

### Anti-Agglomeration of Micro-sized Valsartan in CO<sub>2</sub> for Dissolution rate Enhancement

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Valsartan is widely used to control high blood pressure, treat congestive heart failure, and improve survival rates for people who have had a heart attack. Oral bioavailability of valsartan is very low (less than 40%) due to its poor water solubility. In this work, we have improved dissolution rate of valsartan by preparing single particles without excipients. This will help certain takers with pre-existing renal impairment because some organic excipients mixed with valsartan can potentially harm those patients. The fine valsartan particles with mean diameter of 0.1  $\mu\text{m}$  were obtained without excessive agglomeration by ASES (Aerosol Solvent Extraction system) using subcritical CO<sub>2</sub> in the condition of 70 bar and 5°C. It is found that the particles obtained from the condition of lower temperature were less likely to be agglomerated. It is believed that melting point depression of valsartan took place because CO<sub>2</sub> might be included in solid phase of valsartan. It is observed that valsartan began to melt around 40°C in subcritical CO<sub>2</sub>, differently from that of raw valsartan in air is 100 $\pm$ 0.2°C. Therefore, processed valsartan in subcritical CO<sub>2</sub> at low temperature improved its dissolution rate because of the small sized and little agglomerated particles.