

**Table 4.9 Studies on coffee drinking and oxidative stress and antioxidant status in non-human mammals in vivo**

Species, strain (sex)	Tissue	End-points	Test	Description of exposure <sup>a</sup> and controls	Response <sup>b/</sup> significance	Comments	Reference
<i>Rat</i>							
Rat, Wistar (M)	Urine	DNA damage, lipid peroxidation	8-OHdG, F2-isoprostanes	3 groups ( <i>n</i> = 16 each), instant coffee (0.62%), instant coffee (1.36%), control; 90, 110, 130 days	Coffee vs control increased 8-OHdG [ <i>P</i> < 0.05] No change in isoprostanes	Coffee dose equivalent to 9 and 20 cups/day	Sakamoto et al. (2003)
Rat, Wistar (M)	Liver	DNA damage, lipid peroxidation, proteomics, mRNA	8-OHdG, F2-isoprostanes	4 groups ( <i>n</i> = 6 each), HFD + filtered decaf coffee; HFD + water, ND + filtered decaf coffee, ND + water; 3 months	Coffee HFD vs water HFD: decreased F2-isopr and 8-OHdG [both <i>P</i> < 0.05]	Rats with induced NAFLD (HFD for 3 months); coffee dose equivalent to 2 cups of filtered coffee/day	Salomone et al. (2014)
Rat, Sprague-Dawley (M)	Liver, plasma	Lipid peroxidation	TBARS	4 groups, unfiltered coffee ( <i>n</i> = 7), unfiltered coffee + CCl <sub>4</sub> ( <i>n</i> = 10), CCl <sub>4</sub> ( <i>n</i> = 7), control ( <i>n</i> = 7); 8 days	No change in TBARS with coffee alone. Coffee+CCl <sub>4</sub> vs control+CCl <sub>4</sub> : increased plasma [ <i>P</i> < 0.05] and liver [ <i>P</i> < 0.01] TBARS.	CCl <sub>4</sub> used to induce liver damage	Poyrazoglu et al. (2008)
Rat, Wistar (M)	Muscle (anterior tibialis)	Lipid peroxidation, protein oxidation, antioxidant enzymes	Carbonyls, TBARS, SOD and GPx activity	8 groups ( <i>n</i> = 8 each): coffee + exercise, decaf + exercise, caffeine + exercise, water + exercise, 4 other controls; 21 days	Caffeinated coffee+ exercise vs water + exercise: decreased carbonyls [ <i>P</i> < 0.05] and TBARS [ <i>P</i> < 0.05] No change with decaffeinated coffee or caffeine alone	Coffee dose equivalent to 4 cups (50 ml) coffee/day	Viana et al. (2012)
Rat, Wistar (M)	Liver, serum	Lipid peroxidation, antioxidants	tGSH, GSH/GSSG, FRAP, TBARS	5 groups ( <i>n</i> = 6 each): HFD + decaf coffee; HFD + coffee polyphenols; HFD + coffee melanoidins; HFD + water; standard diet + water; 1 month, after 2 months on HFD except control	HFD+Coffee vs HFD+water: serum HFD+decaf coffee TBARS –25% [ <i>P</i> < 0.05]	Coffee dose equivalent to 6 cups espresso/day; HFD to develop nonalcoholic steatohepatitis	Vitaglione et al. (2010)

					FRAP -15% [ $P < 0.05$ ] tGSH -20% [ $P < 0.05$ ] GSH/GSSG +60% [ $P < 0.05$ ] In liver tissue similar effects, no effects on GST activity, except for HFD+coffee -15% [ $P < 0.05$ ]		
Rat, Sprague-Dawley (M)	Plasma	Lipid peroxidation, antioxidants, antioxidant enzymes	TBARS, tGSH, SOD	4 groups ( $n = 6$ each), coffee, sucrose, coffee + sucrose, water; 12 weeks	Coffee vs water TBARS + 8% [ $P > 0.05$ ] SOD +10% [ $P > 0.05$ ] tGSH + 6% [ $P > 0.05$ ]		Morakinyo et al. (2013)
Rat, Sprague-Dawley (M)	Liver	Lipid peroxidation, antioxidants, antioxidant enzymes	PCR, TBARS, tGSH, SOD	4 groups ( $n = 8$ each): 100 or 300 mg/kg coffee + DMN, DMN only; control; 4 weeks	Coffee + DMN vs DMN only: reduced TBARS [ $P < 0.05$ ]; increased catalase [ $P < 0.01$ ], GSH [ $P < 0.05$ ] and SOD +70% [ $P < 0.01$ ] in liver	DMN induced liver fibrosis	Shin et al. (2010)
Rat, Wistar (M)	Liver	Antioxidant enzymes, antioxidant capacity	SOD, CAT, and GPx activity, ORAC	8 groups ( $n = 6$ each), single dose of filtered coffee (2 ml); sacrificed 1, 2, 3, and 4 hours after gavage, dose response 1 hour after gavage (0.5, 1.0, 1.5, 2.0 ml coffee) control: single dose of water (2 ml); sacrificed 1 hour after gavage	Coffee vs control water (1 hour) 2 ml dose, only at 1 hour significantly different GPx increased [ $P < 0.05$ ] SOD increased [ $P < 0.05$ ] CAT increased [ $P < 0.05$ ] No significant change: ORAC	Dose response enzymes: only 1.5–2.0ml significantly different (except for CAT)	Vicente et al. (2011)
Rat, SHR/Izm (spontaneously hypertensive rat) (M)	Thoracic aorta	NAD(P)H oxidase components Nox-2, p22 <sup>phox</sup> , p47 <sup>phox</sup>	PCR	2 groups ( $n = 6$ each), HHQ-free coffee, physiological saline; 8 weeks	HHQ-free coffee vs physiological saline NAD(P)Hox decreased [ $P < 0.05$ ]		Suzuki et al. (2006)

