Chapter 1. An introduction to Bile Acids

This introductory chapter is a review on the literature of bile acids. Attempts have been made to encompass chemistry, physiology and pathophysiology of bile acids.

Bile acids (Figure 1) conjugated with glycine and taurine participate in a number of important physiological processes such as in the emulsification of neutral fats and the solubilization of cholesterol. Due to their facial amphiphilicity, bile salts aggregate to form micelles, and in some cases gels depending on the number and position of the hydroxyl group, concentration, pH, ionic strength etc. Bile salts together with lipids/fats/cholesterol form mixed micelles in the intestine to enable fat digestion and absorption through the intestinal wall.

Chemical structures of bile acids differ in three respects, (i) the side-chain structure, (ii) the stereochemistry of A/B ring fusion and (iii) the distribution of the number, position and stereochemistry of the hydroxyl groups in the steroid nucleus. It is interesting to learn that the bile acid structure represents a pattern of progressive molecular development along the line of vertebrate evolution.

Avicholic acid, a major constituent of the bile of several avian species, was synthesized in 8 steps from readily available chenodeoxycholic acid in 9% overall yield using remote functionalization strategy in a key step Chlorination at C-17 was performed using the substrate 1 under the radical relay condition The regio-selective introduction of the $\Delta^{16}$ double bond was achieved by refluxing the 17-chloro-steroid in pyridine Hydroboration-oxidation of the $\Delta^{16}$-steroid (BH$_3$ THF, followed by H$_2$O$_2$-NaOH) yielded the side-chain reduced product, which was oxidized in one step to avicholic lactone by TEMPO-mediated N-chlorosuccinimide oxidation in a biphasic mixture using a phase transfer catalyst The cleavage of the lactone (5% KOH/MeOH), acidification and quick extraction yielded the desired product, avicholic acid Micelle formation and equilibrium cholesterol solubilization properties were studied with avicholate in aqueous solution

Chapter 3. A Molecular Hydrogel from a Tripodal Bile Acid Derivative

Tripodal cholamide 2 is a supergelator of aqueous fluids A variety of physical techniques including cryo-TEM, CD, steady-state fluorescence, time-resolved fluorescence and dynamic light scattering were employed in order to understand the structure and dynamics of the gel. The cryo-TEM showed the presence of entangled nanofibers in the gel (Figure 2) Fluorescence studies with hydrophobic probes (pyrene and ANS) indicated the
presence of highly hydrophobic pockets in the gel-network. Both the fluorescent probes reported a step-wise aggregation process leading to gelation in a predominantly aqueous medium. Since the approach of two pyrene molecules is restricted in gels due to an increase in the viscosity, the rate of the excimer formation is reduced. Fluorescence lifetime measurements with pyrene reveal ineffective quenching of pyrene fluorescence by oxygen, possibly caused by slower Brownian diffusion due to the enhanced viscosity in the gel phase. A thermochromic gel [color change from sol (yellow) to gel (green)] was obtained when the gel was doped with a pH sensitive dye bromophenol blue. This was attributed to the preferential binding of one of the forms of the pH sensitive dye to the gel network.

Chapter 4. Ultrafast Dynamics in Gels

Rotational dynamics of polarity sensitive fluorescent dyes (ANS and DPH) in a non-polymeric aqueous gel derived from tripodal cholamide 2 was studied using ultrafast time-resolved fluorescence technique. Results were compared with that of naturally occurring di- and trihydroxy bile salts. ANS in the gel showed two rotational correlation time (τφ) components, 13 2 ns (bound to the hydrophobic region of the gel) and 1 0 ns (free aqueous ANS), where as DPH showed only one.

Figure 2. Cryo-TEM image of the gel derived from 2

Figure 3. Typical time-resolved fluorescence anisotropy decay profiles of ANS obtained in a double-kinetics experiment during the gelation of 2 at 25 °C.
component (4.8 ns) In the sol state, faster rotational motion was observed, both for ANS and DPH. The study of the gelation kinetics by monitoring the ultrafast dynamics of ANS revealed a progressive increase in the aggregate size, and the microviscosity of the aqueous pool encompassed by the self-assembled fibrilar network (SAFIN), during the gelation (Figure 3). The time-course of the dynamics of free aqueous ANS (characterized by a short rotational correlation time, $\phi_R$) seemed to be interesting. After 4 min of the mixing, $\phi_R$ was $\approx$ 0.2 ns, which is very close to the value ($ca$ 0.1 ns) obtained for ANS in an aqueous solution of low viscosity ($\approx$1 cP). As the gelation progresses, $\phi_R$ becomes progressively longer (from 0.2 ns to 1.0 ns) which is an indicative of incremental change in the microviscosity of the aqueous phase suggesting micro-structural changes caused by the rigidification of the aqueous pool encompassed by the networked nanofibers.

Chapter 5. Application of Hydrogels as Templates for the Synthesis of Inorganic Nanotubes

The tripodal cholamide (2)-based hydrogel composed of nanofibers has been used as a template to synthesize inorganic nanotubes, such as $SiO_2$, $TiO_2$, $ZrO_2$, $WO_3$ and $ZnO$, $ZnSO_4$, $BaSO_4$ (Figure 4). An advantage of the use of the hydrogel is that metal alkoxides are not required for the synthesis of the oxide nanotubes. The nanotubes have been characterized by X-ray diffraction and transmission electron microscopy.

Figure 4. TEM images of the titania ($TiO_2$) nanotubes (a) as-synthesized, (b)–(d) after calcination. Inset. SAED pattern taken on a single nanotube.