



TURMERIC
THE SALT OF THE ORIENT
IS
THE SPICE OF LIFE



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Turmeric / Fenugreek - The Magic Ingredients of the Indian Kitchen



Kamala Krishnaswamy

Former Director (NIN)

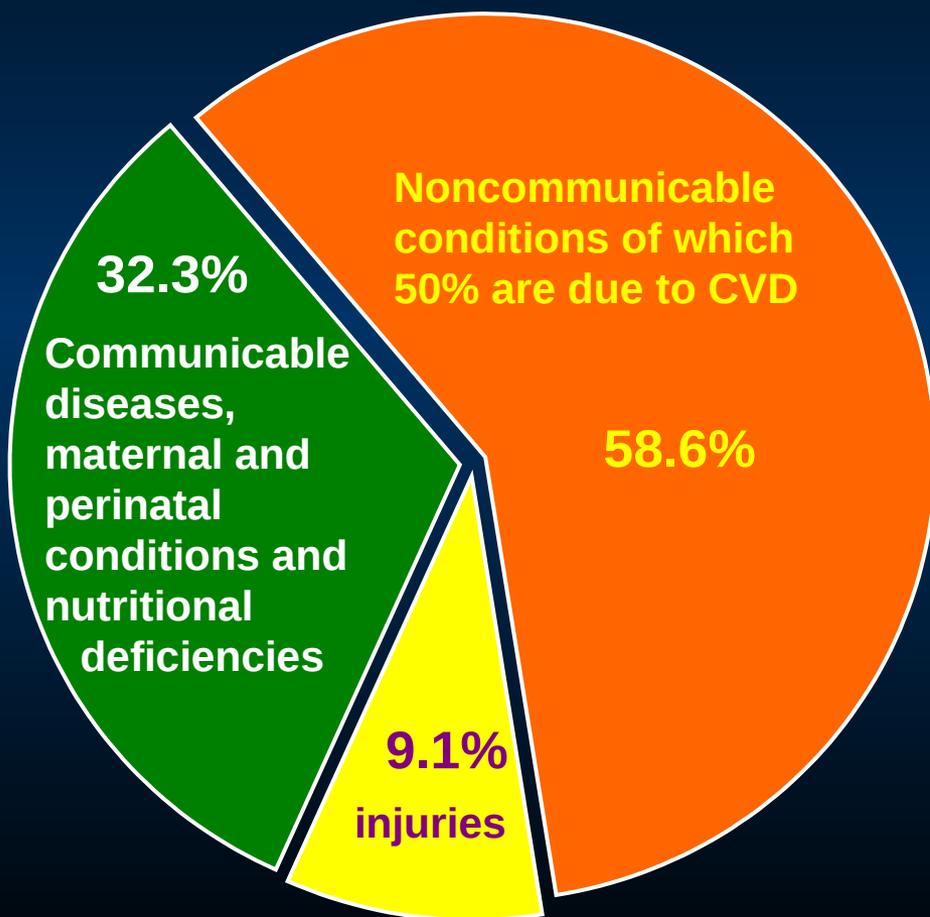


National Institute of Nutrition, Jamai Osmania
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Deaths, by broad cause group estimates for 2002

Total deaths: 57,027,000



Chronic Diseases of Clinical /Public Health Significance

- Cardiovascular and cerebrovascular diseases
- Diabetes and complications
- Chronic inflammatory diseases
- Obesity
- Cataract
- Osteoporosis
- Neurodegenerative diseases
- Aging

Ancient quotes on food and health

- You are what you eat – Rigveda
- Oh, God , Give us food which does not cause any disease and also gives us strength – Yajurveda
- He, who takes food in proper measures lives a long life and lives without disease, gets strength and alertness of mind. His children are born healthy and without any deformity or disease - Mahabharatha

International Trade of Spices

- **India is a land of spices and herbs from time immemorial**
- International trade in spices has grown by leaps and bounds in the last decade
- Estimated exports from India – US \$ 793 x 10⁶ *
- An estimated 500,000 tonnes of spices and herbs are imported globally every year
- **An impressive 46% of the supply comes from India**
- Turmeric export 51,500 tons

* 2006-07

Source : Economic intelligence service 2007



Curcuma longa linn

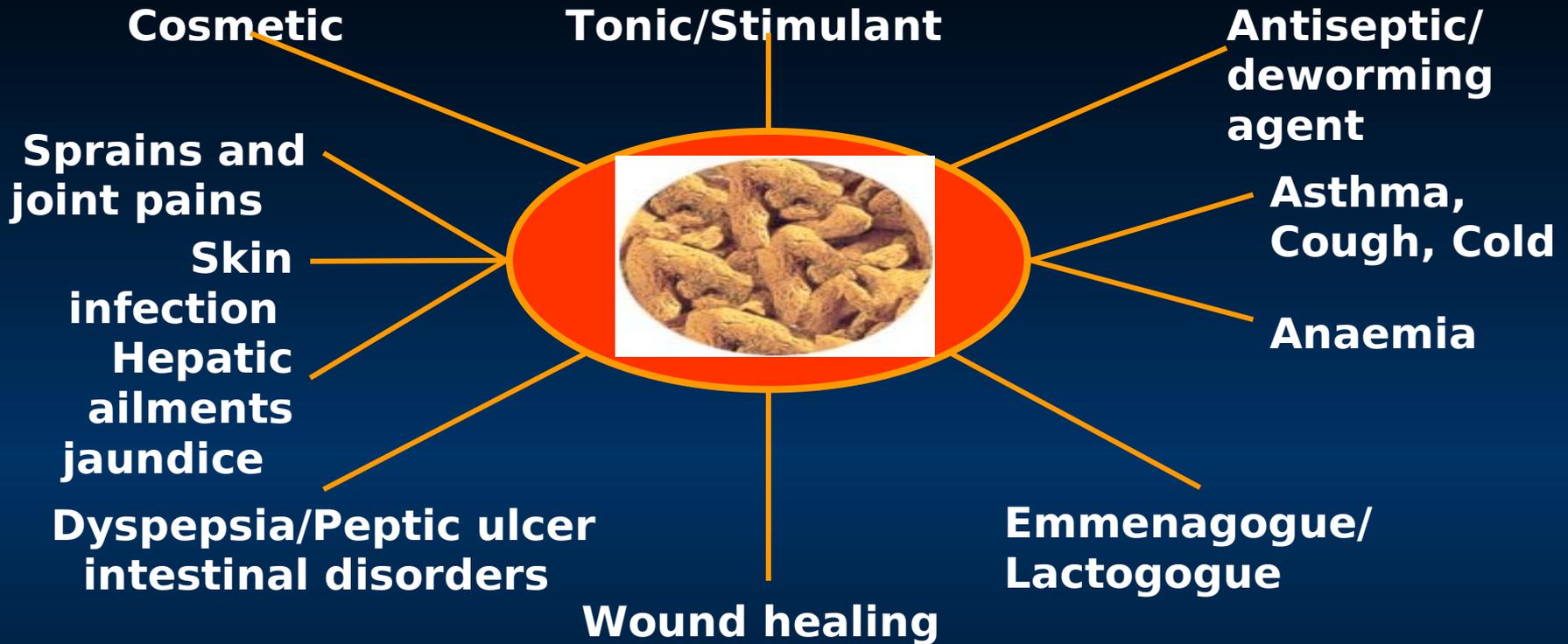


Curcuma longa linn (turmeric)



Curcumin

TRADITIONAL USES OF TURMEIC



Scientific evidences for traditional uses

Antioxidant, anti-inflammatory anti-infective (H-Pylori), anti-spasmodic, Digestive, Choleric, Chologogue, Hypo-lipedemic, Hepato-Protective, Anti-Toxic, Antifibrotic, Wound healing (iNOS)

KALEIDOSCPIC EFFECTS

Chemical Composition of Curcuma longa Linn

		(%)	
Essential Oils	-	2 - 4	
Fatty Oils	-	2 - 3	
Ash	-	4 - 8	Mehra and Puri, 1971
Curcuminoids	-	2 - 5	Srimal and Dhawan, 1985
Phytosterols	-	0.82 *	** Personal Observations
Linolenic acid	-	0.6 - 1 **	(3.9-9.4%) of fatty acids
Moisture	-	3 - 7	

Nutrient Composition per 100g

Proximate Principles

Energy	-	354 Kcal*	Protein	-	7.83g *	Carbohydrate	-	64.9g *
Fat	-			-	9.9g*		-	

Micronutrients

Carotene	-	0.03 mg	Iron	-	15.000 mg	Calcium	-	150 mg
Thiamin	-	0.03 mg	Copper	-	0.394 mg	Phosphate	-	280 mg
Riboflavin	-	0.19 mg	Manganese	-	8.380 mg	Magnesium	-	190 mg
Niacin	-	2.30 mg	Zinc	-	2.720 mg	Sodium	-	30 mg
Vitamin B6	-	1.8 mg *	Chromium	-	0.069 mg	Potassium	-	250 mg
Vitamin C	-	50.00 mg	Selenium	-	0.067 mg	Fibre	-	21.1 gm*
Folic acid	-	18.00 µg	Vitamin E	-	0.07 mg *		-	

CHANGES IN CANCER CELL

Development of Neoplasia

Chemicals, Physical, Radiation, Biological

Normal Cell ← Repair

Mutations ← DNA damage ← Detoxification
in the genome

Initiation

Altered DNA in cells (Adducts)

Mutations * in
Genome of
Somatic
cells

Initiated cells

(fixed altered DNA)

Promotion

DNA - altered clones

Progression

Ex. of altered
Gene
products

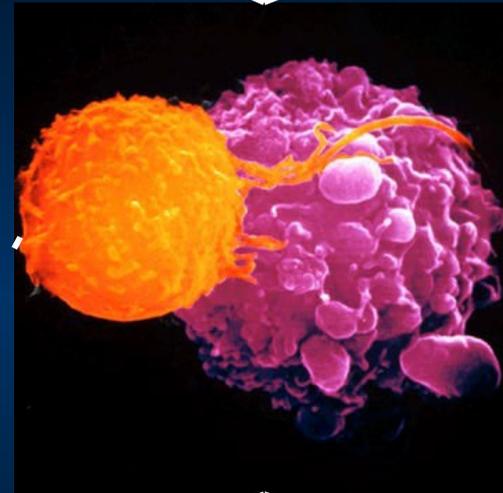
Tumor formation

Invasion, metastasis

Continuous
multiplication
(Proliferation)

Self signals to
growth (Tumor
growth)

Escapes
programmed
cell death
(Apoptosis)



Escapes
growth
restraints
(Tumor
growth)

Sustained
vascularisation
(Angiogenesis)

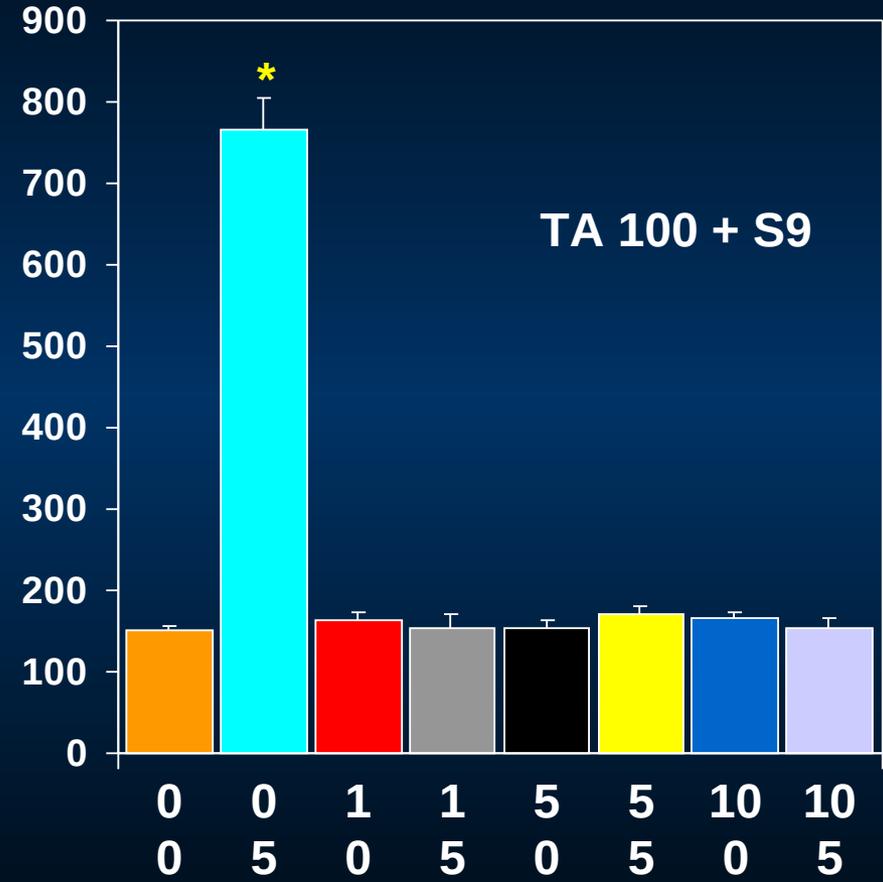
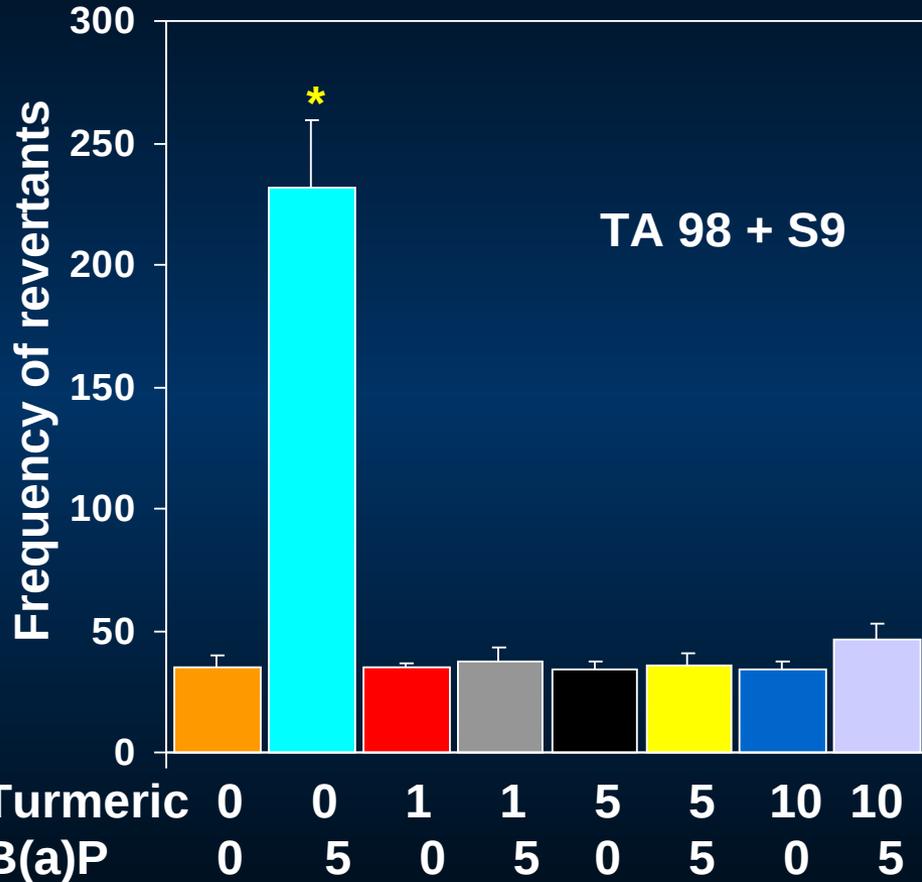
Invasion
(Metastasis)

