Grains and Cancer

(穀類與癌症)

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2008/08/23

Introduction

Grains

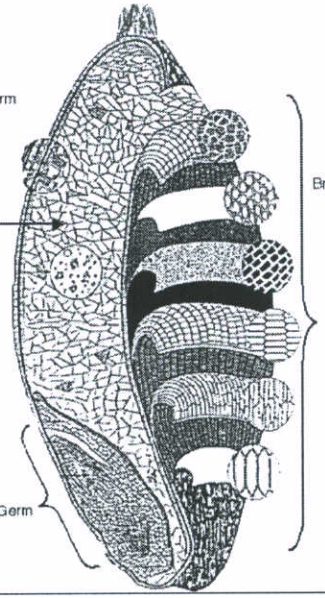
- **Major grains:**
  Wheat, Rice, and Maize
- **Minor grains:**
  Oats, Rye, Barley, Triticle, Sorghum, Millet, and Adlay (Job's tears)
- **Other grains (not botanically true grains):**
  Buckwheat, Wild rice, and Amaranth

Whole grains

The intact, ground, cracked or flaked caryopsis, whose principal anatomical components, the starchy endosperm, germ and bran, are present in substantially the same relative proportions as they exist in the intact caryopsis.

Structure of a whole grain

Providing energy
(Carbohydrate & protein)



Protecting seed
(Fiber, oil, B vitamins, & trace minerals)

Nourishment for the seed
(Antioxidants, vitamin E, & B vitamins)

(Slavin, 2004)

Whole grains and human cancer

Integrated series of case-control studies in Italy

Intake (days/week)	OR (95% CI) score[1]		Chi-square trend
	Intermediate[2]	High[2]	
Type of neoplasm	**(1-3 d/wk)**	**(>3 d/wk)**	
Oral cavity, pharynx and oesophagus	0.4 (0.2–0.6)	0.3 (0.2–0.5)	29.4[4]
Stomach	0.9 (0.7–1.1)	0.5 (0.4–0.7)	14.1[4]
Colon	0.9 (0.7–1.1)	0.5 (0.3–0.6)	21.1[4]
Rectum	0.8 (0.6–1.1)	0.7 (0.5–1.0)	6.1[3]
Liver	0.8 (0.5–1.1)	0.6 (0.4–0.9)	6.8[4]
Gallbladder	0.3 (0.1–1.0)	0.5 (0.2–1.4)	3.8[3]
Pancreas	0.9 (0.7–1.3)	0.8 (0.5–1.2)	0.9
Larynx	0.2 (0.1–0.5)	0.2 (0.0–0.5)	20.2[4]
Breast	0.9 (0.8–1.0)	0.9 (0.8–1.0)	4.6[3]
Endometrium	1.0 (0.8–1.2)	0.9 (0.7–1.1)	1.4
Ovary	0.9 (0.8–1.1)	0.6 (0.5–0.8)	11.6[4]
Prostate	0.9 (0.5–1.6)	0.8 (0.4–1.7)	0.4
Bladder	0.8 (0.5–1.1)	0.4 (0.3–0.7)	12.3[4]
Kidney	0.8 (0.5–1.2)	0.4 (0.2–0.8)	6.9[4]
Thyroid	1.9 (1.3–2.6)	1.3 (0.9–2.0)	6.1[3]
Hodgkin's disease	0.9 (0.4–1.7)	0.6 (0.2–1.5)	1.2
Non-Hodgkin's lymphomas	1.0 (0.6–1.5)	0.4 (0.2–0.8)	5.1[3]
Multiple myeloma	1.0 (0.6–1.7)	0.5 (0.2–1.1)	2.1
Controls			

Higher frequency of whole grain food intake is an indicator of reduced risk of several neoplasms.

(Chatenoud et al., 1998)

Meta-analysis of case-control studies

Table 3. Summary Findings of Epidemiologic Case-Control Studies of High vs. Low Intake of Whole Grains, by Cancer Studied[a]

Cancer Studied	Total Mentions	No. of Mentions <1	No. of Mentions With $p < 0.05$	Pooled Odds Ratios[b]	95% CI
Colorectal, colon, rectum, colon polyps	10	9	5	0.79	0.69–0.89
Colorectal, colon, rectum, colon polyps[c]	3	1	0	1.10	0.68–1.52
Gastric	7	7	7	0.57	0.47–0.67
Gastric[c]	1	0	1	1.60	
Oral, pharyngeal, tongue	4	4	3	0.57	0.38–0.76
Esophageal	2	2	2	0.52	0.09–0.95
Larynx[c]	1	1	0	0.60	
Pancreatic	4	4	2	0.70	0.54–0.86
Prostate	1	1	0	0.90	
Breast	2	2	0	0.86	0.67–1.05
Endometrial	3	3	1	0.55	0.41–0.69
Ovarian	1	1	1	0.63	
Brain	3	2	1	0.67	0.48–0.86
Myeloma	1	1	0	0.50	
Liver	1	1	0	0.58	
Thyroid	1	1	1	0.60	
Bladder	1	1	0	0.46	
Soft tissue sarcoma	1	1	1	0.20	
Soft tissue sarcoma[c]	1	1	1	0.40	
Non-Hodgkin's lymphoma	2	2	2	0.41	0.37–0.45
Hodgkin's lymphoma	1	1	0	0.60	

Whole-grain intake protects against various cancers.

(Jacobs et al., 1998)

The Case-Control Study of the KPMCP (US)

TABLE 3
Associations between plant food intakes (servings/d) and rectal cancer in men and women

	Men			Women			All subjects, OR (95% CI)[1]
	Cases	Controls	OR (95% CI)[1]	Cases	Controls	OR (95% CI)[1]	
	n	*n*		*n*	*n*		
Whole grains **(servings/d)**							
≤0.50	121	118	1.00	91	97	1.00	1.00
0.51–1.25	139	151	1.00 (0.70, 1.41)	115	156	0.85 (0.57, 1.25)	0.92 (0.71, 1.19)
1.26–2.0	125	152	0.86 (0.60, 1.23)	81	125	0.79 (0.51, 1.22)	0.82 (0.63, 1.08)
2.1–3.0	88	115	0.85 (0.58, 1.25)	70	94	1.05 (0.67, 1.67)	0.88 (0.66, 1.18)
>3.0	86	137	0.67 (0.46, 0.98)	36	60	0.74 (0.43, 1.27)	0.69 (0.51, 0.94)
P for linear trend							0.03
P for interaction[2]							0.27

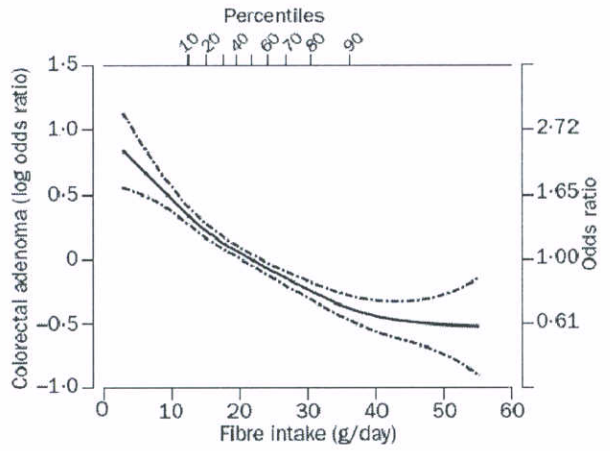
Rectal cancer is inversely associated with intakes of whole-grain products.

(Slattery et al., 2004)

KPMCP: Kaiser Permanente Medical Care Program in northern California

Dietary fiber of whole grains and human cancer

The PLCO Cancer Screening Trial (US) (Case-control)



Total dietary fibre (g/day) and distal colorectal adenoma

Risk of colorectal adenoma decreases with increasing fiber intake.

