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Solubility of atorvastatin calcium in water-ethanol mixture: Solution-mediated phase transformation

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Background and Aims: Solubility is one of the most important physicochemical properties of drugs. If a compound has a low aqueous solubility, it may be subjected to dissolution rate-limited or solubility-limited absorption within the gastrointestinal tract. Solution mediated transformation is a mechanism that influence main powder to another crystalline or amorphous form of drug. The cosolvency (using an organic solvent such as ethanol) , is the most common method to increase the aqueous solubility of drugs. Atorvastatin calcium (ATC) is used in the treatment of primary hypercholesterolemia and dyslipidemia that is classified in class II (low solubility and high permeability) according to the biopharmaceutical classification system. So, it is valuable to investigate solubility of ATC in ethanol-water mixtures and crystalline form of ATC in solution.
Methods: The solubility of ATC in water- ethanol was determined at 25C after the equilibrium condition. The saturated solutions were filtered, then diluted and samples were analysed by spectrophotometer at 246 nm. The characteristics of powders after saturation of the solutions were checked using XRD.
Results: The solubility of ATC in binary water- ethanol mixture is increased (until 80% of ethanol) at 25 C. The solubility is then decrease with further increase in ethanol concentration and finally reached the maximum concentration in pure ethanol. The results of XRD indicate that the crystalline form of ATC was converted to amorphous form in neat ethanol .This form show a significant increase in solubility of ATC in ethanol rich area of the ninaru solvent.
Conclusions: Mixing solvents of water and ethanol could create a solvent system that increase the solubility of ATC and pure ethanol solution mediated transformation crystalline form of ATC to amorphous form and increase in solubility of ATC.

Keywords: Atorvastatin calcium; Solubility; Cosolvency; Amourphous form; Solution-mediated phase transformation