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DETERMINATION OF URINARY LIGNANS AND PHYTOESTROGEN METABOLITES, POTENTIAL ANTIESTROGENS AND ANTICARCINOGENS, IN URINE OF WOMEN ON VARIOUS HABITUAL DIETS. H. Adlercreutz, T. Fotsis, C. Bannwart, T. Mäkelä, K. Wähälä, G. Brunow and T. Hase. Departments of Clinical Chemistry and Chemistry, University of Helsinki, Helsinki, Finland.

The purpose of this investigation was to determine in urine of women on various habitual diets the recently detected diphenolic lignans and isoflavonoid phytoestrogens and their metabolites including the lignans enterolactone (Enl) and enterodiol (End) and the phytoestrogens daidzein (Da), equol (Eq) and O-desmethylangolensin (O-DeA). Some of these compounds have interesting properties e.g. antiestrogenic, anti-tumor promoting or aromatase inhibiting effects. The lignan excretion has been shown to correlate with dietary fiber intake, especially grain intake, and is low in breast cancer patients. The method used is based on ion exchange chromatography and isotope dilution mass spectrometry (selected ion monitoring). For this purpose deuterium-labeled Enl, End ,Da, Eq and O-DeA were synthesized. In women consuming habitually a vegan diet containing no animal products, the excretion of these diphenols varies in preliminary experiments (5 subjects) between 40,000 and more than 120,000 nmol/24 h. In young Finnish lactovegetarian women (n = 12) the mean urinary excretion of Enl, End, Da, Eq and O-DeA is about 4900, 540,1300, 70 and 120 nmol/24 h, respectively and in young Finnish omnivoric women (n = 12) the mean ewxcretion is about 2900, 300, 300, 100 and 25 nmol/24 h, respectively. Thus both the lignan and phytoestrogen excretion was considerably higher in women on a vegan or lactovegetarian diet than in omnivoric women. It is suggested that these compounds may exert a protective effect with regard to breast cancer because of their biological activities and because vegetarian women have low incidence of breast cancer.

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STEROID DYNAMICS IN THE NORMAL AND PATHOLOGICAL MAMMARY GLAND.
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As an approach to the study of the origin of estrogens in breast cancer tissue, the concentration of estrogens and their androgen precursors, as well as aromatase and 17β-dehydrogenase activities in normal glandular (GL) and cancerous (CA) breast tissue were determined and correlations with plasma levels and/or receptor status were studied. In both normal GL and CA breast tissue, steroid concentrations were significantly higher than plasma conc., except for dehydroepiandrosterone sulphate (DHEAS), estrone sulphate (E_1S) and testosterone (T). Androgen conc. were lower, but estrogen conc. were higher in CA than in GL breast tissue. Estradiol (E_2) conc. was positively correlated with the E_2R conc., mean E_2 conc. corresponding to an estimated E_2R occupancy of about 25%. Aromatase and 17β-hydroxysteroid dehydrogenase (E_2DH) ($E_2 \rightarrow E_1$) activities were observed in all breast CA and GL tissues aromatase accounting probably only for a small fraction of tissue estrogens. E_2DH, but not aromatase activity, was significantly higher in E_2R+ than in E_2R- tissues and was negatively correlated with tissue dehydroepiandrosterone (DHEA) and DHEAS conc.; the latter two steroids are non competitive inhibitors of E_2DH which inactivates E_2 to E_1. Conclusion : in both normal and carcinomatous breast tissue, conc. of E_1 and E_2 are significantly higher than in plasma, suggesting either uptake or local synthesis. As to the latter, aromatase activity accounts probably only for a minor fraction of the tissue estrogens. Breast CA tissue has higher aromatase and E_2DH activity than normal glandular tissue, E_2 conc. and E_2DH activity being higher in E_2R+ hormone sensitive, tumors than in E_2R- tumors. Tissue conc. of DHEA(S) which inhibitis oxidative inactivation of E_2, is negatively correlated with E_2DH activity and may have an important modulating role in intratissular estrogen metabolism.