Includes American Indian/Alaska Native, and persons of more than one race.

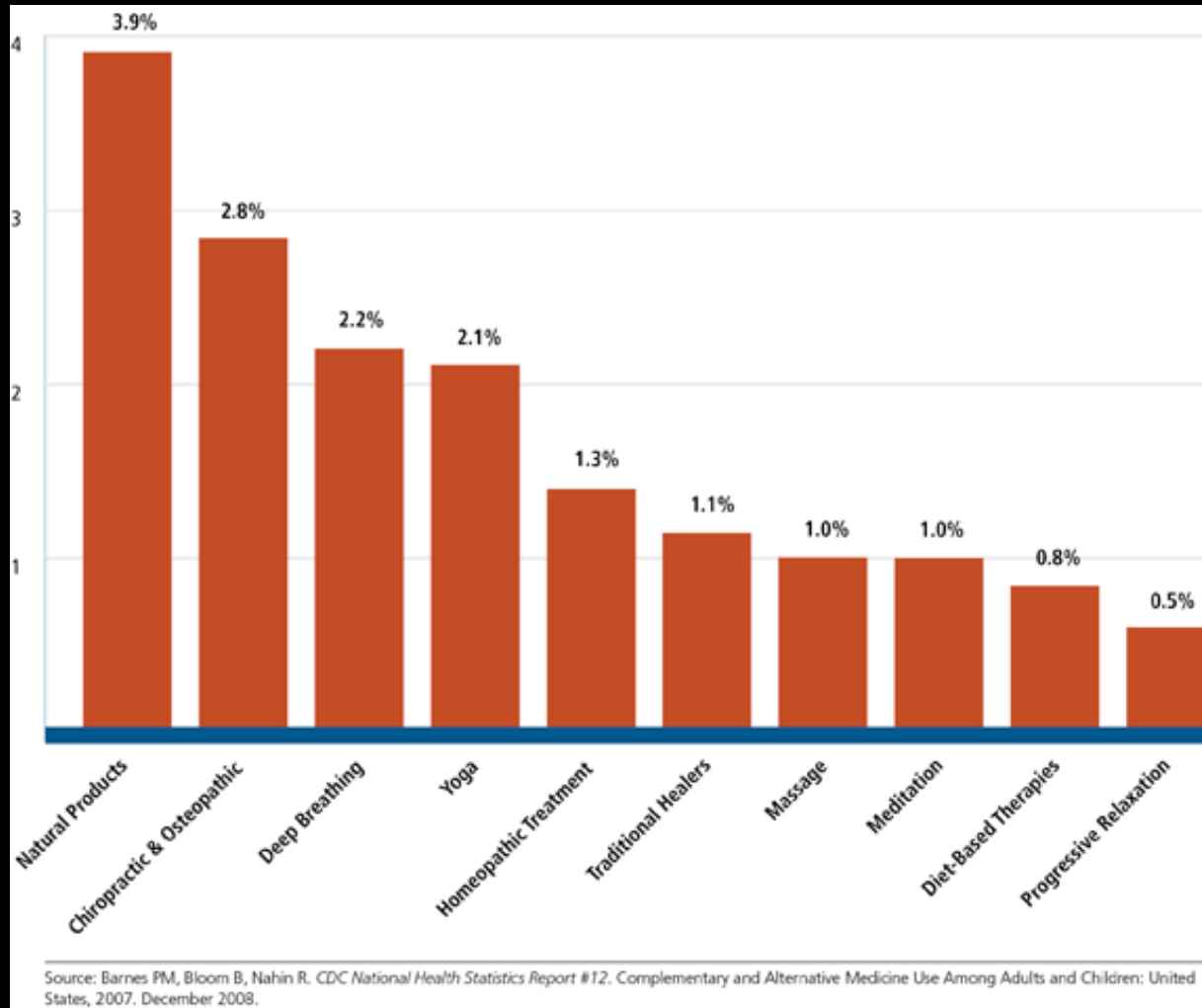


COMMON CAM THERAPIES



Source: Barnes, PM; Bloom, B; Nahin, R. CDC National Health Statistics Report #12. Complementary and Alternative Medicine Use Among Adults and Children: United States, 2007. December 2008