Mouse

Mouse, ICR (M)	Liver	DNA damage, 8-OHdG, genes for antioxidant enzymes	8-OHdG, TBARS	4 groups ( $n = 7-9$ each), normal diet + instant coffee, low vitamin diet + instant coffee, low vitamin diet + water, normal diet + water; 8 months	Coffee vs water in normal diet and low vitamin diet  No significant change in:  8-OHdG, SOD, TBARS, $\gamma$ GCS, GR1, Trx1, Trx2, TR1, TR2, TPx2, iNOS, CAT (except for decreased GPx1 expression [ $P < 0.05$ ])		Morii et al. (2009)
Mouse B6, transgenic EpRE luciferase (Cgene) (M)	Whole body, organs (liver, kidney, spleen, thymus, brain, muscle, adipose tissue, skin, heart)	EpRE activation	Imaging	2 groups ( $n = 6$ each): LPS + coffee (extract in corn oil, Equation 0.6 g coffee bean); control (LPS)	Coffee vs control Luminescence  Whole body increased [ $P < 0.05$ ]  Liver increased [ $P < 0.05$ ]  Thymus decreased [ $P < 0.05$ ]	Probably the dark roasted coffee was used	Paur et al. (2010)
Mouse, $nrf2^{-/-}$ , $nrf2^{+/+}$ C57BL/6 (M)	Liver, small and large intestine	Nrf2 transcription	PCR, immunoblot	6 groups ( $n = 3$ each), coffee 3%, coffee 6%, and control for both $nrf2^{-/-}$ and $nrf2^{+/+}$ ; 5 days	Coffee vs control  In $nrf2^{+/+}$ mouse: liver GST $\uparrow$ , NQO1 $\uparrow$ ;  Small intestine and colon NQO1 $\uparrow$ , GST $\uparrow$ and GCLC $\uparrow$		Higgins et al. (2008)
Mouse Swiss albino (M)	Liver	Sulphydryl content, GST activity	Cytosolic GST activity spectrophotometric with 1-chloro-2,4-dinitrobenzene; sulphydryls with modified Ellman method	3 groups ( $n = 5$ ), instant coffee (70 140, 280 mg/kg bw per day), decaffeinated instant coffee (70 140, 280 mg/kg bw per day), water; 10 days	Coffee vs water (control)  Caffeinated and decaf coffee increased sulphydryls, GST activity		Abraham & Singh (1999)

<sup>a</sup> unless otherwise specified, the term coffee is used to mean brewed, caffeinated coffee

<sup>b</sup> +, positive; -, negative; differences: exposed vs control

8-OHdG, 8-hydroxydeoxyguanosine; AKR, aldo-keto reductase; AOM, azoxymethane; ARE, antioxidant response element; CAT, catalase; CGA, chlorogenic acid; DMN, dimethylnitrosamine;  $\gamma$ -GCL,  $\gamma$ -glutamylcysteine ligase;  $\gamma$ -GCS,  $\gamma$ -glutamylcysteine synthetase; EpRE, electrophile response element; FRAP, ferric reducing antioxidant potential; GR1, glutathione reductase 1; GPx1, glutathione peroxidase 1; GST, glutathione-S-transferase; HHQ, hydroxyhydroquinone; HFD, high fat diet; iNOS, inducible nitric oxide synthase; LPS, lipopolysaccharide; NAFLD, nonalcoholic fatty liver disease; ND, normal diet; NQO1, NAD(P)H-quinone oxidoreductase; ORAC, oxygen radical absorbance capacity; Prx1, peroxiredoxin 1; TBARS, thiobarbituric acid-reactive substances, Trx, thioredoxin; TR, thioredoxin reductase; TPx, thioredoxin peroxidase

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