Studies on the Occurrence of Cholesterol in Water-Containing Liquid-Crystalline Form

III. Formation of Cholesterol-containing Mesomorphous Phases by the Interaction of Sodium Caprylate Solutions with Solid Cholesterol Crystals

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Whereas salts of fatty acids from nonylic acid upwards are able to cause solid crystalline cholesterol to change into the mesomorphous state already when their concentrations exceed their limiting association concentrations (LAC) [1], the same process is not effected by the sodium salt of the next lower fatty acid, caprylic acid, before the concentration of this salt exceeds the critical micelle concentration (CMC). The formation of the mesophase takes place only very slowly in caprylate solutions immediately above the CMC at room temperature. High concentrations of caprylate are necessary to cause the process to proceed rapidly at this temperature. An increase in temperature, however, accelerates the process also at low caprylate concentrations, but the mesomorphous cholesterol-containing phase is not produced by caprylate solutions even at high temperatures unless the concentration of the latter exceeds the CMC.

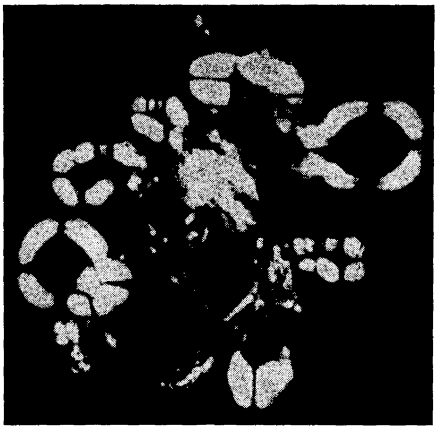

Fig. 1b. Crossed Nicols. 200 ×.

The mesomorphous substance that is formed in concentrated caprylate solutions down to that containing about 2.4 moles of sodium caprylate in 1 000 g of water consists of strongly doubly-refracting matter which rapidly coalesces to more or less spherical globules (Figs. 1a and 1b). In solutions from about 2.4 M down to the CMC, the mesomorphous matter forms long, narrow, often curved spool-shaped doubly-refracting structures (Fig. 2).

Fig. 1a. Ordinary light. 200 ×.

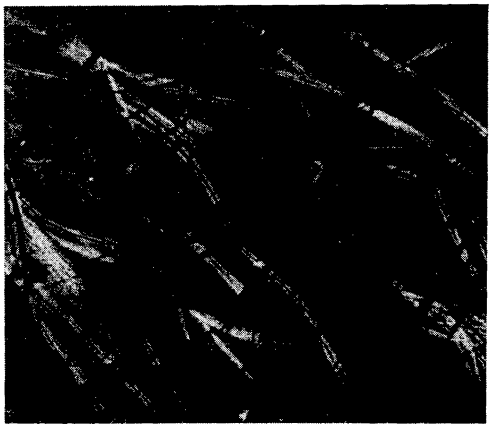

Fig. 2. Crossed Nicols. 200 ×.

Fig. 3. Crossed Nicols. 200 ×.

The appearance of the spherical particles does not change when the temperature rises, but the spool-shaped mesomorphous substance does undergo a change. When the latter substance is warmed in its mother liquor on a heated stage between 34 and 38°C, it changes into a weakly doubly-refracting semiliquid mass (Fig. 3). The same change occurs when the mesomorphous substances is first freed of its mother liquor. The temperature where the change takes place varies for the mesomorphous substances that have separated from solutions containing different caprylate concentrations: it increases from about 34°C for the substance that is formed in solutions at the highest concentration studied to about 38°C for the substance formed near the CMC of sodium caprylate.

Thus cholesterol forms at least two water-containing mesomorphous phases under the influence of caprylate solutions at 20°C. The two phases are formed at different caprylate concentrations and they differ in appearance and temperature stability. Whether the mesomorphous phase that is produced when the spool-shaped liquid crystals are warmed to 34—38°C is identical with the phase that separates from highly concentrated caprylate solutions or represents a third mesomorphous phase has not yet been investigated.

These studies confirm that the chain length of the parent fatty acid is of decisive importance in determining the properties of the water-containing cholesterol mesophases and the conditions under which these phases are produced.

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IV. The Solubility of Cholesterol in Sodium Caprylate Solutions at 20°C

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It has been stated in the literature that cholesterol is almost insoluble in water [1] and we have been unable to find any reliable solubility data for this sterol. It is, however, known that the solubility of cholesterol in water increases appreciably in the presence of association colloids of the bile salt type owing to micellar solubilisation. Thus, Bashour and Baumann have reported rather high solubilities of cholesterol in solutions of different bile acid salts [2]. Also Ekwall has found cholesterol to dissolve in appreciable amounts in sodium cholate solutions. However, the values of the latter author were much lower than the values given by the former [3]. Values of the solubility of cholesterol in solutions of fatty acid salts or other association colloids of the paraffin-chain type seem not to have been reported.

We have found that cholesterol in the finely divided form in which it exists after its solubilisation in association colloid micelles undergoes rapid oxidation at temperatures over 40°C. This confirms the observation of Bergström that cholesterol in the colloidal state (in the presence of sodium stearate) is oxidised at high tem-