PB-31

Sorption of Selected Estrogenic Compounds into Synthetic Membrane Vesicles

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Several *in vitro* methods, such as the receptor binding assay system and the recombined yeast assay system, have been developed to detect and screen endocrine disrupting effects of numerous numbers of chemical compounds. Most of these systems, however, lack the consideration of the penetration of chemical compounds across the plasma (or nuclear) membrane, which is the first and could be the rate limiting step in the sequential hormonal action. Additionally, translocation or sorption of chemical compounds from bulk phase (aqueous or gaseous phase) to biological phase is one of the most important steps for the biodegradation of these compounds. Therefore, the tanslocation of endocrine disruptors through biological membrane was investigated in this study.

Conventionally, the bioconcentration factor measurement has been used to directly evaluate bioaccumulation or bioavailablity of chemical compounds while the octanol-water partitioning system has been used as the simplified model biological phase-water partitioning system. However, the former system has limitations in cost, time and reproducibility whereas the latter system has limitations in simplification due to the difference between the real and the model biological phase (i.e., 1-octanol). Intermediate systems such as the micelle-water and the membrane vesicle (liposome)-water system have recently become popular. Synthetic membrane vesicles were manufactured from phospholipids, the main component of biological membrane, and used as a model biological phase in this study.

Total of nine compounds were selected as model estrogenic compounds, which included four estrogens (i.e., 17β -estradiol, estrone, estriol, and 17α -ethynylestradiol) and five estrogenic compounds (i.e., *p*-nonylphenol, *p-tert*-octylphenol, bisphenol-A, dibutylphtalate, and butylbenzylphthalate). Palmitoyl-oleoyl phosphatidylcholine (POPC), dipalmitoyl phosphatidylcholine (DPPC), and the mixture of DPPC and cholesterol (60:40 wt%) were used to prepare liposomes. The sorption coefficient into liposomes (K_{lipw} value) was determined using the procedure called "equilibrium dialysis" technique.

The log K_{lipw} values obtained in this study did not showed strong but weak or moderate linear correlation with the logarithm of the octanol-water partitioning coefficients (log K_{ow} values) of each selected estrogenic compound. These results suggest the relatively reasonable prediction of bioavailability using the linear free energy relationship (LFER) and/or quantitative activity-structure relationship (QSAR) from the log K_{ow} value. However, some of the selected compounds, especially bisphenol-A, were far off the regression line. Bioavailability or the actual uptake of bisphenol-A could be underestimated if K_{ow} values are solely used for the prediction in LFER or QSAR. In addition, the K_{lipw} values were higher for the liposomes prepared from POPC followed by DPPC and the mixture of DPPC/cholesterol. The looser conformation of the lipid bilayer is suggested as the reason for the higher penetration of estrogenic compounds across the membrane prepared from POPC compared with DPPC. Further investigation is necessary to determine K_{lipw} values for larger number of compounds with a wide variety of chemical structure and to examine the effects of lipid components to prepare liposomes.