Charge-Assisted Bond N⁺-H Mediates the Gelation of Amorphous Lurasidone Hydrochloride during Dissolution
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Purpose
Lurasidone hydrochloride (LH), the hydrochloride form of lurasidone with a charge-assisted bond N⁺-H, is a atypical antipsychotropic agent for the treatment of schizophrenia. In this study, amorphization approach was employed in order to improve the solubility of this BCS II drug, however, powders of amorphous LH quickly aggregated when contacting the dissolution media (water, 37 °C), and formed a sticky gel adhering on the paddle with a significantly lower dissolution (in comparison to crystalline LH). The aim of the current study was to explore the gelation mechanism of amorphous LH.

Methods
Amorphous LH and L (the base form of LH) were prepared by solvent evaporation method from their corresponding methanol solutions. Polarizing light microscope (PLM), scanning electron microscopy (SEM), differential scanning calorimetry (DSC), X-ray powder diffractometry (XRPD) and FTIR were applied to investigate the materials before and after dissolution of amorphous LH and L in 37 °C water.

Results
After dissolution, amorphous LH formed sticky gel. SEM revealed that the product of amorphous LH represented as spherical particles and adhered together to form the framework of the gel. PLM, XRPD, DSC, and IR indicated that amorphous LH transformed to crystalline LH during dissolution. On the other hand, no such gelation phenomenon of amorphous lurasidone (L, the base of LH) was observed under the same dissolution condition. However, the gel would reform when dropping concentrated hydrochloric acid (HCl) slowly into the bottom of the medium during the dissolution of amorphous L, and XRPD/DSC/FTIR indicated that the regenerated gel was consisted of crystalline LH.

Conclusion
In conclusion, the reformed gel from amorphous L by adding HCl suggested that the charge-assisted bond N⁺-H in the structure of LH mediated the gel formation of amorphous LH during its dissolution process. (BK20141351 and BK20151438 of Natural Science Foundation of Jiangsu Province; Priority Academic Program Development of Jiangsu Higher Education Institution)