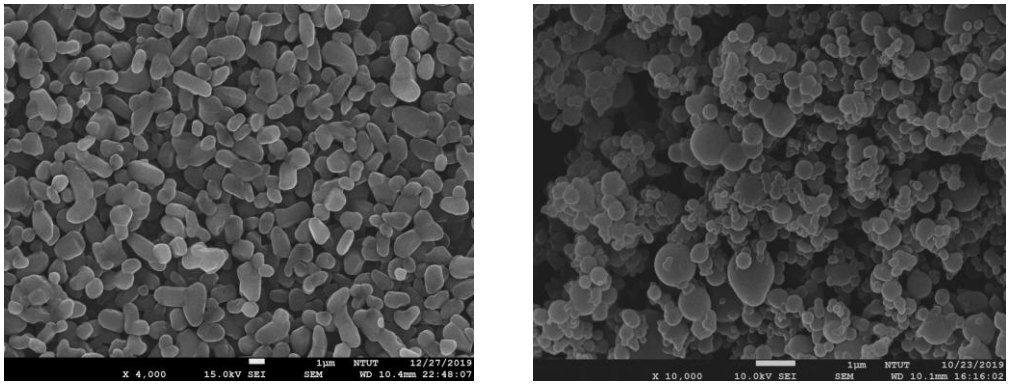
Particle design of an anticancer drug, p-toluenesulfonamide, using supercritical fluid technology

Wei-Ju Chen[a], Li-Ting Lu[a], Chuan-Ching Yang[b], Yung-Ho Chiu[c], Chie-Shaan Su[*,a]

(a) Department of Chemical Engineering and Biotechnology, National Taipei University of Technology, Taipei, Taiwan
(b) Gongwin Biopharm Co., Ltd., Taipei, Taiwan
(c) Taiwan Supercritical Technology Co., Ltd., Changhua, Taiwan

p-Tolenesulfonamide is a developing new drug used in treatment of central lung cancer severe airway obstruction and passed phase III clinical trial in China. Due to the hydrophobic and poorly water-soluble natures, current formulation of p-tolenesulfonamide requires multiple excipients and brings challenges in large-scale manufacturing. Particle design of p-tolenesulfonamide is a strategy to overcome the solubilization issue and further develop novel formulation for other indications. Supercritical fluid particle design processes such as the rapid expansion of supercritical solutions (RESS) and supercritical antisolvent (SAS) provide advantages in controlling the solid-state property of pharmaceutical solid such as the particle size, crystal form, crystal habit and residual solvent content. In this study, particle design of p-tolenesulfonamide through supercritical fluid technology was demonstrated for producing microparticle of p-tolenesulfonamide and designing solid dispersion dosage form with polymeric carrier, polyvinylpyrrolidone. Regarding the microparticle production, as presented in **Fig. 1**(a), p-tolenesulfonamide microparticles with mean size of 1 μm were successfully obtained. The crystal form, thermal property and spectrometric behavior were confirmed consistent with the unprocessed sample by the analytical results of PXRD, DSC and FTIR. To further design solid dispersion dosage form, **Fig. 1**(b) shows the production of spherical drug/polymer composite nanoparticle with mean size of 300 nm by supercritical fluid process was feasible. In addition, the effect of process parameter in supercritical fluid process was systematically investigated and discussed. These results show supercritical fluid technology is an efficient tool to manipulate the solid-state property of p-tolenesulfonamide for further formulation design.



(a) (b)

Fig. 1 SEM images of (a) microparticles of p-toluenesulfonamide and (b) powders of solid dispersion of p-toluenesulfonamide in polyvinylpyrrolidone.