## Abstract

**Introduction:** Diabetes is a disease that caused by continual high blood sugar level**.** Antidiabetic drugs are used to control the blood sugar level in type 2 diabetes. Rapaglinide is an oral antidiabetic drug that is practicaly insoluble in water and has a short elimination half-life time. Furthermore, the extent of bioavailability of this drug is low and so novel drug delivery systems (NDDS) were used to overcome these problems. Nanocarriers are of the most important examples of NDDS. In this study, it was tried to load repaglinide into nanostructured lipid carriers (NLC) with coated with chitosan polymer and then the effect of developing such structure has been investigated on physicochemical and biological properties of drug.

**Methods**: To preparthe NLC nanoparticles, two distinct ethanolic and aqueous solutions were prepared. The ethanolic solution contained lipidic components and the drug. The aqeous phase composed from water and surfactant/stabilizer. Next, the alcohol phase was pored dropwise into the aqueous phase under stirring condition. The effects of different parameters such as concentration of stearic acid, glyceryl mono stearate, oleic acid and tween 80, on quality, morphology and nanoparticles size was investigated and these parameters were optimized. After that, the properties of prepared nanoparticles were investigated by using various techniques including Fourier Transfer Infra Red (FTIR), Scanning Electron Microscopy (SEM), Thermal Gravimetric Analysis/Differential Thermal Gravimetric (TGA/DTA) and Dynamic Light Scattering (DLS). The concentration of repaglinide was determined and calibrated by spectrophotometric method (UV-Vis spectrometry). The drug release profile from pure drug and nanocarrier-loaded drug was determined using dialysis bag method. Furthermore, oral administration of drug to mouses was done and the effect of loading the drug on the blood sugar level of mices was evaluated through blood sampling from tail vein.

**Results, discussion and conclusion:** The size of nanostructured lipid carriers was verified in nano scale (less than 100 nm) diameters. Effect of various parameters on nanoparticles size were evaluated and based on the obtained results, increasing the stearic acid concentration (SA) lead to the increase in the lipid carrier particles size and furthermore increase in concentration of glycerol mono stearate (GMS) caused to the decrease of particles size. After optimizing of conditions and preparation of particles in nano scales, based on obtained FTIR results, the presence of electrostatic bonds indicated the chemical interaction between carboxylic group of stearate on the surface of NLC and amin group of chitosan polymer chains and therefore, formation of chitosan coating was proved. The results of TGA analysis represented that after loading thenanostructured lipid carriers loaded with repaglinide and coating with chitosan, the thermal stability and also the mechanical and chemical stabilities were increased remarkably. SEM images showed that nanostructured lipid carriers containing drug has spherical morphology and chitosan layer was located in the form of long strings around it. Releasing results showed that the release of repaglinide in chitosan-coated nanostructures lipid carriers is significantly slower than common nanoparticles without any coating and also the release of drug in this nanoparticles occurred in longer times rather than in nanoparticles without coating which were reached to steady level more quickly.The invivo study through oral administration of samples to mouses showed that simple repaglinide can decrease the blood sugar, but this effect in nano-repaglinide samples was significantly more than simple drug samples. Also, the duration of action of nano-drugs was longer than pure drug sample.

**Keywords:** Nanostructured lipid carriers (NLC), Repaglinide, chitosan, diabetes type 2, oral antidiabetic drugs