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Fruit Extract, Rich in Polyphenols and Flavonoids, Modifies the Expression of *DNMT* and *HDAC* Genes Involved in Epigenetic Processes

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Introduction

Plant based polyphenols

1. Can be found in many fruits and vegetables.
2. Anti-cancer properties.
3. Inhibition of angiogenesis.
4. Stimulation of the immune system.



Introduction

DNMTs

HDACs



Objectives



- Investigate if regular intake of an aqueous extract derived from the seed and peel of a fruit, abundant in polyphenols, exerts an impact on the expression levels of DNMT and HDAC genes.
- polyphenols/flavonoids, could prevent the early stages of tumor formation following carcinogenic DMBA exposure by modulating DNMT and HDAC mRNA levels.

Materials and Methods

- male CD1 mice were used for this study, with six animals in each group



		Fluid Consumption (for 28 Days)		Carcinogenic Exposure (on Day 27) **	
Group 1	Control	Tap water	ad libitum	Vehicle	
Group 2	DMBA	Tap water	ad libitum	DMBA	20 mg/kg bw
Group 3	FC	Fruit seed and peel extract	Human-equivalent dose *	Vehicle	
Group 4	FC + DMBA	Fruit seed and peel extract	Human-equivalent dose *	DMBA	20 mg/kg bw

The experimental animals received ad libitum water after full consumption of the polyphenolic fruit seed and peel extract (FC; *) and purified corn oil as the vehicle or DMBA (7,12-dimethylbenz(a)anthracene) dissolved in purified corn oil was administered intraperitoneally 24 h prior to cervical dislocation and dissection (**).

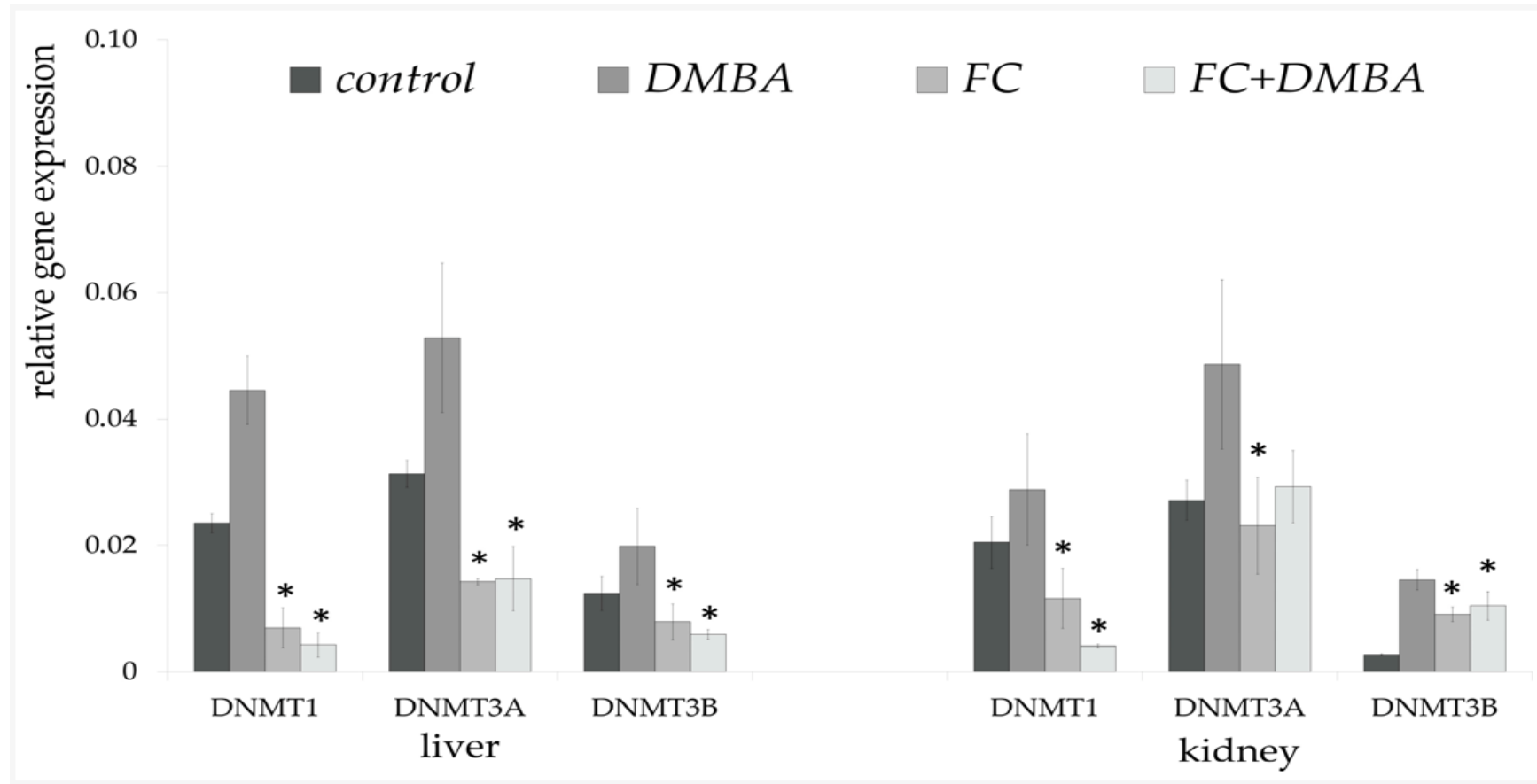
Materials and Methods

- Autopsy and collecting samples from liver and kidneys.
- RNA isolation, ExtraZol Tri-reagent protocol.
- RT-PCR SYBR Green protocol.
- Statistical analysis.