(Peters et al., 2003)

PLCO: Prostate, Lung, Colorectal , and Ovarian

	10% and 90% percentiles (g/day)	Base model*		Multivariate-adjusted analyses†	
		Odds ratio (95% CI)	P_{trend}	Odds ratio (95% CI)	P_{trend}
Fibre source					
Total fibre	12·6–36·4	0·77 (0·73–0·81)	<0·0001	0·91 (0·86–0·97)	0·002
Fibre from:					
Grains/cereals	3·3–14·1	0·75 (0·68–0·82)	<0·0001	0·88 (0·79–0·97)	0·008
Legumes	0·9–5·6	0·88 (0·73–1·67)	0·22	0·99 (0·78–1·20)	0·90
Vegetables	2·7–10·7	0·96 (0·84–1·10)	0·59	1·00 (0·89–1·15)	0·99
Fruits	1·4–8·7	0·58 0·51–0·67)	<0·0001	0·80 (0·71–0·93)	0·003

*Adjusted for age, centre, sex, and energy intake. †Adjusted for age, centre, sex, energy intake, ethnic origin, education attainment, smoking, alcohol intake, aspirin use, ibuprofen use, physical activity, body-mass index, red meat intake, folate intake, calcium intake, and other fibre food sources (for analysis of fibre from grains and cereals, legumes, vegetables and fruits)

Table 3: **Association between fibre food groups and distal colorectal adenomas**

Dietary fiber, particularly from grains, cereals, and fruits, is associated with decreased risk of distal colon adenoma.

(Peters et al., 2003)

The EPIC Study (European) (Prospective)

	Quintile					Hazard ratio for each quintile increase	p
	1	2	3	4	5		
Cereal fibre (g)	4·72 (2·28)	6·61 (2·82)	7·93 (3·31)	9·35 (3·91)	12·05 (5·71)	..	
Hazard ratio (95% CI)	1·00	0·89 (0·74–1·08)	0·85 (0·69–1·03)	0·88 (0·71–1·08)	0·78 (0·62–0·98)	0·950 (0·901–1·002)	0·060
Vegetable fibre (g)	2·83 (1·72)	3·77 (2·10)	4·42 (2·42)	5·11 (2·81)	6·48 (3·85)	..	
Hazard ratio (95% CI)	1·00	0·94 (0·77–1·15)	0·95 (0·77–1·16)	1·00 (0·81–1·24)	0·88 (0·70–1·11)	0·983 (0·932–1·035)	0·517
Legumes fibre (g)	0·45 (0·68)	0·65 (0·92)	0·85 (1·14)	1·14 (1·47)	1·73 (2·17)	..	
Hazard ratio (95% CI)	1·00	1·02 (0·83–1·26)	1·10 (0·91–1·34)	1·18 (0·97–1·43)	1·04 (0·84–1·30)	1·025 (0·976–1·077)	0·311
Fruit fibre (g)	2·21 (1·56)	3·41 (2·00)	4·29 (2·38)	5·36 (2·87)	7·76 (4·40)	..	
Hazard ratio (g)	1·00	0·69 (0·57–0·85)	0·76 (0·63–0·92)	0·82 (0·66–0·99)	0·78 (0·64–0·97)	0·967 (0·922–1·015)	0·174

Analyses are done with Cox's regression using age, weight, height, sex, non-fat energy, energy from fat, and stratified by centre.

Table 4: **Intakes of fibre and colorectal cancer by quintile of sex-specific source of fibre intake**

An inverse association between intake of fiber from cereals and risk of colon cancer.

(Bingham et al., 2003)

EPIC: European Prospective Investigation into Cancer and Nutrition

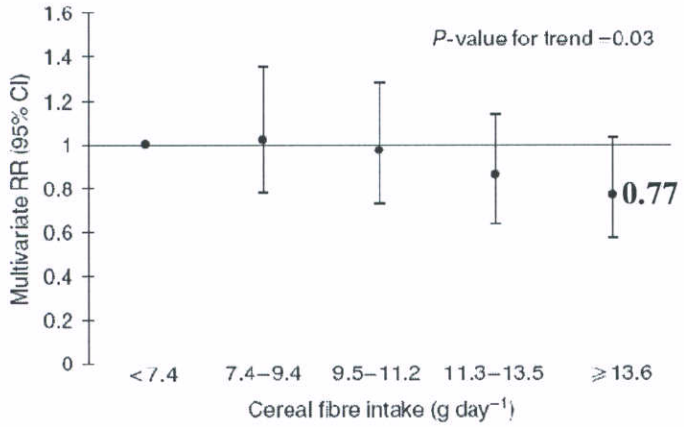
The Swedish Mammography Cohort Study (Prospective)

Table 2 RR and 95% CI of colorectal cancer according to consumption of whole grains

	Categories of whole grain consumption (servings day^{-1})					
	<1.5	1.5–2.4	2.5–3.4	3.5–4.4	⩾4.5	P-value for trend
Colorectal cancer						
All cases						
Number of cases	187	201	191	132	94	
Age-adjusted RR (95% CI)	1.00	0.99 (0.81–1.22)	1.05 (0.85–1.29)	0.97 (0.77–1.22)	0.80 (0.62–1.03)	0.14
Multivariate RR (95% CI)[a]	1.00	1.00 (0.81–1.24)	1.05 (0.84–1.30)	0.96 (0.75–1.23)	0.80 (0.60–1.06)	0.16
Excluding cases with follow-up <2 years						
Number of cases	176	187	175	119	84	
Multivariate RR (95% CI)[a]	1.00	0.99 (0.80–1.23)	1.02 (0.81–1.29)	0.93 (0.72–1.21)	0.76 (0.56–1.03)	0.10
Colon cancer[b]						
All cases						
Number of cases	136	135	131	88	57	
Age-adjusted RR (95% CI)	1.00	0.92 (0.72–1.16)	1.00 (0.78–1.28)	0.90 (0.68–1.18)	0.67 (0.49–0.91)	0.03
Multivariate RR (95% CI)[a]	1.00	0.94 (0.73–1.21)	1.02 (0.79–1.33)	0.91 (0.67–1.23)	0.67 (0.47–0.96)	0.06
Excluding cases with follow-up <2 years						
Number of cases	129	125	124	79	52	
Multivariate RR (95% CI)[a]	1.00	0.91 (0.70–1.18)	1.02 (0.78–1.34)	0.86 (0.63–1.18)	0.65 (0.45–0.94)	0.04
Rectal cancer[b]						
All cases						
Number of cases	50	66	57	43	36	
Age-adjusted RR (95% CI)	1.00	1.22 (0.84–1.78)	1.14 (0.77–1.68)	1.17 (0.77–1.78)	1.16 (0.75–1.80)	0.61
Multivariate RR (95% CI)[a]	1.00	1.17 (0.80–1.72)	1.09 (0.72–1.64)	1.09 (0.69–1.72)	1.11 (0.67–1.83)	0.85
Excluding cases with follow-up <2 years						
Number of cases	46	62	48	39	31	
Multivariate RR (95% CI)[a]	1.00	1.21 (0.81–1.81)	1.02 (0.66–1.58)	1.11 (0.69–1.79)	1.07 (0.62–1.82)	0.99

High consumption of whole grains may decrease the risk of colon cancer in women.

(Larsson et al., 2005)



The observed reduction in colon cancer risk associated with high consumption of whole grains may partly be attributed to cereal fiber.