MOST COMMON THERAPIES AMONG CHILDREN



THE REASONS WHY PATIENTS TURN TO CAM

- Prevent chronic disease ; cancer, CVS
- Hope of minimizing ADR to treatment
- Treatment cancer



A BIG CHALLENGE FOR PHARMACIST



- Beliefs of use complementary medicine



- Clinical trials



- Summarized as recommended in cancer patient



WHAT TO CONSIDER ABOUT USE OF CAM

Precaution &
contraindicatio
n

Clinical
trials

Interact with
CMT or RT or Sx

Dosing &
administratio
n

Increase toxicity

Web site
with reliable
information

Potential side
effect

Quality control
→biologic potency
& contaminate



CANCER PREVENTION AND CAM

- Beliefs of use complementary medicine: supplements can prevent or treat chronic Disease
- 50% of adults use micronutrient
 - Antioxidant
 - Vitamin D, Ca, Selenium
 - Soybeans



ANTIOXIDANTS

- Antioxidant vitamin
 - Vit. A
 - Vit C
 - Vit E
 - Beta carotene
- Epidemiologic evidence suggests that a number of micronutrients may ↓ incidence of cancers of epithelial cell origin (lung, breast, oropharynx, stomach, bladder, prostate, colon)

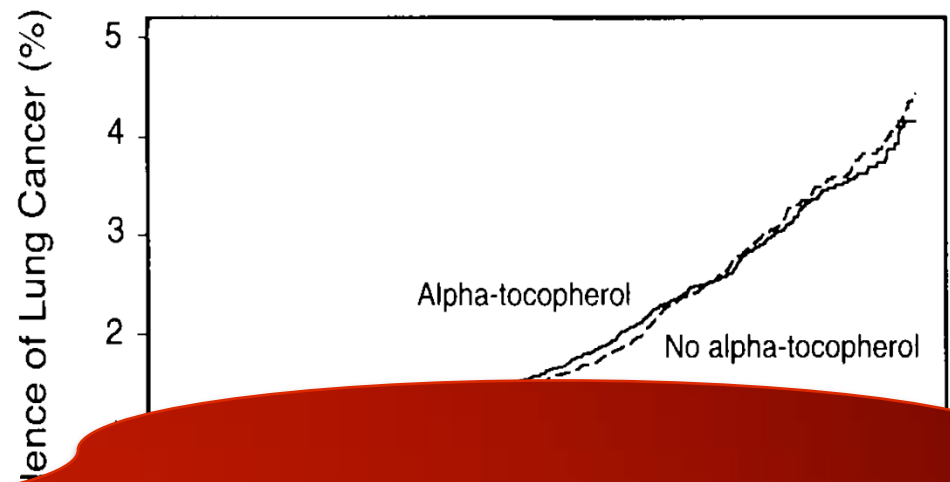


ANTIOXIDANTS: CLINICAL TRIALS

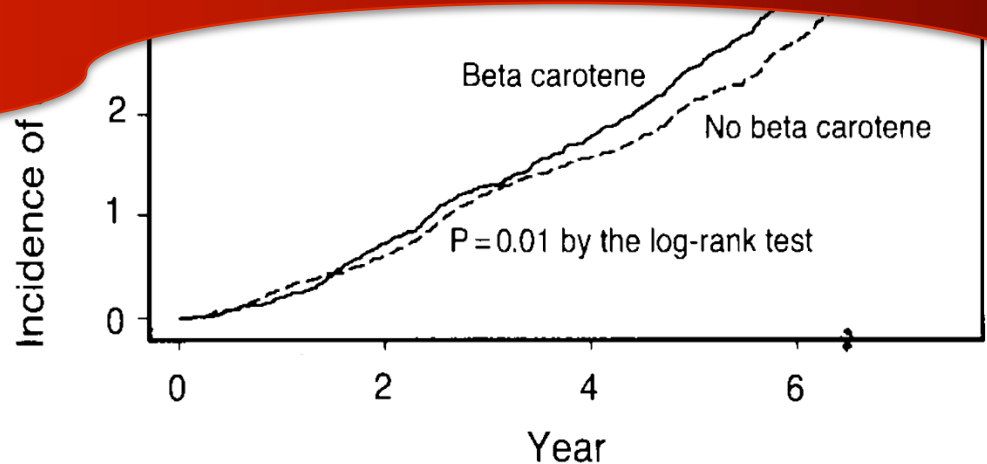
○ CARET trials

- β -carotene 30 mg + retinyl palmitate 25,000 IU
- 29,000 male smokers aged 50-69
- Mean pack-year = 36
- After a mean follow-up of 4.0 years: the group that received vitamins had a 28% greater incidence of lung cancer (RR 1.28, 95% CI 1.04 to 1.57; *P* 0.02)

ALPHA TOCOPHEROL BETA CAROTENE TRIALS (ATBC)



Both CARET and ATBC trial clearly established “supplement containing carotene were harmful to cigarette smokers or asbestos exposure: ↑risk of lung cancer and ↑overall mortality”

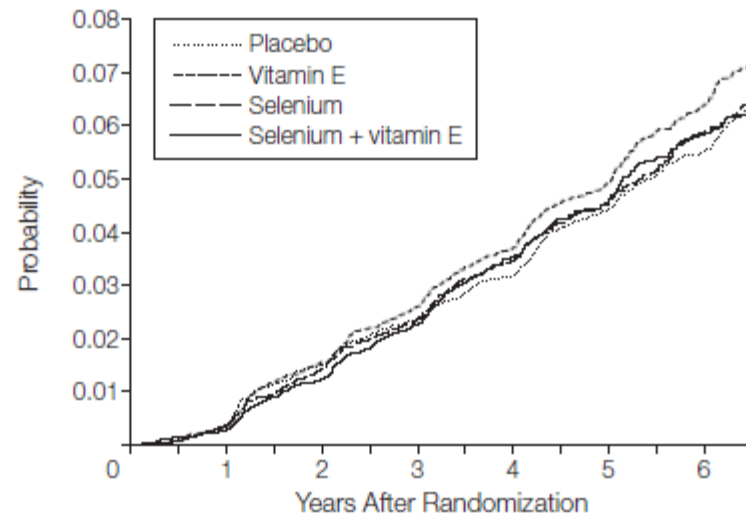


VITAMIN D, CALCIUM, SELENIUM

- SELECT trials (Selenium & Vit E Cancer prevention)
 - 35,000 men high risk of developing Prostate cancer
 - 4 arms: Se 200 mcg, Vit E 400 IU
 - Vit E alone HR = 1.13;
 - Se + Vit E
 - Se alone
 - No reduction in risk of prostate cancer by either of the agents alone or in combination

SELECT TRIALS

Figure 2. Cumulative Incidence of Prostate Cancer Detected Each Year by Intervention Group

