

# This Week's Citation Classic

**Hofmann A F & Small D M.** Detergent properties of bile salts: correlation with physiological function. *Annu. Rev. Med.* **18**:333-76, 1967. [Gastroenterol. Unit, Mayo Clinic and Foundation, Rochester, MN; and Dept. Med., Boston Univ. Sch. Med., Boston, MA]

This interpretative review summarized the behavior of amphipathic molecules in water and then considered the physical chemistry of bile acid solutions and the behavior of physiologically relevant additives. It discussed the composition of bile, gallstone formation, and fat digestion in physico chemical terms. [The SC® indicates that this paper has been cited over 280 times since 1967.]

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June 24, 1980

"This review was a labor of love written by Donald Small, who is now director of the division of biophysics in the department of medicine at Boston University, and myself, when I was a member of the department of medicine of the Mayo Clinic.

"The review had two aims. The first was to describe the detergent properties of bile acids using the language and principles of colloid chemistry. The second was to correlate the distinctive detergent properties with their physiological role of lipid transport, in particular, the transport of cholesterol in bile and of triglyceride digestion products in the intestinal lumen. The review has been popular, I think, because it was among the first discussions of micelle formation in the medical literature and because it attempted to relate human physiology and disease to colloid chemistry.

"Both Small and I had been trained in internal medicine. I had spent three years in the department of physiological chemistry at the University of Lund, Sweden, working with Bengt Borgstrom. Here I had shown that bile acids readily solubilize fatty acids and monoglycerides to form mixed micelles and then had isolated a micellar phase by ultracentrifugation of intestinal content obtained during the digestion of a meal in

man. Small had worked at the Institut Pasteur in Paris with the great biophysicist, Dervichian, defining the phase equilibria of simulated bile, as well as the surface properties of bile acids.

"There are some novel ideas in the review. We reversed the McBain phase diagram for the soapwater system, putting the aqueous side on the left; we drew structures of molecular organization of the mesomorphic phases; and we proposed the term 'critical micellar temperature' to replace the older term 'Krafft point.' We used the term 'swelling amphipath' and stressed the importance of transition temperatures for liquid crystalline states.

"Since then I have continued as a clinical investigator, studying the metabolism of bile acids in health and disease; more recently, I have worked on the medical dissolution of cholesterol gallstones with certain bile acids. Small has focused on the structure and function of lipoproteins and has become a world authority on cholesterol metabolism. Interest in bile acids has expanded enormously (even though they are not yet an ASCA® topic). Small and I have each received the Distinguished Achievement Award of the American Gastroenterological Association, and we shared (together with Jan Sjövall) the Eppinger Prize.

"We like to think that our review helped to make certain biological processes comprehensible to colloid chemists and showed that understanding of simple concepts of colloid chemistry aids in understanding the pathogenesis of digestive disease. The physical chemistry of bile acids as it relates to bile and gallstone formation has subsequently been characterized in greater detail,<sup>1</sup> and micelles and liquid crystalline phases have moved from the detergent literature into the exploding areas of membranology.<sup>2,3</sup> Finally, research on the biological effects of bile acids has also expanded greatly; bile acid researchers gather biennially for an international conference sponsored by the Falk Foundation."<sup>4</sup>

1. **Carey M C & Small D M.** The physical chemistry of cholesterol solubility in bile. Relationship to gallstone formation and dissolution in man. *J. Clin. Invest.* **61**:998-1026, 1978.
2. **Helienius A & Simons K.** Solubilization of membranes by detergents. *Biochem. Biophys. Acta* **415**:29-79, 1975.
3. **Mazer N A, Carey M C & Benedek G B.** Quasielastic light scattering studies of aqueous bilayer lipid systems. Mixed micelle formation in bile salt/lecithin solutions. *Biochemistry* **19**:601-15, 1980.
4. **Paumgartner G, Stiehl A & Gerok W,** eds. *Biological effects of bile acids. Proceedings of the 26th Falk Symposium, 5th Bile Acid Meeting, Freiburg im Breisgau, West Germany, June, 1978.* Lancaster, UK: MTP Press, 1979. 318 p.271