The Effects of Black & Green Tea on Cancer
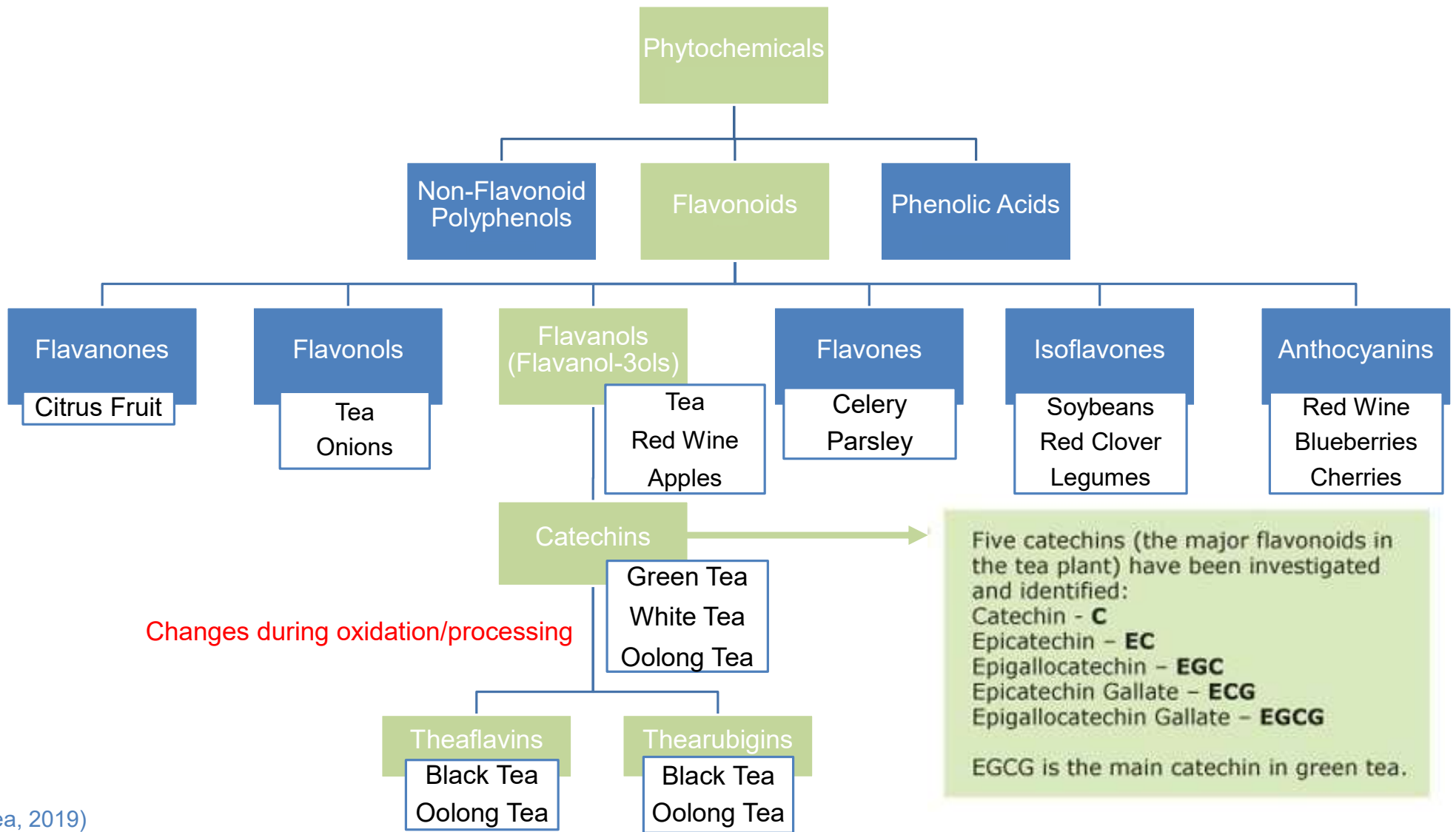
Erin Diederich

☕ Objectives

1. Tea Origins
2. Compounds in Tea
3. Cancer
4. Diagnosis
5. Cancer TNM Stages

6. Treatments
7. MNT for Cancer Prevention
8. Research Articles
9. Future Anticancer Drug

Tea Origins

- *Camellia sinensis* plant

- Oxidation process & length determines color & taste
  - White, dark, green, oolong, black and fermented pu'erh tea.

- Subtypes based on growing region

Photo by Sergi Montaner from FreeImages

(The Tea, 2019) (Types, 2018)

Phytochemicals

Non-Flavonoid Polyphenols · Flavonoids · Phenolic Acids

Flavanones — Citrus Fruit

Flavonols — Tea, Onions

Flavanols (Flavanol-3ols) — Tea, Red Wine, Apples

Flavones — Celery, Parsley

Isoflavones — Soybeans, Red Clover, Legumes

Anthocyanins — Red Wine, Blueberries, Cherries

Catechins — Green Tea, White Tea, Oolong Tea
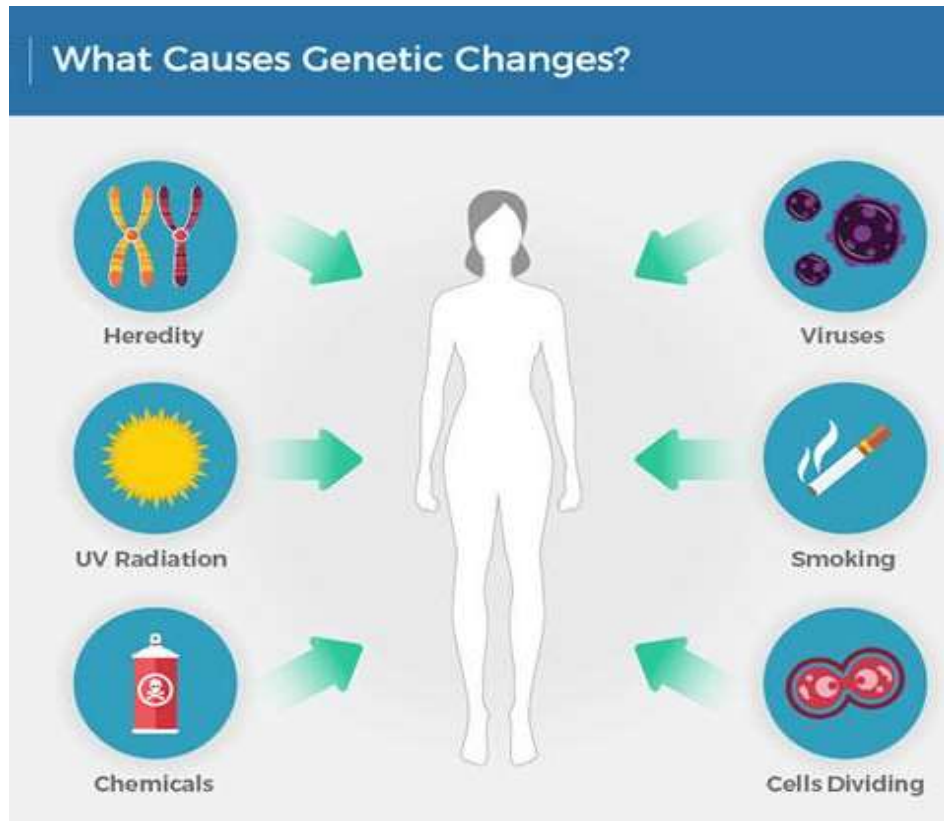
Five catechins (the major flavonoids in the tea plant) have been investigated and identified:
Catechin - **C**
Epicatechin – **EC**
Epigallocatechin – **EGC**
Epicatechin Gallate – **ECG**
Epigallocatechin Gallate – **EGCG**

EGCG is the main catechin in green tea.

Changes during oxidation/processing

Theaflavins — Black Tea, Oolong Tea

Thearubigins — Black Tea, Oolong Tea

(Tea, 2019)

Cancer: Cause & Effect

What Causes Genetic Changes?

Heredity

UV Radiation

Chemicals

Viruses

Smoking

Cells Dividing

Effect:

- DNA damage

- Oncogenes

- Tumor Suppressor Genes

(What, 2019)

Diagnosis

- Imaging:
  - CT Scan
  - MRI
  - Nuclear Scan
  - Bone Scan
  - PET Scan
 - Ultrasound
  - X-rays

- Biopsy

- Lab tests

(Team, 2019)

(What, 2019) (How, 2019)

Cancer TNM Stages

Stage	What it means
Stage 0	Abnormal cells are present but have not spread to nearby tissue. Also called carcinoma in situ, or CIS. CIS is not cancer, but it may become cancer.
Stage I, Stage II, and Stage III	Cancer is present. The higher the number, the larger the cancer tumor and the more it has spread into nearby tissues.
Stage IV	The cancer has spread to distant parts of the body.