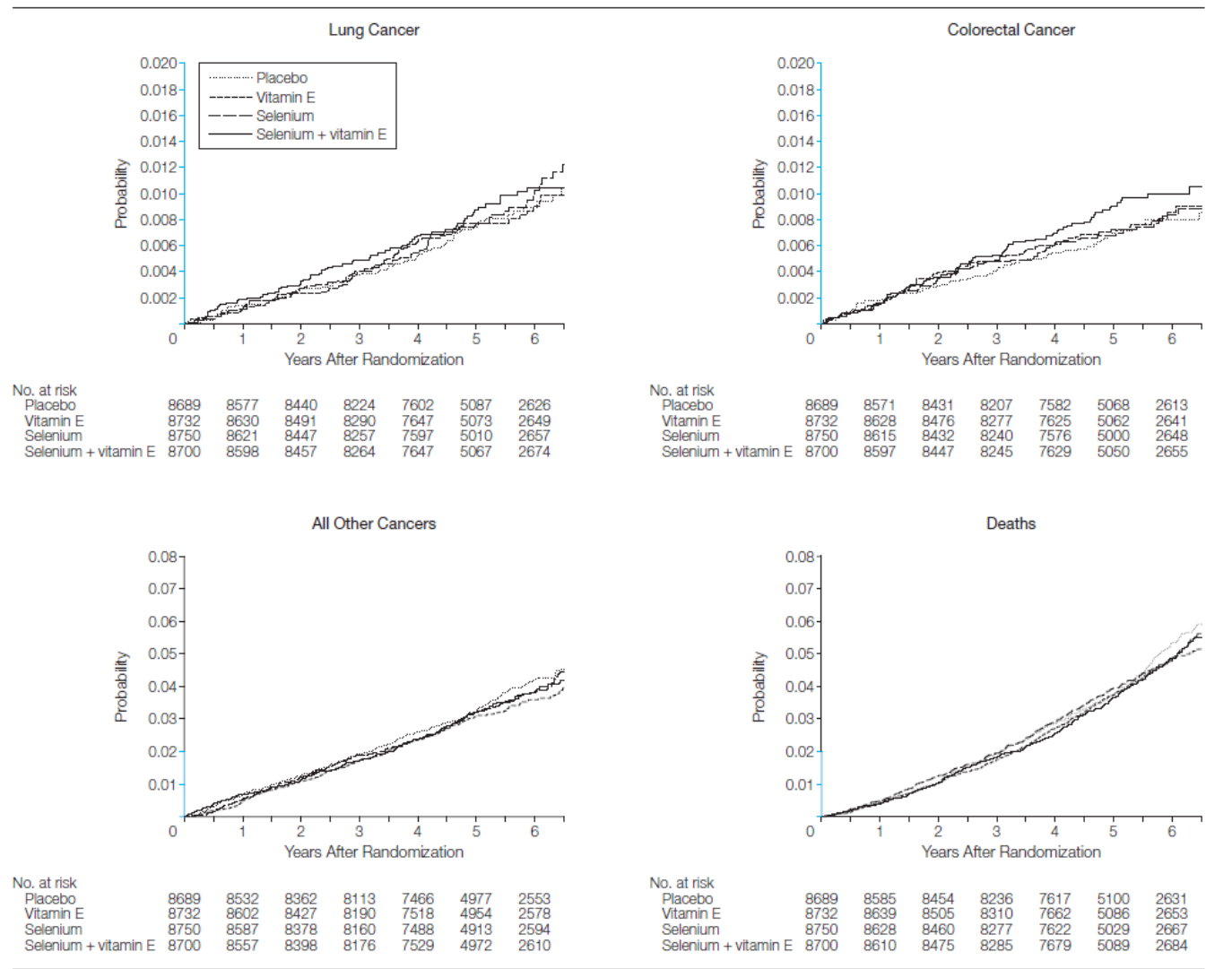


No. at risk							
Placebo	8689	8553	8328	8039	7389	4892	2516
Vitamin E	8732	8610	8373	8098	7401	4867	2537
Selenium	8750	8597	8341	8083	7393	4848	2558
Selenium + vitamin E	8700	8585	8371	8097	7428	4894	2580

Compared with placebo, there was a statistically nonsignificant increase in prostate cancer in the vitamin E group ($P=.06$) and not in the selenium + vitamin E group ($P=.52$) or the selenium group ($P=.62$).

SELECT TRIALS

Figure 3. Cumulative Incidence of Lung Cancer, Colorectal Cancer, All Other Primary Cancers, and Deaths by Intervention Group



There were no significant differences in any prespecified secondary cancer or death end points (all $P > .15$). The blue portions of the y-axes indicate 0 to 0.02 cancer probability.