(Larsson et al., 2005)

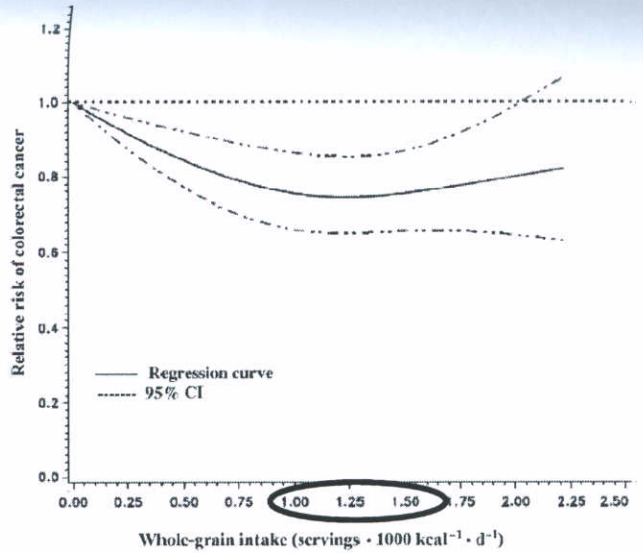
The NIH-AARP Diet and Health Study (US) (Prospective)

TABLE 4
Relative risks (and 95% CIs) of colorectal cancer by quintiles of whole-grain intake

	Quintile					P for trend
	1	2	3	4	5	
Colorectal cancer						
Median intake **(servings/kcal/d)**	0.2	0.4	0.6	0.8	1.3	
Cases/person-years	717/424 327	614/425 549	611/426 196	523/426 211	509/426 243	
Age-and sex-adjusted	1.00	0.87 (0.78, 0.96)	0.85 (0.76, 0.94)	0.71 (0.63, 0.79)	0.67 (0.60, 0.75)	<0.001
Multivariate[1]	1.00	0.92 (0.82, 1.02)	0.93 (0.83, 1.04)	0.81 (0.72, 0.91)	0.79 (0.70, 0.89)	<0.001
Colon cancer						
Cases/person-years	500/424 327	422/425 549	449/426 196	378/426 211	391/426 243	
Age- and sex-adjusted	1.00	0.85 (0.75, 0.97)	0.89 (0.78, 1.01)	0.73 (0.64, 0.84)	0.74 (0.64, 0.84)	<0.001
Multivariate[1]	1.00	0.91 (0.79, 1.03)	0.98 (0.86, 1.12)	0.83 (0.73, 0.96)	0.86 (0.75, 0.99)	0.03
Proximal colon cancer						
Cases/person-years	266/424 327	211/425 549	247/426 196	208/426 211	207/426 243	
Age- and sex-adjusted	1.00	0.79 (0.66, 0.95)	0.91 (0.76, 1.08)	0.74 (0.62, 0.89)	0.72 (0.60, 0.86)	<0.001
Multivariate[1]	1.00	0.84 (0.70, 1.01)	1.00 (0.84, 1.19)	0.85 (0.70, 1.02)	0.84 (0.69, 1.01)	0.10
Distal colon cancer						
Cases/person-years	217/424 327	192/425 549	190/426 196	152/426 211	163/426 243	
Age- and sex-adjusted	1.00	0.90 (0.74, 1.09)	0.88 (0.72, 1.07)	0.69 (0.56, 0.85)	0.72 (0.59, 0.88)	<0.001
Multivariate[1]	1.00	0.96 (0.79, 1.17)	0.98 (0.80, 1.19)	0.79 (0.64, 0.98)	0.85 (0.69, 1.06)	0.05
Rectal cancer						
Cases/person-years	221/424 327	197/425 549	166/426 196	150/426 211	124/426 243	
Age- and sex-adjusted	1.00	0.90 (0.75, 1.10)	0.75 (0.61, 0.92)	0.66 (0.54, 0.82)	0.54 (0.43, 0.67)	<0.001
Multivariate[1]	1.00	0.95 (0.78, 1.16)	0.82 (0.67, 1.01)	0.76 (0.61, 0.94)	0.64 (0.51, 0.81)	<0.001

(Schatzkin et al., 2007)

NIH-AARP: National Institutes of Health-American Association of Retired Persons



Whole-grain intake is inversely associated with colorectal cancer risk. (Schatzkin et al., 2007)

TABLE 3
Relative risks (and 95% CIs) of colorectal cancer by source of dietary fiber intake

	Quintile					
	1	2	3	4	5	*P* for trend
Fiber from grains						
Median intake (g · 1000 kcal^{-1} · d^{-1})	1.7	2.5	3.2	4.0	5.7	
Cases/person-years	652/424 227	660/425 715	583/425 996	569/426 245	510/426 344	
Age-and sex-adjusted	1.00	0.98 (0.88, 1.09)	0.85 (0.76, 0.95)	0.81 (0.73, 0.91)	0.71 (0.63, 0.79)	<0.001
Multivariate[1]	1.00	1.03 (0.92, 1.15)	0.94 (0.83, 1.05)	0.94 (0.83, 1.06)	0.86 (0.76, 0.98)	0.01
Fiber from fruit						
Median intake	0.5	1.2	2.0	2.9	4.8	
Cases/person-years	678/424 344	613/424 958	563/425 460	527/426 776	503/426 089	
Age-and sex-adjusted	1.00	0.86 (0.77, 0.96)	0.78 (0.70, 0.87)	0.73 (0.65, 0.81)	0.83 (0.74, 0.92)	0.001
Multivariate[1]	1.00	0.95 (0.85, 1.06)	0.91 (0.81, 1.03)	0.90 (0.80, 1.02)	1.08 (0.95, 1.23)	0.14
Fiber from vegetables						
Median intake	1.7	2.5	3.2	4.2	6.0	
Cases/person-years	689/423 597	599/425 480	586/425 353	550/426 468	550/427 128	
Age-and sex-adjusted	1.00	0.88 (0.79, 0.98)	0.87 (0.78, 0.97)	0.83 (0.74, 0.93)	0.87 (0.77, 0.97)	<0.001
Multivariate[1]	1.00	0.91 (0.81, 1.02)	0.93 (0.83, 1.04)	0.92 (0.81, 1.03)	1.01 (0.89, 1.15)	0.70
Fiber from beans						
Median intake	0.2	0.5	0.8	1.3	2.3	
Cases/person-years	623/425 769	620/425 785	561/425 569	595/425 566	575/425 737	
Age-and sex-adjusted	1.00	0.98 (0.87, 1.09)	0.87 (0.78, 0.98)	0.91 (0.81, 1.02)	0.89 (0.79, 0.99)	0.04
Multivariate[1]	1.00	0.98 (0.88, 1.09)	0.88 (0.78, 0.99)	0.92 (0.83, 1.04)	0.93 (0.83, 1.04)	0.25

Only fiber from grains is associated with a low risk of colorectal cancer. (Schatzkin et al., 2007)

A Case-Control Study in San Francisco (US)

TABLE 2. Association between consumption of whole-grain foods and risk of pancreatic cancer in a population-based case-control study, San Francisco Bay Area, California, 1995–1999

Whole grain (serving size) and frequency of consumption	Cases		Controls		Model 1*		Model 2†	
	No.‡	%	No.‡	%	OR§	95% CI§	OR	95% CI
Total whole grains¶								
Never or <1 serving/day	473	90	1,455	86	1.0	Referent	1.0	Referent
1 serving/day	40	8	188	11	0.62	0.43, 0.88	0.69	0.47, 1.0
≥2 servings/day	13	2	58	3	0.57	0.31, 1.1	0.60	0.31, 1.2
Trend-*p*					0.002		0.04	

Consuming more whole-grain foods may reduce the risk of pancreatic cancer.