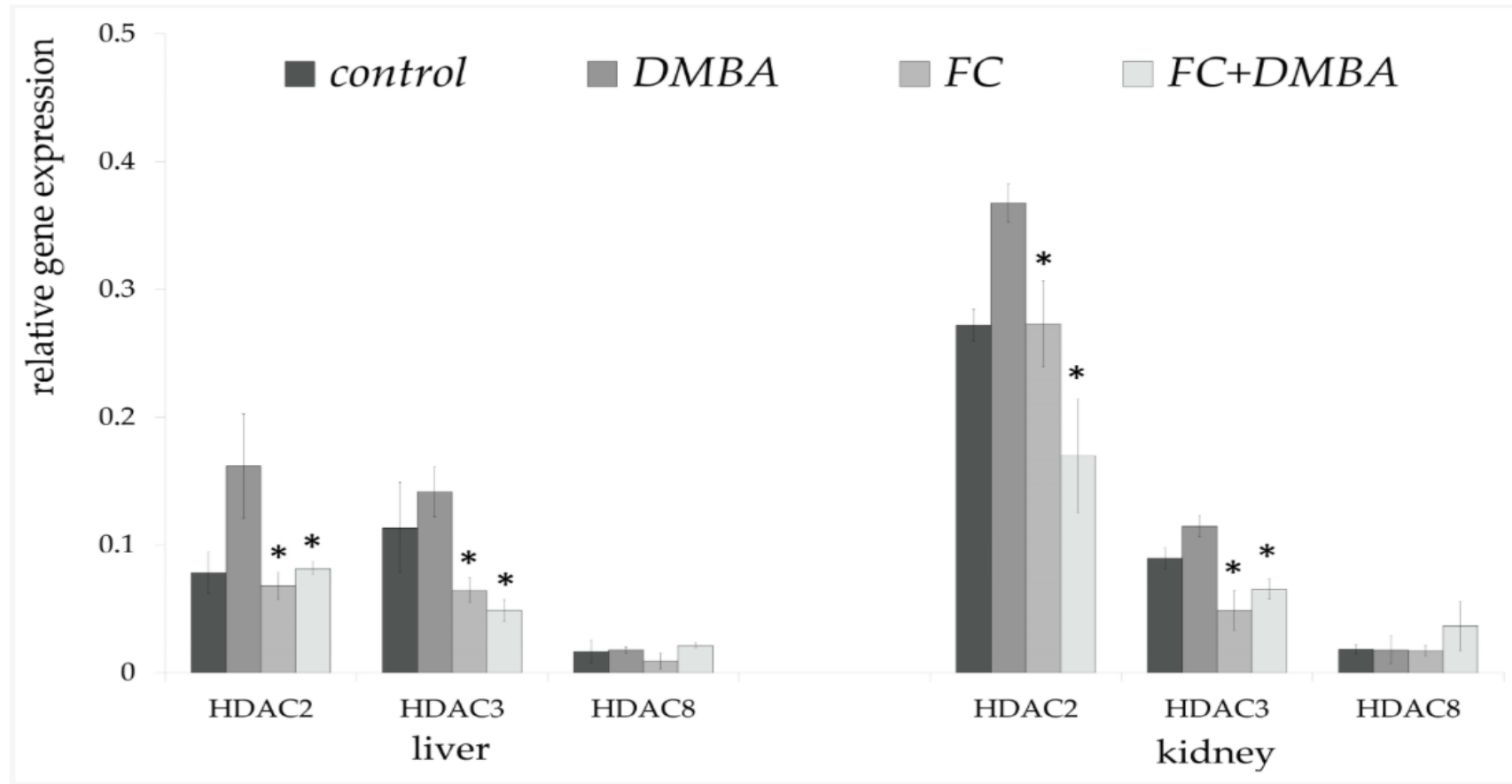
Gene Name	Forward Primer	Reverse Primer
DNA methyltransferase 1 (<i>DNMT1</i>)	F-AAGAATGGTGTGTCTACCGAC	R-CATCCAGGTTGCTCCCCTTG
DNA methyltransferase 3A (<i>DNMT3A</i>)	F-GAGGGAAGTCTGAGACCCAC	R-CTGGAAGGTGAGTCTTGCCA
DNA methyltransferase 3B (<i>DNMT3B</i>)	F-AGCGGGTATGAGGAGTGCAT	R-GGGAGCATCCTTCGTGTCTG
Histone deacetylase 2 (<i>HDAC2</i>)	F-GGAGGAGGCTACACAATCCG	R-TCTGGAGTGTCTGGTTGTCA
Histone deacetylase 3 (<i>HDAC3</i>)	F-GCCAAGACCGTGGCGTATT	R-GTCCAGCTCCATAGTGAAGT
Histone deacetylase 8 (<i>HDAC8</i>)	F-ACTATTGCCGGAGATCCAATGT	R-CCTCCTAAAATCAGAGTTGCCAG
Hypoxanthine phosphoribo-syltransferase 1 (<i>HPRT1</i>)	F-TCAGTCAACGGGGGACATAAA	R-GGGGCTGTACTGCTTAACCAG

Sequences of primers used for qRT-PCR are listed.

Results



Results



Discussion and Conclusion

- The results of this study indicated that fruit and peel extract administered to mice at human-equivalent doses protected against the DMBA-induced upregulation of *DNMT* and *HDAC* genes.
- Our results suggest that an extract derived from fruit peels and seeds provides effective protection against early gene expression changes of genes involved in epigenetic processes induced by the carcinogen DMBA.





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Thank you for your attention