

**SECOND DERIVATIVE SPECTROPHOTOMETRIC
DETERMINATION OF THE PARTITION COEFFICIENTS OF
NEWLY-SYNTHEZED PHENOTHIAZINES BETWEEN
THE PHOSPHATIDYLCHOLINE PHASE AND WATER**

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Chlorpromazine and other phenothiazines are clinically useful as tranquilizers [1]. Drug-lipid bilayer interactions include processes such as drug adsorption, distribution and accumulation in cell membranes and inside cells, and thus are important for their therapeutic or toxic effects [2]. The partition coefficients (K_p) between PC unilamellar vesicles of size 100 nm and a buffer (pH = 7.4) for newly-synthesized phenothiazines were determined using the second derivatives of ultraviolet absorption spectra. The absorption spectra of all the investigated phenothiazine derivatives in the presence of PC vesicles showed a bathochromic shift, induced by an increase in the concentration in the vesicles. The relatively high background signal appearing in these spectra, derived from light scattering caused by liposome suspension was entirely eliminated in the second derivative absorption spectra [3]. After the elimination procedure, all the second derivative of phenothiazine spectra clearly showed two isosbestic points, indicating that these compounds exist in two distinct states - free and bound to the lipid vesicles [4]. The derivative intensity change (ΔD) of each compound was measured at λ_{max} for each absorption spectrum, and the K_p values were calculated from the relationship between ΔD and the PC concentration. The K_p values for all the phenothiazine derivatives are around of 10^5 and increased about 1.7-fold when the alkyl phenothiazine chain was lengthened by one $-CH_2$ group. Substituting $-CF_3$ for $-H$ at position 2 of the phenothiazine ring results in an about 3.5-fold increase in the K_p values.

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