CALCIUM AND VIT D

- Calcium and Vit D with risk of colorectal cancer
 - 864 patients with a history of polyps
 - Calcium 1.5 g/day
 - High Ca intake may be associated with a reduction in risk of recurrent adenomas, especially among individuals on high fat diets¹
 - Vit D & Ca interact synergistically to protect against adenoma recurrence and colorectal cancer²

1. Hyman J, et al. Cancer Epidemiol Biomarkers Prev 1998;7:291-295

2. Hartman T, et al. J Nutr 2005;135:252-159

SOYBEANS

- Primary food source for isoflavone glycosides genistin and daidzin; PHYTOESTROGEN
- Evidence suggests that
 - Soybean α ↓cancer mortality rates, particularly for cancers of the colon, breast, prostate, uterine, ovarian
- In animal study and in vitro study
 - soy protein Bowman-Birk trypsin inhibitor (BBI) suppress carcinogenesis



SOYBEANS

- Effect of soy foods on breast cancer risk depends on the age when they are consumed
 - High soy intake by young women: protection
 - Soy intake after menopause: unclear benefit or harmful



SOYBEANS

- It is unclear how they might affect the growth of estrogen receptor-positive breast cancers.
- Until this issue is resolved,
“Many oncologists recommend that **people taking tamoxifen or AI and estrogen-sensitive breast tumors should avoid** adding large amounts of soy, including soy supplements or isoflavones, to their diets”



HOPE OF MINIMIZING ADR TO TREATMENT

- Ginseng¹
 - 53 Breast cancer
 - 3000 mg of ginseng
 - Improve QOL
- Ginger
 - Reduce CINV caused by platinum-based CMT

1.Kim JH, et al. J clini pharm ther 2006;31:331-334.



GINGER: *IN VITRO* STUDY

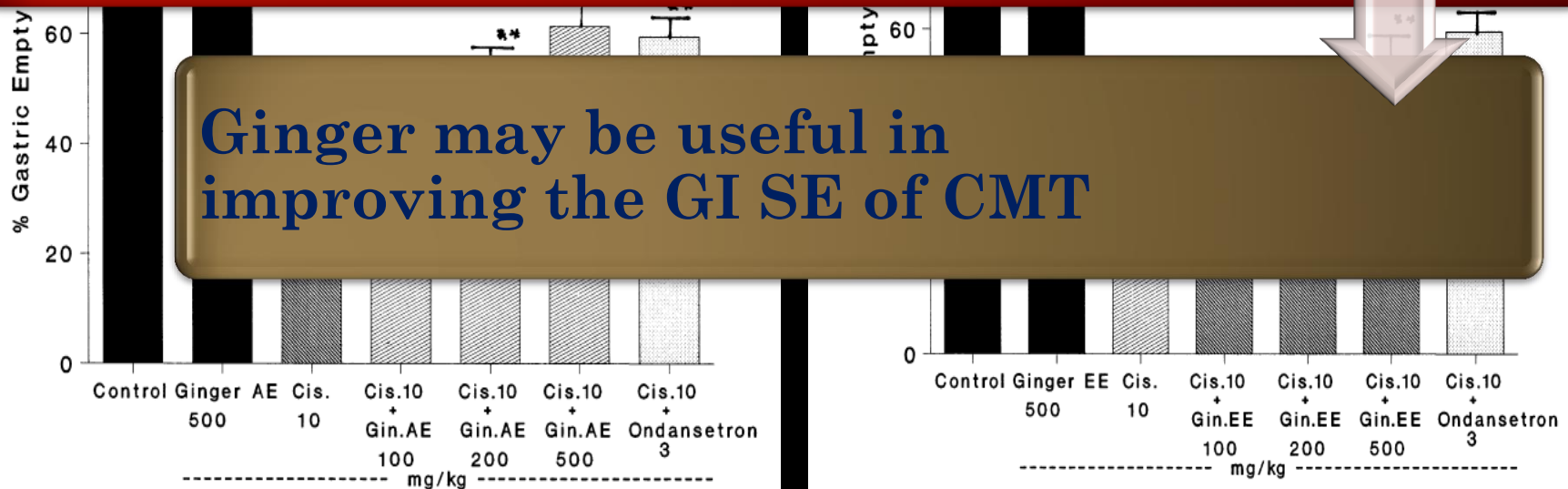
- Mode of action of 6-,8-,10-gingerol, 6-shogaol on 5-HT₃ receptor
 - inhibit contraction of guinea pig ileum induced by SR57227A (highly selective 5-HT₃ receptor agonist)
 - Weak anti-cholinergic
 - Weak anti-neurokininergic activity
 - It may be conclude that 6-,8-,10-gingerol, 6-shogaol exert antiemetic effect via 5-HT₃ antagonist