* Activation of growth promoting and Inactivation of suppressor and apoptosis genes

Studies and Methods

Ames test	S. typhimurium
SOS response	E.coli
P32 post label assay	DNA adducts
Drug metabolising enzymes	AHH GSHT UDPGT
Antioxidant	TBARS Liver enzymes Antioxidant enzymes
SSbs	S.Cerevisiae
Tumor induction	Histopathology
Comet assay	Lymphocytes
Cataract	Induction
Lipids	Hypolipidemic effects
Human studies	Mutagens in Urine DNA adducts and Micronuclei in vivo Nitrosation

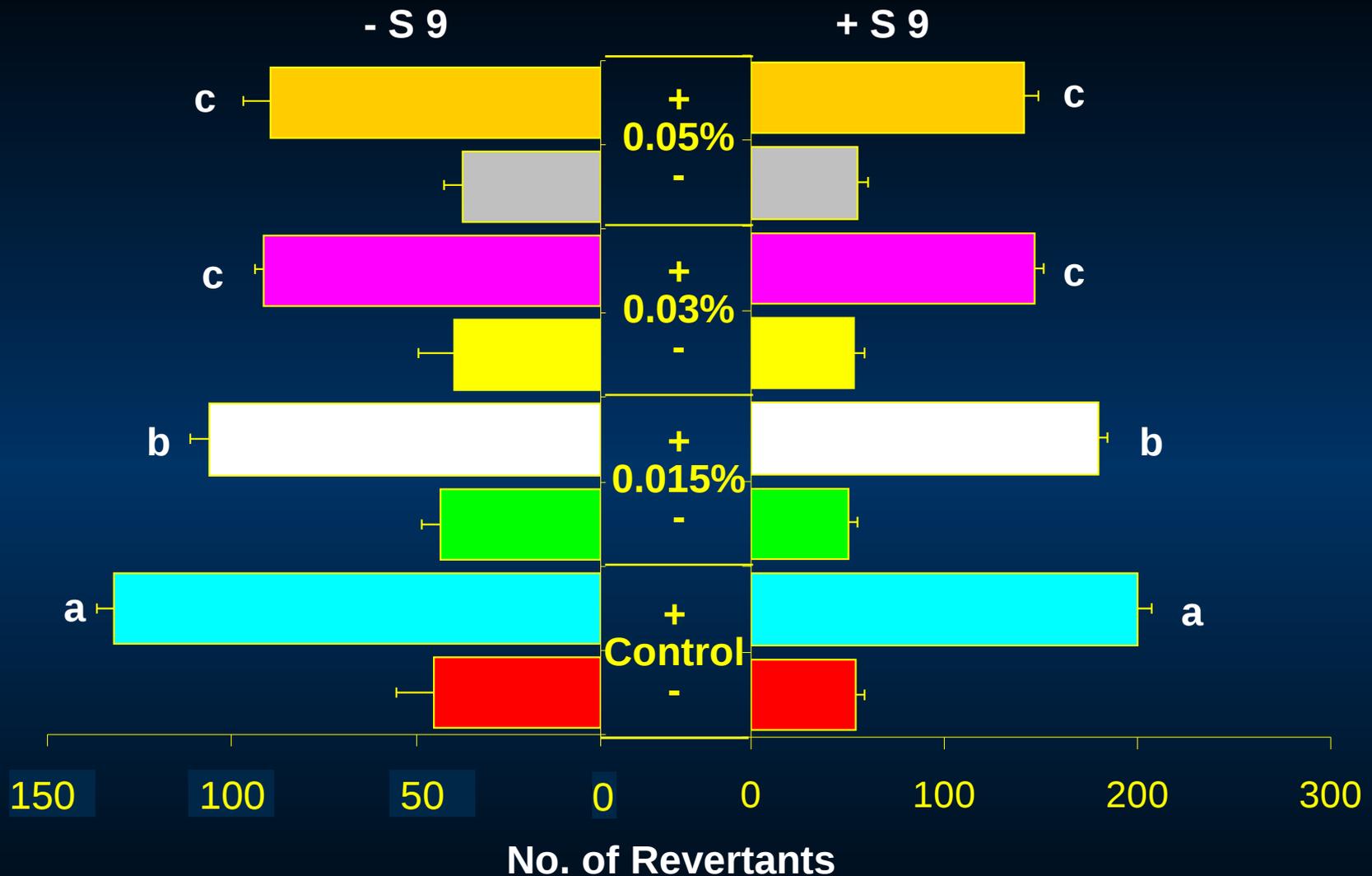
Mutagens Load in Urine in Turmeric Fed Rats



* p < 0.001

Similar results were seen with 0.1%, 0.5% turmeric with both B(a)P and 3MC

Effects of Curcuminoids* on Urinary Mutagens TA 98

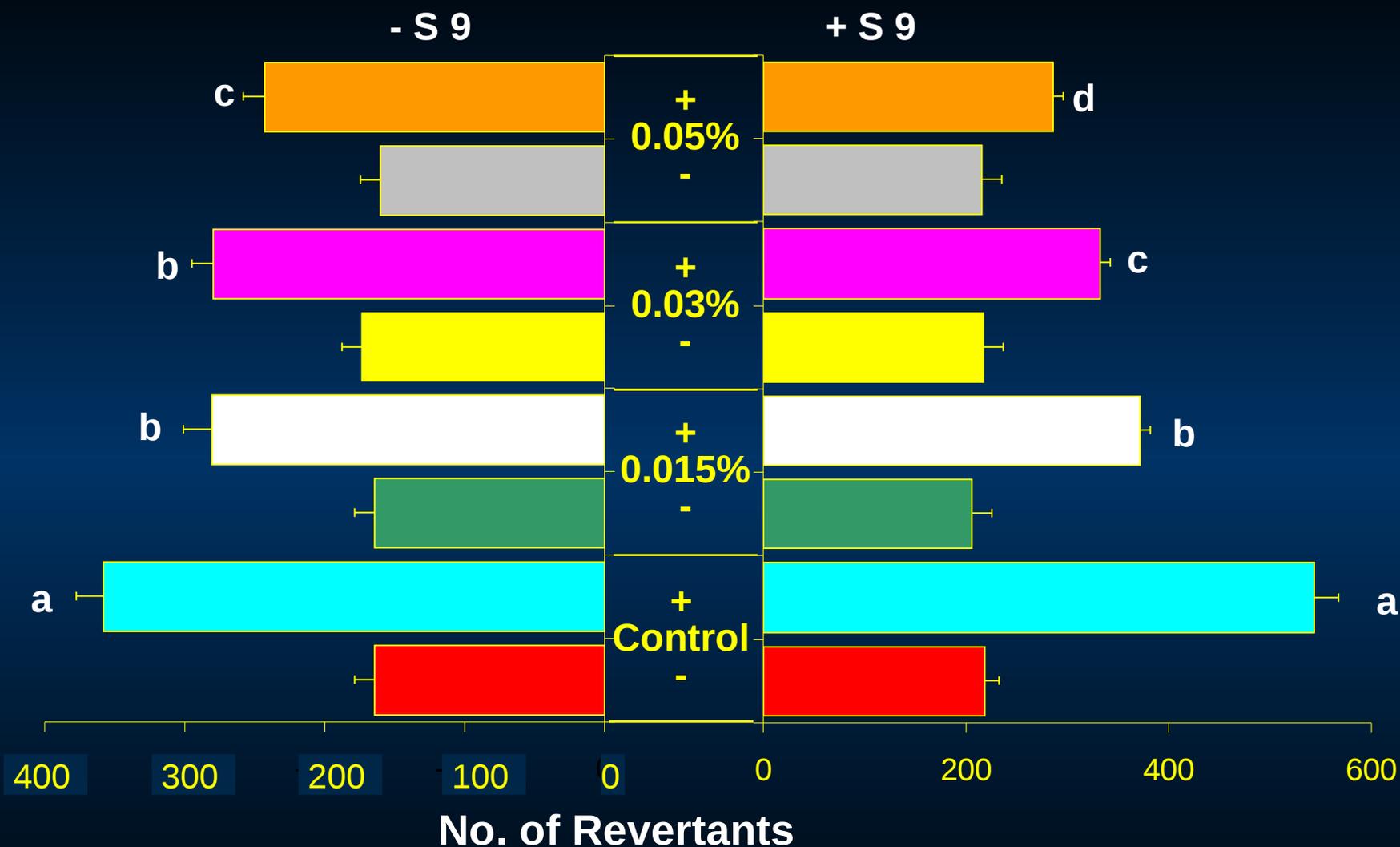


* I – Diferuloyl methane, II – Demethoxy curcumin, III – Bisdemethoxy curcumin

+ With B (a)P (1mg / Rat) - Without B(a)P; S9 : activated MFOs'

Values bearing different superscripts are significantly different : $p < 0.05$ (Anova)

Effects of Curcumin on Urinary Mutagens TA 100

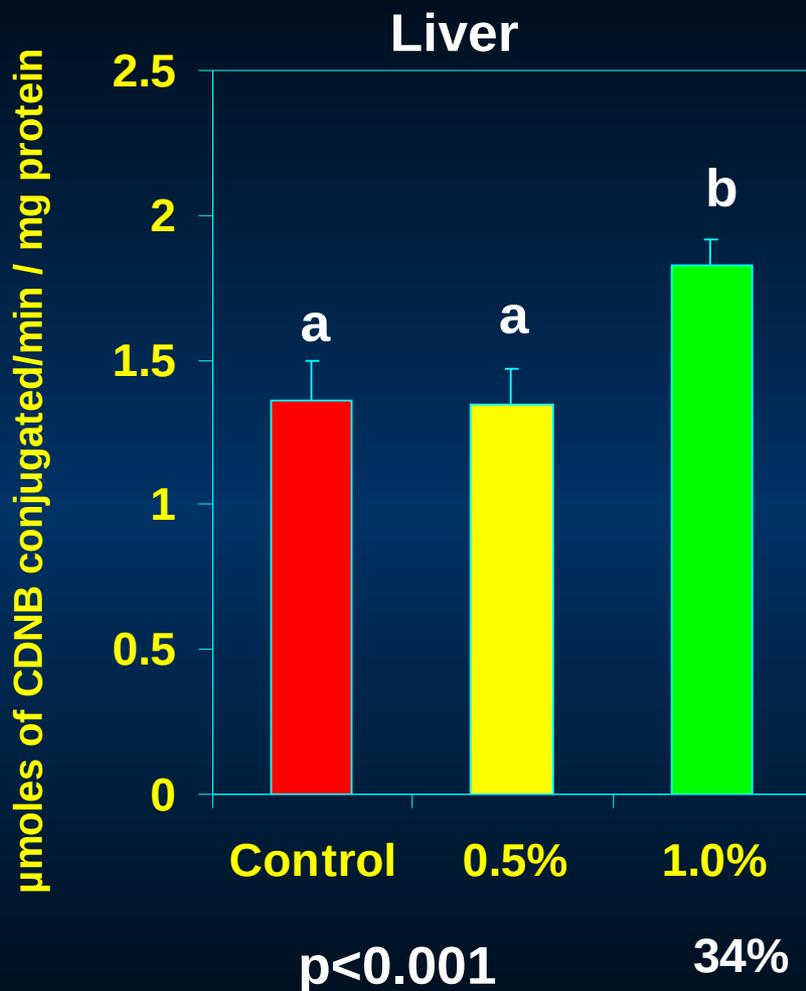


+ With B (a)P (1mg / Rat) - Without B(a)P; S9 : activated MFOs'
 Values bearing different superscripts are significantly different : p<0.05 (Anova)

SUMMARY OF ANTIMUTAGENIC ACTIVITY

- Water and alcohol extracts, curcumin free water extracts, I, II,III curcumins, salicyl/anisyl curcumin, turmerin (a peptide)
- In vivo/ in vitro – varying doses
- Beedi /cigarettes smoke condensate, masher, food mutagens (cooked)
- B(a)P, 3-Mc, DMBA, aflatoxin, 4-nitrophenylene diamine, methyl nitrosoguanidine.
- Curcumin I,II-more active than curcumin III
- Parahydroxy groups/diketone moiety-important for activity.

