

## Coffee and Hormones

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Coffee has an impact on hormone metabolism.

Major polyphenolic components present in coffee were found to inhibit human catechol-O-methyltransferase (COMT)-mediated O-methylation of catechol estrogens. (Zhu, Wang et al. 2009)

### Women

A case-control study nested in the prospective Women's Health Study (WHS) found a relationship between coffee and SHBG in postmenopausal women with newly diagnosed type 2 diabetes. Caffeinated coffee was positively associated with SHBG but not with sex hormones. Multivariable-adjusted geometric mean levels of SHBG were 26.6 nmol/l among women consuming  $\geq 4$  cups/day of caffeinated coffee and 23.0 nmol/l among nondrinkers (P for trend = 0.01). In contrast, neither decaffeinated coffee nor tea was associated with SHBG or sex hormones. The multivariable-adjusted odds ratio (OR) of type 2 diabetes for women consuming  $\geq 4$  cups/day of caffeinated coffee compared with nondrinkers was 0.47 (95% CI 0.23-0.94; P for trend = 0.047). The association was largely attenuated after further adjusting for SHBG (OR 0.71 [95% CI 0.31-1.61]; P for trend = 0.47). In addition, carriers of rs6259 minor allele and noncarriers of rs6257 minor allele of SHBG gene consuming  $\geq 2$  cups/day of caffeinated coffee had lower risk of type 2 diabetes in directions corresponding to their associated SHBG. (Goto, Song et al. 2011)

A cross-sectional study found that caffeine may alter circulating levels of luteal estrogens and SHBG. The study examined 524 premenopausal and 713 postmenopausal women from the Nurses' Health Study (NHS) and NHSII. In premenopausal women, caffeine intake was inversely associated with luteal total and free estradiol, and positively associated with luteal progesterone levels (P-trend = .02, .01, .03, respectively). Coffee intake was significantly associated with lower luteal total and free estradiol levels, but not luteal progesterone levels (P-trend = .007, .004, .20, respectively). Among the postmenopausal women, there was a positive association between caffeine and coffee intake and SHBG levels (P-trend = .03 and .06, respectively). (Kotsopoulos, Eliassen et al. 2009)

Rancho Bernardo community-based study found a positive association of caffeine with estrone and its inverse association with bioavailable

testosterone in postmenopausal women. Caffeine intake was inversely associated with age and waist/hip ratio and positively associated with alcohol consumption. Significant inverse associations were noted between caffeine intake and bioavailable testosterone, which persisted after adjustment for age, waist/hip ratio, body mass index, alcohol intake, cigarette smoking, and physical activity ( $r = -0.10$ ,  $p = 0.02$ ). At high doses (equivalent to more than 2 cups of coffee or four cans of caffeinated soda daily), caffeine intake was positively associated with plasma estrone before and after adjustment for confounders ( $r = 0.26$ ,  $p = 0.05$ ). Sex hormone-binding globulin levels were positively associated with increasing caffeine intake (adjusted  $r = 0.09$ ,  $p = 0.03$ ). (Ferrini and Barrett-Connor 1996)

## 2/16 Ratio

A study examined the change in the ratio between the pre-operative visit and first follow-up visit three to six months post-operatively among 59 women with primary ER positive breast cancer tumors. The pre-operative ratio was not correlated with tumor characteristics, but was significantly higher in women who consumed three or more cups of coffee daily ( $p = 0.009$ ). The ratio increased between the two visits in 69.5% of the women. The factors associated with a significant increase in the ratio were concomitant tamoxifen and radiotherapy ( $p = 0.006$ ), increasing alcohol consumption ( $p = 0.006$ ), and a high coffee consumption ( $p = 0.03$ ). Breast cancer patients who started tamoxifen during radiotherapy and who had a moderate coffee and alcohol consumption demonstrated a significant improvement in their estrogen metabolite profile between the pre- and post-operative visits. (Klug, Bageman et al. 2006)

The strongest factors predicting discordance between the urinary and plasma 2OHE1/16alphaOHE1 ratios among non-OC users were a baseline urinary 2OHE1/16alphaOHE1 ratio in the three upper quartiles ( $p < 0.001$ ), the menstrual cycle phase ( $p = 0.001$ ), and the number of cups of coffee consumed per day ( $p = 0.006$ ). (Bradlow, Jernstrom et al. 2006)

