Development of In Situ Depot Forming Dosage Form for Long-Acting Contraception
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Purpose
Birth control is still a major concern worldwide. Although an extensive research has been made to develop long acting injectable hormonal contraceptives, still there is an unmet need for injectable contraceptives which can provide contraception for more than three months after single shot. The purpose of this study is to develop injectable polymeric depot forming dosage form containing levonorgestrel (LNG) for contraceptive effect for six months after single injection that help to reduce unintended pregnancies with high patient compliance and low cost.

Methods
A prototype in-situ depot forming formulation was prepared using poly (lactide-co-glycolide) and polyactic acid and a mixture of solvents N-methyl-2-pyrrolidone and triethyl citrate. The syringeability of the formulation through 21G needle was evaluated. The in-vitro LNG release kinetics in PBS (pH 7.4) was investigated by quantifying LNG release content using HPLC. The formulation was subcutaneously injected into female SD rats (40mg/kg dose), blood and vaginal secretions were collected as a function of time for four months. Plasma samples were analyzed for LNG concentration using UFLC/MS/MS and the vaginal secretions were subjected to microscopic cytology evaluation.

Results
Manual syringeability test showed that the formulation can go through 21G needle. In vitro release data from figure 1 show that prototype formulation can continuously release LNG for more than four months. In vivo data from figure 2 show that the formulation can continuously release LNG in-vivo that can achieve plasma LNG levels within a range of 0.5-3 ng/mL for four months after the sub-Q injection in rats. Vaginal cytology studies revealed that all of the cells are either at early diestrus, diestrus or proestrus stages but not at the estrus stage.

Conclusion
The prototype formulation can be injected through 21G needle, and can constantly release LNG in-vivo to cause contraception for four months. The data showed that the prototype formulation has a great potential for sustained release of LNG for longer-acting contraception.