Effect of Turmeric on Drug Metabolising enzyme GST Activity

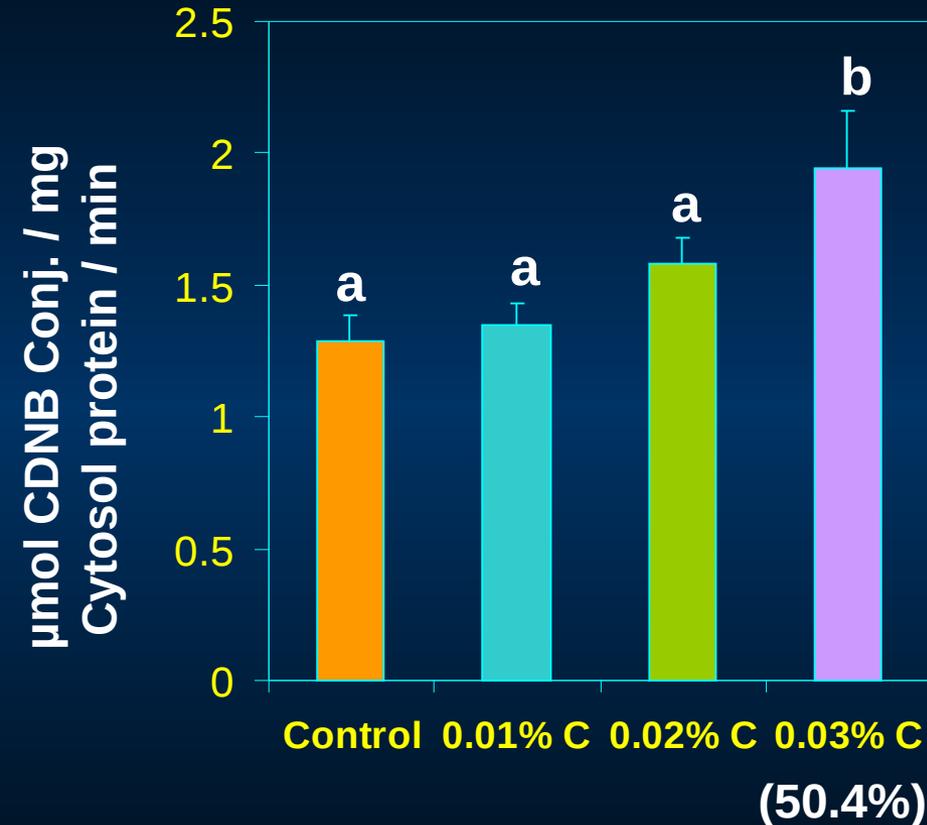


Each value is a pool of 3 animals;
Values bearing different superscripts are significant

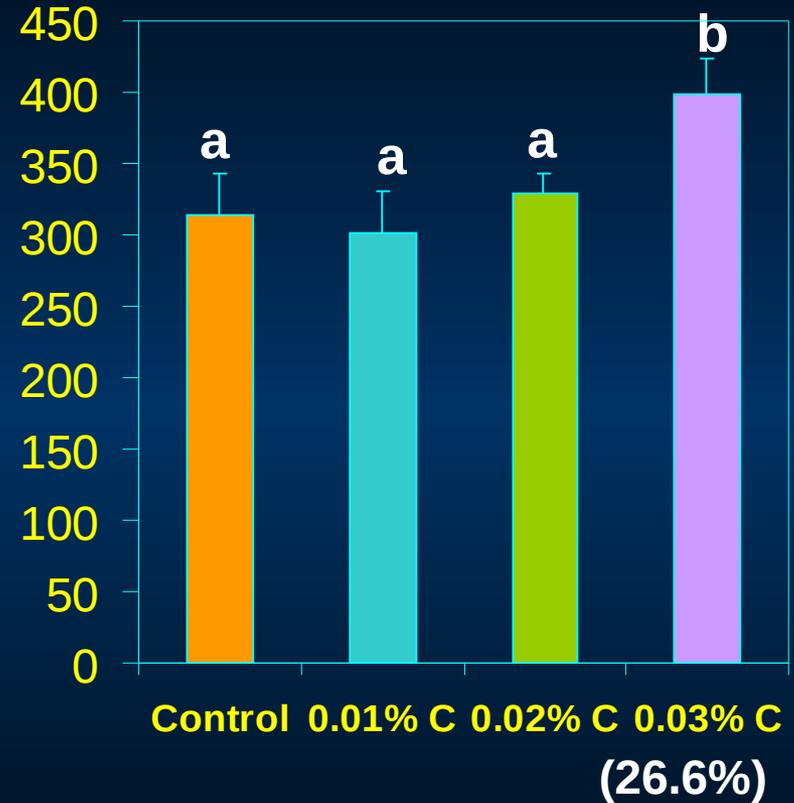
No. of pooled samples - 7

Effect of Curcumin on GST Activity

Liver



Intestine



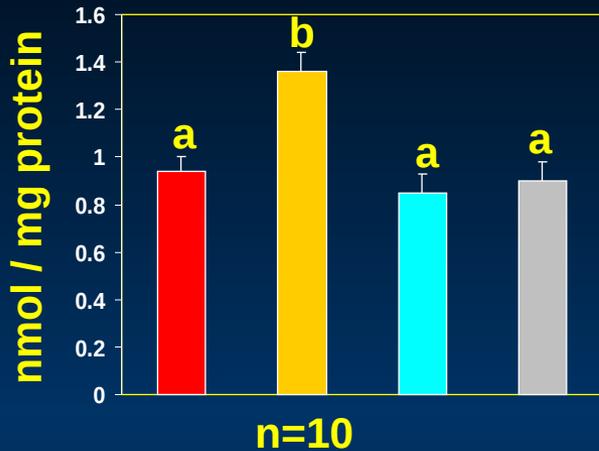
Values are Mean \pm SE of 6 observations;
Each observation is a pool of 3 animals
a,b : $p < 0.05$ between groups (Anova)
Different superscripts are significant

↑ QR, UDPGT, EH

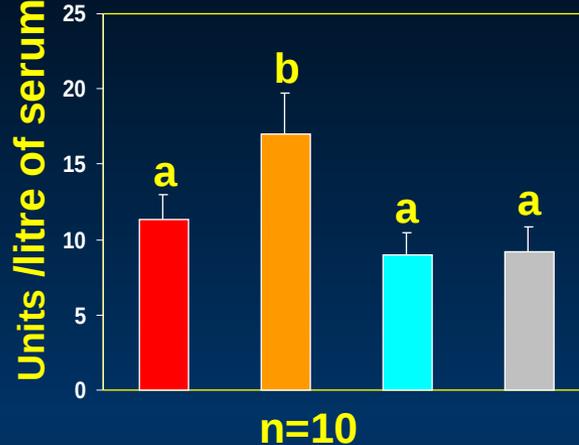
↓ CYP-1A1,

Effect of Curcumin on ACAP Induced Lipid Peroxidation

Liver MDA levels

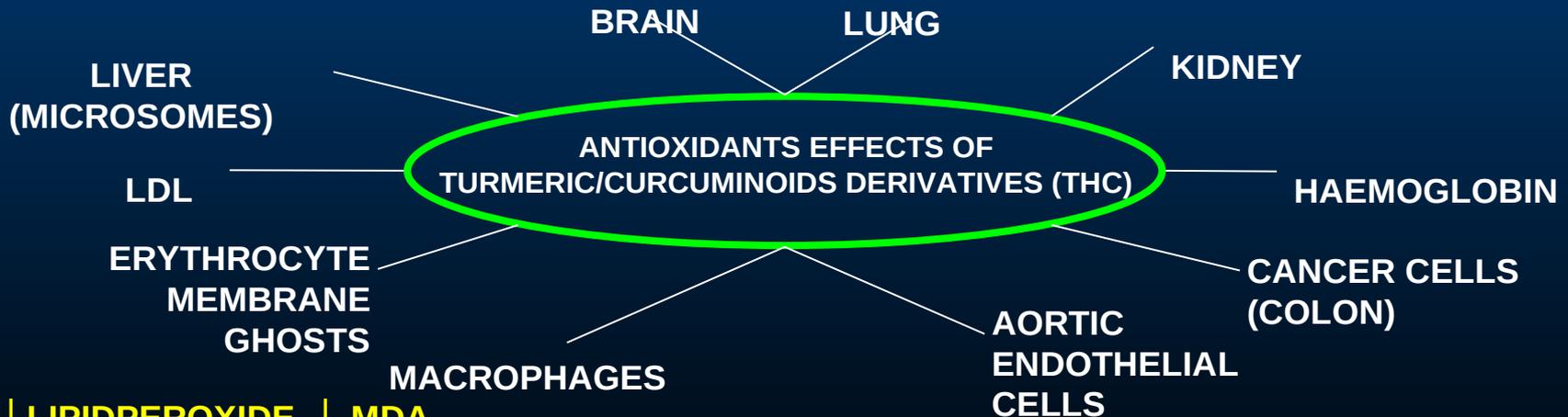


Serum ALT levels



Values are Mean \pm SE;
a,b : p<0.05 between groups (Anova)
Different superscripts are significant

- Control
- Control + ACAP
- 0.015% Curcumin
- 0.03% Curcumin



↓ LIPIDPEROXIDE, ↓ MDA

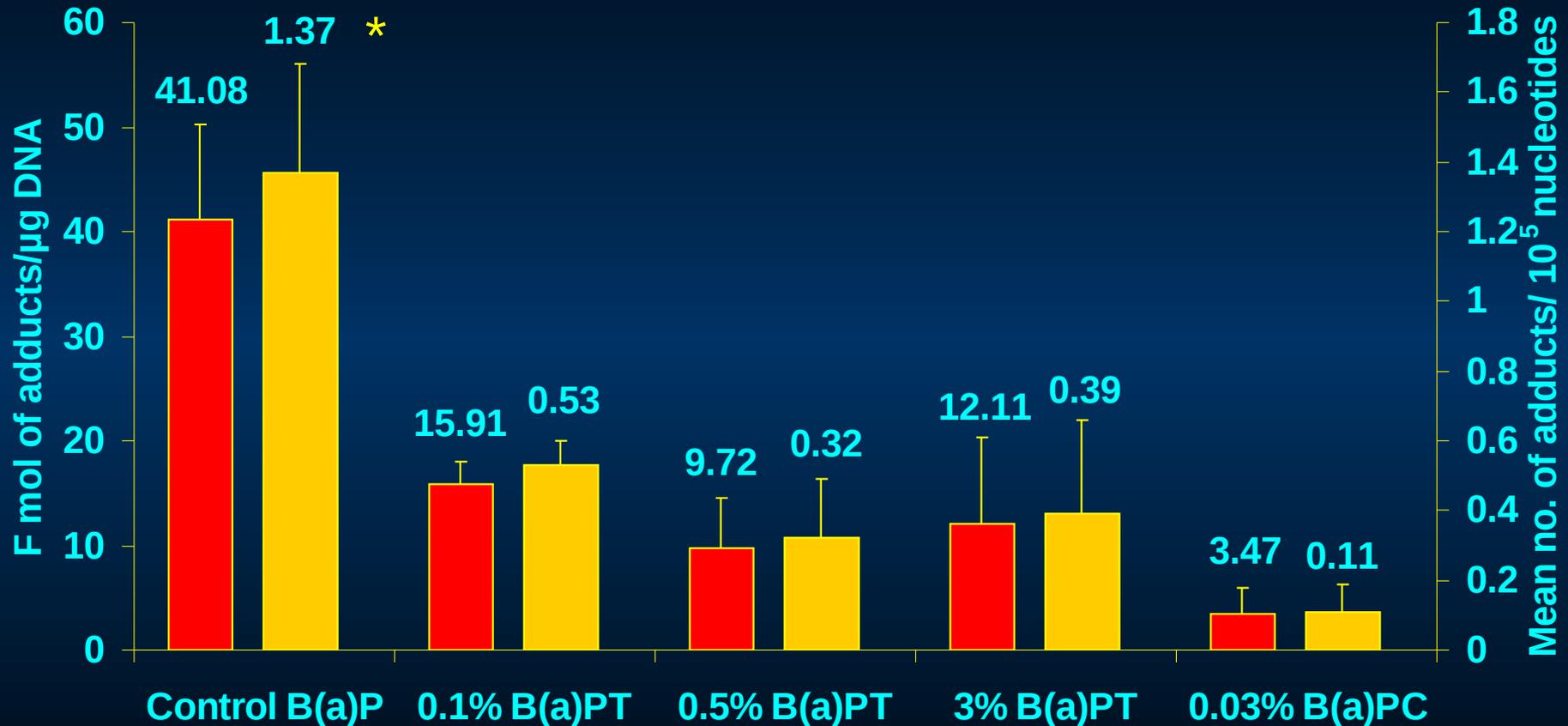
MECHANISMS: OXYGEN RADICAL SCAVENGERS, LIPID PEROXIDE SCAVENGERS, QUENCHING OF SINGLET OXYGEN

↓ LIPOXYGENASE AND CYCLOXYGENASE, ↑ HO-1MRNA, ↓ PEROXISOME, (↑ GPX, G6PD, SOD, GLUTATHIONE), ↓ NF KB

DNA ADDUCTS - CANCER

- In vivo carcinogenic potential
 - In vitro cell transformation
 - Target organ specificity
 - Sensitive species
 - Activates oncogenes
 - Levels high in smokers
 - Human sample similar to animals
 - Genetic correlations
-

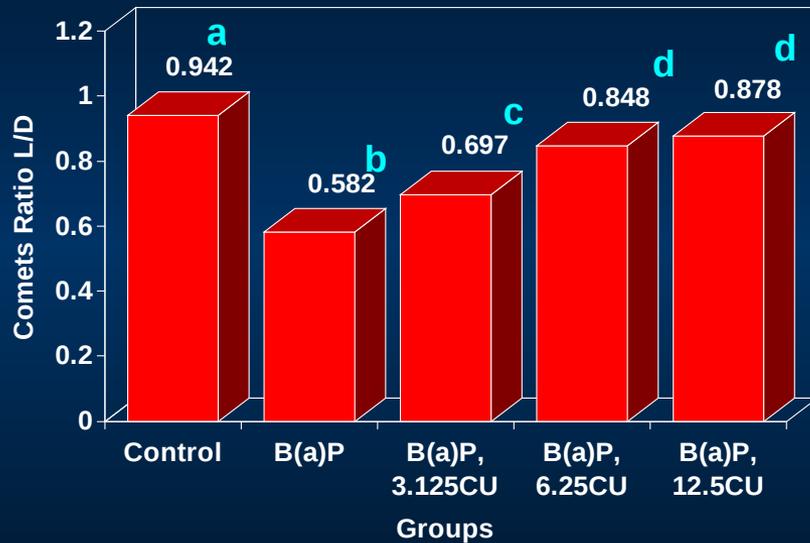
Effect of Turmeric and Curcumin on B(a)P-DNA Adducts in Hepatic Tissue