(Cancer, 2019)
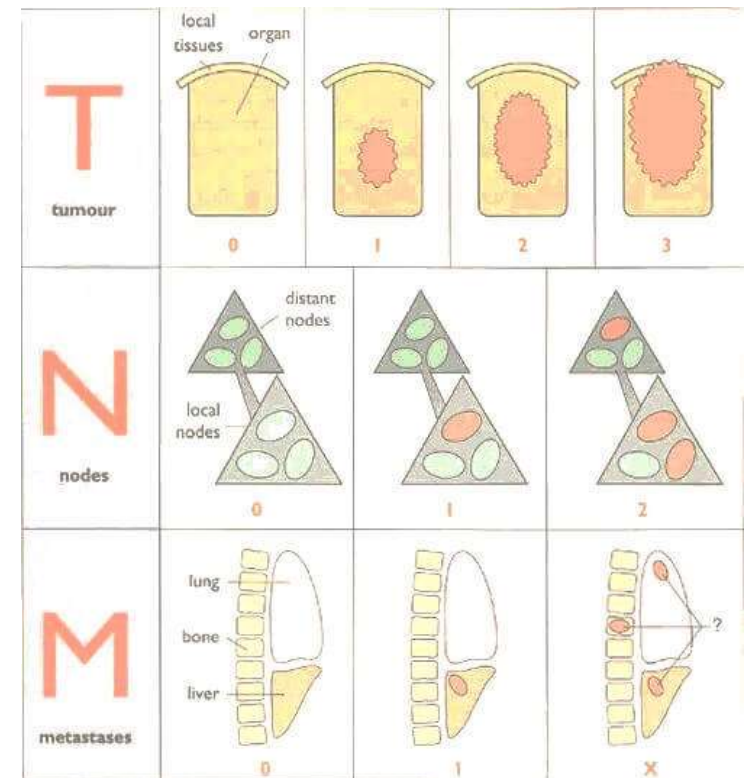
(Epomedicine, 2016)

Treatments

Surgery

Radiation Therapy

Chemotherapy

Immunotherapy to Treat Cancer

Targeted Therapy

Hormone Therapy

Stem Cell Transplant

Precision Medicine

(Complimentary, 2019)

MNT for Cancer Prevention

<u>Therapeutic Options:</u>

- Eat plant sources of protein

- 5+ servings of fruits & veggies

- Whole grains & high-fiber

- Limit red meat & whole eggs

- Decrease saturated fat intake
  - Choose monounsat. & polyunsat.

- Bake or broil foods & choose low-fat dairy

- Exercise 5x/wk. for 30 min.

- Maintain healthy weight

- Balance calorie intake with exercise

- Limit alcohol to ≤ 2 drinks men, ≤ 1 women

(The most, 2019)

Research Article:

Inhibitory effect of black tea (Camellia Sinensis) theaflavins and Thearubigins against HCT 116 colon cancer cells and HT 460 lung cancer cells

Background

Study Design:

- In vitro controlled trial

Purpose:

- to investigate the in vitro anti-oncogenic ability of black tea-isolated Theaflavins and Thearubigins alone and in combination against colon cancer cell lines (HCT 116) and lung cancer cell lines (HT 460).

Participants:

- HCT 116 & HT 460 (2,000 cells/well) were seeded in 96 well plates each

(Imran, 2019)

Criteria

Inclusion

- Viable cells

- Cancerous

Exclusion

- Nonviable cells

Abbreviations

HCT 116 = colon cancer
HT 460 = lung cancer

TF = Theaflavins
TR = Thearubigins

(Imran, 2019)

HCT 116 & HT 460 cells in separate wells

Control
No Intervention

TF
50, 100, 150, 200, and 250 μg/mL

TR
50, 100, 150, 200, and 250 μg/mL

TF + TR ½ dose for each was used in serum complete media (200 μl)

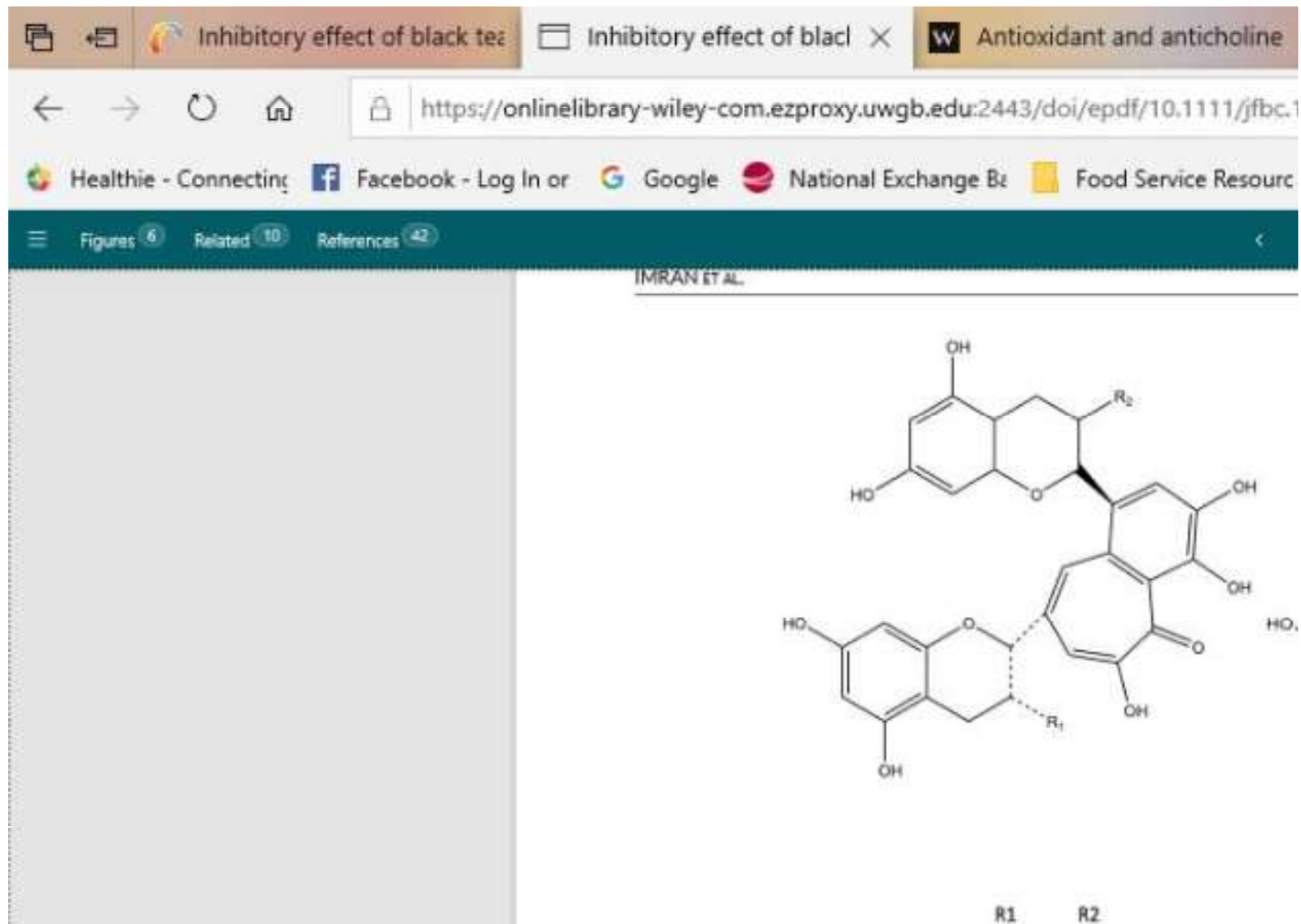Incubated 24 hours

Incubated 24 hours

Incubated 24 hours

Incubated 24 hours

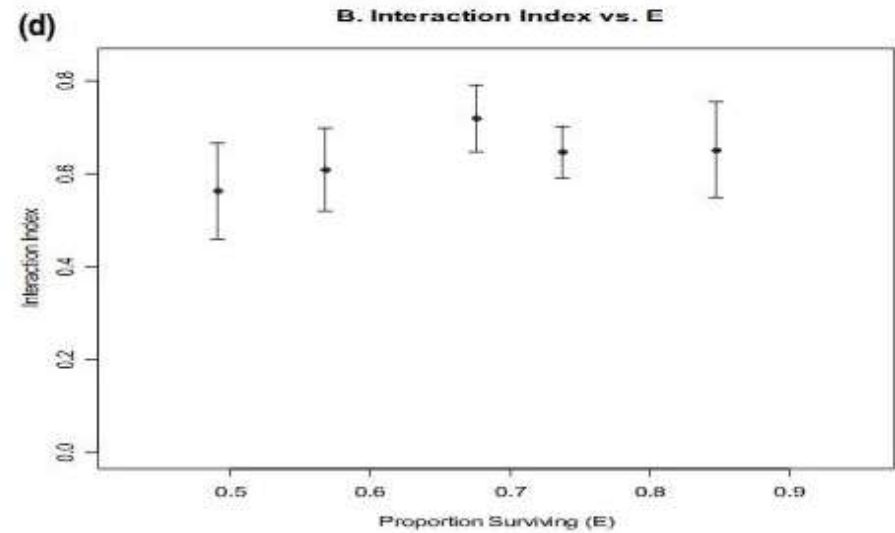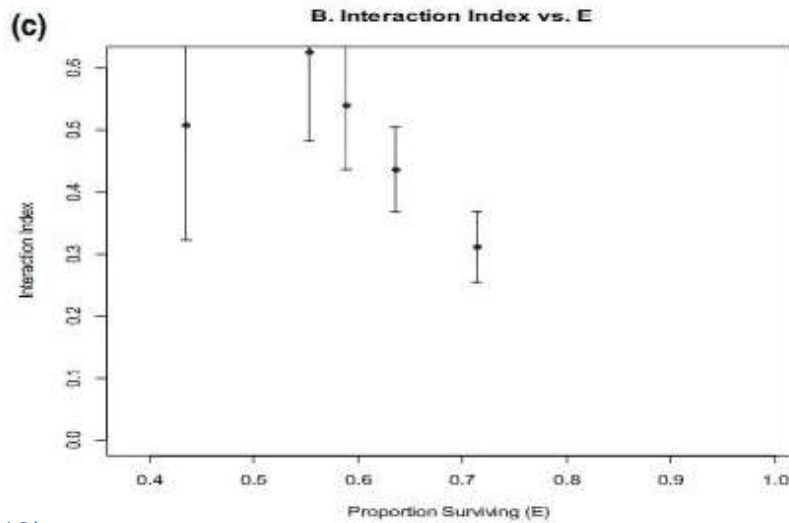After 72 hours of exposure to Intervention → MTT Assay → Incubated 60 min. @ 37°C