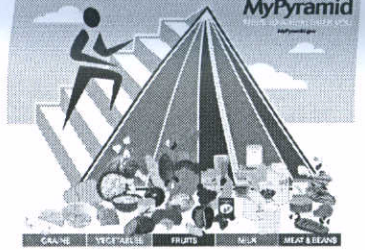
(Chan et al., 2007)

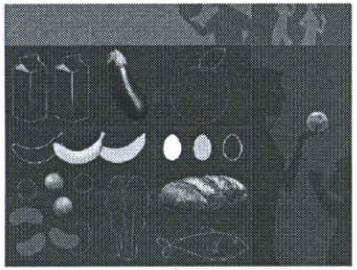
TABLE 5. Association between consumption of carbohydrate and fiber and risk of pancreatic cancer in a population-based case-control study, San Francisco Bay Area, California, 1995–1999

Dietary component and quartile of consumption	Cases		Controls		Model 1*		Model 2†	
	No.‡	%	No.‡	%	OR§	95% CI§	OR	95% CI
Dietary fiber (g/day)								
Q1 (≤15.6)	157	32	371	25	1.0	Referent	1.0	Referent
Q2 (15.7–20.4)	125	26	370	25	0.80	0.60, 1.1	0.86	0.64, 1.1
Q3 (20.5–26.4)	122	25	370	25	0.78	0.59, 1.0	0.90	0.67, 1.2
Q4 (≥26.5)	81	17	371	25	0.53	0.39, 0.72	0.65	0.47, 0.89
Trend-*p*					0.0001		0.02	

Dietary fiber is inversely associated with risk of pancreatic cancer.

(Chan et al., 2007)





Dietary Guidelines for Americans 2005

GRAINS

Make half your grains whole

Eat at least 3 oz. of whole-grain cereals, breads, crackers, rice, or pasta every day

1 oz. is about 1 slice of bread, about 1 cup of breakfast cereal, or 1/2 cup of cooked rice, cereal, or pasta

(USDA, 2005)

The Wheat Bran Fiber Trial (US) (Intervention)

Table 3. Crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for adenoma recurrence by quartile of baseline dietary fiber intake for the 1304 participants in the Wheat Bran Fiber trial

Quartile*	Median baseline dietary fiber intake, g/day	No. of participants with recurrence of adenomas	No. of participants with no recurrence of adenomas	OR (95% CI)	Adjusted OR (95% CI)†	P_{trend}‡
1	10.1	175	151	1.00 (referent)	1.00 (referent)	
2	15.3	158	168	0.81 (0.60 to 1.10)	0.79 (0.56 to 1.12)	
3	20.0	149	177	0.73 (0.53 to 0.99)	0.76 (0.54 to 1.08)	
4	27.7	156	170	0.79 (0.58 to 1.08)	0.83 (0.57 to 1.19)	.31

No association is found between amount of fiber consumed and adenoma recurrence.

(Jacobs et al., 2002)

Table 4. Crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for adenoma recurrence by quartile of baseline dietary fiber intake from the leading sources of fiber for the 1304 participants in the Wheat Bran Fiber trial

Fiber source	Total No. of participants	No. of participants with recurrence of adenomas	No. of participants with no recurrence of adenomas	OR (95% CI)	Adjusted OR (95% CI)*	P_{trend}†
Fruits, median g/day						
1.5 (Q1)	326	165	161	1.00 (referent)	1.00 (referent)	
3.7 (Q2)	329	162	167	0.95 (0.70 to 1.29)	0.89 (0.63 to 1.25)	
6.2 (Q3)	323	149	174	0.81 (0.61 to 1.14)	0.86 (0.60 to 1.21)	
11.5 (Q4)	326	162	164	0.96 (0.71 to 1.31)	0.92 (0.64 to 1.32)	.62
Vegetables, median g/day						
1.5 (Q1)	327	164	163	1.00 (referent)	1.00 (referent)	
2.7 (Q2)	325	157	168	0.93 (0.68 to 1.26)	0.98 (0.70 to 1.38)	
3.4 (Q3)	326	144	182	0.79 (0.58 to 1.07)	0.86 (0.6 to 1.20)	
6.8 (Q4)	326	173	153	1.12 (0.83 to 1.53)	1.34 (0.94 to 1.91)	.21
Cereals, breads, and crackers, median g/day						
1.4 (Q1)	326	167	159	1.00 (referent)	1.00 (referent)	
2.8 (Q2)	329	165	164	0.96 (0.71 to 1.30)	0.92 (0.65 to 1.29)	
4.4 (Q3)	323	150	173	0.83 (0.61 to 1.12)	0.88 (0.62 to 1.24)	
8.8 (Q4)	326	156	170	0.87 (0.64 to 1.19)	0.84 (0.59 to 1.19)	.31

Fiber intake, whether considered as a whole or from specific sources, does not modify the effect of treatment group.

(Jacobs et al., 2002)

Wheat and cancer

Wheat bran and colorectal tumor: The Wheat Bran Fiber Trial (US) (Intervention)

TABLE 4. RISK OF RECURRENT ADENOMAS.*

FOLLOW-UP PERIOD	NO. ANALYZED	HIGH-FIBER GROUP	LOW-FIBER GROUP	ADJUSTED ODDS RATIO (95% CI)†	HIGH-FIBER GROUP	LOW-FIBER GROUP	ADJUSTED RELATIVE RISK (95% CI)‡
		no. with ≥1 recurrent adenomas/total no. (%)			mean no. of recurrent adenomas		
After randomization	1303	338/719 (47.0)	299/584 (51.2)	0.88 (0.70–1.11)	0.61	0.57	0.99 (0.71–1.36)
After colonoscopy at 1 year	889	168/468 (35.9)	153/421 (36.3)	1.04 (0.79–1.38)	0.60	0.53	1.08 (0.71–1.64)

Wheat bran fiber does not protect against recurrent colorectal adenomas.

(Alberts et al., 2000)

Wheat bran and colorectal tumor: Interventional trial for colorectal cancer prevention in Osaka (Japan)

TABLE III – RISK OF TUMOR OCCURRENCE WITH WHEAT BRAN BISCUITS

	Year	Wheat bran (groups A + C) (n = 191)	No treatment (groups B + D) (n = 189)	Crude relative risk	Crude (95% CI)	Adjusted OR	Adjusted (95% CI)†
Number of tumors							
At least one	2	119 (62.3%)	106 (56.1%)	1.11	(0.94–1.31)	1.31	(0.87–1.98)
	4	106 (55.5%)	93 (49.2%)	1.13	(0.93–1.37)	1.31	(0.87–1.97)
≥ 2	2	57 (29.8%)	60 (31.7%)	0.94	(0.70–1.27)	0.92	(0.60–1.43)
	4	51 (26.7%)	53 (28.0%)	0.95	(0.69–1.32)	0.95	(0.60–1.50)
≥ 4	2	11 (5.8%)	14 (7.4%)	0.78	(0.36–1.67)	0.78	(0.34–1.76)
	4	11 (5.8%)	12 (6.3%)	0.91	(0.41–2.00)	0.91	(0.39–2.13)
Size of largest tumor (mm)							
≥ 3	2	95 (49.7%)	88 (46.6%)	1.07	(0.87–1.32)	1.14	(0.76–1.72)
	4	97 (50.8%)	76 (40.2%)	1.26	(1.01–1.58)	1.57	(1.04–2.37)
≥ 4	2	51 (26.7%)	52 (27.5%)	0.97	(0.70–1.35)	0.97	(0.61–1.54)
	4	52 (27.2%)	51 (27.0%)	1.01	(0.73–1.40)	1.02	(0.65–1.60)
≥ 10	2	4 (2.1%)	4 (2.1%)	0.99	(0.25–3.90)	1.00	(0.25–4.06)
	4	7 (3.7%)	0 (0.0%)	—	$p < 0.01$‡		
Atypia of tumors							
With moderate	2	64 (33.5%)	66 (34.9%)	0.96	(0.73–1.27)	0.94	(0.61–1.44)
	4	77 (40.3%)	74 (39.2%)	1.03	(0.80–1.32)	1.06	(0.70–1.60)

No significant difference in the development of new colorectal tumors is observed with administration of wheat bran.