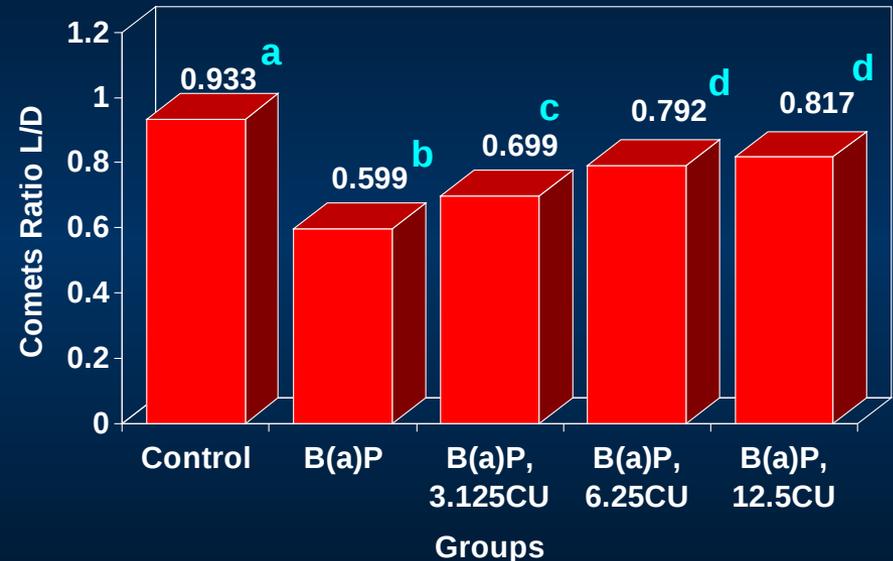
* p < 0.01

Protective Effect of Curcumin - B(a)P Induced DNA Damage

Women



Men

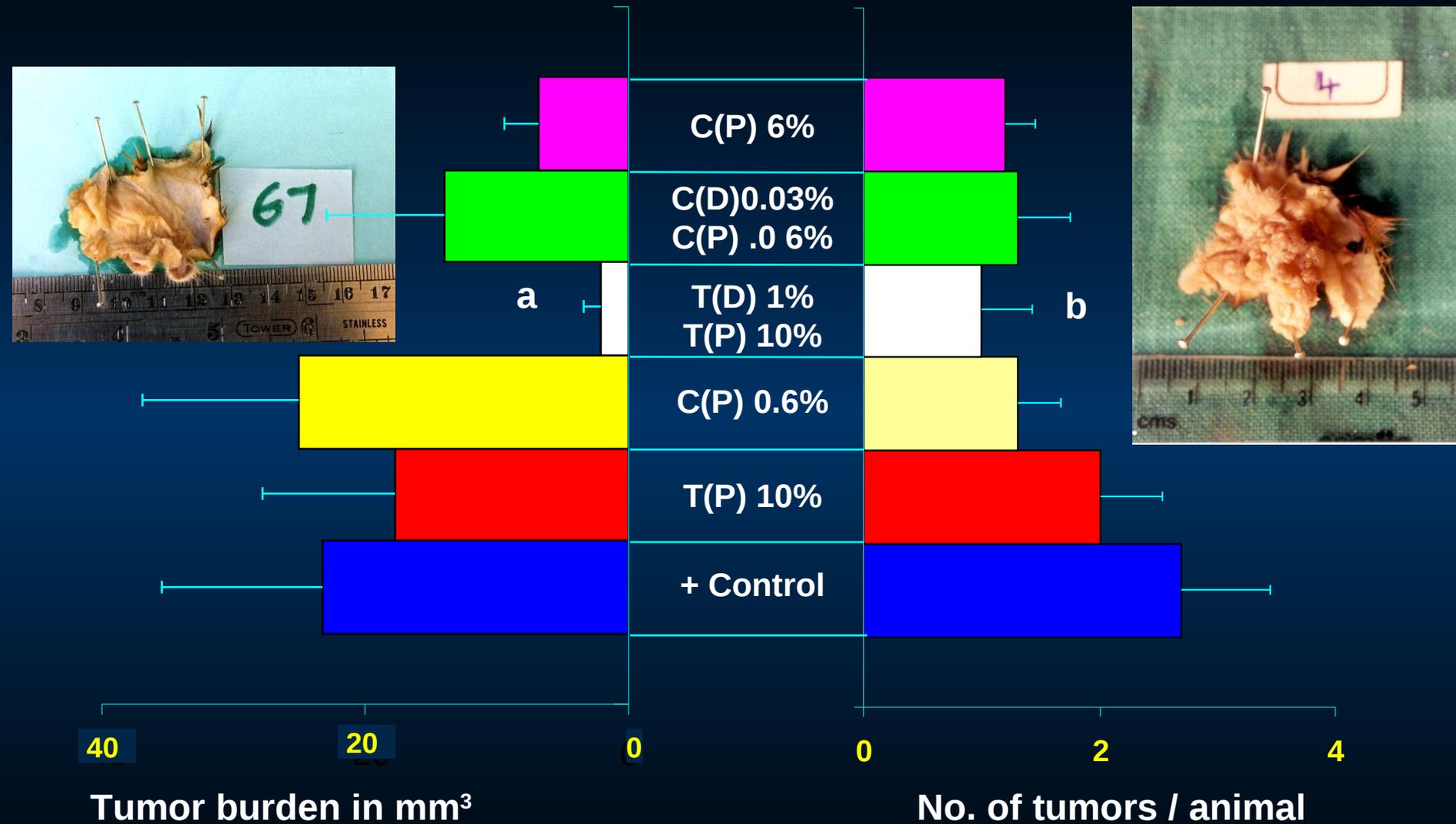


CU : Curcumin in micromoles

Different superscripts are significantly different, Anova with Duncan Multiple range test

Strand breaks (SSBs) in *S.cerevisiae* diploid strain repaired

Effects of T/C on DMBA Induced Tumorigenesis (Hamster Cheekpouch Model)



a,b : p<0.05
Duration : 14 Weeks;

P : Painting - 3 Weeks;
DMBA : 600 µg / 2 wks

D : Diet;

Experimental Design : B(a)P Induced Fore Stomach Carcinogenesis

Groups



NEOPLASTIC INDEX (CELLULAR EVENTS IN CARCINOGENESIS)

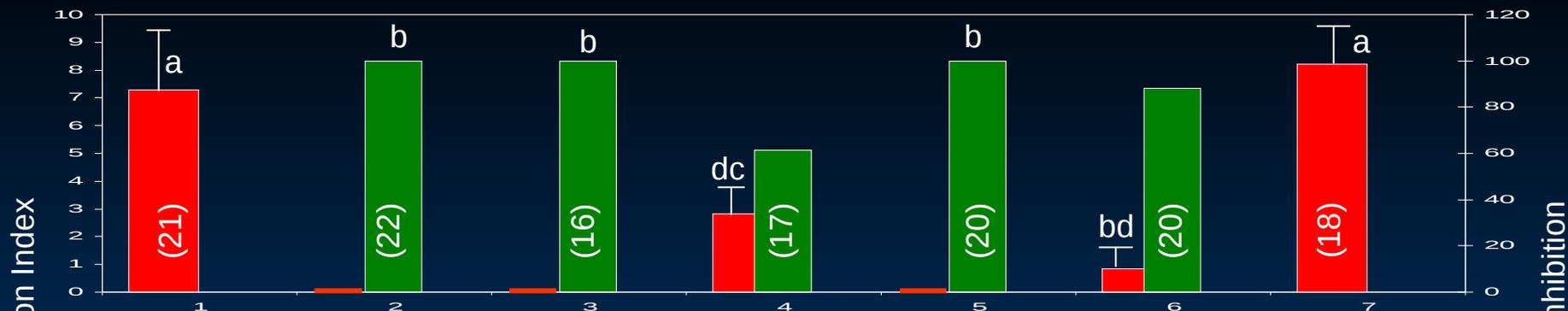
1. Normal mucosa
2. Hyperkeratosis
3. Acanthosis focal
4. Acanthosis diffuse
5. Papillary focal
6. Hyperplasia diffuse
7. Papillomas & adenomas
8. Dysplasia focal
9. Carcinoma in situ
10. Invasive squamous cell carcinoma (ISCC)

Strain : swiss mice (Male)
 Duration : 60 wks
 Dose : 1.5mg x 4 / 10 wks
 Route : Gavage
 Target organ : Forestomach
 Initiation : 0-10 wks
 Post initiation : 11-60 wks

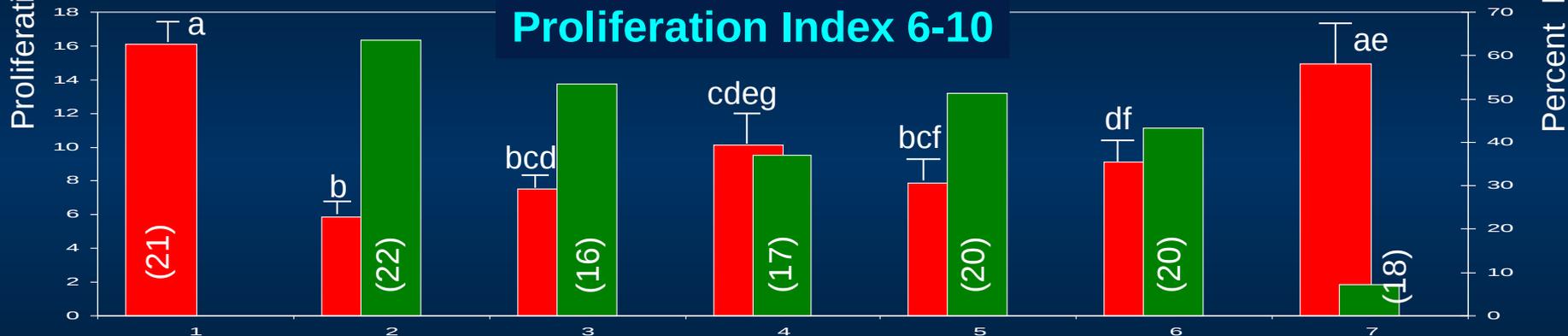
B(a)P B(a)P + 0.02% Curcumin
 1% Turmeric 0.02% Curcumin
 B(a)P +1% Turmeric Stock Diet

Effect of T / C on B(a)P Induced Forestomach Carcinogenesis

Proliferation Index 1-10



Proliferation Index 6-10



B(a)P	+	-	+	+	-	+	+
T	-	+	+	+	-	-	-
C	-	-	-	-	+	+	+
				PI			PI

T= Turmeric 1%

C= Curcumin 0.02%

I = Initiation (10wks)

PI= Post Initiation (50wks)

Values are Mean ± SE

() : No. of Animals

█ Proliferation index

█ Percent inhibition

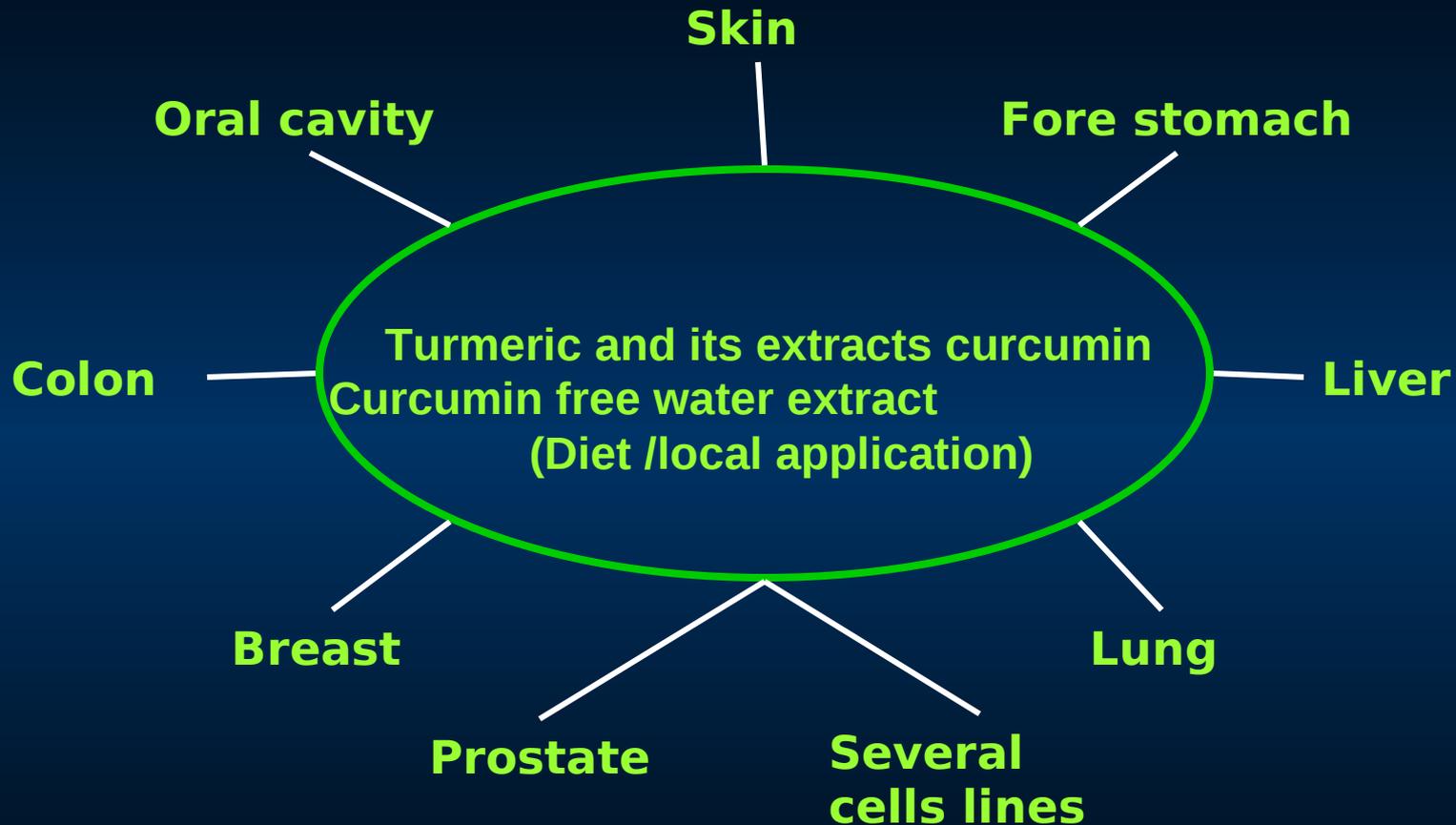
Non Parametric Test

p < 0.001 or 0.01

Dose B(a)P 1.5mg x 4 / 10 wks

By gavage

CHEMOPREVENTIVE /TUMORICIDAL EFFECTS OF TURMERIC /CURCUMIN



(B(a) P/TPA, DMBA/TPA, Nitrosamine, AOM, DMH, Radiation/viral - induced tumors) Delay in onset, ↓ number/volume