(Imran, 2019)

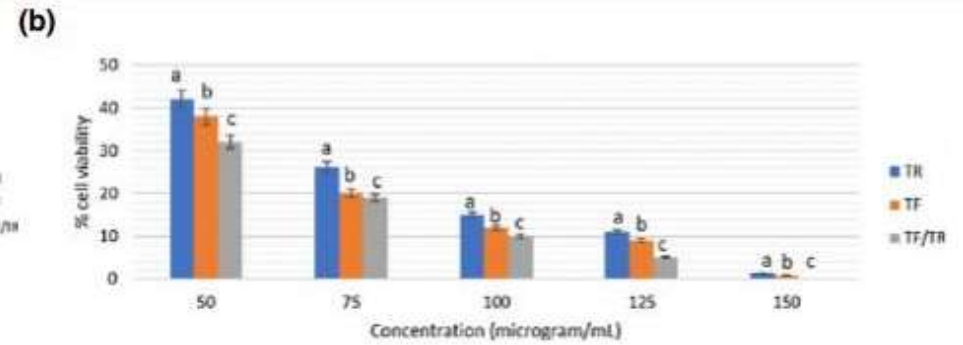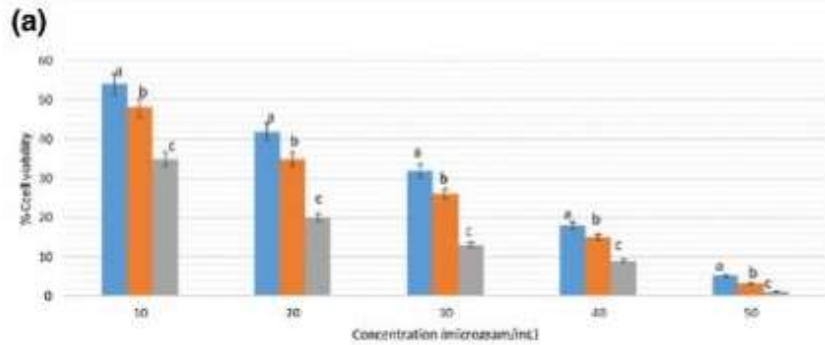# What are Theaflavins & Thearubigins?

Cell Viability [Fig. 2]

The Cell Cycle and the Checkpoints

3. Mitosis Checkpoint

2. DNA Synthesis Checkpoint

1. Cell Growth Checkpoint

M

G2

G1

S

G0
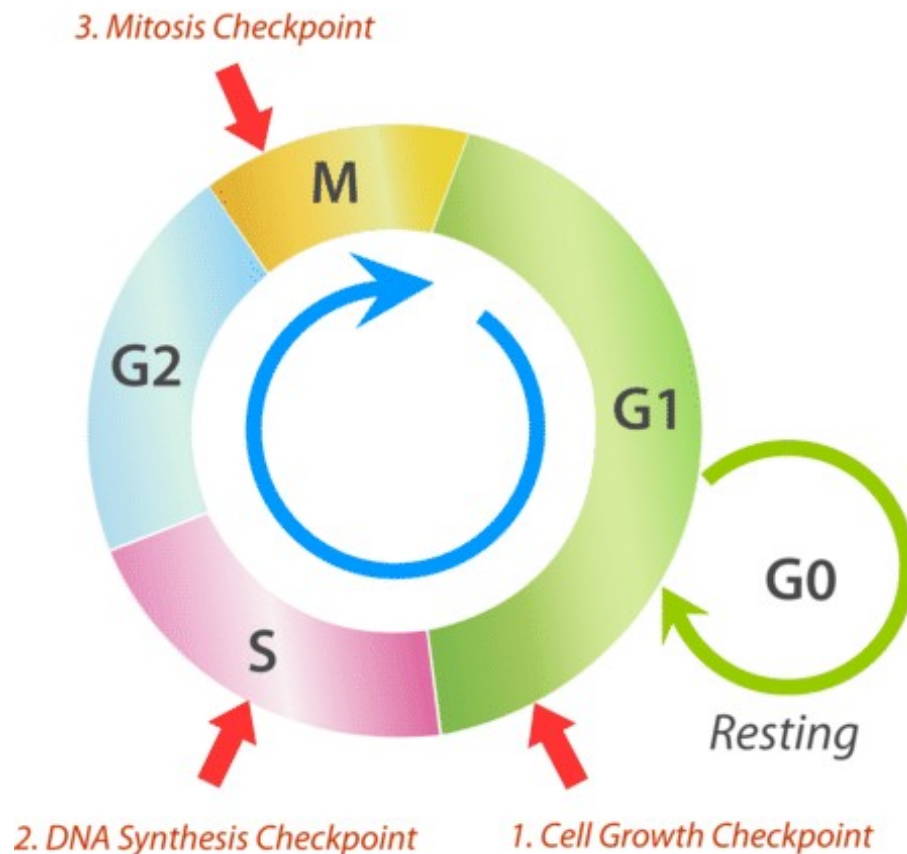
Resting

1. Cell Growth Checkpoint

- Occurs toward the end of growth phase 1 (G1).
- Checks whether the cell is big enough and has made the proper proteins for the synthesis phase.
- If not, the cell goes through a resting period (G0) until it is ready to divide.

2. DNA Synthesis Checkpoint

- Occurs during the synthesis phase (S).
- Checks whether DNA has been replicated correctly.
- If so, the cell continues on to mitosis (M).

3. Mitosis Checkpoint

- Occurs during the mitosis phase (M).
- Checks whether mitosis is complete.
- If so, the cell divides, and the cycle repeats.

Effect on Cell Cycle Progression of HCT 116 [Fig. 3]
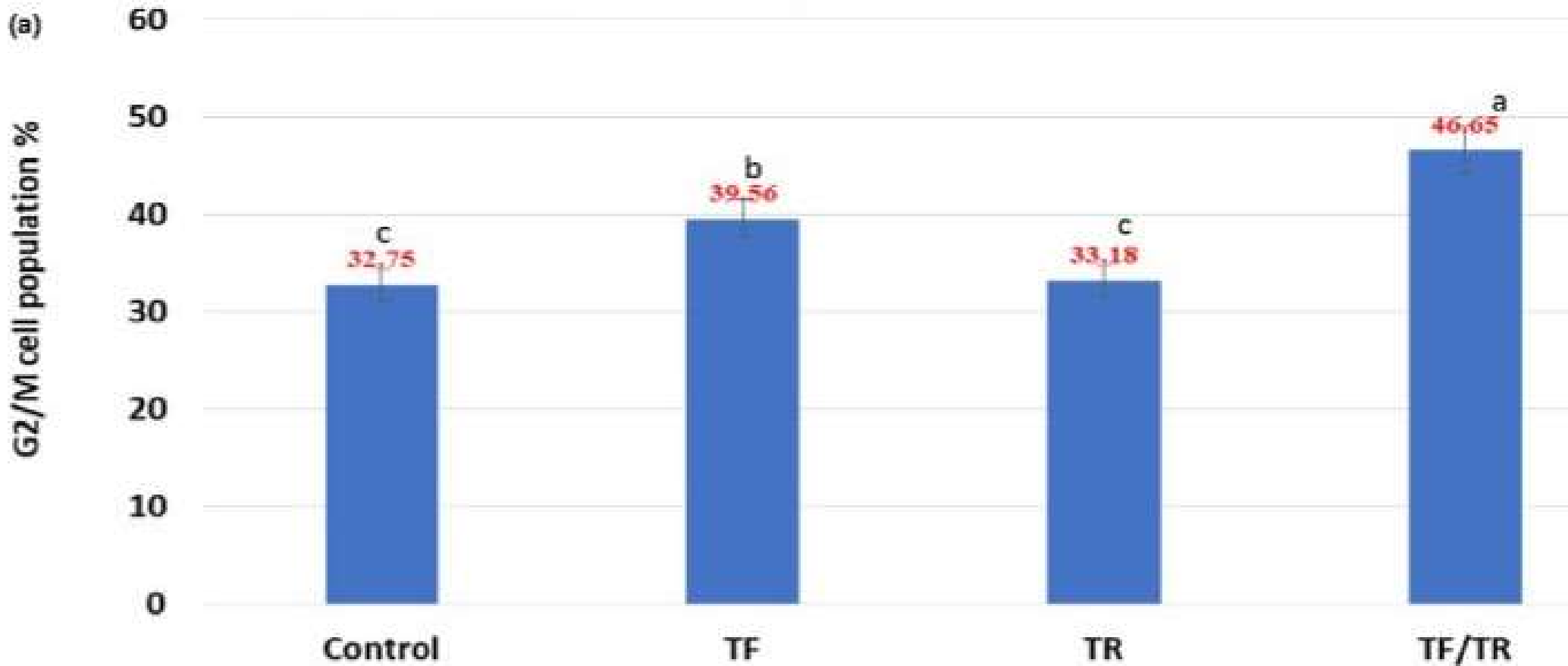
(Imran, 2019)