(Ishikawa et al., 2005)

Wheat bran and intestinal tumor: meta-analysis

Summary of dietary prevention of colorectal tumors in humans, rats, and mice

Table 3
Summary of dietary prevention of colorectal tumours in rats, mice and humans: Efficacy of agents to reduce polyp recurrence in humans, tumour incidence in rats, and polyp number in mice

Agent or diet	Humans, mean polyp recurrence		Carcinogen initiated rats, colon tumour incidence			Min mice, polyp number (small bowel)		
	RR[c]	N[e]	RR (95%CI)[c]	Rats/men	N[e]	PR (95%CI)[d]	Mice/men	N[e]
Aspirin[a]	0.85 S[d]	4	0.86 (0.77–0.96)	OK[b]	8	0.94 (0.73–1.15)[f]	±OK	7
β-carotene	1.00 NS[d]	4	0.72 (0.47–1.08)[g]	OK	4	No study		0
Calcium	0.79 S	3	0.92 (0.85–1.00)	OK	13	1.09–1.21	NO	1
Wheat bran	0.96 NS	3	0.87 (0.77–0.97)	±OK	12	0.64 (0.54–0.84)	NO	5

Rodent models roughly predict effect in humans.

(Corpet and Pierre, 2005)

Wheat bran and colon tumor: meta-analysis

Table 2
Meta-analysis of chemoprevention studies in carcinogen-initiated rats, dealing with aspirin, beta-carotene, calcium and wheat bran protection

Treatment	2 × 2 table: no. of rats		RR	95% CI	P value
	With tumour	Total			
Wheat bran treated rats	307	595	0.83	0.75–0.91	0.0002
No wheat bran controls	355	569	0.87	0.77–0.97	0.015
Wheat bran in high fat diets			*0.79*	*0.66–0.93*	*0.006*
Wheat bran in low fat diets			*0.91*	*0.78–1.07*	*0.26*

Wheat bran reduces colon tumor incidence in rats.

(Corpet and Pierre, 2005)

Wheat bran fractions and colon tumor

Preventive Potential of Wheat Bran Fractions against Experimental Colon Carcinogenesis: Implications for Human Colon Cancer Prevention[1]

Bandaru S. Reddy,[2] **Yoshinobu Hirose, Leonard A. Cohen, Barbara Simi, Indrane Cooma, and Chinthalapally V. Rao**

Nutritional Carcinogenesis and Chemoprevention Program, American Health Foundation, Valhalla, New York 10595

[CANCER RESEARCH 60, 4792–4797, September 1, 2000]

The lipid fraction of wheat bran has strong colon tumor inhibitor properties.

The modulation of tumorigenesis by this fraction is associated with the alteration of iNOS and COX-2 activities.

iNOS: inducible nitrogen oxide synthase
COX-2: cyclooxygenase-2

Wheat bran oil and intestinal tumor

Wheat Bran Oil and Its Fractions Inhibit Human Colon Cancer Cell Growth and Intestinal Tumorigenesis in *Apc*$^{min/+}$ Mice

SHENGMIN SANG,[†] JIHYEUNG JU,[†] JOSHUA D. LAMBERT,[†] YONG LIN,[‡] JUNGIL HONG,[†] MOUSUMI BOSE,[†] STEVEN WANG,[†] NAISHENG BAI,[§] KAN HE,[§] BANDARU S. REDDY,[†] CHI-TANG HO,[⊥] FREDERICK LI,[∥] AND CHUNG S. YANG*,[†]

Department of Chemical Biology, Ernest Mario School of Pharmacy, Rutgers University, 164 Frelinghuysen Road, Piscataway, New Jersey 08854-8020, Cancer Institute of New Jersey, New Brunswick, New Jersey 08903, Pure World Botanicals, 375 Huyler Street, South Hackensack, New Jersey 07606, Department of Food Science, Rutgers University, 65 Dudley Road, New Brunswick, New Jersey 08901-8520, and Department of Epidemiology, Dana Farber Cancer Institute, Harvard University, Boston, Massachusetts 02115

J. Agric. Food Chem. 2006, *54*, 9792–9797

min: multiple intestinal neoplasia

Wheat aleurone flour and colon tumor

Wheat Aleurone Flour Increases Cecal β-Glucuronidase Activity and Butyrate Concentration and Reduces Colon Adenoma Burden in Azoxymethane-Treated Rats

Graeme H. McIntosh, Peter J. Royle and Greg Pointing[1]

CSIRO Health Sciences and Nutrition, Adelaide, SA 5000, Australia

J. Nutr. 131: 127–131, 2001.

Wheat germ extract and colon tumor

Wheat germ extract inhibits experimental colon carcinogenesis in F-344 rats

Attila Zalatnai[1,5], Károly Lapis[1], Béla Szende[1], Erzsébet Rásó[2], András Telekes[2], Ákos Resetár[3] and Máté Hidvégi[4]

[1]1st Institute of Pathology and Experimental Cancer Research, Semmelweis University, Budapest, Hungary, [2]National Institute of Oncology, Budapest, Hungary, [3]Biromedicina Co., Budapest, Hungary and [4]Department of Biochemistry and Food Technology, Budapest University of Technology and Economics, Budapest, Hungary

[5]To whom correspondence should be addressed
Email: zalatnai@korb1.sote.hu

Carcinogenesis vol.22 no.10 pp.1649–1652, 2001

A wheat germ extract prevents colonic cancer in laboratory animals.

Wheat with high phenolic acids and intestinal tumor

Antitumor Activity of Wheats With High Orthophenolic Content

Kelly Drankhan, John Carter, Ron Madl, Carol Klopfenstein, Frank Padula, Yemen Lu, Thomas Warren, Neil Schmitz, and Dolores J. Takemoto

NUTRITION AND CANCER. 47(2), 188–194, 2003

When fiber content is equal in diets, the content of orthophenolic acids in wheats predict the anti-tumor activity in vivo (Min mice).

Rye and cancer

Rye bran and colon tumor

Effects of soy or rye supplementation of high-fat diets on colon tumour development in azoxymethane-treated rats

Margaret J.Davies, Elizabeth A.Bowey, Herman Adlercreutz[1], Ian R.Rowland[2] and Paul C.Rumsby[3]

Carcinogenesis vol.20 no.6 pp.927–931, 1999

BIBRA International, Woodmansterne Road, Carshalton, Surrey SM5 4DS, UK and [1]Department of Clinical Chemistry, University of Helsinki and Folkhalsan Research Center, PO Box 60, FIN-00014, Helsinki, Finland

[2]Present address: Northern Ireland Centre for Diet and Health, School of Biomedical Sciences, University of Ulster, Coleraine BT52 1SA, UK

[3]To whom correspondence should be addressed
Email: prumsby@bibra.co.uk

Rye bran supplementation decreases the frequency of colonic tumors.

Rye bran and intestinal tumor

Beef induces and rye bran prevents the formation of intestinal polyps in *Apc*^{Min} mice: relation to β-catenin and PKC isozymes

Marja Mutanen[1], Anne-Maria Pajari and Seija I.Oikarinen

Carcinogenesis vol.21 no.6 pp.1167–1173, 2000

Department of Applied Chemistry and Microbiology (Nutrition), PO Box 27, University of Helsinki, Helsinki, FIN-00014, Finland

[1]To whom correspondence should be addressed
Email: marja.mutanen@helsinki.fi

The mice fed rye bran diet have the lowest number of polyps in the entire intestine.