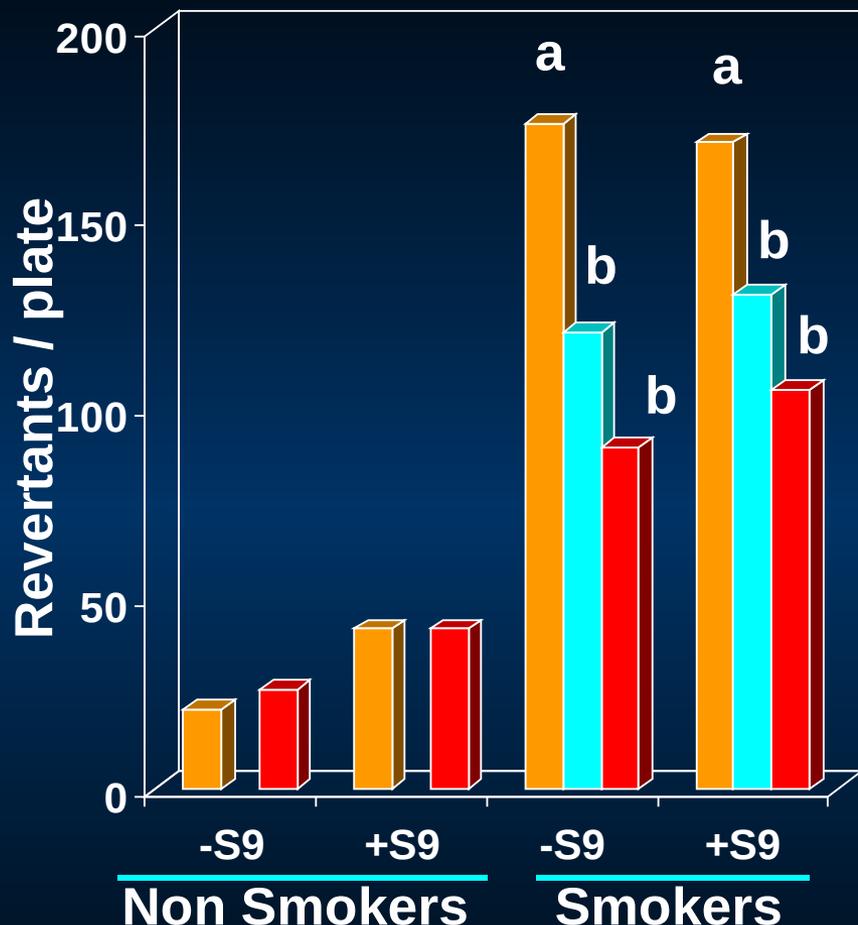
Turmeric Doses in Diet and Relevance to Humans

% of Turmeric in Diet	0.1	0.5	1.0
Diet intake 15 g/day	15 mg	45 mg	150 mg
Human Doses *			
mg/kg	8.9	44.6	89.2
g/50kg	0.45	2.3	4.5
g/70kg	0.62	3.1	6.2

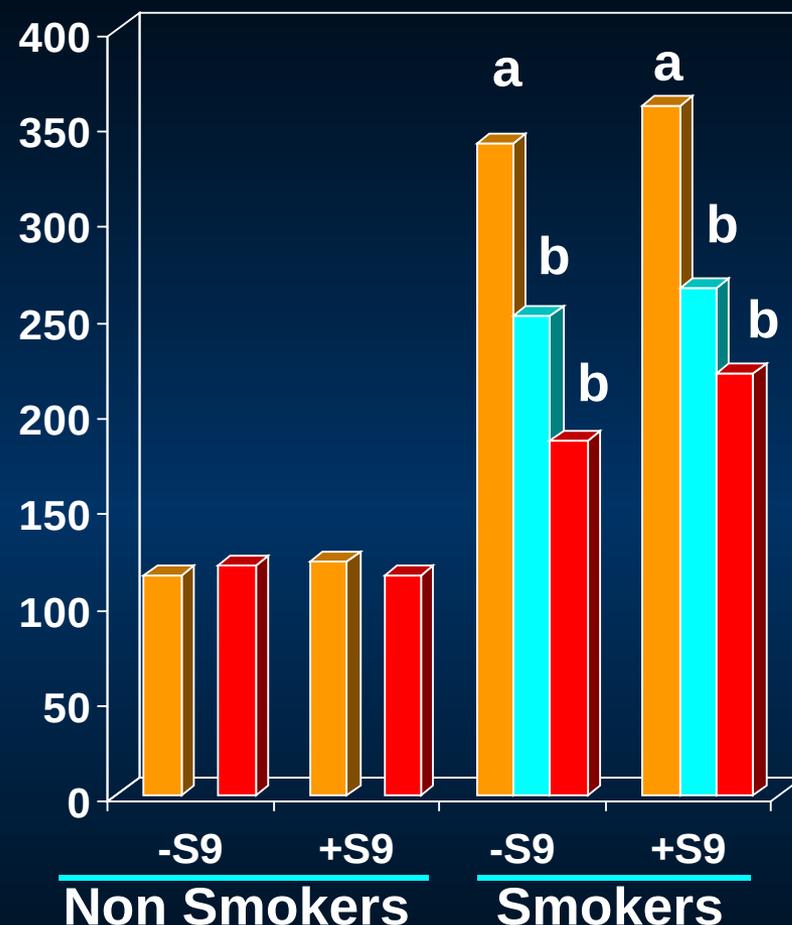
* Pharmacological basis
Freireich *et al.*, 1966.

Urinary Mutagens - In Smokers

TA 98



TA 100



Basal 15 days 30 days

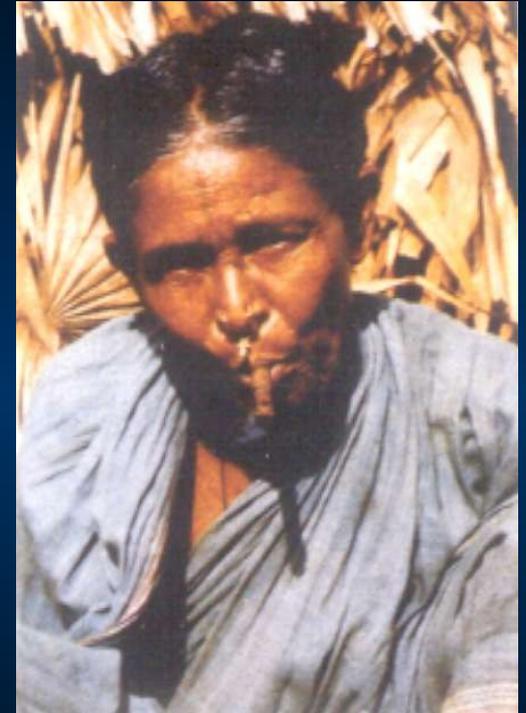
Basal 15 days 30 days

Values bearing different superscripts are significantly different ($p < 0.001$) within each category

EPIDEMIOLOGY

Prevalence of Preneoplastic lesions	- 200 / 1000
Incidence of Preneoplastic lesions	- 106 / 1000
Malignant transformation	- 0.6 / 1000 / yr
Incidence of malignancy	- 14 / 100,000

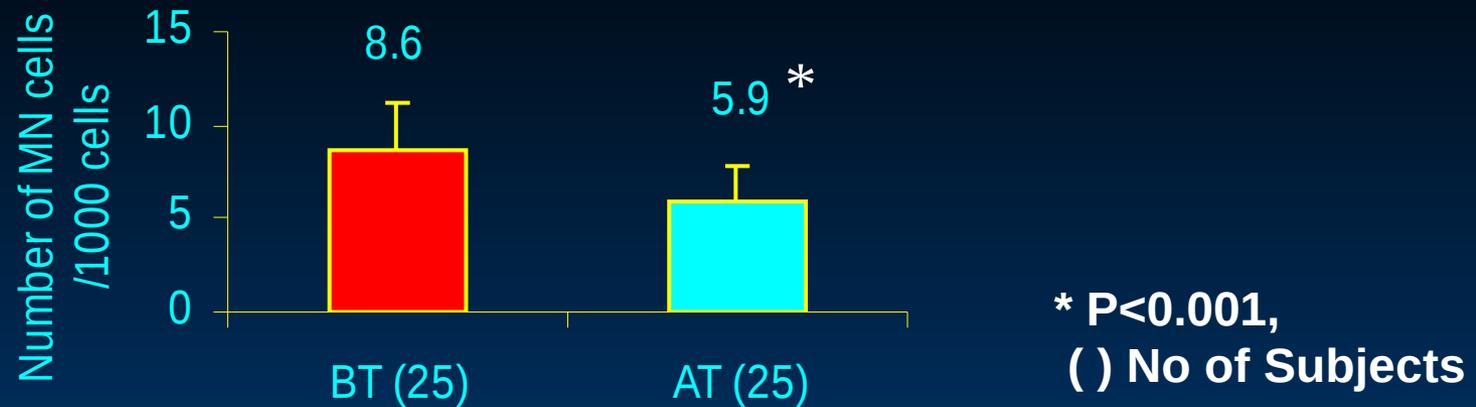
Mehta et al, 1980





**50% showed remission
within 9 months vs
10% natural remissions**

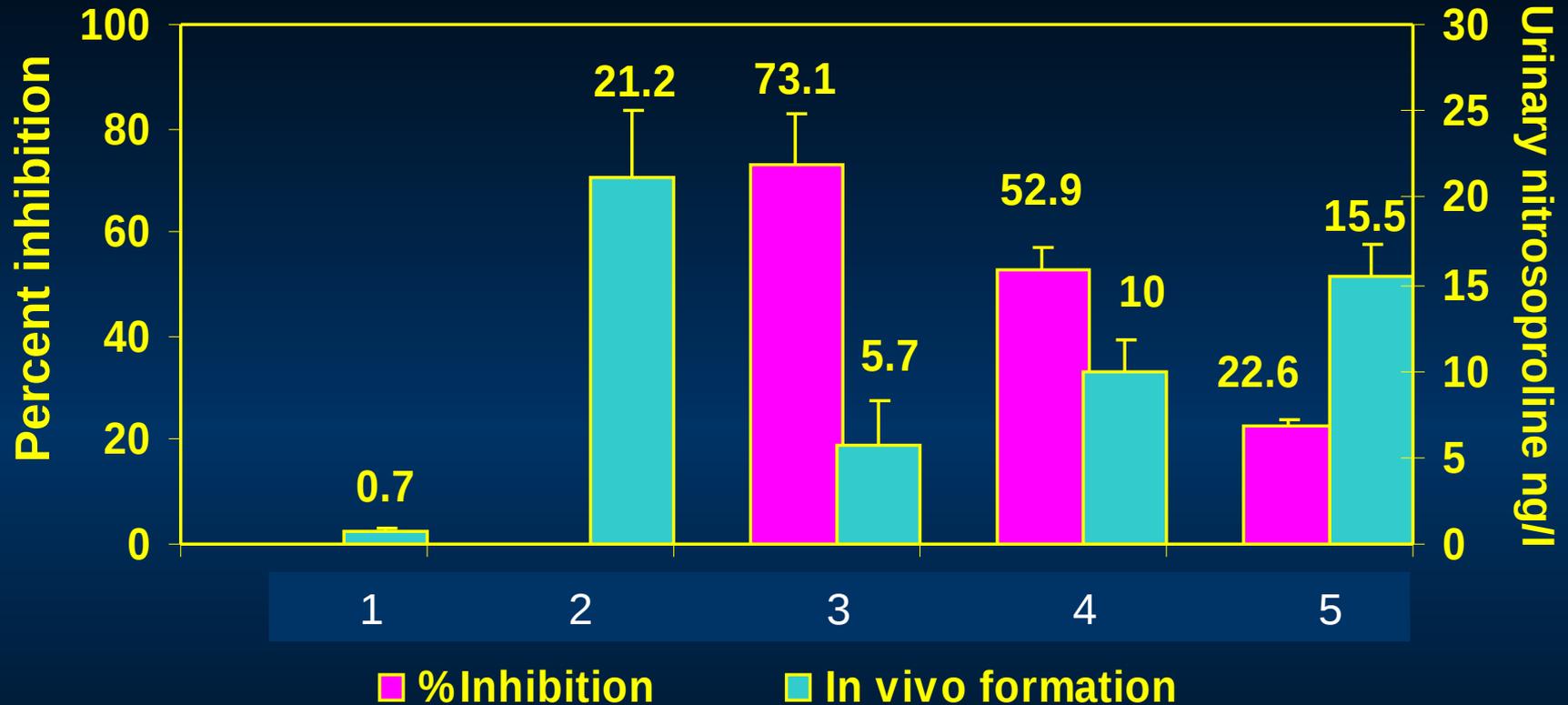
Effect Of Turmeric (1g/d) On Micronuclei



Effect of Turmeric (1g/d) on DNA adducts



In Vivo Nitrosation (L-Proline Test)



