Thin-layer Chromatographic separation of intermediates of Simvastatin synthesis

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Simvastatin is an orally administered prodrug, hydrolysed in body to β - hydroxyacid simvastatin, the active metabolite 3-Hydroxy-3-methyl-glutaryl-coenzyme A (HMG CoA) reductase inhibitor. As it is potent inhibitor of cholesterol biosynthesis it is widely used in the treatment of hypercholesterolemia.

It is synthesised from lovastatin in four phases.

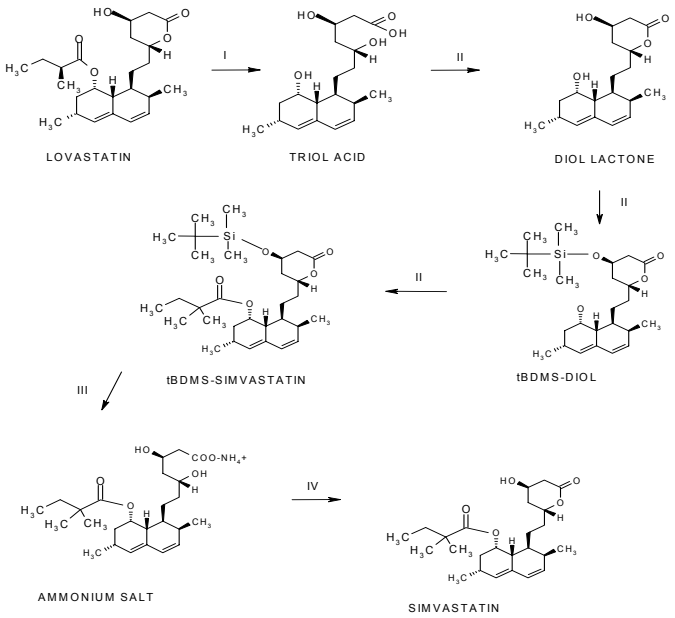

Figure 1 Synthesis of Simvastatin from Lovastatin

It is very complex process with intermediates with different polarity, solubility and stability. The aim was to develop the method which will separate all the intermediates, lovastatin (starting material) and simvastatin and qualifie and quantifie them in terms of percent against the sum of all peaks. Controlling of synthesis during all stages of reaction has to be fast and simple and for that reason TLC was the method of choice.

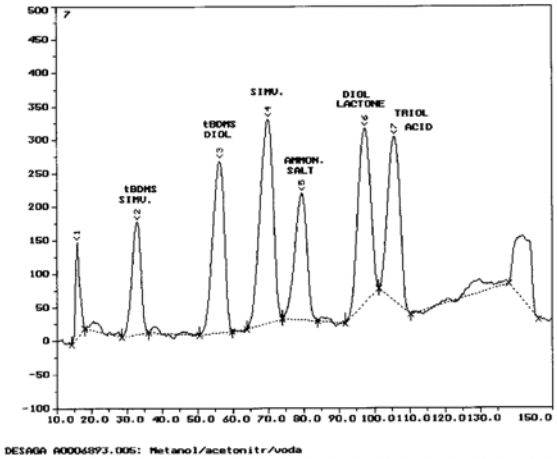

Figure 2 Chromatographic separation of simvastatin synthesis intermediers

Chromatographic conditions: samples solution were dissolved in methanol accept silil derivates which were dissolved in aceton, containing approx. 14 mg ml-1 of each on Rp-18 F_{254} TLC plates (200x200 mm, Merck, 1.15389) prewashed with acetonitril; developed with methanol : acetonitril : water (16+4+2) in a twin-trough chamber Camag without saturation (migration time, ca 40 min); applied volume, 4µl in 5mm band, corresponds to approx. 1 ug substance per spot . Densitometric evaluation by UV λ = 254 nm.