Rye bran and intestinal tumor

Plasma enterolactone or intestinal *Bifidobacterium* levels do not explain adenoma formation in multiple intestinal neoplasia (Min) mice fed with two different types of rye-bran fractions

S. Oikarinen[1]*, S. Heinonen[2], S. Karppinen[3], J. Mättö[3], H. Adlercreutz[2], K. Poutanen[3] and M. Mutanen[1]

[1]*Department of Applied Chemistry and Microbiology, Division of Nutrition, PO Box 27, FIN 00014 University of Helsinki, Finland*
[2]*Institute for Preventive Medicine, Nutrition and Cancer, Folkhälsan Research Centre and Division of Clinical Chemistry, FIN-00014 University of Helsinki, Finland*
[3]*VTT Biotechnology, PO Box 1500, FIN-02044 VTT, Finland*

British Journal of Nutrition (2003), 90, 119–125

The soluble extract of rye bran increases number and size of adenomas in the distal small intestine.

Rye bran and intestinal tumor

Lignan Precursors From Flaxseed or Rye Bran Do Not Protect Against the Development of Intestinal Neoplasia in *Apc*^{Min} Mice

Henk J. van Kranen, Alicja Mortensen, Ilona K. Sørensen, Jolanda van den Berg-Wijnands, Rudolf Beems, Tarja Nurmi, Herman Adlercreutz, and Coen F. van Kreijl

NUTRITION AND CANCER, 45(2), 203–210, 2003

With the rye bran diet a statistically significant enhancement of the number of small intestinal tumors in female mice is observed.

The number of colon tumors is comparable between the control and rye bran-fed mice of either sex.

Oat and cancer

A Case-Control Study in San Francisco (US)

TABLE 2. Association between consumption of whole-grain foods and risk of pancreatic cancer in a population-based case-control study, San Francisco Bay Area, California, 1995–1999

Whole grain (serving size) and frequency of consumption	Cases		Controls		Model 1*		Model 2†	
	No.‡	%	No.‡	%	OR§	95% CI§	OR	95% CI
Cooked oatmeal or oat bran (1 cup)								
<1/month	235	45	851	50	1.0	Referent	1.0	Referent
1/month–1/week	155	29	491	29	1.1	0.90, 1.4	1.2	0.94, 1.5
≥2/week	136	26	359	21	1.3	1.0, 1.7	1.3	1.0, 1.7
Trend-*p*					0.05		0.02	

Consumption of cooked breakfast cereals (oatmeal/oat bran) is positively associated with the risk of pancreatic cancer.

(Chan et al., 2007)

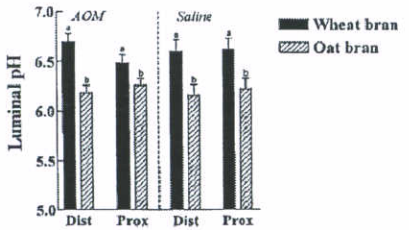
Oat bran and colon tumor

Wheat Bran Diet Reduces Tumor Incidence in a Rat Model of Colon Cancer Independent of Effects on Distal Luminal Butyrate Concentrations[1,2]

Debra L. Zoran, Nancy D. Turner, Stella S. Taddeo, Robert S. Chapkin and Joanne R. Lupton[3]

Faculty of Nutrition, Texas A&M University, College Station, TX 77843-2471

J. Nutr. 127: 2217–2225, 1997.



Rats consuming oat bran have significantly more development of colon tumors.

Large luminal butyrate concentration in the distal colon alone are not protective of tumor development.

Oat bran and intestinal tumor

Table II. Effect of beef, cereal brans and inulin on tumor development in the small intestine and colon of Min mice, mean and SD

Dietary group	Number of tumors			Tumor incidence (%) in colon and caecum
	Total small intestine	Distal small intestine	Colon and caecum	
AIN93-G	35.3 (11.6)	19.6 (6.8)	1.5 (0.9)	83
Non fiber	34.6 (7.1)	22.7 (5.6)	1.4 (1.7)	71
Rye	26.4 (12.1)[a]	15.4 (8.7)[b]	1.4 (2.1)	33
Wheat	35.0 (8.2)	21.0 (6.2)	2.1 (1.8)	75
Oat	46.9 (13.8)	29.9 (11.3)	1.8 (1.0)	83
Inulin	49.3 (16.3)	32.9 (14.3)	2.4 (1.0)	100
Beef	52.8 (13.2)	36.6 (9.4)[c]	3.2 (2.3)	89

[a]Significantly different from the beef group ($P = 0.004$) and from the inulin group ($P = 0.031$).
[b]Significantly different from the inulin group ($P = 0.017$).
[c]Significantly different from the AIN93-G group ($P = 0.009$), the rye-bran group ($P = 0.001$) and from the wheat-bran group ($P = 0.02$).

The number of intestinal tumors is comparable between the control and oat bran-fed mice.

(Mutanen et al., 2000)

Rice and cancer

A Case-Control Study in San Francisco (US)

TABLE 2. Association between consumption of whole-grain foods and risk of pancreatic cancer in a population-based case-control study, San Francisco Bay Area, California, 1995–1999

Whole grain (serving size) and frequency of consumption	Cases		Controls		Model 1*		Model 2†	
	No.‡	%	No.‡	%	OR§	95% CI§	OR	95% CI
Brown rice (1 cup)#								
<1/month	407	77	1,184	70	1.0	Referent	1.0	Referent
1/month–1/week	97	18	418	25	0.65	0.50, 0.83	0.71	0.55, 0.93
≥2/week	22	4	99	6	0.60	0.37, 0.97	0.72	0.44, 1.2
Trend-*p*					0.0003		0.01	

An inverse association is observed between brown rice and risk of pancreatic cancer.

(Chan et al., 2007)

Rice bran and intestinal tumor

Evaluation of the cancer chemopreventive efficacy of rice bran in genetic mouse models of breast, prostate and intestinal carcinogenesis

RD Verschoyle[1], P Greaves[1], H Cai[1], RE Edwards[2], WP Steward[1] and AJ Gescher*,[1]
[1]Cancer Biomarkers and Prevention Group, Department of Cancer Studies and Molecular Medicine, University of Leicester, Leicester LE2 7LX, UK
[2]Medical Research Council Toxicology Unit, University of Leicester, Leicester, UK

British Journal of Cancer (2007) 96, 248 – 254

Consumption of rice bran reduces numbers of intestinal adenomas in Min mice.

The fibrous constituents of the bran mediate chemopreventive efficacy.

Rice bran hemicellulose and colon tumor

The water-soluble rice bran hemicellulose play a preventive role in 1,2-dimethylhydrazine (DMH)-induced large bowel carcinogenesis in Fischer 344 rats.

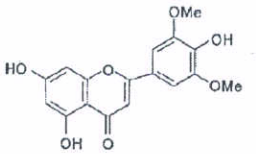
(Aoe et al., 1993)

Tricin from rice bran and intestinal tumor

The rice bran constituent tricin potently inhibits cyclooxygenase enzymes and interferes with intestinal carcinogenesis in *Apc^{Min}* mice

Hong Cai,[1] Mohammad Al-Fayez,[1] Richard G. Tunstall,[1] Sharon Platton,[1] Peter Greaves,[2] William P. Steward,[1] and Andreas J. Gescher[1]

[1]Cancer Biomarkers and Prevention Group, Department of Cancer Studies and Molecular Medicine and [2]Medical Research Council Toxicology Unit, University of Leicester, Leicester, United Kingdom



Mol Cancer Ther 2005;4(9). September 2005

Rice bran oil and liver tumor

Suppression of diethylnitrosamine and 2-acetylaminofluorene-induced hepatocarcinogenesis in rats by tocotrienol-rich fraction isolated from rice bran oil

J Iqbal[1], M Minhajuddin[2] and Z H Beg[3]

European Journal of Cancer Prevention 2004, 13:515–520

Tocotrienol-rich fraction of rice bran oil reduces cancer risk by preventing hepatic lipid peroxidation and protein oxidation damage due to its antioxidant actions.