1. Baseline

2. 500mg Proline

3. 500mg Proline + 5g Turmeric

4. 500mg Proline + 2g Turmeric

5. 500mg Proline + 1g Turmeric

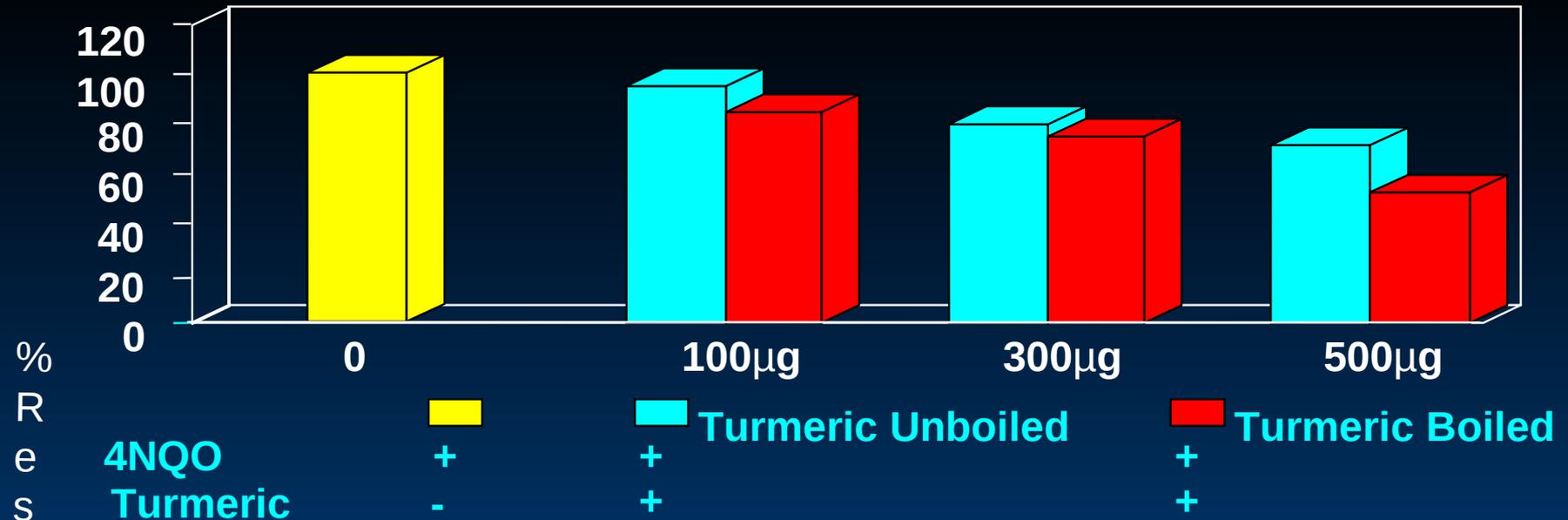
2 vs 3,4,5 :- $p < 0.05$

ED.50 - 1.95g

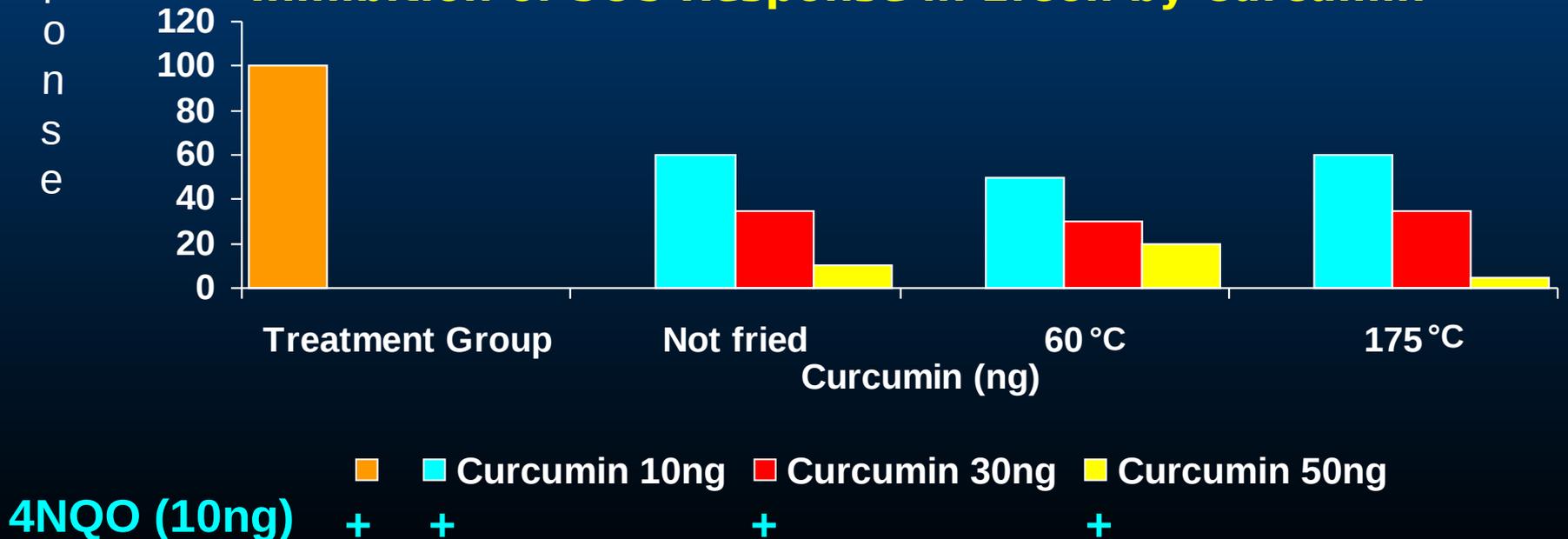
In-vitro ED.50 - 1.15 to 3.54 g

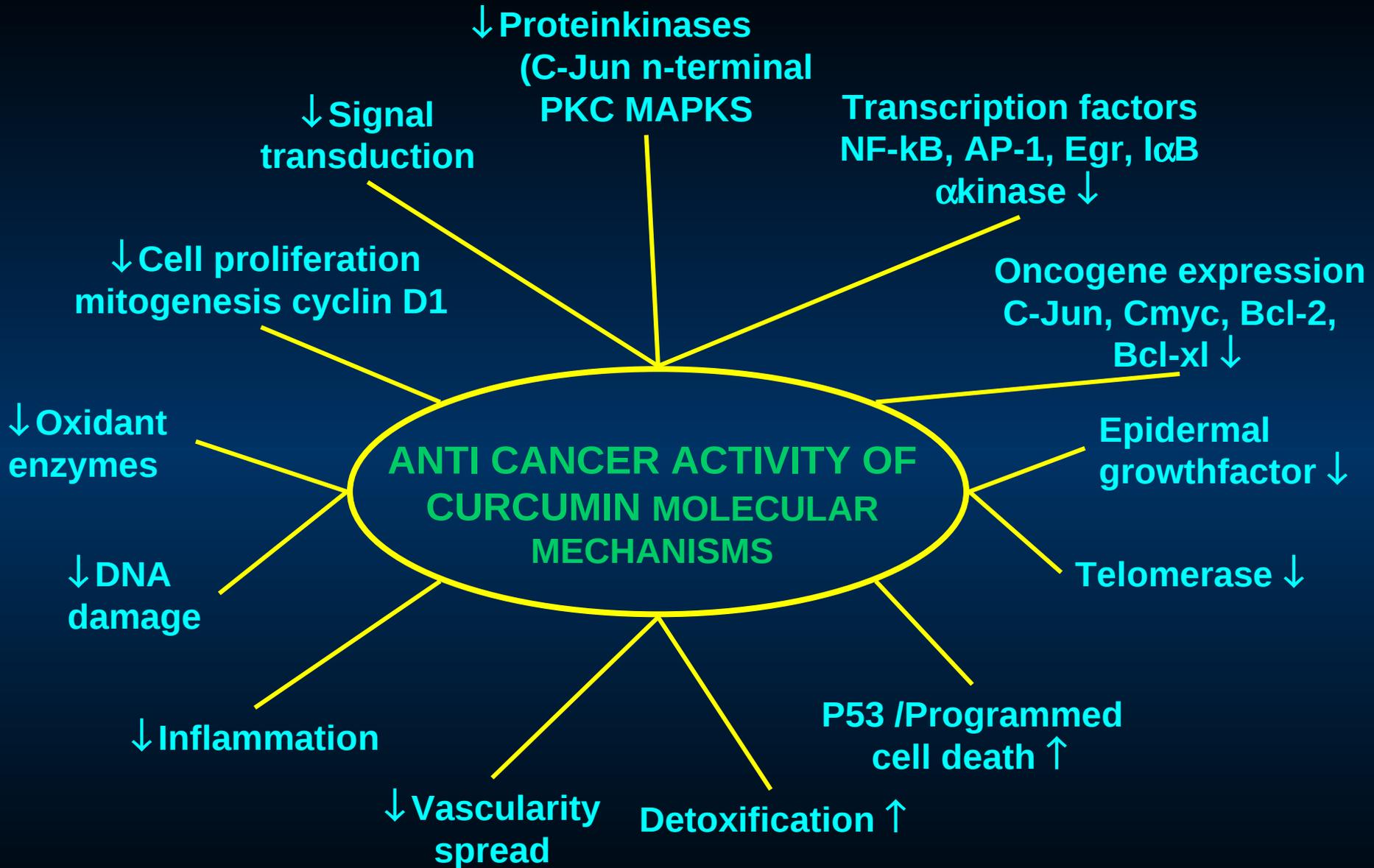
KK - 2007

INHIBITION OF SOS RESPONSE IN E. COLI BY TURMERIC

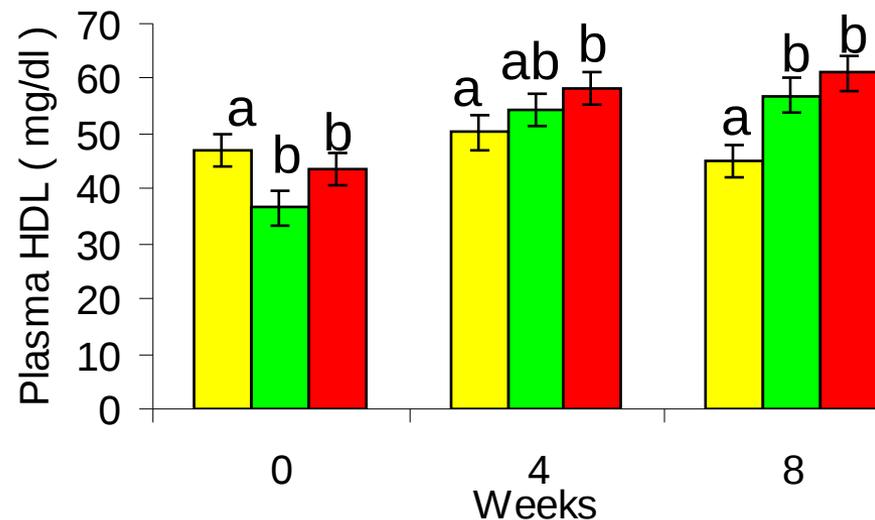
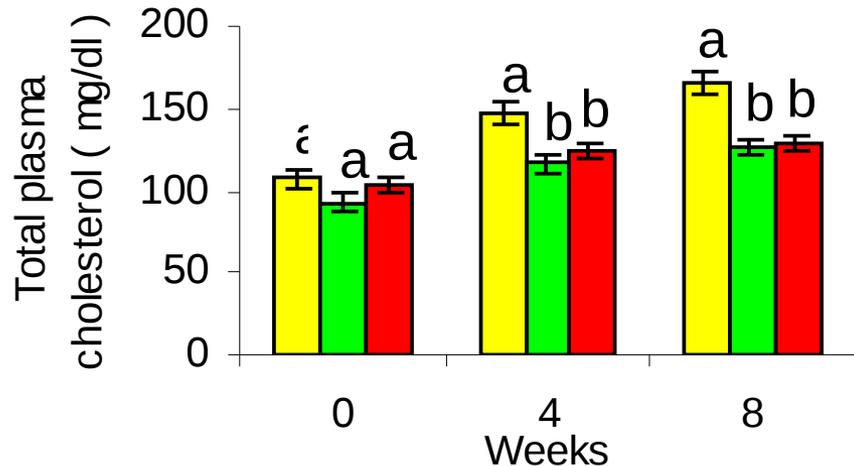


