MOLECULAR ARCHITECTURE OF PHOSPHATIDYLCHOLINE SMALL UNILAMELLAR VESICLES (PC SUV'S)

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Vesicular drug delivery systems have traditionally employed phospholipids, however synthetic amphiphiles offer a valuable alternative. The synthesis of vesicle-forming amphiphiles, with predetermined aggregation properties and surface characteristics will lead to vesicles with improved physiochemical and biological stability. A computer program VESICA has been developed which will aid the design of novel vesicle-forming amphiphiles, by allowing prediction of the vesicular properties of their aggregates prior to synthesis. This program has been used to investigate proposed model structures of dipalmitoylphosphatidylcholine (DPPC) SUV's (Lawrence et al 1990) and the results obtained have validated the modelling approach of Cornell et al (1980). Following the same procedures we have now used the experimental values for the hydrated vesicle radii (Cornell et al 1982) and bilayer phosphate-phosphate separations (Lewis and Engelman 1983) to compute the internal architectures of other SUV's in the series (Table 1).

LIPID	Ro*	Rop	Rho	Rpi	Ri	Rhi	Rint	no	ni	do	di
DLPC (C12)	116.0	112.4	108.8	81.90	77.45	86.35	96.21	2022	1274	12.67	9.78
DMPC (C14	101.8	98.20	94.60	64.20	59.75	68.65	79.56	1529	805	15.0	10.94
DSPC (C18)	109.0	105.4	101.8	64.90	60.45	69.35	82.49	1771	822	19.31	13.14

Table 1: SUV parameters R: radius (Å), o: outer, i: inner, p: phosphate group, h: hydration, n: number of lipids, d: monolayer thickness, int: inner and outer monolayer interface. *Cornell et al (1982).

For each SUV the calculated thickness of the hydrocarbon region (do + di, see Table 2) is in close agreement with the observed values (Lewis and Engelman 1983).

	DLPC	DMPC	DPPC	DSPC
l	22.5	26.0	29.7	32.5
l^a	18.8	22.3	26.0	28.8
l^b	19.5	23.0	26.0	29.5

Table 2: Hydrocarbon bilayer thickness (l = do + di, Å) includes the glycerol region; subtracting 3.7Å removes this region (l^a) to compare with the data (l^b) of (Lewis and Engelman 1983)

The lengths of the inner and outer alkyl chains in the SUV's are respectively 60% and 80% of the extended chain length, the former providing a limit to the minimal size of the vesicle. From previous work (Lawrence et al 1990) we have noted that the inner head group conformation would also limit the minimal size of the vesicle; we therefore believe that the lower vesicle size limit is governed not simply by chain packing in the hydrocarbon region (Israelachvili et al 1976) or by the inner polar head group interactions (Cornell et al 1980), but a combination of both of these factors.

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