Rice germ and colon tumor

Dietary prevention of azoxymethane-induced colon carcinogenesis with rice-germ in F344 rats

Kunihiro Kawabata, Takuji Tanaka[1], Taro Murakami[2], Tadashi Okada[2], Hiromichi Murai[2], Tomohiro Yamamoto[3], Akira Hara[3], Masahito Shimizu, Yasuhiro Yamada, Kengo Matsunaga, Toshiya Kuno, Naoki Yoshimi, Shigeyuki Sugie and Hideki Mori[4]

Carcinogenesis vol.20 no.11 pp.2109–2115, 1999

First Department of Pathology, Gifu University School of Medicine, 40 Tsukasa-machi, Gifu 500-8705, [1]First Department of Pathology, Kanazawa Medical University, 1-1 Daigaku, Uchinada, Ishikawa 920-0293, [2]Oryza Oil and Fat Chemical Co. Ltd, Ichinomiya 493-8001 and [3]Department of Biochemistry, Gifu Pharmaceutical University, 5-6-1 Mitahorahigashi, Gifu 502-0003, Japan

[4]To whom correspondence should be addressed.
Email: hidmori@cc.gifu-u.ac.jp

Dietary exposure to rice germ during the initiation phase significantly reduces the incidence of colonic adenocarcinoma.

A significant anticancer property of rice-germ preparations may be partly due to their antiproliferative effects.

Adlay and cancer

Adlay seed and lung tumor

Antiproliferative and Chemopreventive Effects of Adlay Seed on Lung Cancer in Vitro and in Vivo

HUI-CHIU CHANG,[†] YU-CHUN HUANG,[‡] AND WEN-CHUN HUNG*[,§]

Department of Physiology, Graduate Institute of Medicine, and School of Technology for Medical Sciences, Kaohsiung Medical University, Kaohsiung 807, Taiwan, Republic of China

J. Agric. Food Chem. **2003**, *51*, 3656–3660

Feeding with diet containing powdered adlay seed reduces the number of surface lung tumors.

Adlay seed and lung tumor

Methanolic Extract of Adlay Seed Suppresses COX-2 Expression of Human Lung Cancer Cells via Inhibition of Gene Transcription

WEN-CHUN HUNG[†] AND HUI-CHIU CHANG*[,§]

School of Technology for Medical Sciences and Department of Physiology, Kaohsiung Medical University, Kaohsiung 807, Taiwan, Republic of China

J. Agric. Food Chem. **2003**, *51*, 7333–7337

Treatment of the methanolic extract of adlay seed reduces the PGE_2 level in serum and inhibits COX-2 expression of tumor tissues in nude mice.

PGE_2: prostaglandinE_2

Dehulled adlay and colon tumor

Effects of adlay on azoxymethane-induced colon carcinogenesis in rats

Chun-Kuang Shih [a,b,*], Wenchang Chiang [b], Min-Liang Kuo [c,*]

[a] *School of Nutrition and Health Sciences, Taipei Medical University, Taipei 110, Taiwan*
[b] *Graduate Institute of Food Science and Technology, National Taiwan University, Taipei 106, Taiwan*
[c] *Graduate Institute of Toxicology, College of Medicine, National Taiwan University, Taipei 100, Taiwan*

Food and Chemical Toxicology 42 (2004) 1339–1347

Dehulled adlay significantly reduces the number of colonic aberrant crypt foci (ACF).

Rats fed dehulled adlay have less COX-2 protein expression in tumors.

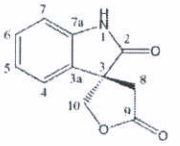
Adlay bran lactam and cancer

Isolation and characterization of new lactam compounds that inhibit lung and colon cancer cells from adlay (*Coix lachryma-jobi* L. var. *ma-yuen* Stapf) bran

Ming-Yi Lee [a], Huan-You Lin [b], Faiwen Cheng [a], Wenchang Chiang [a,*], Yueh-Hsiung Kuo [a,b,c,d,*]

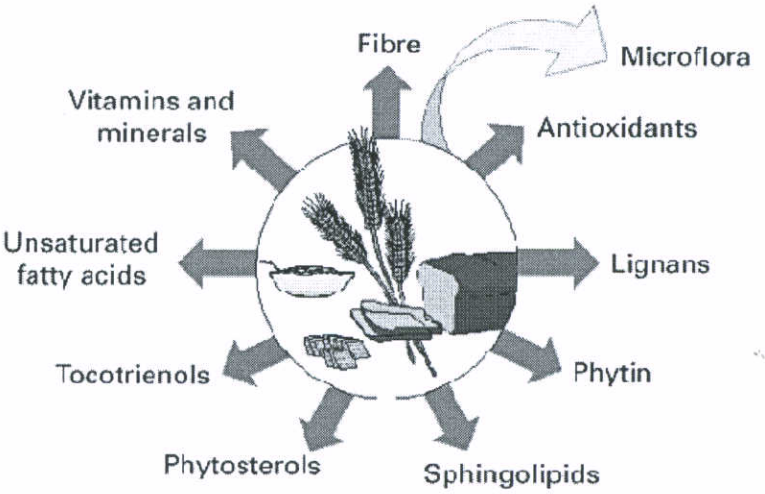
[a] *Graduate Institute of Food Science and Technology, Center for Food and Biomolecules, College of Bioresources and Agriculture, National Taiwan University, Taipei 106, Taiwan*
[b] *Department of Chemistry, National Taiwan University, Taipei 106, Taiwan*
[c] *Tsuzuki Institute for Traditional Medicine, China Medical University, Taichung 404, Taiwan*
[d] *Agricultural Biotechnology Research Center, Academia Sinica, Taipei 115, Taiwan*

Food and Chemical Toxicology 46 (2008) 1933–1939



Anti-cancer components in whole grains

Active components in whole grains



(Slavin, 2003)

Dietary fiber

Table 1. *Possible mechanisms for the protective action of dietary fibre on colorectal oncogenesis*

Physical
Increased bulk and dilution of carcinogen
Decreased contact time due to more rapid transit
Binding of carcinogen
Binding of bile salts

Prebiotic and metabolic action of flora
Alteration of colonic microflora; numbers and species balance
Inhibition of carcinogen activation
Stimulation of flora to increase bulk
Alteration of bile salt metabolism to reduce conversion to secondary bile salts

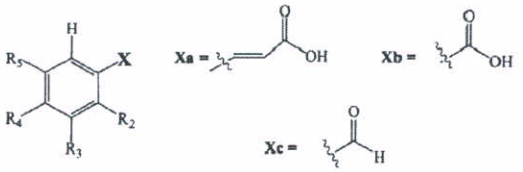
Fermentative
Lowering of pH
Reduced solubility of bile salts
Increased production of SCFAs, especially butyrate

Metabolic
Reduced insulin resistance and hyperinsulinaemia

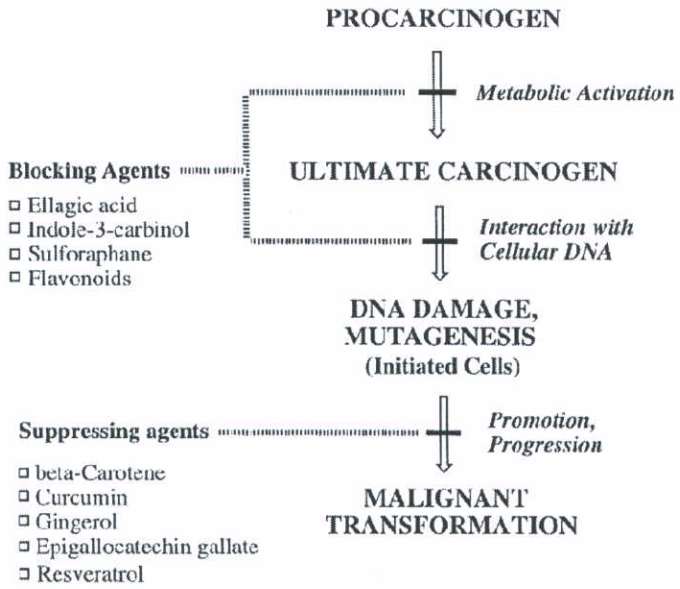
(Young et al., 2005)

