Process Development of Pitavastatin, a Potent HMG-CoA Reductase Inhibitor : Comparison between Optical Resolutions and Asymmetric Synthesis

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Pitavastatin calcium(LIVALO®) is an antihyperlipemic agent, launched in September, 2003 in Japan. It has two asymmetric centers in the desmethylmevalonic acid chain like other HMG-CoA reductase inhibitors. Naturally, in the process research it was the most important problem to construct (*3R,5S*)1,3-*syn*-diol part successfully. In this symposium, we show the outline of the practical manufacturing process focusing on the following methods.

① Optical resolution via diastereomeric salt formation using α-methylbenzylamine as a resolving agent, which is the method in the early stage of the development.
② Recrystallization and following chromatographic optical resolution of racemic DOLE by a simulated moving bed(SMB) system.
③ Asymmetric synthesis characterized by aldol reaction using Ti-catalyst to obtain optically active MOLE from ENAL, which is the comparatively new method found several years ago.