

Physicochemical Characterization of Mixed Ck2-13/AOT & Ck2-13/C8 β G1 Microemulsions for Drug Delivery Applications

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Research Description

1,3 Dioxolane surfactants proved to form microemulsions which are transparent, thermodynamically stable, isotropic mixtures of oil, water, surfactant, and frequently cosurfactant. In our research we are planning to characterize the physicochemical behavior of microemulsion systems that need to be performed before being applied to their potential as multipurpose drug delivery vehicles. Based on that, two mixed surfactant microemulsion systems were produced by combining mainly a pH-degradable nonionic surfactant synthesized in our lab, cyclic ketal polyethylene oxide 1, 3-dioxolane, Ck2-13 with: a) an ionic surfactant sodium bis (2-ethylhexyl) sulfosuccinate, AOT and b) a nonionic surfactant n-octyl- β -D-glucopyranoside, C8 β G1. In order to achieve our goal, we have successfully determined the conditions which yield stable microemulsion systems for the Ck2-13/AOT and Ck2-13/C8 β G1 binary systems. In addition, we have characterized the mixed Ck2-13/AOT in how the two surfactants interact with each other at the interface by verifying the structural changes of surfactant aggregates using the electrical conductivity and the dynamic light scattering techniques and revealing the local interactions in the vicinity of core water molecules using the Fourier Transform Infrared (FTIR) analysis. However, we still need to understand the molecular origins of how the two surfactants interact with each other. Accordingly, it is crucial to determine directly the interfacial composition of both surfactants at different types of interface, especially oil/water interface. Small angle neutron scattering (SANS) is able to achieve this goal, for curved interfaces, using neutron contrast variation. The model system we are going to use is a single phase (w/o) microemulsion system where water droplets are dispersed in a continuous oil phase which is isotocane. The stabilizing layers are the mixed surfactant mentioned before with controlled composition. Furthermore, SANS could also be used to probe the nature of the oil penetration into the interfacial surfactant monolayer of the microemulsion. It is of interest to note that Ck2-13 is stable in the basic media but loses its surface activity when it gets hydrolyzed in the acidic media. So, SANS would tell us what happens when the system comes in contact with acidic conditions. Are there any transient effects that occur as the surfactant system changes from Ck2-13-rich to AOT- or C8 β G1- rich? The results of SANS would shed light on surfactant behavior in real-life situations.

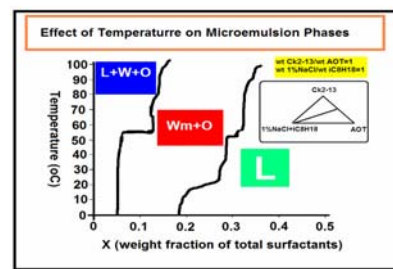
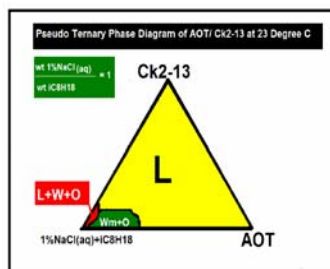
Background and Significance

Microemulsions systems have recently attracted pharmaceutical scientists since they have great potential to serve as drug delivery vehicles through dissolving a wide range of drug molecules. They possess the ability to solubilize large amounts of both water-soluble and oil-soluble drugs. They improve the drug bioavailability, e.g., in topical administration and in oral administration of peptide and protein drugs, sparingly soluble lipophilic drugs, and drugs labile at the conditions in the stomach. In addition, microemulsions compared to other drug delivery systems are easy to sterilize and inject due to their ease of filtration and low viscosity. However, there is still lack of fundamental research that characterizes the physicochemical behavior of microemulsions that needs to be performed before being applied to their potential as multipurpose drug delivery vehicles. This does not mean that microemulsions offer any less potential as delivery systems than alternative vehicles such as liposomes. Indeed, it is pertinent to note that it took considerably less time for a microemulsion product (i.e. Neraol) to get onto the market than the first liposomal drug delivery system [1].