Phenolic acids

- Inhibition of carcinogen activation
- Induction of phase II enzymes
- Inhibition of arachidonic acid metabolism
- Modulation of oncogenes, tumor suppressor genes, and signal transduction pathways
- Antioxidative properties



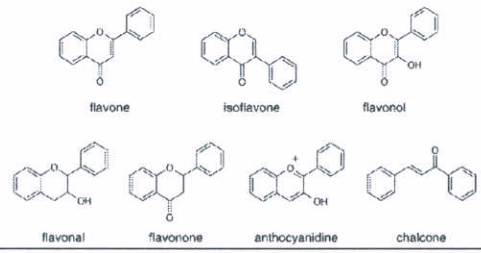
(Robbins, 2003)



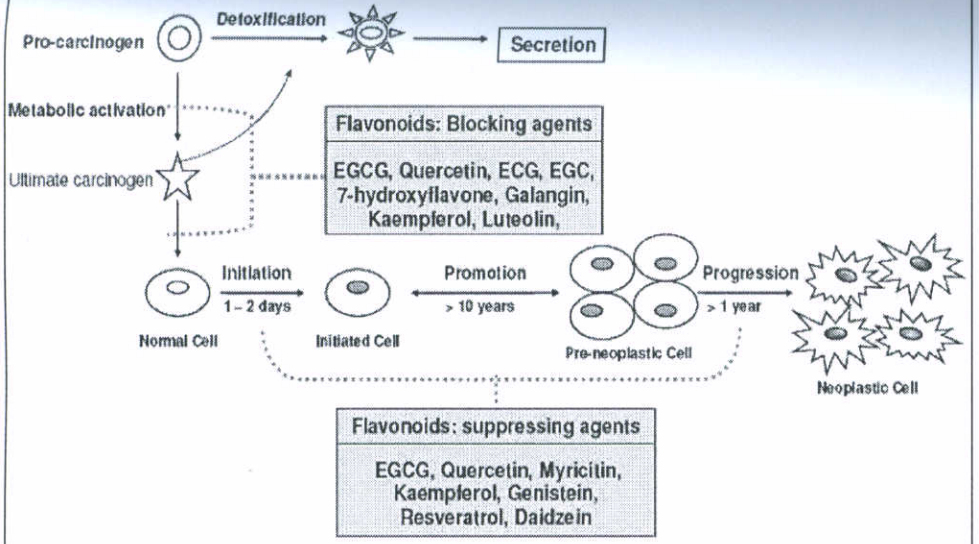
(Surh, 1999)

Flavonoids

- Antioxidative activity
- Anti-inflammatory activity
- Anti-proliferative activity
- Inhibition of bioactivating enzymes
- Induction of detoxifying enzymes



(Boots et al., 2008)



(Kale et al., 2008)

Phytic acid (Inositol hexaphosphate, IP6)

Table 1 Mechanisms of action: phytic acid (IP6)

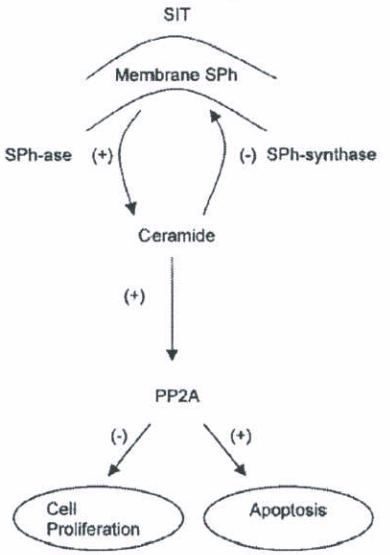
Gene function
- Interference with signal transduction by blocking phosphatidyl inositol 3 kinase
- Stimulation of p53 suppressor gene
- Stimulation of tumor suppressor gene p21 WAF1/Cip1
- Decreasing mitosis by arresting proliferation in the G0/G1 phase

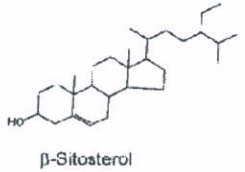
Enhanced immunity
- Increase NK cell function
- Antagonizing fibroblast growth factors

Antioxidant properties
- Forms an iron chelate thereby inhibiting iron mediated oxidative reactions

(Fox and Eberl, 2002)

Phytosterol





β-Sitosterol

FIGURE 2 Proposed mechanism by which β-sitosterol inhibits tumor growth and stimulates apoptosis. Abbreviations: SIT, β-sitosterol; SPh, sphingomyelin; PP2A, protein phosphatase 2A; SPh-ase, sphingomyelinase; SPh-synthase, sphingomyelin synthase.

(Awad and Fink, 2000)

Vitamin E

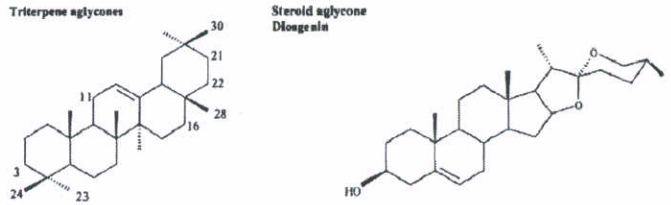
- Antioxidative activity
- Maintaining selenium in the reduced state
- Inhibition of nitrosamines formation

Selenium (Se)

- Antioxidative activity
- Suppressive action on cell proliferation

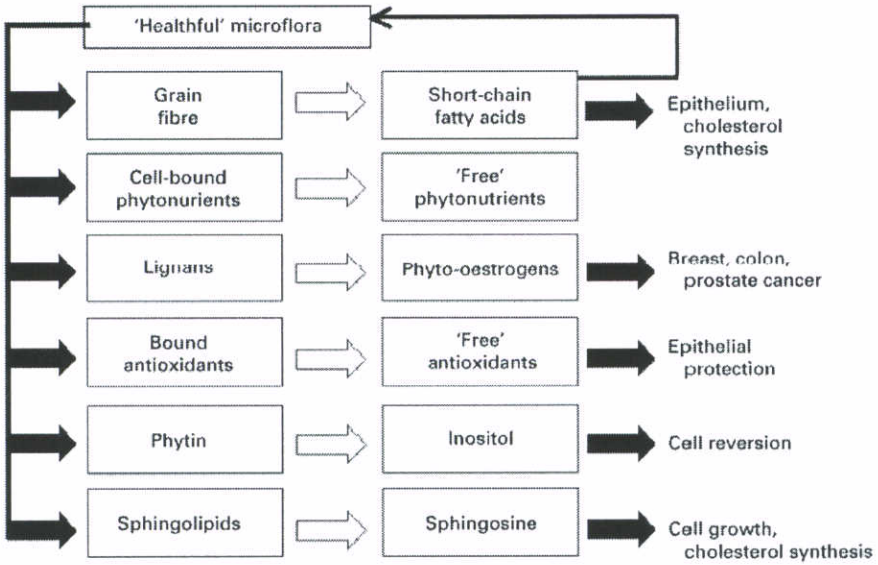
Saponin

- Cytotoxic and growth inhibitory effects against tumor cells
- Immnne-modulatory effects
- Binding to bile acids
- Normalization of epithelial cell proliferation



(Rao and Sung, 1995; Guclu-Ustundag and Mazza, 2007)

Components in whole grains and the microflora



(Slavin, 2003)

The whole is greater than the sum of the parts!