Purpose
The development of sustained release suspension of water soluble drug was challenging due to the dissolution in water of the formulation. The purpose of this study was to develop a sustained release suspension utilizing ion complex to reduce the solubility and dissolution rate in suspension.

Methods
Mirabegron (MB) was used as a model compound with water-soluble and pH-dependent solubility. The suspension is composed of ion complex and water-insoluble polymer. Several kinds of ion complex were prepared using a precipitation method and evaluated drug solubility and dissolution rate. Ethylcellulose aqueous dispersion (Aquacoat® ECD) was utilized as a water-insoluble polymer to adjust the dissolution rate by preparing the dried granules. The dried granules were dispersed in water at the MB-equivalent concentration of 10 mg/mL. In-vitro drug release was examined by paddle method.

Results
Ion complex with sodium lauryl sulfate (SLS) has significantly reduced the solubility of MB in the pH range of 2-8 and showed sustained release dissolution profile. MB has an amine group and a thiazol group, while SLS is a salt with a sulfate group. The positively charged MB bound with the negatively charged sulfate group of SLS, thus precipitated out of the solution. SLS has an alkyl chain and the solubility of complex reduced with the alkyl chain length, indicating that the alkyl chain length affects the dissolution rate. The utilization of Aquacoat® ECD effectively controlled the drug release dissolution profile by preparing the dried granules. The particle size of granules is less than 200 μm in diameter to protect a gritty sensation during administration. There were no differences in sustained release dissolution profile between dried granules and suspension. In addition, the suspension showed unchanged release dissolution profile for 2 weeks at room temperature due to the low solubility of drug in the complex.

Conclusion
The sustained release suspension of MB was successfully achieved by the use of ion complex formed with SLS as well as the utilization of Aquacoat® ECD to control the drug release. The sustained release suspension exhibited the stable release dissolution after storage.