Structure of ganglioside/cholesterol mixture

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Introduction

Polysialogangliosides, glycosphingolipids containing more than one sialic acid residue, are abundant in neuronal synapse membranes and are speculated to be involved in various membrane-mediated physiological phenomena. Due to their strong amphiphilic properties and bulky headgroups, polysialogangliosides form small micelles in an aqueous solution. However, compared with that of phospholipid mixtures, structural information on the association of polysialogangliosides with other membrane lipid components is still limited and ambiguous. In this present study, the characteristics of the structures of ganglioside (GD_{1a})/cholesterol mixed micelles with various molar ratios were investigated by using SR-SAXS. According to the shell-modeling method [1], we assumed the structures of the micelles as a triple-shell structure composed of the three regions, *i.e.*, a core, an inner-shell and an outer-shell, because incorporated cholesterol within the hydrophobic region of the micelles is predicted to be anchored with its hydroxyl group at the hydrophilic-hydrophobic interface.

Materials and Methods

Disialoganglioside (G_{D1a}) and cholesterol were purchased from SIGMA Chemical and used without further purification. The final concentration of ganglioside for all samples was 0.5 % w/v. The molar ratios of [ganglioside]/[cholesterol] for each sample was 1/0, 1/0.05, 1/0.1, 1/0.2, 1/0.4, 1/0.7 and 1/1. SAXS measurements were carried out by a SAXS spectrometer installed at the BL-10C beam line of PF at KEK. The X-ray wave length, the sample-to-detector distance, and the exposure time were 1.49 Å, 198 cm, and 480 seconds respectively. The obtained scattering data were analyzed based on the same procedures presented previously [1].

Results and Discussions

Fig. 1 summarizes the cholesterol dependence of the structure parameters of the mixed micelle. These results indicate that most of the steroid rings of cholesterol molecules are located in the inner-shell region of the micelle. Therefore, the decrease of the outer-shell contrast would be explained by the increase of the amount of water molecules within the outer-shell region, that is, the incorporation of cholesterol molecules within the inner-shell region tends to give a more distance between the ganglioside sugar heads in the outer-shell region. Alternatively, cholesterol molecules have a role as a kind of spacer molecules at the hydrophilic-hydrophobic interface of the mixed micelles.

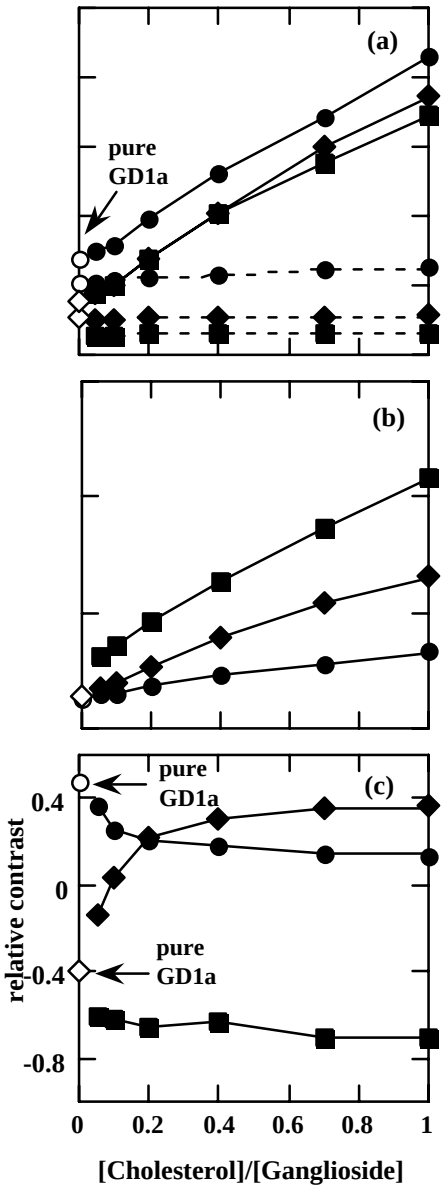

Fig. 1. Structural parameters from the model fitting. (a) axis length; (b) axial ratio; (c) contrast. Circles (●) for outer-shell; diamonds (◆) for inner-shell; square (■) for core. In (a), dashed lines correspond to the short-axis (radius), and full lines for the long-axis.

References

[1] M. Hirai,et al., Biophys. J., 70, 1761 (1996); J. Phys. Chem., 100, 11675 (1996); Biophys. J., 74, 3010 (1998); J. Phys. Chem. B, 103, 10136 (1999).

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