-Acetone and 50% ethanol
extract 100, 200, 500 mg/kg PO
-Ginger juice 2, 4 ml/kg PO

Reversal of cisplatin-induced delay in gastric emptying in rats
by ginger (*Zingiber officinale*)

Both Ginger Extract and ginger juice reversed
cisplatin-induced delay in gastric emptying



GINGER: *IN VIVO* STUDY

Arch Pharm Res Vol 32, No 4, 565-573, 2009
DOI 10.1007/s12272-009-1413-9



Archives of
Pharmacal
Research

www.springer.com/12272

Gingerol Inhibits Cisplatin-induced Vomiting by Down Regulating 5-Hydroxytryptamine, Dopamine and Substance P Expression in Minks

Effect	Ondansetron	Ginger 200 mg/kg PO
No. of retching/vomiting	↓	↓
Level of 5-HT	↓	↓
Level of Dopamine	↔	↓
Level of SP	↔	↓

GINGER: PHASE II/III

A Phase II/III Randomized, Placebo-Controlled, Double-Blind Clinical Trial of Ginger (*Zingiber officinale*) for Nausea Caused by Chemotherapy for Cancer: A Currently Accruing URCC CCOP Cancer Control Study

Jane T. Hickok, Joseph A. Roscoe, Gary R. Morrow, Julie L. Ryan



GINGER: PHASE II/III

3 d prior CMT + 5HT₃
antagonist

Placebo x 6 d

GE 0.5 g x 6 d

GE 1.0 g x 6 d

GE 1.5 g x 6 d

644 patient with
nausea
experience from
CMT

-all doses of
ginger
significantly
reduced nausea
-0.5 g & 1 g of
ginger occur the
greatest
reduction(40%)

EMETOGENIC CMT

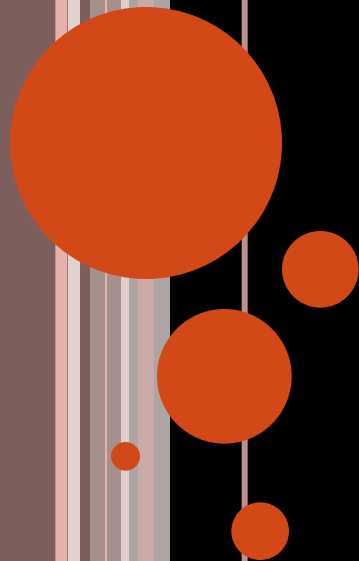
Symptom assessed	Groups (N = 57)		P-Value (Pearson Chi-square test) (comparing none-mild vs. moderate-severe)
	Control (n = 30) (%)	Experimental (n = 27) (%)	
Acute phase (days 1-4)			
CIN			
None	0 (0)	0 (0)	0.003 ^a
Mild	2 (06.7)	12 (44.4)	
Moderate	6 (20)	11 (40.7)	
Severe	22 (73.3)	4 (14.8)	
CIV			
None	1 (3.3)	4 (14.8)	0.002 ^a
Mild	6 (20)	14 (51.8)	
Moderate	10 (33.3)	6 (22.2)	
Severe	13 (43.3)	3 (11.1)	
Delayed phase (days 5-10)			
CIN			
None	0 (0)	6 (22.2)	<0.001 ^a
Mild	8 (26.7)	14 (51.8)	
Moderate	10 (33.3)	4 (14.8)	
Severe	12 (40)	3 (11.1)	
CIV			
None	3 (10)	9 (33.3)	0.022 ^a
Mild	13 (43.3)	14 (51.8)	
Moderate	8 (26.7)	3 (11.1)	
Severe	6 (20)	1 (3.7)	

