A Novel Enhancement of Statins' Solubility with Hydroxypropyl BETA-Cyclodextrin Inclusion Complex via Molecular Dynamics and in vitro Validation

Khan, Elyas (School: Dar AlFikr Schools)

The prediction and optimization of drug solubility in various formulations play a pivotal role in drug development. Statins (STN), a widely prescribed cholesterol-lowering drug family, exhibit poor aqueous solubility, limiting their bioavailability and therapeutic efficacy. In this study, the solubility enhancement of three STNs, atorvastatin, simvastatin, and lovastatin in hydroxypropyl beta-cyclodextrin (HP-BCD) inclusion complexes through a combination of molecular dynamics simulations and experimental evaluations was explored. To predict the change in solubility of STNs' in a complexation with HP-BCD, Materials Science Maestro (MSM), a molecular dynamics simulation, was utilized to calculate the Hildebrand and Hansen solubility parameters. This was achieved by formulating disordered systems that go through a cycle called a relaxation protocol. An in vitro validation was then formulated with a hydroalcoholic mixture and an excess of the selected STNs. The MSM results showed an increase in the system's solubility according to the mentioned parameters. These results were further verified and psychochemically characterized. In the presence of the HP-BCD solution, the solubility of STNs increased to 1229.73 ± 10.69 µg/mL at polymer concentrations ranging from 20-40 mM. The experimental results were then compared with the MSM predictions, allowing for a comprehensive computational model validation. These insights help in developing optimized drug formulations to enhance the bioavailability and therapeutic effectiveness of poorly water-soluble drugs. This is a noteworthy example of the alignment between the MSM and experimental validation, showcasing the potential for advancing pharmaceutical research and facilitating the development of innovative drug enhancement systems.

Awards Won:
Third Award of $1,000
The Scientific and Technological Research Council of Türkiye TUBITAK: 1st Prize Award