42b Surfactant Design for Hydrofluoroalkane-Based Pmdis: a Microscopic Investigation Using Chemical Force Microscopy

Libo Wu and Sandro R. P. da Rocha

Pressurized metered dose inhalers (pMDIs) are the most common vehicles for the delivery of drugs to the lungs, accounting for approximately 80 % of the prescribed aerosols. They are also excellent candidates for the delivery of biomolecular species. However, the development of pMDI-based formulations has been confronted with several challenges since the replacement of CFCs with the more environmentally friendly hydrofluoroalkanes (HFAs). In spite of the fact that the operation of pMDIs with HFAs is similar to those containing CFCs, previous formulations are not compatible due to the significantly different physicochemical properties between these two classes of fluids. For example, none of the FDA approved surfactants commonly used in the CFC-based formulations are soluble in HFAs. Surfactants are generally required excipients in pMDIs, with functions including dispersion stabilization and throttle lubrication. Co-solvents are necessary in order to solubilize amphiphiles with methylene-based tails. However, co-solvents may increase toxicity, change the vapor pressure of the pMDI, and negatively affect the stability of the dispersed drug particles. Fluorinated-based tails have also been proposed for the stabilization of aggregates in HFAs.

Stability of dispersed aggregates in HFAs depends on both tail-tail and solvent-tail interactions. In this work, the interaction of hydrogenated and fluorinated-based tails in 2H, 3H-perfluoropentane (HPFP), a mimic solvent for HFAs, is investigated. The adhesion force between chemically modified substrate and AFM tip is determined by Chemical Force Microscopy. Johnson-Kendall-Roberts (JKR) theory is used to determine single molecule forces. The results in HPFP are compared and contrasted with those in isooctane, a good solvent for methylene-based tails. Although HPFP is a good solvent for the fluorinated-based tails, it is not capable of solvating such moieties as well as hydrogenated tails are solvated in isooctane. Single molecule forces indicate that the interaction between fluorinated-based tails in HPFP is lower but the same order of magnitude than that in isooctane. As expected, a very large adhesion force is observed for hydrogenated modified tip and substrate in HPFP.

Keywords: HFA; pMDI; CFM; adhesion force, drug delivery, biomolecules, atomic force microscopy, reverse microemulsions.