Effect on Cell Cycle Progression of HT 460 [Fig. 4]

(a)

Apoptosis

(Jockers, 2019)
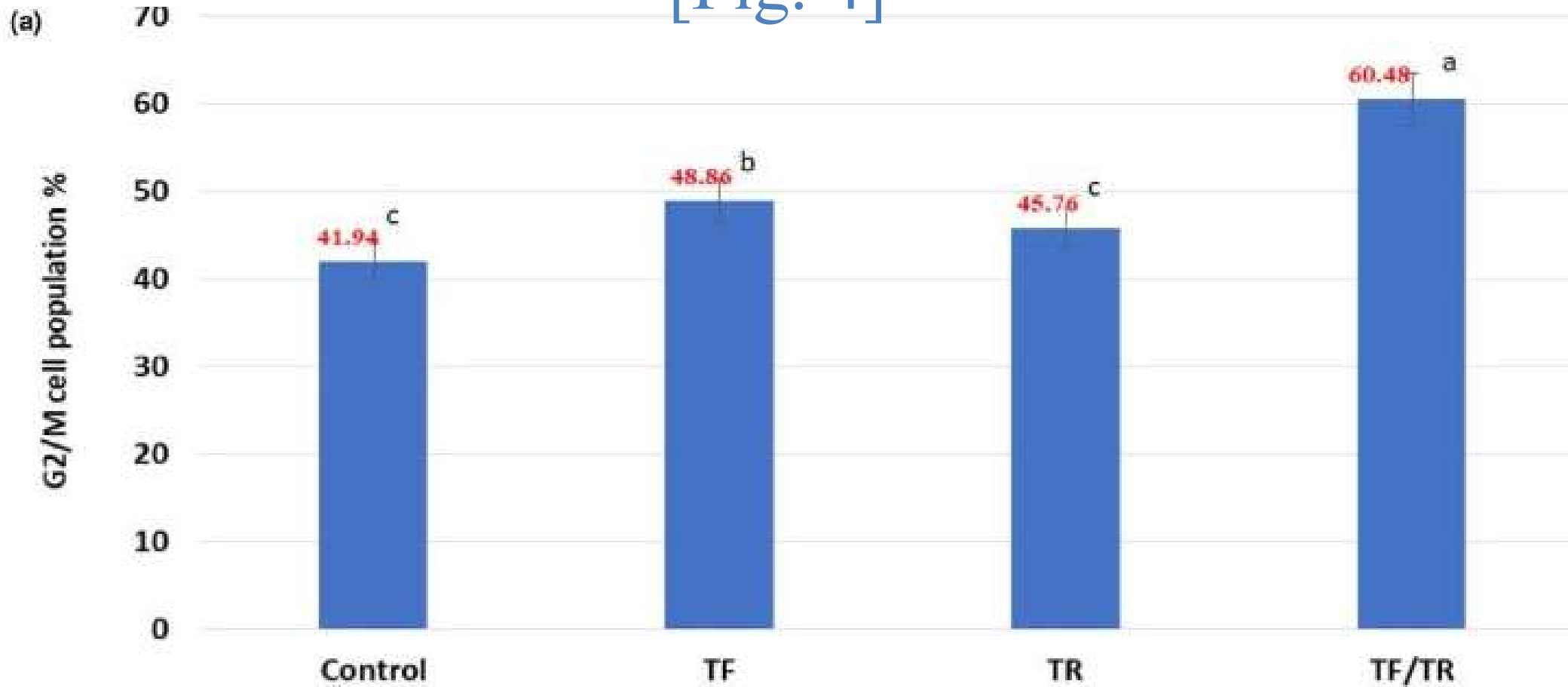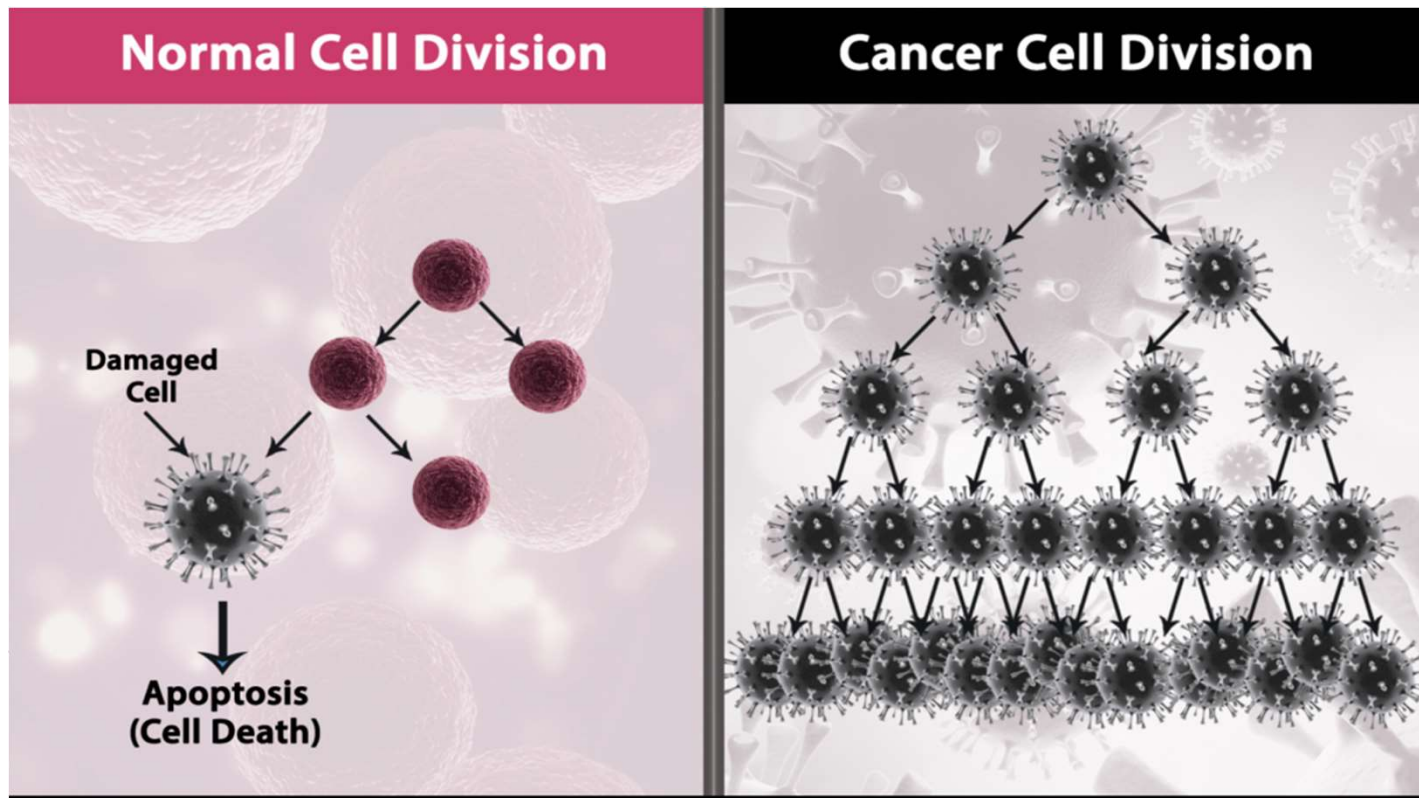
Effect on Apoptosis of HCT 116 [Fig. 5]
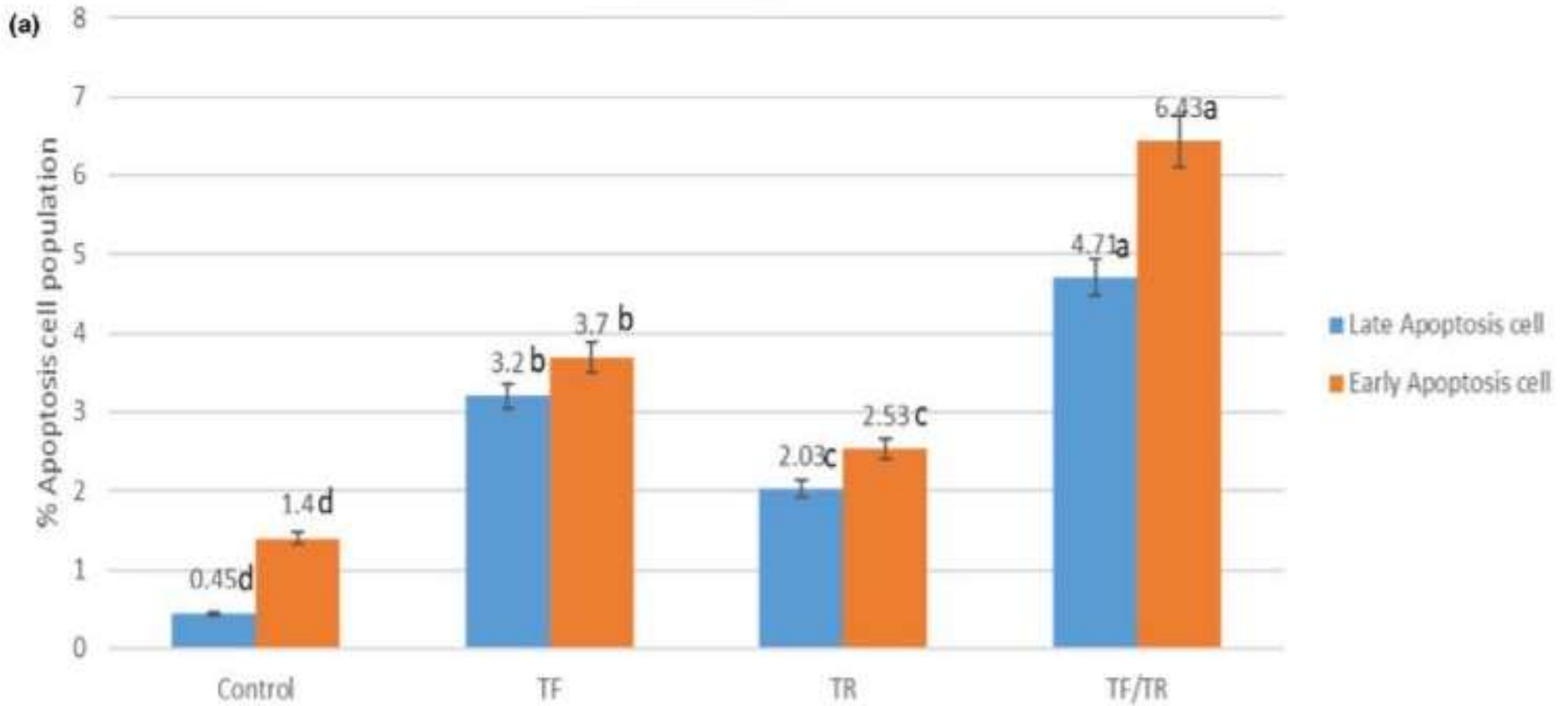
(Imran, 2019)