^aSignifies difference at $P < 0.05$.

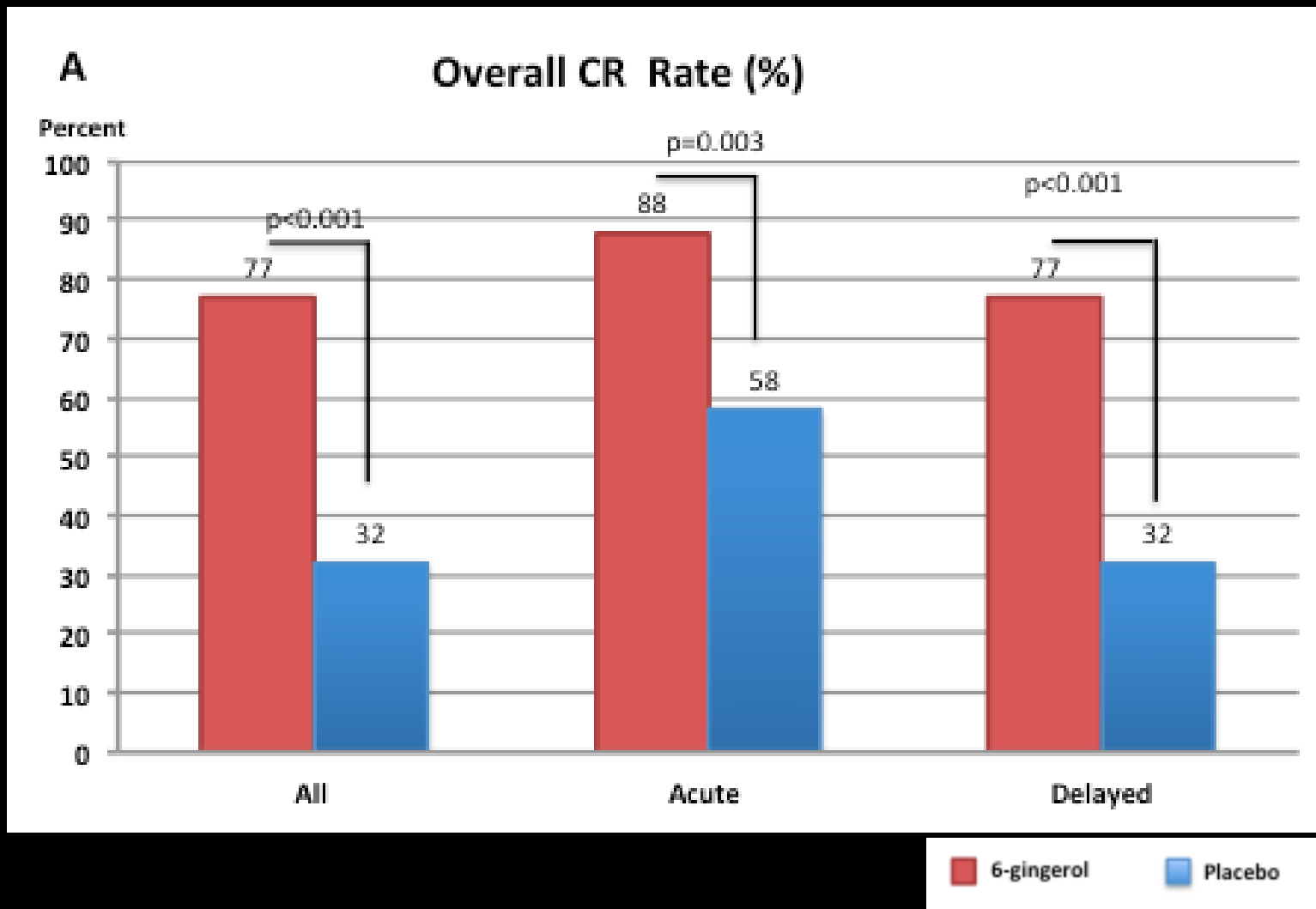


A PHASE II RANDOMIZED DOUBLE-BLIND PLACEBO
CONTROLLED STUDY OF 6-GINGEROL AS AN ANTI-
EMETIC IN SOLID TUMOR PATIENTS RECEIVING
MODERATELY TO HIGHLY EMETOGENIC
CHEMOTHERAPY

Jitprapa K., Kwanjit D., Nuttapong N., Suphat S.



OVERALL CR RATE



DRUG INTERACTION

- Ginger as anti-platelet activity
 - In vitro: >5 g of ginger may have this activity
 - In human: taking 5 g of ginger daily for a week
 - ➔ No change in platelet activity
 - ➔ No abnormal bleeding



DIET AND NUTRITION: MEGADOSE

VITAMIN C

- Use of Vit. C for **Treatment** cancer has been publicized for many year

Megadose Vitamin C **is not recommended** for prevention or treatment of cancer

- Survival
- Symptom & Appetite

1. Cameron E, et al. Proc Natl Aced Sci USA 1976;73:3685-3689.

2. Creagan ET, et al. NEJM 1979;301:687-690.

CAM AND TOXICITIES

- Drug interaction
 - Change in Effectiveness of CMT or RT
 - ↑Toxicity
- Impairment of Renal and Hepatic function



POTENTIAL INTERACTION BETWEEN HERBAL VS CONVENTIONAL DRUGS

Herbs	Drugs	Potential interaction
Feverfew, garlic, ginseng, ginkgo, ginger, dong quai	Warfarin	Altered bleeding time
Evening primrose oil	Anticonvulsants	Lowered seizure threshold
Ginseng	-Phenelzine sulfate -Estrogens, corticosteroids	-Headache, tremulousness, manic episodes -Additive effects
