

Chemical Reaction



The New Polymer Frontier

UPM technology has enormous implications for the development of advanced treatment cosmetics, with greatly enhanced delivery of active ingredients. **BY STEVE HERMAN**

"All animals are equal, but some animals are more equal than others."

—George Orwell, "Animal Farm"

LIKE THE DENIZENS in "Animal Farm," all meetings are equal, but some meetings are more equal than others. The September 5, 2001, NYSCC meeting was more equal than most, due to the presence of a dynamic speaker, Dr. Kathryn Uhrich of Rutgers University, who presented a technically exciting topic. Dr. Uhrich introduced her work on unimolecular polymeric micelles (UPM), a technology of great potential that has yet to be exploited by the personal-care industry. The phrase "cutting edge" is greatly overused, but here it is entirely appropriate. UPM expands our understanding of possible micelle structures, the delivery of actives, and protection of unstable materials.

This field can be considered the new frontier of polymer applications. This is reflected in

the many terms recently coined to denote variations of the new structures: dendrimers (and their monomeric units, dendrons), lock and key micelles, Starburst polymers, micellane, and amphiphilic star-like macromolecules (ASMs). New names seem to arise as quickly as new structures and applications are identified. Just as conventional emulsifiers can be anionic, cationic, or nonionic, the new polymers are able to assume many guises.

Micelles are well known to all cosmetic chemists, being the essential structural feature of most emulsions. In their simplest form, micelles are droplets of oil with surfactant molecules on the surface dispersed in an external water phase (Figure 1). The surfactant molecules, being partly lipophilic and partly hydrophilic, provide a solubility

bridge between the otherwise incompatible components of the emulsion. If the core shrinks to the size of a molecule and unites into a single molecule, the result is similar to a unimolecular micelle.

Does that mean a single molecule can be considered a micelle? Yes and no. Some UPM are indeed single molecules, with a hydrophobic core covalently bonded to a number of polymers terminating in lipophilic structures. One advantage of these structures over conventional micelles and liposomes is their stability at very low concentrations, down to 10^{-6} M.

Other versions of UPM function through an association of separate molecular structures. Assume the UPM is being compared to the micelle of an oil-in-water nonionic emulsion. The core area is not exactly equivalent to the oil phase of the emulsion, but is rather a nonpolar area of the polymer. It can be designed to contain a lipophilic pocket capable of capturing and holding an oil soluble ingredient under controlled circumstances. In one environment, the lipophilic active can effectively be encapsulated, while another environment >>>>

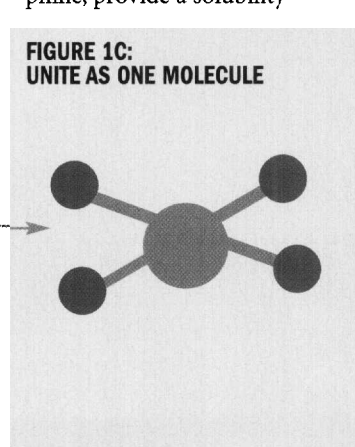
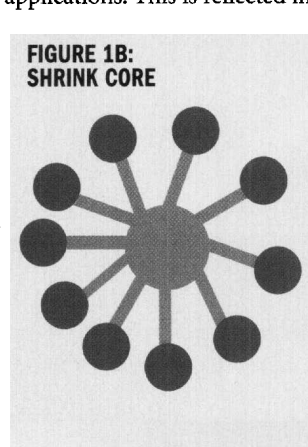
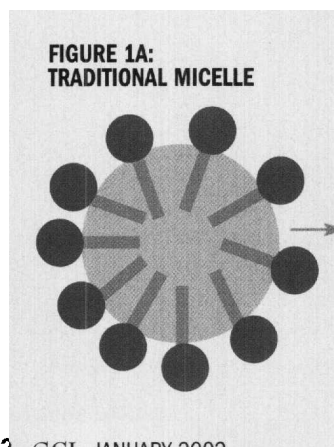
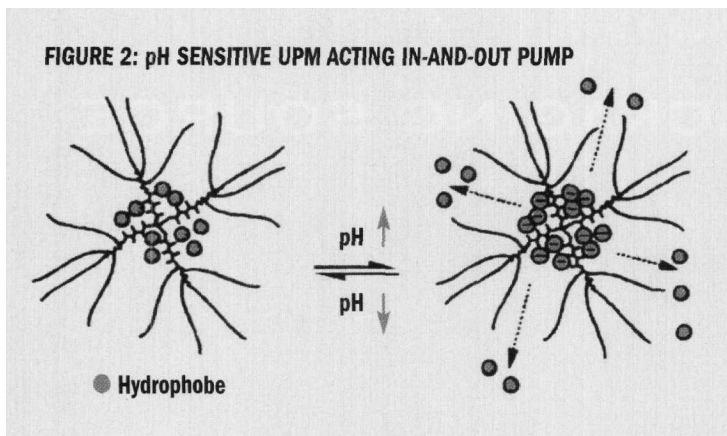


