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UTICAJ VELIČINE ČESTICA NA OSLOBAĐANJE SIMVASTATINA IZ TABLETA

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Slaba rastvorljivost supstanci jedan je od ograničavajućih faktora za oslobađanje iz čvrstih farmaceutskih oblika. Veličina čestica i površina su dva važnija faktora koja utiču na brzinu rastvaranja supstanci i potencijalno njenu biološku raspoloživost. Cilj ovog rada je bio da se ispita uticaj veličine čestice aktivne supstance(simvastatina) na *in vitro* oslobađanje simvastatina iz tableta sa trenutnim oslobađanjem.

Simvastatin je beo ili skoro beo kristalni prašak, gotovo nerastvoran u vodi (0.03mg/ml). U ispitivanju su korišćene tri serije uzoraka simvastatin tableta sa različitim veličinama čestica (različit granulometrijski sastav) aktivne supstance, proizvedene od strane različitih proizvođača. Tablete simvastatina 20mg su izrađene tehnikom prekompresije i sve dobijene tablete imale su slične fizičke karakteristike (prosečna masa, dijametar, tvrdoća, habanje itd).

Ispitivanje brzine rastvaranja je izvedeno u aparaturi sa lopaticama (aparatura II ,USP 27) u 900ml medijuma za ispitivanje (0.5% natrijumlauril sulfat u 0.01M natrijumfosfatnom puferu), pH=7±0.1, T=37±0.5°C na 50rpm. Sadržaj oslobođenog simvastatina je određen spektrofotometrijski na 238 nm. Uzorci su uzimani na svakih 5 minuta u toku 30 minuta ispitivanja i dobijeni rezultati za prvu seriju simvastatin tableta sa veličinom čestica d(0.9)=28µm su bili: 39.84%, 87.97%,91.72%, 93.97%,95.49%,99.72%. Rezultati dobijeni za drugu seriju sa veličinom čestica d(0.9)=11µm bili su: 44.21%, 97.77%,99.32%, 100.35%,100.31%, 100.69%. Za treću seriju tableta sa veličinom čestica d(0.9)=5µm dobijeni su sledeći rezultati: 32.58%, 87.97%,92.19%, 102.51%, 103.39%, 100.98%.

Poređenje profila brzine rastvaranja simvastatina iz ispitivanih tableta ukazuje da razlika u veličini čestica simvastatina nema značajan uticaj na brzinu njegovog oslobađanja iz tableta.

EFFECT OF PARTICLE SIZE ON DISSOLUTION RATE IN SIMVASTATIN TABLETS

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The low solubility is one of the limiting factors for solid dosage forms dissolution rate. The particle size and surface area are two very important factors influencing on dissolution rate and potentially on bioavailability. The focus of this investigation was an evaluation of simvastatin particle size influence on *in vitro* release behavior of simvastatin from immediate release tablets.

Simvastatin is white or almost white, crystalline powder, practically insoluble in water (0.03mg/ml). In this study tree different series of simvastatin tablets were used with different particle size of active substance made by different manufactures. The tablets containing 20mg of simvastatin were made by precompression technique. All of them got similar physical characteristics such as average weight, diameter, hardness, friability etc.

The dissolution test was preformed according to the paddle method (apparatus II ,USP 27) in 900ml of dissolution medium (0.5% of sodium lauryl sulfate in 0.01M sodium phosphate buffer), pH=7±0.1, T=37±0.5°C at 50rpm. The simvastatin content was determined spectrophotometrically at 238 nm. The samples were taken every 5 minutes for 30 minutes of dissolution test and the results for the first series of simvastatin tablets with particle size d(0.9)=28μm were: 39.84%, 87.97%,91.72%, 93.97%,95.49%,99.72%. For the second series d(0.9)=11μm: 44.21%, 97.77%,99.32%,100.35%,100.31%, and 100.69%. The third series with particle size d(0.9)=5μm: 32.58%,87.97%,92.19%,102.51%,103.39%,and 100.98%.

The results obtained indicate that particle size of simvastatin in tested tablets had no significant impact in dissolution profiles in simvastatin tablets