A Novel Sustained-Release Injection System Using Liquid Crystal Technology for Monthly Delivery of Leuprolide
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Purpose
The aim of the present study was to provide a new injectable liquid crystal-forming system (LCFS) composed of sorbitan monooleate (SMO) for sustained release of leuprolide.

Methods
The LCFS is a liquid form composed of SMO, phosphatidyl choline, tocopherol acetate as core components without polymers, and contains 3.75 mg of leuprolide acetate in about 0.1 ml of formulation for a one month dose. Cryo-TEM and polarized optical microscopy (PLM) were investigated to observe the structure of the liquid crystal formed after exposure to water. LCFS containing 3.75 mg of leuprolide acetate were subcutaneously injected into the back of the rat and beagle dog, respectively. Leuprolide concentrations in plasma sample taken from the SD rats and beagle dogs were monitored for 28 days using a UPLC-MS/MS method.

Results
The LCFS lost the flow property of a liquid and changed into a spherical semi-solid form to minimize the contact surface with water, exhibiting a semi-transparent and light yellow appearance after injected into the water. The LCFS with SMO exhibited typical characteristics of the liquid crystalline phase, which were classified into the hexagonal phase in terms of their structure observed by Cryo-TEM and PLM. The LCFS showed reduced initial burst ($C_{\text{max}}$ values) after subcutaneous injection in rats and dogs compared with a commercial depot formulation of leuprolide (reference). Despite the significantly reduced $C_{\text{max}}$ values, LCFS showed a similar steady state of plasma concentrations and AUC$_{\text{last}}$ compared with the reference.

Conclusion
A new injectable liquid crystal-forming system (LCFS) based on SMO was developed for the sustained delivery of leuprolide. The LCFS is expected as a potential system for the controlled release of a wide range of drugs which can substitute the well-known PLGA microparticle system due to the terms of safety, ease of preparation, and suitability of controlled release properties. This is a partial encore presentation, since some data were presented at the ‘41st Annual Meeting & Exposition of the Controlled Release Society (2014)’ in July.