

## Synthesis and physicochemical control of adapalene

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**Background and Aims:** Adapalene is a third-generation topical retinoid which is primarily used in the treatment of mild to moderate acne and is also used to treat keratosis pilaris as well as other skin conditions. The present study was aimed at the optimization of adapalene synthesis from adapalene methyl ester.

**Methods:** Different hydrolysis conditions were tried such as type and amount of solvent, reaction temperature, type and concentration of alkaline reagent. Yield and run time for the reaction were used as the two parameter to decide about the optimum condition. Final purification of adapalene was achieved by recrystallization from a mixture of organic solvent such as THF, methanol, toluene, heptane, ethyl acetate and DMSO. Melting point, IR, Mass, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR spectroscopies were used to confirm the identity of adapalene and HPLC-UV was used for purity evaluation. General pharmacopeial physicochemical controls including residue on ignition, loss on drying and heavy metal tests were used to verify the compliance of the compound with commercial requirement.

**Results:** Hydrolysis in a mixture on THF and water using 50% NaOH gave the best results. The sodium salt of adapalene thus obtained is converted to free acid using acetic acid. Crystalization from THF/Ethyl acetate (70:30) gave the final product with the purity of 99.9%. The overall yield was 82%.

**Keywords:** Adapalene; Physicochemical control