Inhibition of SOS Response in E. coli by Curcumin



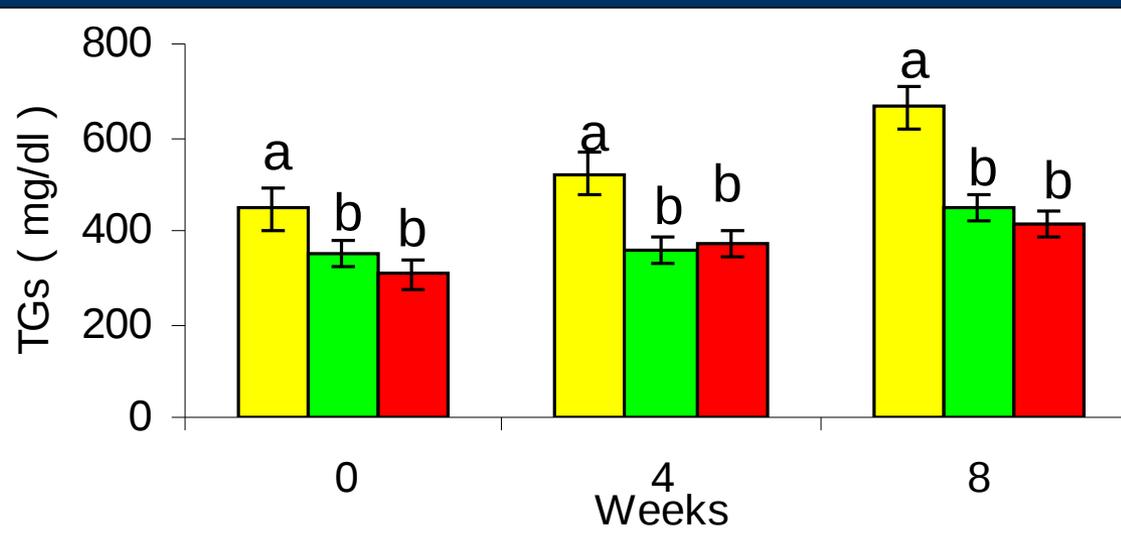


Effect of turmeric on lipid profile of WNIN/Ob rats

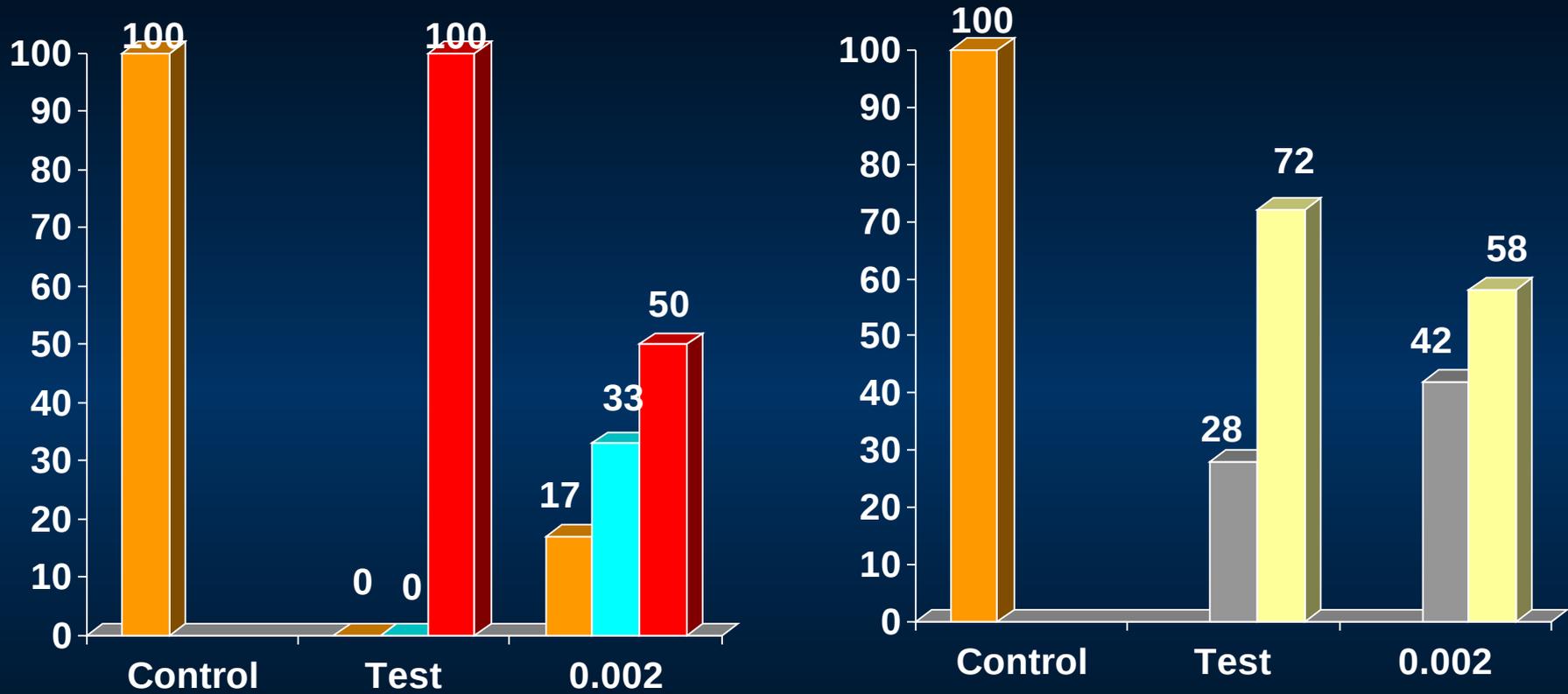


↓ LDL oxidation
 ↓ Platelet aggregation
 ↓ Fatty streaks
 ↓ Adhesion molecules / Tissue factor
 ↓ Smooth cell proliferation
 ↓ Endothelial cell proliferation
 ↓ CoX II , LOX
 ↓ Thromboxane

↑ Prostacyclin
 ↑ Choloretic

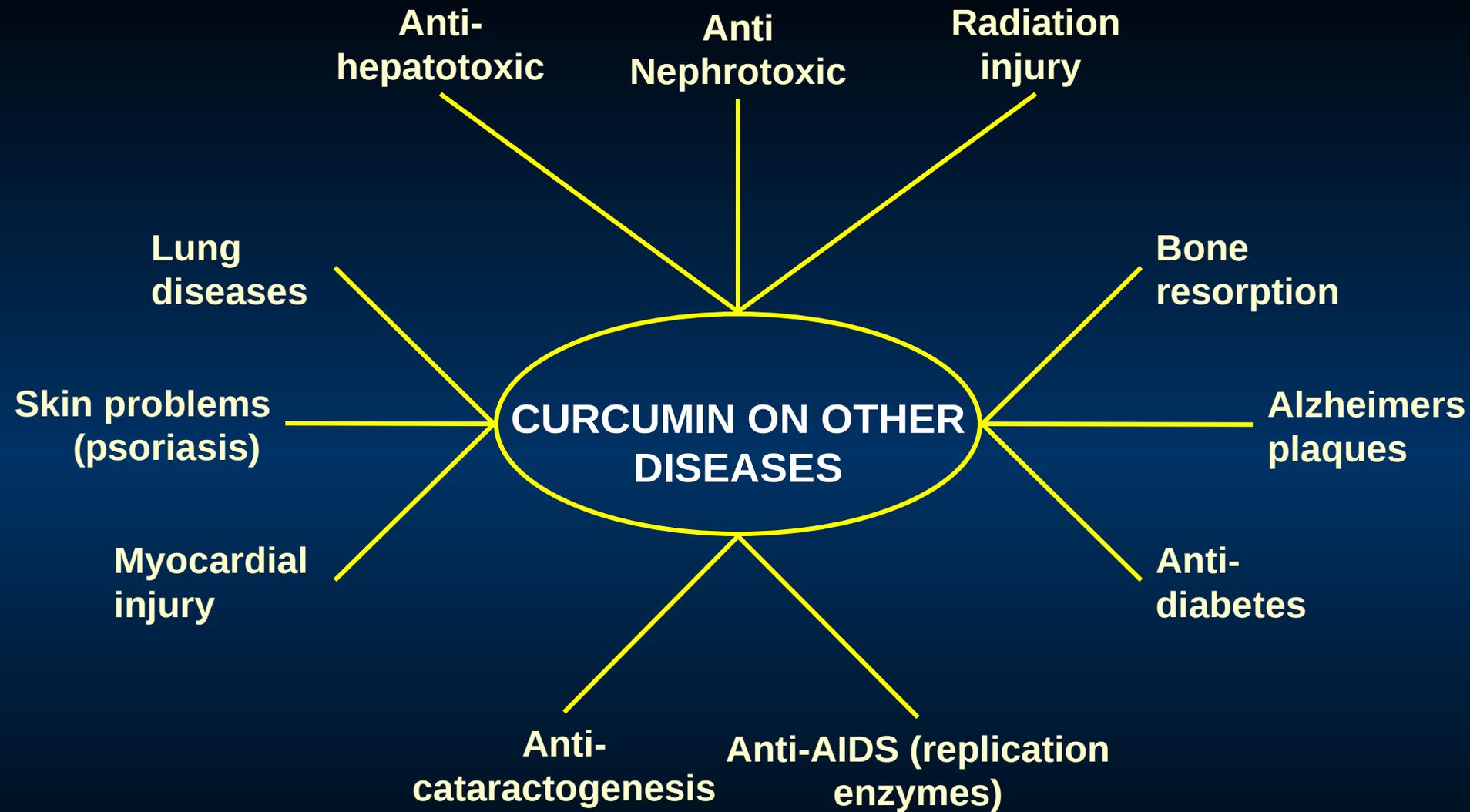


Galactose (30%) induced cataract - Delayed by curcumin (0.002%) - 4 weeks



Lipid peroxidation ↓
 GSH ↑
 Protein aggregation ↓

- Clear
- Stage I
- Stage II
- Stage III
- Stage IV



ANTIOXIDANT & ANTI-INFLAMMATORY EFFECTS

Toxicology Evaluation Studies on Turmeric / Curcumin

Animal model	Toxicity test	Dosage Schedule	Effect
Rat Mouse	Acute Curcumin	80-1800 mg / kg x7D	Not lethal
Rat	Chronic	1800 mg, 800 mg/kg body wt. x 900 Curcumin	No Evidence of abnormalities
Mice Rabbit	Terato- genic	800-1600 300-600 mg/kg body wt. Curcumin	Not teratogenic
Mice Rabbit Monkey	Genetic	Same as above	No significant change in chromo- somal aberrations

CLINICAL TRIALS IN HUMANS



ANTI-INFLAMMATORY ACTIVITY

1. Rheumatoid arthritis
2. Post operative inflammation
3. Idiopathic orbital tumors
4. Chronic anterior Uveitis

OTHER EFFECTS

1. Peptic ulcer (Healing)
2. Psoriasis (pH/histology)
3. Hyperlipidemia
4. Normal Volunteers (cholekinetic)

ANTI CANCER

1. Precancer and Cancer
2. Oral pre cancerous lesions
3. Colo rectal cancers
4. Mutagens in smokers
5. DNA damage in lymphocytes

Double blind cross over, Open trials, Laboratory studies,
Oral curcumin and turmeric, Ointment of turmeric, TE, TOR

Dose: Turmeric 1-1.5 g/d ;
Curcumin 500 mg - 12g/day

Duration : 5d-9 months

Most studies :4-6 months

Curcumin Proposed as chemopreventor

Multiple myeloma
Pancreatic cancer
Colon Cancer
Prostate Cancer
Cervical Cancer

GI Tract cancer
Melanoma
Alzheimer's Disease
Myelodysplastic syndrome

PLEIOTROPIC EFFECTS OF CURCUMIN

Turmeric -The salt of the Orient Is the Spice of life

ANTICANCER



ANTI-ATHEROSCLEROTIC

ANTI-INFLAMMATORY

ANTI-INFECTIVE

ANTI-DEGENERATIVE

CANCER

**CARDIO VASCULAR
DISEASES**

**DEGENERATIVE
DISORDERS**

**INFLAMMATORY
DISORDERS**

RR 2007

Nutrient Composition of Fenugreek (*Trigonella foenum graecum*) Macronutrients (g/100g)

Component	Leaves	Seeds
Moisture	86.1	2.4
Protein	4.4	25.4
Fat	0.9	7.9
N3 fatty acids	0.2	2.0
Total dietary fiber	4.7	48
Insoluble dietary fiber	3.2	28
Soluble dietary fiber	1.5	20
Ash	1.5	3.9
Carbohydrate	6	3.6

Source : Gopalan et al 2000 (Nutritive value of Indian foods)

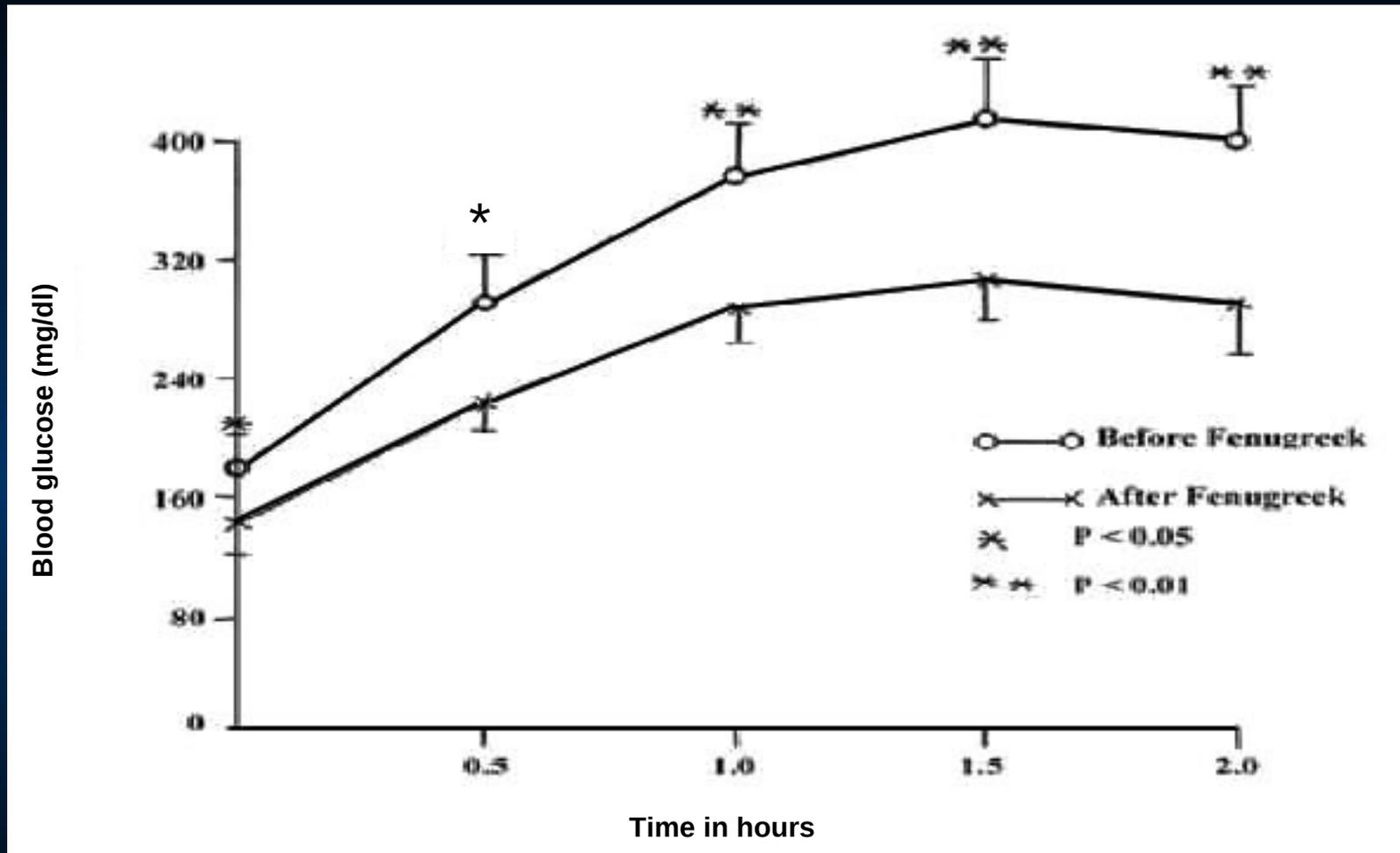
Sridhar & Lakshminarayana, 1993

PUS Rao & Sharma , 1987.