FIGURE 2: pH SENSITIVE UPM ACTING IN-AND-OUT PUMP



will make the system decompose, releasing the active to a precisely targeted area.

The first micellar polymers, which were introduced by George Newkome, consisted of lipophilic, aliphatic polymers with hydrophilic ends. Some recent work by Uhrich and her group¹ uses a sugar (mucic acid), fatty acids, and polyethylene glycols (PEG) to produce biocompatible structures. By using linkages that break under known conditions, such as ester or amide bonds, the molecule becomes biodegradable. The polar outer branches enable the molecule to be dispersed in water. Balancing the lipophilic and hydrophilic components allows a manipulation of polarity balance equivalent to the HLB system of conventional nonionic emulsions.

The nomenclature used by Uhrich to describe the chemical composition of amphiphilic polymers² is not obvious to the average cosmetic chemist. The polymers contain sections of varied composition and polarities. In one example of the naming process, MA(hex) is mucic acid acylated by hexanoyl chloride. Core(hex) results from the coupling of MA(hex) with tris(hydroxyphenyl) ethane. Core(hex)PEG5 has an interior of Core(hex) and exterior of PEG of molecular weight 5,000.

The HLB numbers derived

by Uhrich do not have the same values cosmetic formulators are familiar with from the work of Griffin. The usual definition of HLB derives from the weight percent of the hydrophilic portion of the amphiphilic molecule, but the number is arbitrarily divided by five. The reason was simply to produce smaller numbers, typically 1 to 20. In the simplest case, where the hydrophilic portion is ethylene oxide and the hydrophobic portion is a hydrocarbon, $HLB = E/5$, where E is the weight percent of oxyethylene.

The polymeric micelle definition is $HLB = M_H / (M_L + M_H)$, where M_L and M_H are the molecular weights of the lipophilic and hydrophilic portions. Since this is a simple decimal rather than a percent, and no factor of 5 is used, the values range from 0 to 1. The relationship between the two methods is:

$$HLB_{Griffin} = (HLB_{Uhrich} \times 100\%) / 5 = HLB_{Uhrich} \times 20.$$

Since an important use of the polymers is to solubilize oil soluble material for drug delivery, it would seem reasonable to expect them to have an HLB range of 10 to 18, which in the Uhrich system would be 0.50 to 0.90, with structures as high as 0.99 reported in the literature.

A pharmaceutical application,³ the "In-and-Out Drug Pump," is shown in Figure 2. It consists of a hydrophilic shell and a pH-responsive ionizable core. The drugs are concentrated in the core of the micelles when the pH of the surrounding medium encourages interaction with the core.

A change of pH, causing either protonation or deprotonation of the core, will increase polarity and release the drug.

The UPM technology has enormous implications for the development of advanced treatment cosmetics, with greatly enhanced delivery of active ingredients. Also possible is the stabilization of materials that are currently difficult to formulate with traditional systems, utilizing custom molecules conforming to rigorous pharmaceutical standards of safety and efficacy. The wealth of technology arising from a variety of disciplines makes it clear that there is virtually unlimited potential for creating personal-care products of ever-increasing value. **GCI**

References

The father of the new polymeric structures, including unimolecular micelles, has recently coauthored a book: Newkome, George R., Moorefield, Charles N., and Vogtle, Fritz, "Dendrimers and Dendrons: Concepts, Synthesis, Applications," 2001.

Newkome is also active in the patenting of new polymeric micelles, for example: U.S. 6,130,209, Lock and key micelles, October 10, 2000.

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The UPM technology utilizes custom molecules that can enable the stabilization of materials that are currently difficult to formulate with traditional systems.