Effect on Apoptosis HT 460 [Fig. 6]

(a)

% Apoptosis cell population

- Late Apoptosis cell
- Early Apoptosis cell

Control: 2.43d, 1.4d
TF: 20.3b, 20.27b
TR: 11.4c, 18.67c
TF/TR: 24.87a, 27.37a
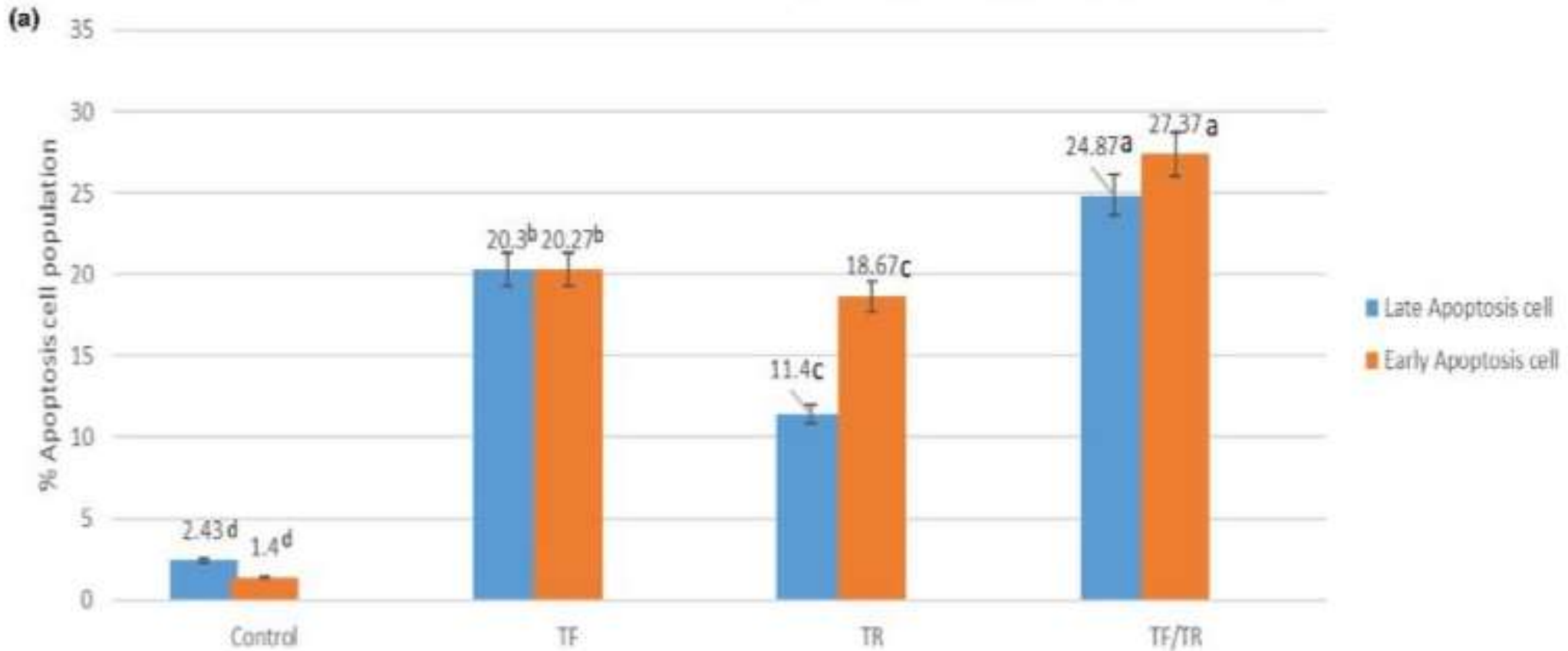
(Imran, 2019)

EAL Worksheet Findings

Strengths

- Defined type of tea

- Defined and supported testing methods

- Cited past studies with similar methods and outcomes

Limitations

- In vitro study

- Natural concentrations of TF & TR

- Exposure time

Research Rating: Positive +

(Imran, 2019)

Research Summary

- In a dose-dependent manner, TF and TR and their combinations, inhibit cancer cell viability

- TF, TR, and their combinations exhibited substantial cell arrest at the G2/M phase

- TF, TR, and their combination can induce apoptosis in HT 460 and HCT 116 cancer cell lines.

(Imran, 2019)

Research Article:

Reduced prostate cancer risk with green tea and epigallocatechin 3-gallate intake among Hong Kong Chinese men

Background

- Study Design:
  - Retrospective case-control study

- Purpose:
  - To determine the association between prostate cancer risk and habitual green tea intake among Chinese men in Hong Kong and explore the relationship with EGCG.

- Participants:
  - Male patients at Hong Kong hospital, diagnosed with prostate cancer and control patients

(P M Y Lee, 2017)

Criteria

Inclusion

- Males

- Hong Kong Chinese ethnicity

- Less than 85 years old

- Diagnosed with primary PCA

Exclusion

- 85+ years old

- Physician-diagnosed cancer in any site

- Communication difficulties

(P M Y Lee, 2017)
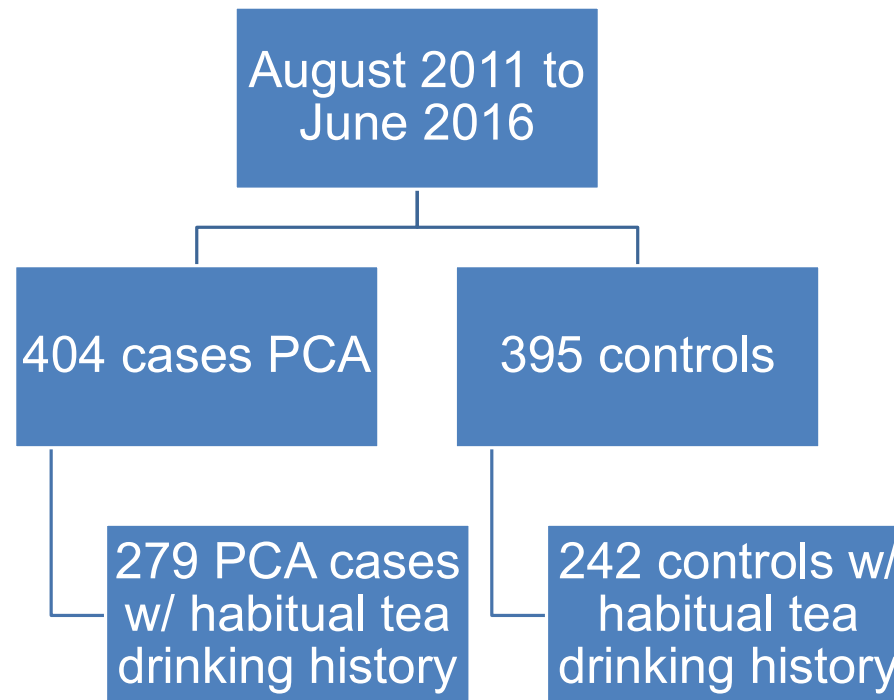
Similarity Between Case & Control