Ghafoorunnisa & Pangrekar J, 1993

Wealth of India (1976), Vol X, published by CSIR

Effect of fenugreek seeds on oral GTT in NIDDM

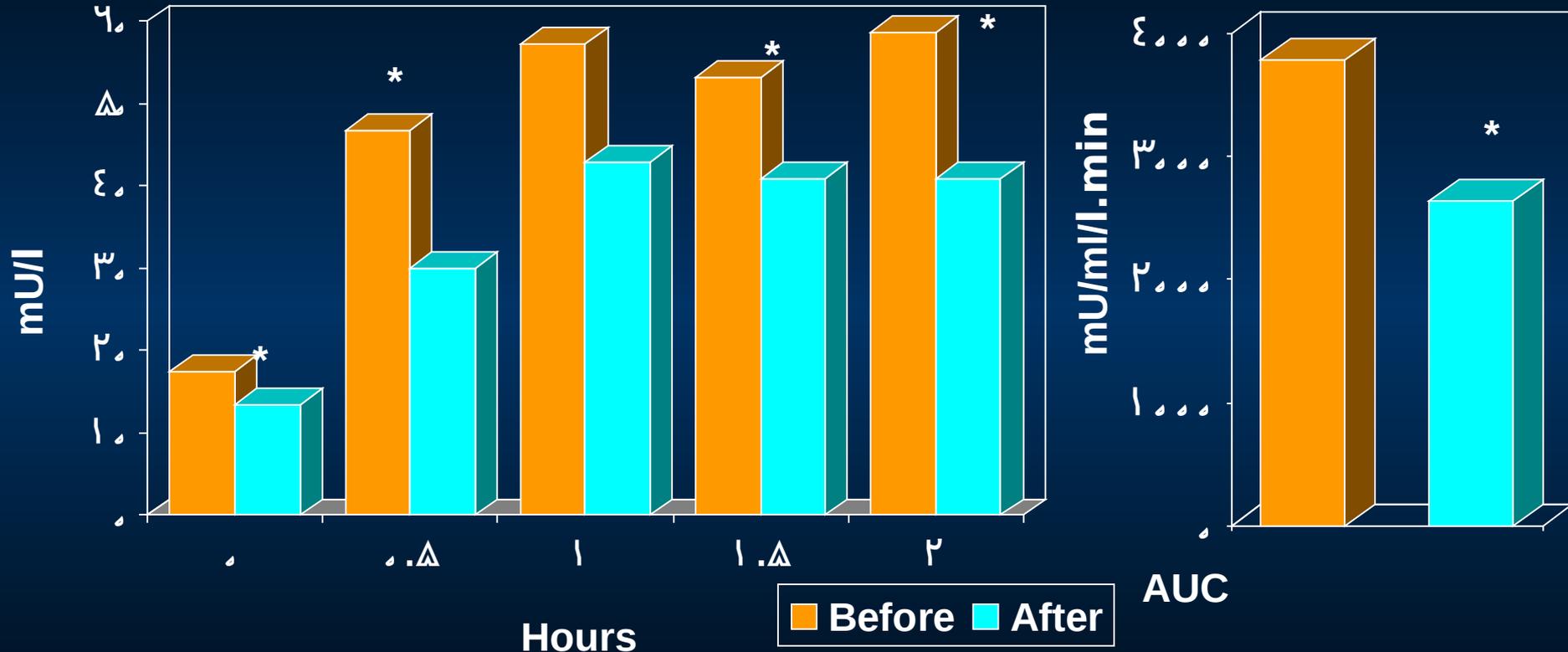


Duration : 10 days

100 g defatted fenugreek seed powder

Source : Sarma, RD and Raghuram TC - Nutr. Res. 1990; 10: 731-9

Effect of Fenugreek Seeds on Serum Insulin Levels

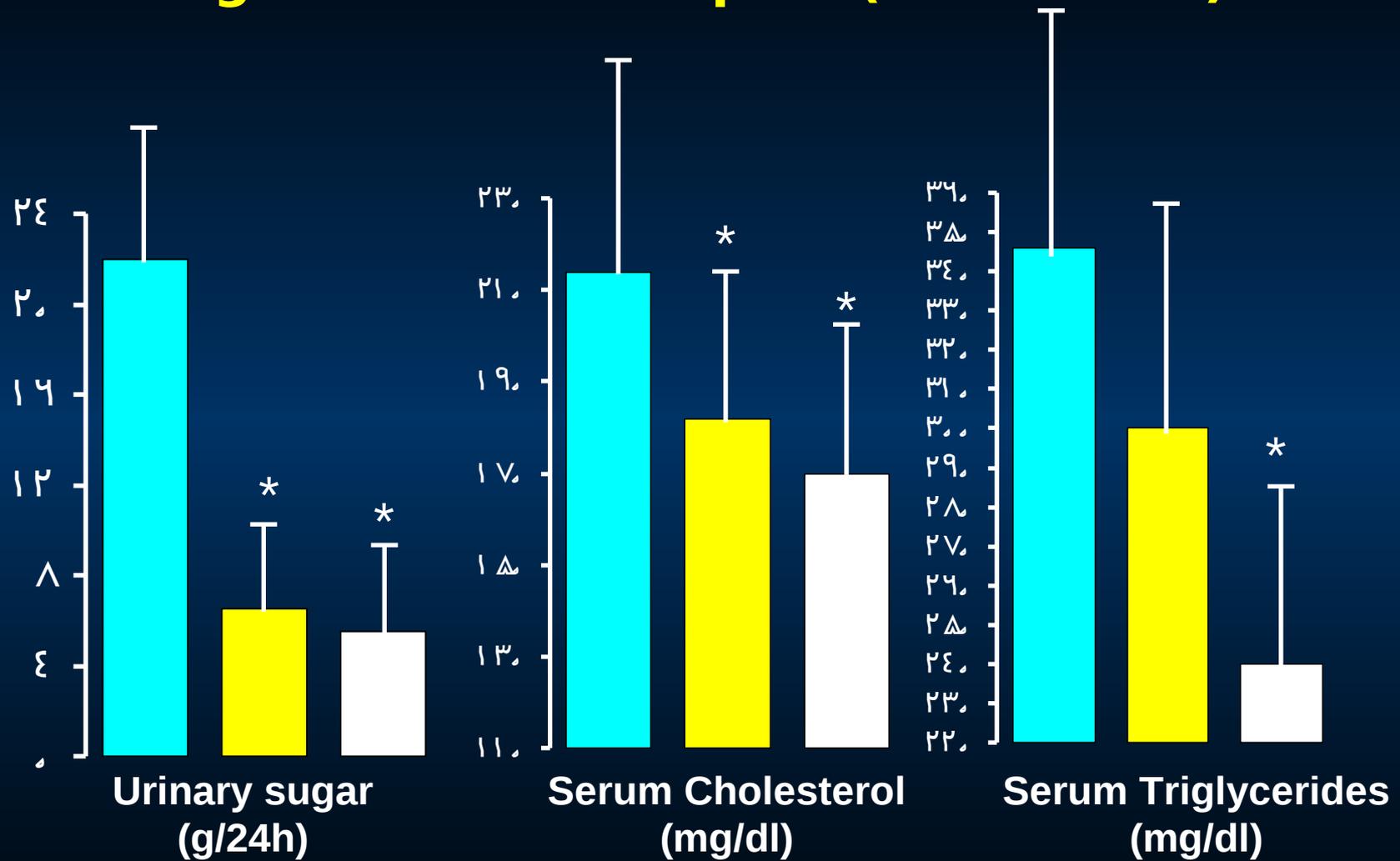


AUC : Area under Curve

Level of significance *p<0.05

Source: Sharma RD and Raghuram TC, 1990

Effect of Fenugreek seeds on 24h Urinary sugar and serum lipids (Mean \pm SE)



* p<0.05

Before

After 10 days

After 20 days

Source: Sharma RD and Raghuram TC, 1990

KK - 2007

Effect of Fenugreek on IV GTT in 10 Type 2 Diabetes

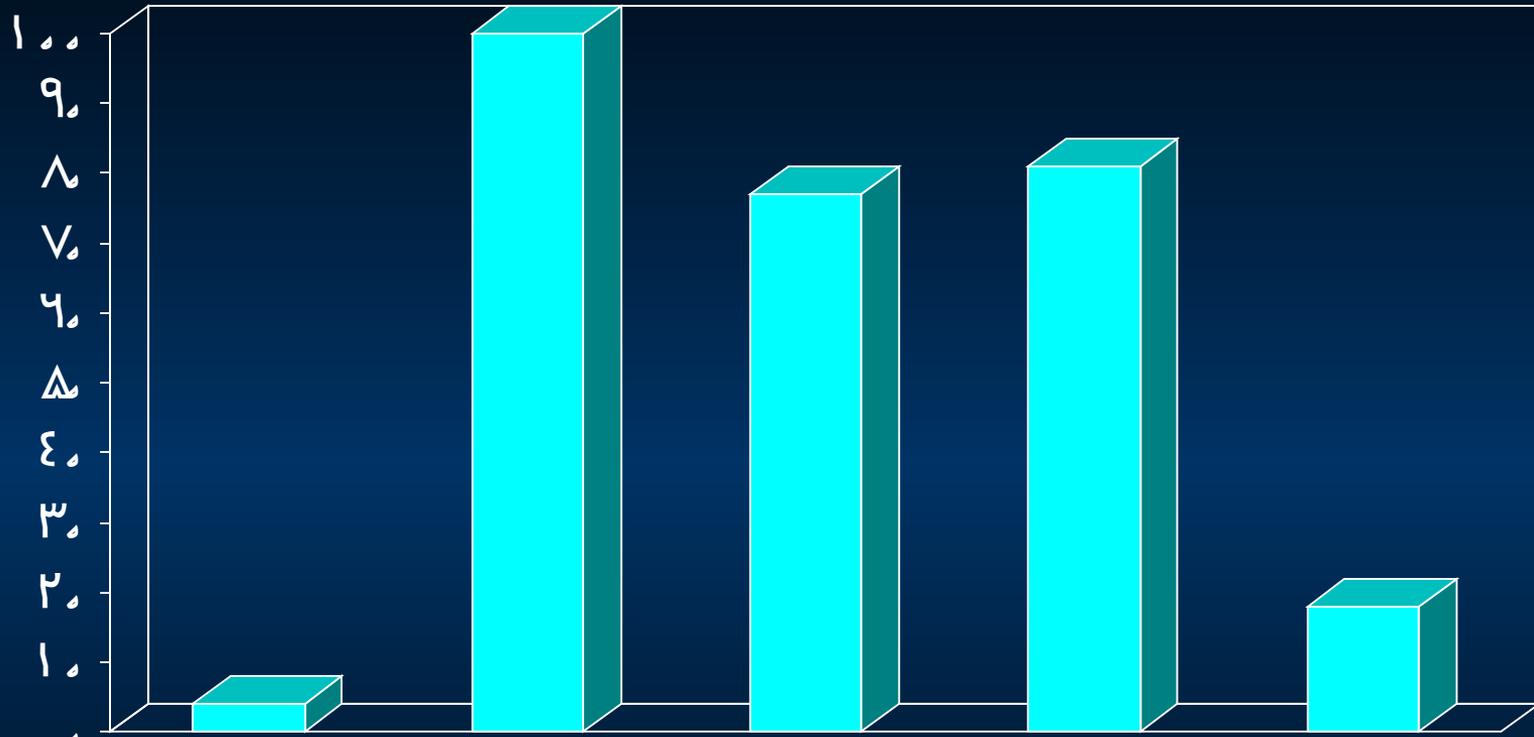
Parameter	Control diet	Fenugreek diet (25g / day)
<u>Blood glucose</u>		
AUC (mg/ml. min)	152.4 ± 10.8	138.8 ± 6.2 *
Half life (hours)	1.75 ± 0.13	1.34 ± 0.07 **
Clearance (ml/min)	216.6 ± 19.2	229.1 ± 18.1***
Volume of distribution (L)	31.9 ± 2.6	26.5 ± 2.1 **
RBC insulin receptors (ng/ml)	14.5 ± 5.9	16.1 ± 7.2 **

Statistical analyses by paired 't' test.

* P <0.05; ** P <0.01; *** P <0.01;

Source : Raghuram et al, 1994

Fenugreek and Cataract (Experimental Studies)



STZ (Diabetic) -

+

+

+

+

Fenugreek (%) -

-

5

10

20

↓ Water content

↓ Aldose reductase

↑ GSH

↓ Glucose content (liver / plasma)

↓ Sorbital dehydrogenase

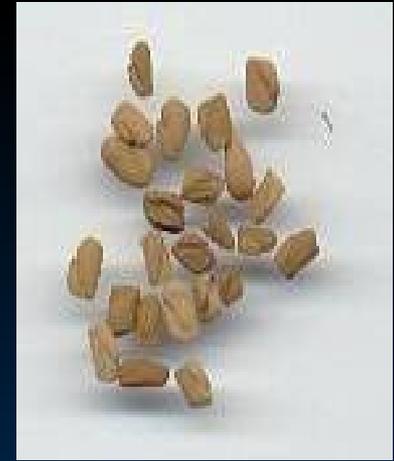
↓ Oxidative stress ↓ Osmotic stress

EFFECTS OF ONIONS AND GARLIC

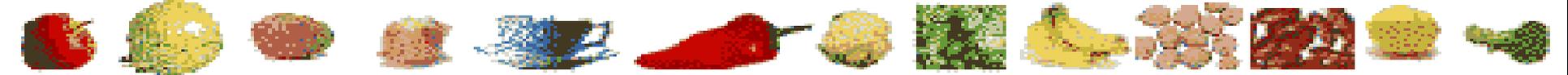
- Counteracted mutagenicity of B(a)P, 3MC (AMES & COMET assay)
 - Boiled / fried garlic & onion same effect in SOS responses (*E. coli* PQ 37)
 - Garlic has hypolipidaemic & anti-aggregator effects
 - Decrease in DNA adducts (in-vivo & in-vitro)
 - Increase in conjugating enzymes
-



Conclusions



- Turmeric is a strong antimutagen, detoxificant, antioxidant, anti inflammatory, anti cancer and tumouricidal agent
- Turmeric is a hypolipidaemic anti aggregatory agent
- Onion and garlic have anti-cancer , hypolipidaemic & antiaggregatory effects.
- Fenugreek is hypoglycemic and hypolipidaemic agent
- Aggregate effects of spices in small doses (1-2g) may have sustainable beneficial effects
- Food based approaches are best for prevention and / or control of chronic diseases



**MAN IS A PRODUCT OF NATURE /
NURTURE AND NUTRITION**

**Eat well
Live well**

**DIETARY APPROACHES
FOR PREVENTION OF CHRONIC DISEASES
IS
COST EFFECTIVE, CULTURALLY ACCEPTABLE
AND SUSTAINABLE**



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Thank you