## Cancer

A recent meta-analysis found that coffee consumption may reduce the total cancer incidence and it also has an inverse association with some type of cancers. Compared with individuals who did not or seldom drink coffee per day, the pooled RR of cancer was 0.87 (95% CI, 0.82-0.92) for regular coffee drinkers, 0.89 (0.84-0.93) for low to moderate coffee drinkers, and 0.82 (0.74-0.89) for high drinkers. Overall, an increase in consumption of 1 cup of coffee per day was associated with a 3% reduced risk of cancers (RR, 0.97; 95% CI, 0.96-0.98). In subgroup analyses, we noted that, coffee drinking was associated with a reduced risk of bladder, breast, buccal and

pharyngeal, colorectal, endometrial, esophageal, hepatocellular, leukemic, pancreatic, and prostate cancers. (Yu, Bao et al. 2011)

### Breast Cancer

A recent study found that high daily intake of coffee was associated with a statistically significant decrease in ER-negative breast cancer among postmenopausal women. In the Swedish study, coffee consumption was associated with a modest decrease in overall breast cancer risk in the age-adjusted model (OR > 5 cups/day compared to OR ≤ 1 cup/day: 0.80, 95% CI: 0.64, 0.99, P trend = 0.028). In the stratified case-control analyses, a significant reduction in the risk of ER-negative breast cancer was observed in heavy coffee drinkers (OR > 5 cups/day compared to OR ≤ 1 cup/day : 0.43, 95% CI: 0.25, 0.72, P trend = 0.0003) in a multivariate-adjusted model. The breast cancer risk reduction associated with higher coffee consumption was significantly higher for ER-negative compared to ER-positive tumours (P heterogeneity (age-adjusted) = 0.004). CONCLUSIONS: A high daily intake of coffee was found to be associated with a statistically significant decrease in ER-negative breast cancer among postmenopausal women. (Li, Seibold et al. 2011)

Trigonelline (Trig), a niacin-related compound, is a natural constituent of coffee accounting for approximately 1% dry matter in roasted beans. Trig stimulated MCF-7 cell proliferation in a dose-responsive manner and significantly enhanced cell growth at concentrations as low as 100 pmol/L. (Allred, Yackley et al. 2009)

### Prostate Cancer

A prospective analysis of 47 911 men in the Health Professionals Follow-up observed a strong inverse association between coffee consumption and risk of lethal prostate cancer. The association appears to be related to non-caffeine components of coffee. Men who consumed six or more cups per day had a lower adjusted relative risk for overall prostate cancer compared with nondrinkers (RR = 0.82, 95% confidence interval [CI] = 0.68 to 0.98, P(trend) = .10). The association was stronger for lethal prostate cancer (consumers of more than six cups of coffee per day: RR = 0.40, 95% CI = 0.22 to 0.75, P(trend) = .03). Coffee consumption was not associated with the risk of nonadvanced or low-grade cancers and was only weakly inversely associated with high-grade cancer. The inverse association with lethal cancer was similar for regular and decaffeinated coffee (each one cup per day increment: RR = 0.94, 95% CI = 0.88 to 1.01, P = .08 for regular coffee and RR = 0.91, 95% CI = 0.83 to 1.00, P = .05 for decaffeinated coffee). The age-adjusted incidence rates for men who had the highest (≥6 cups per day) and lowest (no coffee) coffee consumption were 425 and 519 total prostate cancers, respectively, per 100 000 person-years and 34 and 79

lethal prostate cancers, respectively, per 100 000 person-years. (Wilson, Kasperzyk et al. 2011)

### **Insulin Resistance**

The combination of coffee consumption and HRT could lower insulin resistance in postmenopausal women. In overweight women, greater insulin sensitivity is associated with intake of espresso coffee and not with HRT; in normal weight women, only HRT is associated with lower insulin resistance. (Catalano, Trovato et al. 2008)

### **Diabetes**

In a case-controlled human study, those who drank the most coffee cut their risks of diabetes by 67% when compared to those that did not drink coffee. Levels of coffee consumption were positively related to levels of current smoking and inversely related to body mass index, waist circumference, female gender, and hypertension. Compared to those who did not drink coffee, participants who drank 12 or more cups of coffee daily had 67% less risk of developing diabetes during the follow-up (hazard ratio: 0.33, 95% confidence interval: 0.13, 0.81). (Zhang, Lee et al. 2011)

### **Parkinson's disease**

One study found that caffeine reduces the risk of Parkinson's disease but that this hypothetical beneficial effect may be prevented by use of estrogen replacement therapy. After adjustment for age, smoking, and alcohol intake, coffee consumption was inversely associated with Parkinson's disease mortality in men ( $p(\text{trend}) = 0.01$ ) but not in women ( $p = 0.6$ ). In women, this association was dependent on postmenopausal estrogen use; the relative risk for women drinking 4 or more cups (600 ml) of coffee per day compared with nondrinkers was 0.47 (95% confidence interval: 0.27, 0.80;  $p = 0.006$ ) among never users and 1.31 (95% confidence interval: 0.75, 2.30;  $p = 0.34$ ) among users. (Ascherio, Weisskopf et al. 2004)

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