

## Health status is affected, and Phase I/II biotransformation activity altered in young women using oral contraceptives containing Drospirenone/Ethinyl Estradiol

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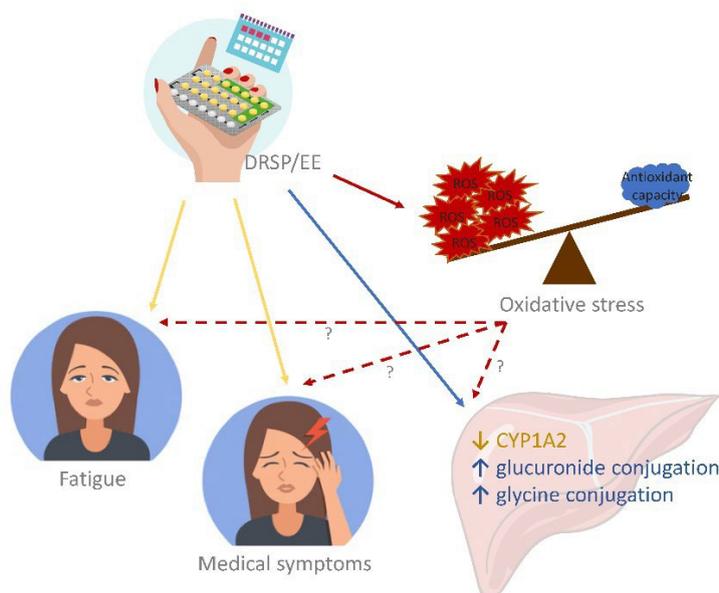


Figure 1. Graphic summary. Health status is affected, and phase I/II biotransformation activity altered in young women using oral contraceptives containing drospirenone/ethinyl estradiol. These effects may be mediated by oxidative stress.

Combined oral contraceptive (COC) use has been associated with various adverse effects. Formulations containing drospirenone (DRSP) and ethinyl estradiol (EE) are generally regarded as milder COCs. Whether long term use of these pills indeed has a low health risk remains questionable. COC use may affect the biotransformation balance by increasing the toxic load or by interfering with the pharmacokinetics of other drugs. This may negatively impact overall health via the production of toxic biotransformation metabolites and induction of oxidative stress. Although individual enzymes involved in biotransformation are known to be regulated by COCs, the effect of COC use on the overall liver biotransformation efficiency has not been reported. Here, we evaluated the general subjective health status and overall liver biotransformation efficiency of healthy young women who were either long term chronic users of COCs containing DRSP/EE, or who were not using any hormonal products. COC users suffered from moderate to severe fatigue and reported more health-related symptoms. Furthermore, phase I (CYP1A2) activity was reduced whereas phase II conjugation reactions (glucuronide conjugation and glycine conjugation) were increased in COC users. Finally, serum peroxide levels were markedly elevated and antioxidant capacity of plasma was reduced in COC users. COCs containing DRSP/EE may, therefore, adversely affect health status and disturb the balance between phase I and II biotransformation reactions. These effects may be mediated by oxidative stress.

**Keywords:** biotransformation, oral contraceptives, fatigue, health status, oxidative stress