One of the major advantages of Ck2-13 is its potential to be applied for target drug applications because it is stable in the basic medium but undergoes hydrolysis at its cyclic ketal bonds in the presence of acid. They produce microemulsions that possess phase behavior and physical properties similar to common alkyl ethoxylate nonionic surfactants, except for lower surfactant efficiency and stronger susceptibility to attractive interaction-limited water solubilization in oil. A major drawback of Ck2-13 is its sensitivity to temperature. Accordingly, it is necessary to mix Ck2-13 with other surfactants having complementary characteristic to improve its microemulsion performance. In particular, mixing Ck2-13 with other surfactants would form microemulsions that are nearly insensitive with respect to temperature. In addition, mixing Ck2-13 with other ionic surfactants results in increasing the microemulsions phase region while decreasing the amounts of the required surfactants. Furthermore, Ck2-13 droplet size will be affected by the added surfactants which indicate that the interfacial packing can be controlled by the mixed systems.

Ck2-13 was mixed with AOT which has been co-formulated with a number of different drugs as a microemulsion dosage form. For example, it has been used for delivery of Vitamine K and steroids such as hydrocortisone, prednisolone, and betamethasone. However, when AOT microemulsions are formulated in combinations with other nonionic surfactants, the extent of microemulsion region is often distinctly increased; additionally, the temperature range over which the microemulsion is stable is generally improved.

Ck2-13 was also mixed with the non-toxic C8 β G1 for dermatological applications. In general, alkyl glucosides are non toxic and accomplish a fast anaerobic and aerobic biodegradation. They are manufactured from renewable resources such as sugar and vegetable oil. However, they are more hydrophilic than the other polyethylene glycol (PEG)-based surfactants, because of their sugar unit which make them more water-soluble and less soluble in hydrocarbons such as alkanes. Therefore, making microemulsions with C8 β G1 is difficult. Their physicochemical behavior in oil-water system is distinctly different from that of conventional non-ionic surfactants. In particular, they do not show the pronounced inverse solubility vs. temperature relationship like the ethoxylates surfactants. Therefore, they are of interest for applications in pharmaceutical and cosmetic formulations. Mixing Ck2-13 with C8 β G1 would increase the performance of both of them in microemulsion systems since Ck2-13 forms microemulsions over a wide range of fractions and C8 β G1 is insensitive for temperature. Also worthy of mention, the presence of a pH-degradable surfactant adds some "tunability" to the microemulsion systems which is absence when alkyl glycosides are the lone surfactant type.



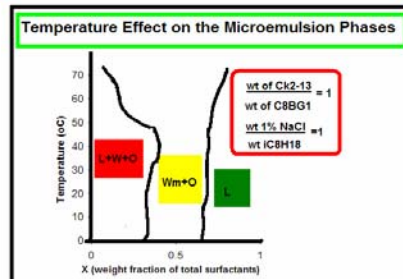
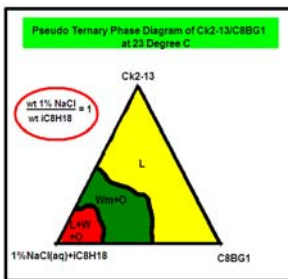
Phase Diagrams of Mixed Ck2-13/AOT

L+W+O regions occur at low overall (CK-2,13+AOT) concentrations over a wide temperature range.

Om+W did not coexist except at very low fraction of Ck2-13 and low temperature (<15 degree C).

Wm+O occurred at several different sets of conditions.

L phases occurred at high fractions of total surfactants (x).



Phase Diagrams of Mixed Ck2-13/C8 β G1

The coexistence of Wm+O and L+W+O phases that are insensitive to temperature is due to the presence of NaCl(aq) in the microemulsion system that decreases the hydrophilicity of both Ck2-13 and C8 β G1 and hence decreases the electrostatic interaction between the two surfactants.

L phase region were more fluid and less viscous which gives an indication of a decrease in interaction between the two surfactants.

References

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