

Pharmacognosy of Simvastatin

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Abstract

Simvastatin is 2, 2 –dimethyl butanoic acid (1S, 3R, 7S, 8S, 8aR) – 1, 2, 3, 7, 8, 8a-hexahydro-3, 7-dimethyl-8-[2- [(2R,4R) tetrahydro -4- hydroxyl- 6 -oxo-2H pyran-2- yl]ethyl-1-naphthalenyl ester1,2 can be considered in the category of statins known as cholesterol-lowering lactones which, in 2011-13, were discovered as being the most broadly and innovatively discovered drug in the universe .This paper deals with the characteristics, structure, use of this drug.

Keywords: *Simvastatin, Statins, Cholesterol, Drug*

INTRODUCTION

Simvastatin is a drug which is having plasma half-life of 2 hrs and poor oral bioavailability (<5%) owing to the extensive initial pass metabolism (Tiwari et al., 2011). To nullify the first pass effect, the possible methods included are transdermal, rectal, buccal, and parenteral routes of administration (Van der Weijden et al., 2009). TDDS (transdermal drug delivery system) can be an effective way for the systemic availability of drugs. Transdermal patches are newly devised

drug delivery systems for the skin application to attain a systemic effect (Tamjidi et al., 2013).

APPLICATION OF THE TDDS SYSTEM OFFERS MANY CLINICAL BENEFITS OVER OTHER ROUTES

Simvastatin (SIM) is a lipid-lowering agent availed for treatment of hypercholesterolemia in humans and animals (Steinhardt et al., 2008). Simvastatin (lactone compound) undergoes hydrolysis to be converted to

the β , δ - dihydroxy acid form, which is a much potent competitive inhibitor of 3-hydroxyglutaryl-CoA reductase, the enzyme catalyzing the rate-limiting step of cholesterol biosynthesis. When this drug is administered orally, SIM is subjected to extensive first-pass metabolism in the liver leading to its low bioavailability (5%) and short half life (2 hrs) (Sohn et al., 2010). There were researchers to formulate and optimize a stable transdermal formulation for delivering SIM in order to avoid the first-pass effect, and consequently enhance SIM bioavailability and therapeutic efficacy leading to reduction in dosing frequency and improvement of patient compliance (Mundy, 1999).

SIMVASTATIN AND SOLUBILITY OF DRUG

In the current scenario, there have been tremendous strides in the solubility enhancement of poorly soluble drugs (Mukozawa et al., 2011). Solubility is a significant criterion for drug efficacy, independent of route of administration (Marie et al., 1995). It also poses a main challenge for pharmaceutical industries, which are developing new pharmaceutical products, since 38-40% of the active substances being identified are either insoluble or poorly soluble in aqueous media (Mehnert et al., 2012). A limiting

factor for in vivo performance of poorly water soluble drugs, following oral administration, is their resistance to being wetted and being dissolved into the fluid in the gastrointestinal tract (v et al., 2014). Aggrandizing the dissolution rate of poorly water soluble drug is typically important for optimizing bioavailability (Muller et al., 2000). The role of solubility enhancement is an attempt to shift the classification of a drug (II $\rightarrow$ I) in order to discard the problems associated with dissolution-limited compounds (Lee et al., 2008). Poor solubility is in most cases associated with poor bioavailability (Liu et al., 2013). There are mainly two basic approaches to overcome the bioavailability problems of these drugs, increase of saturation solubility and dissolution velocity (Muller et al., 2002). Moreover, many of the new compounds, show such a low solubility that micronisation does not lead to a sufficient increase in bioavailability after oral administration. Simvastatin undergoes many compound transformation in the biosynthetic pathway (Fig:1). The solubility of the Simvastatin drug can be raised to another level by integrating nonbio technological approaches (Sreeremya, 2017).

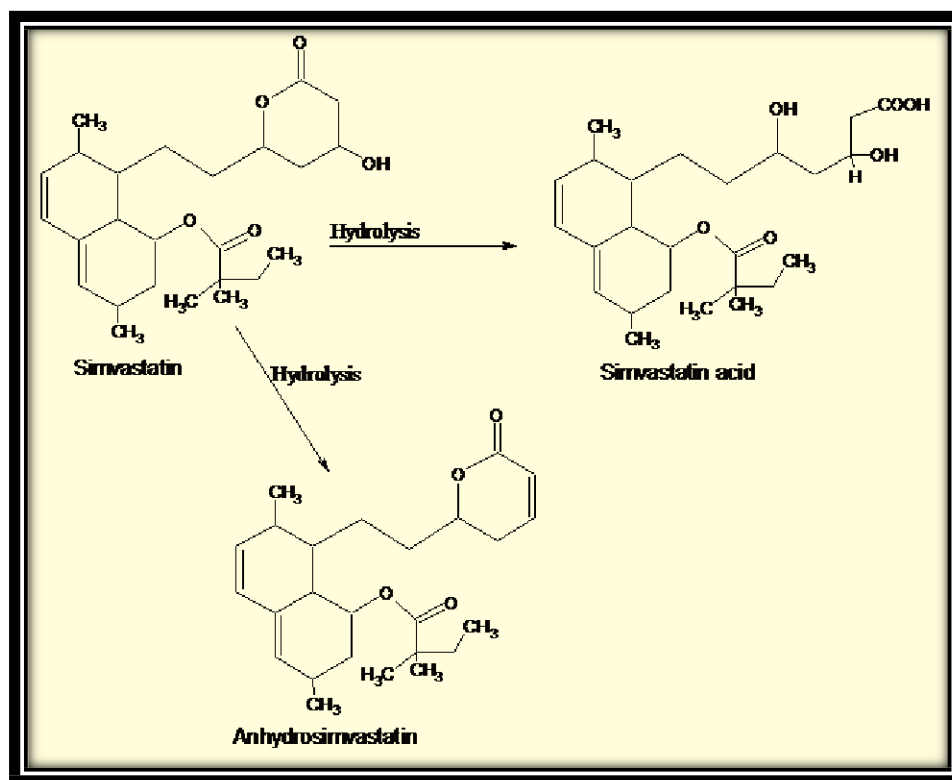


Fig: 1 Structure of Simvastatin

Procedure for Preparation of Simvastatin standard stock solution

10 mg of Simvastatin was added into a 10 mL volumetric flask and the volume was made up to the mark with mobile phase to give 1 mg/mL (1000 µg/mL) solution. From this stock solution, 10 mL of 100 µg/mL solution was prepared and again from this solution 10 mL of 10 µg/mL was prepared (Iqbal et al., 2012).

Preparation of analytical calibration curve solutions:

From the standard stock solution 0.25-2 µg/mL standard solutions were prepared and stored below 4-8°C until further analysis (Kou et al., 2013).

Preparation of blank plasma: Blank plasma (0.2 mL) was transferred into 2.0 mL centrifuge tube and 0.2 mL of precipitating agent (about 10% perchloric acid) was added. Finally made up to 2 mL with the mobile phase. The resulting solution was vortexed for 5-10 minutes and centrifuged at 4000 rpm for 10 minutes. The supernatant layer was separated and assessed (Im et al., 2013).

CONCLUSION

Simvastatin is cholesterol lowering rather a lipid lowering medications. Many of the cholesterol lowering drugs are in market but among the major cholesterol lowering drug Simvastatin has a much potential to

enhance good cholesterol and to decrease the bad cholesterol.

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