**Preparation and Characterization of Entrectinib-Loaded Supersaturated SNEDDS**

**Sung Mo Park**, Kwan Hyung Cho.

Department of Pharmacy, Inje University, Gimhae, Gyeongsangnam-do, Republic of Korea.

**Background and aims.** Entrectinib (ENT) is a poorly water-soluble, BCS class II drug with pH-dependent solubility. This study aimed to develop a supersaturated self-nanoemulsifying drug delivery system (super-SNEDDS) using high-pressure homogenization (HPH) to enhance its solubility and dissolution.

**Methods.** Based on solubility evaluations in various excipients, Capmul MCM C8 and Capryol 90 were selected as oil phases, and Kolliphor HS15 and TPGS as surfactants. ENT was loaded into the oils at 25% (w/w) to prepare HPH-treated oil suspensions, which were mixed with surfactant solutions saturated with ENT and centrifuged to obtain the solubilized phase. PVP K17, selected based on its solubility in both phases, was incorporated as a precipitation inhibitor (PPI). The formulations were evaluated for particle size, drug loading, precipitation inhibition, and dissolution under different pH conditions including pH shift condition.

**Results.** FL2, composed of Capmul MCM C8 and Kolliphor HS15 in a 2/8 ratio (w/w), showed a particle size of 16.3 ± 0.6 nm and a high solubilized drug loading (%, w/w) of 10.49 ± 0.06. FLP2, prepared by adding 3% (w/w) PVP K17 to FL2, exhibited a particle size of 16.6 ± 0.6 nm and improved physical stability. In dissolution testing, both formulations achieved a dissolution rate of over 95% within 10 min under pH 1.2 and 6.8. In the pH shift dissolution test (from pH 1.2 to 6.8), the dissolution rate of FL2 decreased to approximately 90% after the pH shift. In contrast, FLP2, which contained the PPI, showed a temporary decrease but subsequently recovered to over 95% within 5 min, demonstrating enhanced precipitation inhibition and maintained of supersaturation.

**Conclusion/Discussion.** The HPH-treated super-SNEDDS enhanced the solubility and dissolution of ENT and maintained supersaturation under varying pH. These findings suggest that the super-SNEDDS is a promising oral delivery system for poorly water-soluble drugs with pH-dependent solubility.

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**References:**

(1) Rolfo, C. et al (2015) Expert opinion on investigational drugs 24(11):1493-1500

(2) González-Sales, M. et al (2021) Cancer Chemotherapy and Pharmacology 88:997-1007

(3) Tran, P. et al (2021) Journal of Pharmaceutical Investigation 51:439-463

(4) Park, H. et al (2020) Pharmaceutics 12(4):365

(5) Yadav, K. S. et al (2020) Journal of Pharmaceutical Innovation 15:690-701

(6) Xu, S. et al (2013) International journal of pharmaceutics 453(1):36-43