Table 1. Selected characteristics of prostate cancer cases and controls among Hong Kong Chinese men

Characteristic	Cases (N = 404)	Controls (N = 395)	P-value
Age, mean (s.d.)	69.5 (7.1)	68.1 (8.2)	0.011
Tobacco smoking, n (%)			
Never	209 (51.7)	189 (47.9)	
Former	137 (33.9)	130 (32.9)	
Current	58 (14.4)	76 (19.2)	0.173
Alcohol consumption, n (%)			
Non-users	312 (77.2)	304 (77.0)	
Users	92 (22.8)	91 (23.0)	0.933
Educational attainment, n (%)			
Primary or below	172 (42.6)	150 (38.0)	
Secondary	177 (43.8)	198 (50.1)	
Tertiary	55 (13.6)	47 (11.9)	0.204
Family prostate cancer history, n (%)			
No	374 (92.6)	383 (97.0)	
Yes	30 (7.4)	12 (3.0)	0.007
Deep fried food consumption, n (%)			
< 1 time per month	198 (49.0)	207 (52.4)	
1–3 times per month	123 (30.5)	149 (37.7)	
≥ 1 time per week	83 (20.5)	39 (9.9)	< 0.001
Green vegetable consumption, n (%)			
< 1 time per week	4 (1.0)	9 (2.3)	
1–3 times per week	39 (9.7)	31 (7.8)	
≥ 4 times per week	361 (89.3)	355 (89.9)	0.246
Orange fruits, n (%)			
< 1 time per week	50 (12.4)	38 (9.6)	
1–3 times per week	39 (9.7)	48 (12.2)	
≥ 4 times per week	315 (77.9)	309 (78.2)	0.283
Orange vegetable consumption, n (%)			
< 1 time per week	29 (7.2)	23 (5.8)	
1–3 times per week	101 (25.0)	111 (28.1)	
≥ 4 times per week	274 (67.8)	261 (65.1)	0.485
Coffee consumption, n (%)			
Non-users	304 (75.2)	312 (79.0)	
Users	100 (24.7)	83 (21.0)	0.238

(P M Y Lee, 2017)

Exposure Assessment on Tea Drinking & EGCG Estimation

- Habitual tea drinking
  - Drank at least 1x/week over 5 years preceding diagnosis or recruitment

- Provide information on types of tea (that is, green tea, oolong tea, black tea, pu'erh tea),

- Frequency of tea drinking (cups a day, one cup is equivalent to 250 ml)

- Years of drinking & concentration of tea drinking expressed by the amount of tea leaves of intake
  - (light: o2.5 g; moderate: 2.5–5.0 g, heavy: 5.0–7.5 g; very heavy: ⩾7.5 g) in 250 ml water.
  - choose the amount of tea leaves displayed in four different bags (that is, 1.25 g, 2.5 g, 5.0 g, 7.5 g, respectively) to best describe the concentration of their tea drinking.

(P M Y Lee, 2017)

August 2011 to June 2016

404 cases PCA

395 controls

279 PCA cases w/ habitual tea drinking history

242 controls w/ habitual tea drinking history

(P M Y Lee, 2017)

Association between EGCG intake (GT) and PCA

Table 3. Associations between EGCG intake from teas and prostate cancer risk among Hong Kong Chinese men

Variables	Cases N(%)	Controls N(%)	Crude OR (95% CI)	Adjusted OR (95% CI)[a]	P for trend
Habitual EGCG consumption (mg per day)[b]					
Low	101 (36.2)	58 (24.0)	1.00	1.00	
Middle	117 (41.9)	120 (49.6)	0.56 (0.37, 0.85)	0.56 (0.36, 0.86)	
High	58 (20.8)	63 (26.0)	0.53 (0.33, 0.86)	0.56 (0.33, 0.94)	0.015
Cumulative consumption of EGCG from tea (mg × years)[b]					
Low	100 (35.8)	61 (25.2)	1.00	1.00	
Middle	127 (45.5)	113 (46.7)	0.69 (0.46, 1.03)	0.65 (0.42, 1.01)	
High	49 (17.6)	67 (27.7)	0.45 (0.27, 0.73)	0.46 (0.27, 0.79)	0.003

Abbreviations: CI, confidence interval; EGCG, epigallocatechin 3-gallate; OR, odds ratio. [a]Adjusted for age at interview, deep fried food consumption, green vegetable consumption, alcohol consumption, coffee consumption, tobacco smoking, education attainment, family prostate cancer history. [b]Daily intake of EGCG intake was categorized into three levels by interquartile according to the exposure distribution of control (low: < 36 mg; middle: 36–145 mg; high: > 145 mg). [c]Cumulative EGCG intake was categorized into three levels by interquartile according to the exposure distribution of control (low: < 248 086 mg; middle: 248 086–1 587 750 mg; high: > 1 587 750 mg).

(P M Y Lee, 2017)

Results were considered statistically significant at P < 0.05.

Results Summary

- 32 cases and 50 controls reported habitual green tea drinking, showing an adjusted OR of 0.60 (95% confidence interval): 0.37, 0.98).

- A significantly lower intake of EGCG was observed among cases (54.4mg) than the controls (72.5mg), which results in an inverse gradient of PCA risk with the increasing intake EGCG (test for trend P = 0.015).

(P M Y Lee, 2017)

EAL Worksheet Findings

Strengths

- Accounted for confounding factors

- Thorough intake inquiry

- Results were measurable

Limitations

- Small sample size

- Retrospective, recall bias

- Ethnic Group

Research Rating: Positive +

(P M Y Lee, 2017)

Research Summary

Findings show a significantly inverse association between green tea intake and PCA risk, whereas a positive association with consumption of pu'er tea was indicated. Consumption of EGCG may be protective of PCA.

(P M Y Lee, 2017)

Research Article:

Randomized Clinical Trial of Brewed Green and Black Tea in Men With Prostate Cancer Prior to Prostatectomy

Background

Study Design:

- Randomized controlled study

Purpose:

- To determine the effect of GT and BT consumption on biomarkers related to prostate cancer development and progression in malignant RP tissue by immunostaining.
  - Specifically, to determine effects of proliferation (Ki67), apoptosis (TUNEL, Bax, Bcl-2), inflammation (NFκB), and oxidation (8OHDg).

Participants:

