

Table S1: Phase I Detoxification genes

Gene Short name	Gene Denomination	Fold Change over control	SE	p value	Fold Change over control	SE	p value	Fold Change over control	SE	p value
		Nicotine			3R4F (Full Flavor)			Ultralow Nicotine		
NQO2	NAD(P)H Dehydrogenase Quinone 2	1.08	0.037	ns	1.18	0.026	*	1.28	0.0471	***
AKR1B1	Aldo keto reductase family 1, member B1 (aldose reductase)	1.00	0.032	ns	1.23	0.023	**	1.09	0.061	ns
AKR1C3	Aldo-keto reductase family 1, member C3 (3-alpha hydroxysteroid dehydrogenase, type II)	0.78	0.074	ns	1.65	0.086	ns	1.79	0.116	***
CBR4	Carbonyl reductase 4	0.93	0.111	ns	1.42	0.114	*	1.27	0.055	ns

Table S1: Effect of CSE on gene array studies of other genes belonging to Phase I detoxification such as NQO2, AKR1B1, AKR1C3 and CBR4. Data were expressed as mean \pm SEM (fold change over control).

*p<0.05, **p<0.01, ***p<0.001 vs. control. n=6

Table S2: Phase II Detoxification genes

Gene Short name	Gene Denomination	Fold Change over control	SE	p value	Fold Change over control	SE	p value	Fold Change over control	SE	p value
		Nicotine			3R4F (Full Flavor)			Ultralow Nicotine		
GSTA4	Homo sapiens glutathione S-transferase A4	0.89	0.057	ns	1.36	0.076	*	1.44	0.131	**
GSTM2	Homo sapiens glutathione S-transferase M2 (muscle)	0.94	0.038	ns	1.26	0.041	**	1.27	0.041	***

Table S2: Effect of CSE on gene array studies of other genes belonging to Phase II detoxification related genes such as GSTA1 and GSTM2. Data were expressed as mean \pm SEM (fold change over control).

*p<0.05, **p<0.01, ***p<0.001 vs. control. n=6

Table S3: Genes Involved in ABC Efflux Transporters

Gene Short name	Gene Denomination	Fold Change over control	SE	p value	Fold Change over control	SE	p value	Fold Change over control	SE	p value
		Nicotine			3R4F (Full Flavor)			Ultralow Nicotine		
ABCA1	ATP-binding cassette, sub-family A (ABC1), member 1	0.99	0.102	ns	1.33	0.094	*	1.12	0.043	ns
ABCA3	ATP-binding cassette, sub-family A (ABC1), member 3	0.85	0.106	ns	1.20	0.063	*	1.04	0.061	ns
ABCB6	ATP-binding cassette, sub-family B (MDR/TAP), member 6 (ABCB6), nuclear gene encoding mitochondrial protein	0.88	0.065	ns	1.31	0.094	*	1.27	0.019	*
ABCG1	ATP-binding cassette, sub-family G (WHITE), member 1 (ABCG1), transcript variant 2	0.97	0.067	ns	1.27	0.065	*	1.15	0.035	ns

Table S3: Effect of CSE on gene array studies of other genes belonging to ABC efflux transporters involved in cholesterol efflux. Data were expressed as mean \pm SEM (fold change over control). *p<0.05 vs. control. n=6

Table S4: Genes Involved in NADPH Production

Gene Short name	Gene Denomination	Fold Change over control	SE	p value	Fold Change over control	SE	p value	Fold Change over control	SE	p value
		Nicotine			3R4F (Full Flavor)			Ultralow Nicotine		
IDH1	Isocitrate dehydrogenase 1 (NADP+), soluble	0.98	0.074	ns	1.44	0.037	**	1.25	0.104	ns
ME1	Malicenzyme 1, NADP(+)-dependent, cytosolic	1.01	0.180	ns	1.62	0.143	*	1.59	0.120	*
TKT	Transketolase (Wernicke-Korsakoff syndrome) (TKT)	0.90	0.061	ns	1.47	0.082	***	1.28	0.077	*
UGDH	UDP-glucose dehydrogenase	1.02	0.146	ns	1.48	0.109	*	1.43	0.066	*

Table S4: Effect of CSE on gene array studies of other genes belonging to NADPH production. Data were expressed as mean \pm SEM (fold change over control). *p<0.05, **p<0.01, ***p<0.001 vs. control. n=6

Table S5: Primer sequences used in real time qRT-PCR

Target gene	Forward	Reverse
Nrf2	CGGTATGCAACAGGACATTG	AGGATGCTGCTGAAGGAATC
NQO1	TGATCGTACTGGCTCACTCA	GTCAGTTGAGGTTCTAAGAC
P-gp (ABCB1)	GCT CCT GAC TAT GCC AAA GC	TCT TCA CCT CCA GGC TCA GT
MRP-4 (ABCC4)	TGA TGA GCC GTA TGT TTT GC	CTT CGG AAC GGA CTT GAC AT
CYP2S1	ACCCCAACCACTTGTCCACACA	TGAGGGTCCTCGTATGTCCAAAG
CYP51A1	CTACAGTCGCCTGACAACAC	CCACTTTCTCCCAACTCTC
SLC7A11	GGTGGTGTGTTTGCTGTC	GCTGGTAGAGGAGTGTGC
GCLC	AAGCCATTCACTCCAGATTTTACC	ACAACAACTTCAACGCAAAGC
GCLM	ACTGACTTAGGAGCATAACTTACC	AAGAATATCTGCCTCAATGACACC
HO-1	CCAGCCATGCAGCACTATGT	AGCCCTACAGCAACTGTCGC
NFkB p65	ACT GTT CCC CCT CAT CTT CC	TGG TCC TGT GTA GCC ATT GA
β -actin	CTGGCCCGGACCTGACAGA	GCCGCAGTGCCATCTCTT

Table S5: This includes Forward and reverse primer sequences (5' -3') used in real time qRT-PCR