Kelp	Thyroxine	Iodine content of herb may interfere with thyroid replacement
Hawthorn flower, devil's claw, licorice	Digoxin	Alters pharmacodynamics; drug level monitoring is prudent
St. John's wort	Irinotecan, PIs, drugs metabolized by CYP-450 Cyclosporine Oral contraceptives Digoxin	Reduced drug levels

WEB SITES WITH RELIABLE INFORMATION ON CAM

Organization	Web Address
American Botanical Council	http://www.herbalgram.org
American Cancer Society	http://www.cancer.org
M.D. Anderson Cancer Center	http://www.mdanderson.org/departments/cimer
Memorial Sloan-Kettering Cancer Center	http://www.mskcc.org/mskcc/html/11571.cfm
National Cancer Institute	http://www.cancer.gov/cancertopics/pdq/cam/cam-cancer-treatment/Patient
National Center for Complementary and Alternative Medicine	http://nccam.nih.gov
Office of Complementary and Alternative Medicine	http://www.cancer.gov/cam
OncoLink (University of Pennsylvania Cancer Center)	http://www.oncolink.org
Quackwatch	http://www.quackwatch.com

SUMMARY OF KEY POINTS

- Pharmacist must familiarize most common CAM used by cancer pt. so that informed discussions
- Use the evidence base to give the appropriate instruction to our cancer patient
- Pharmacist must warn patients about potential problems with CAM
- Many types of CAM may interact with conventional medications to ↑toxicity or ↓efficacy of CMT



THANK YOU FOR YOUR ATTENTION