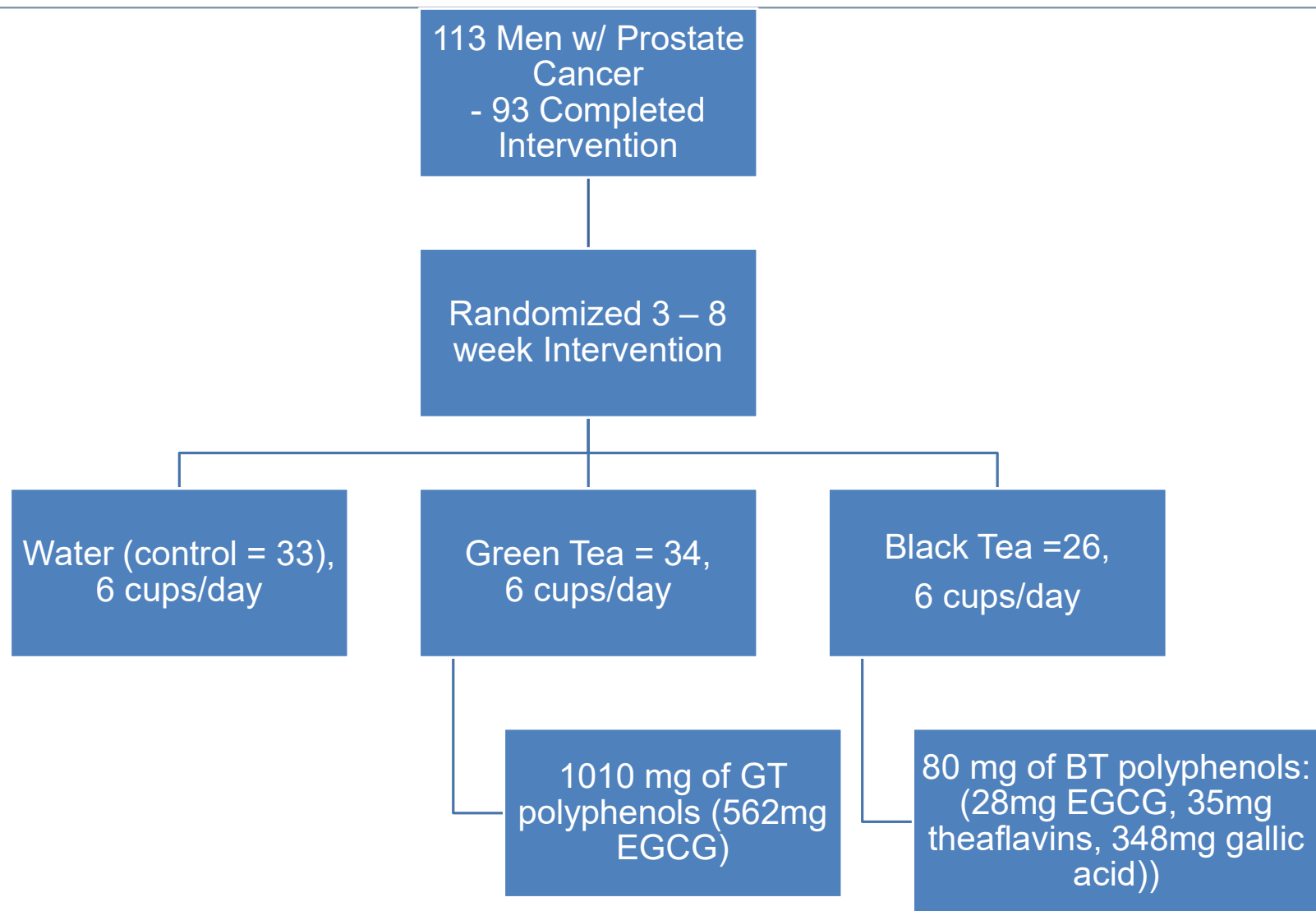- 113 Male patients, 50-70 years old, diagnosed w/ prostate cancer

(Henning, 2015)

Criteria

Inclusion

- Clinically diagnosed localized prostate cancer

- Prostatectomy at least 3 weeks after study entry

Exclusion

- History of hepatitis

- Alcohol abuse and other significant medical or psychiatric conditions

- 5-alpha reductase inhibitors, antiandrogens, or luteinizing hormone-releasing hormone agonists

(Henning, 2015)

```
┌─────────────────────────┐
│   113 Men w/ Prostate   │
│        Cancer           │
│    - 93 Completed       │
│      Intervention       │
└───────────┬─────────────┘
            │
┌───────────┴─────────────┐
│   Randomized 3 – 8      │
│   week Intervention     │
└───────────┬─────────────┘
```

Water (control = 33), 6 cups/day	Green Tea = 34, 6 cups/day	Black Tea =26, 6 cups/day

1010 mg of GT polyphenols (562mg EGCG)

80 mg of BT polyphenols: (28mg EGCG, 35mg theaflavins, 348mg gallic acid))
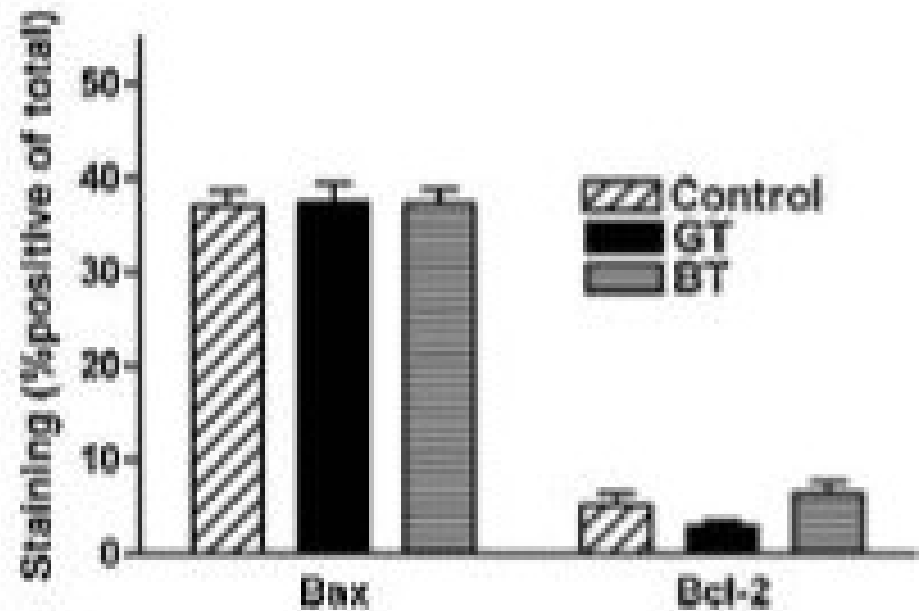
(Henning, 2015)

Immunostaining in Radical Prostatectomy [Fig. 1]

- NFkB Inflammation:

  - GT significantly lower vs. control

  - BT no significant difference vs. control
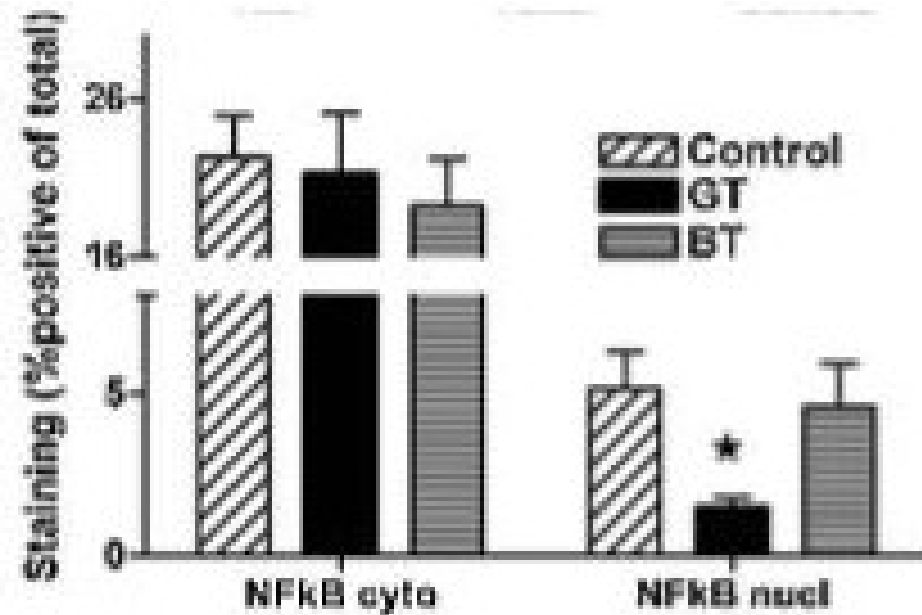

(Henning, 2015)

Immunostaining in Radical Prostatectomy [Fig. 1]

- No significant differences when comparing GT, BT, and control in RP staining for:
  - Apoptosis (Bax and Bcl-2)

(Henning, 2015)

Immunostaining in Radical Prostatectomy [Fig. 1]

- No significant differences when comparing GT, BT, and control in RP staining for:
  - Proliferation (Ki67)
  - Oxidative DNA damage (8OHDg)

(Henning, 2015)
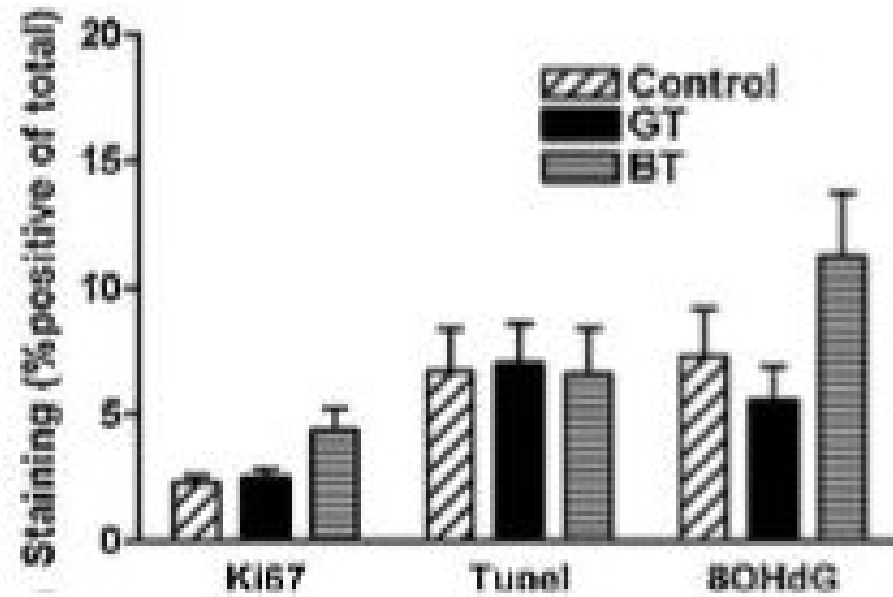
Concentration of Polyphenols in Tissue

TABLE II. Concentration of Tea Polyphenols and Methyl-Metabolites in Prostate Tissue and Urine Collected Before and After the Consumption of GT and BT

	Prostate Tissue Concentration (pmol/g tissue) [†a]		
	Water	GT	BT
EGCG	‡	16.7 ± 12.7[*]	‡
ECG	‡	7.6 ± 5.1[*]	‡
4″-MeEGCG	‡	15.8 ± 10.1[*]	‡
Theaflavin	‡		‡

	Urine Concentration (μmol/g creatinine) [‡a,b]			
	GT-Pre	GT-Post	BT- Pre	BT-Post
EGC	‡	9.2 ± 16[*]	‡	0.4 ± 0.4[*]
EC	‡	4.8 ± 6.1[*]	‡	0.3 ± 0.3[*]
4′-MeEGC	‡	8.0 ± 18[*]	‡	0.2 ± 0.3[*]
Theaflavins	‡	‡	‡	‡

[*]Compared with the control group, $P < 0.01$. n = 34 (GT), 26 (BT), 33 (control), mean ± s.d.
[†a](−)-epigallocatechin-3-gallate (EGCG), (−)-epicatechin-3-gallate (ECG), (−)-epigallocatechin (EGC), (−)-epicatechin (EC), 4′-O-methyl EGC (4′-MeEGC), 4″-O-methylEGCG (4″-O-methylEGCG).
[b]Polyphenols were not detected in urine after water consumption below detection limit.

(Henning, 2015)

Urine Oxidative DNA Damage & PSA
[Fig. 3]

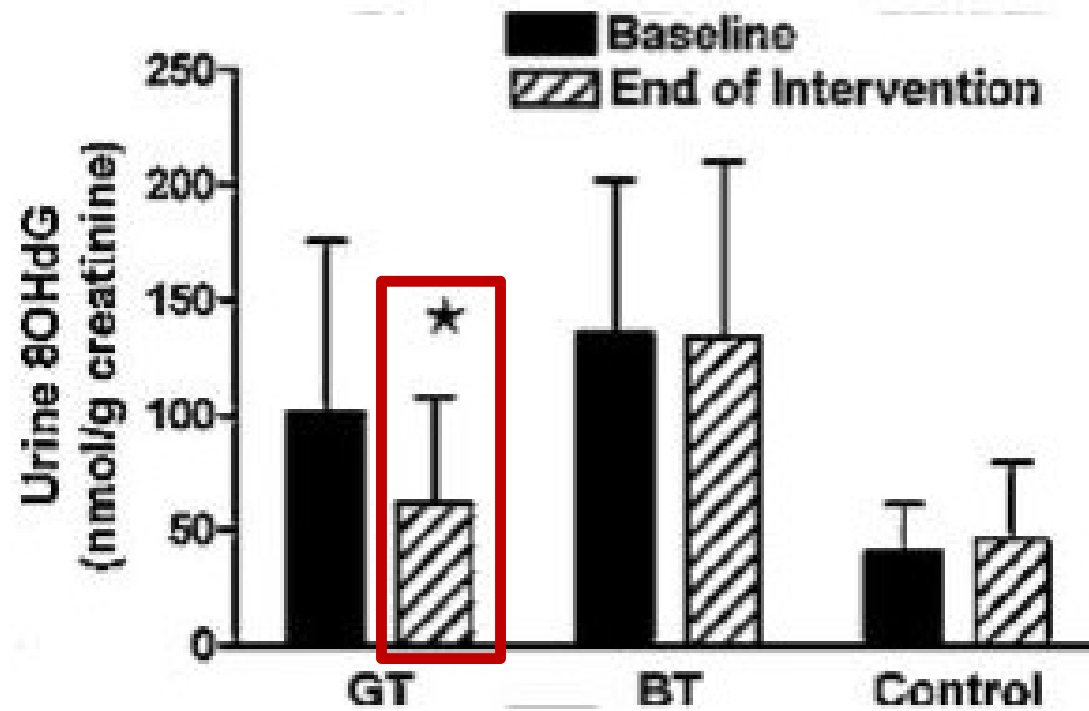Fig. 3. Change in urinary concentration of oxidative DNA damage marker 8OHdG in urine collected at baseline and post-intervention (mean ± SEM; GT n = 14; BT n = 16; Water n = 14).

(Henning, 2015)

Serum PSA

TABLE III. Prostate Specific Antigen Concentrations in Serum Collected from Men Consuming GT, BT or Water Control Collected at Baseline and on the Morning of Radical Prostatectomy (Post-Intervention)

| | Serum PSA $(ng/mL)^a$ | | |
	Water	GT	BT
PSA baseline	9.9 ± 8.5	9.6 ± 5.2	9.2 ± 4.3
PSA post-intervention	10.0 ± 9.0	$8.4 \pm 4.3^*$	9.6 ± 6.0

Data are presented as mean $\pm$ std; n $=$ 30 (control), 30 (GT) and 23 (BT).

[*]PSA changes from pre to post were compared between the 3 groups using Analysis of Variance with pairwise contrasts, $P < 0.05$.

[a]green tea (GT), black tea (BT), prostate specific antigen (PSA).

(Henning, 2015)

EAL Worksheet Findings

Strengths

- Defined brewing strength – one bag/240 mL on boiling water for 5 min.

- Controlled for other dietary confounding factors

Limitations

- Attrition

- Short study (3 to 8 weeks); longer intervention ideal

- Different intervention lengths

- Not blinded

Research Rating: Positive +

(Henning, 2015)

Research Summary

In summary, daily consumption of six cups of brewed GT resulted in uptake of tea polyphenols in the prostate gland, a significant decrease in nuclear NFkB, and a decrease in systemic antioxidant activity as measured by urinary 8OHdG.

(Henning, 2015)

Future Anticancer Drug?

- Animal and Human trials needed

- Addition of green and black teas to Nutrition Care Manual pending successful human trials

  - Safer

  - Better tolerance – No Side Effects

  - Economical

(Imran, 2019)

References – APA Format

- Amaresh, N., Mullaicharam, A., & El-Khider, M. (2011). Chemistry and pharmacology of caffeine in different types of tea leaves. International Journal of Nutrition, Pharmacology, Neurological Diseases, 1(2), 110-115.

- Cancer Staging. (n.d.). Retrieved November 27, 2019, from https://www.cancer.gov/about-cancer/diagnosis-staging/staging.

- Complementary and Alternative Medicine (CAM). (n.d.). Retrieved November 27, 2019, from https://www.cancer.gov/about-cancer/treatment/cam.

- Epomedicine, & Nekhala, D. E. (2016, August 14). TNM Classification and Cancer Staging Simplified. Retrieved November 27, 2019, from https://epomedicine.com/medical-students/tnm-classification-cancer-staging-simplified/.

- Henning, Wang, Said, Huang, Grogan, Elashoff, . . . Aronson. (2015). Randomized clinical trial of brewed green and black tea in men with prostate cancer prior to prostatectomy. Prostate, 75(5), 550-559.

- How Cancer Is Diagnosed. (n.d.). Retrieved November 27, 2019, from https://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis.

- Imran, Ali, Butt, Masood Sadiq, Xiao, Hang, Imran, Muhammad, Rauf, Abdur, Mubarak, Mohammad S., & Ramadan, Mohamed Fawzy. (2019). Inhibitory effect of black tea (Camellia sinensis) theaflavins and thearubigins against HCT 116 colon cancer cells and HT 460 lung cancer cells. Journal of Food Biochemistry, 43(5), N/a.

References

- Jockers, Jockers, Jockers, D., Jockers, & Cathy. (2019, August 23). Special Nutrients that Turn off Cancer Cells. Retrieved November 30, 2019, from https://drjockers.com/special-nutrients-turn-off-cancer-cells/.

- Learning, L. (n.d.). Biology for Non-Majors I. Retrieved November 30, 2019, from https://courses.lumenlearning.com/wmopen-nmbiology1/chapter/cell-cycle-checkpoints/.

- P M Y Lee, C F Ng, Z M Liu, W M Ho, M K Lee, F Wang, . . . L A Tse. (2017). Reduced prostate cancer risk with green tea and epigallocatechin 3-gallate intake among Hong Kong Chinese men. Prostate Cancer and Prostatic Diseases, 20(3), 318-322.

- The most trusted diet manual since 1981. (n.d.). Retrieved November 27, 2019, from https://www.nutritioncaremanual.org/client_ed.cfm?ncm_client_ed_id=136.

- The Tea Association of The USA. (n.d.). Retrieved November 25, 2019, from http://www.teausa.org/.

- Types of Tea. (2018, February 6). Retrieved November 27, 2019, from https://tea-culture.net/types-of-tea/.

- TEA AND HEALTH. (n.d.). Retrieved November 27, 2019, from https://www.octaviatea.com/pages/Tea-Guide-Page-Twelve.html.

- Team, V. U. M. C. W. D. (n.d.). Vanderbilt Health. Retrieved December 17, 2019, from https://www.vanderbilthealth.com/radiology/49780.

- What Is Cancer? (n.d.). Retrieved November 27, 2019, from https://www.cancer.gov/about-cancer/understanding/what-is-cancer.

QUESTIONS?

Thank you!