TERMIJSKE METODE U ISPITIVANJU STABILNOSTI LORATADIN TABLETA

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Aktivna supstanca, Loratadin (etil estar 4-(8-hloro-5,6-dihidro-11*H*-benzo-[5,6]ciklohepta-[1,2-b]piridin-iliden)-1-piperidinkarboksilne kiseline), i preparat Loratadin tablete (antihistamink za sistemsku primenu), kondiconirani su tri meseca na temperaturama od: 4, 40, 50 i 60 ^{o}C, u atmosferi: azota, vazduha i čistog kiseonika. Stresni uslovi, (temperatura, kao i različite atmosfere), su izabrani tako da se eventualni proces degradacije ubrza, odnosno ustanovi uticaj atmosfere na proces razgradnje. Kondicionirani uzorci su ispitivani termijskim metodama, diferencijalnom skenirajućom kalorimetrijom (DSC) i termogravimetrijskom analizom (TGA), sa ciljem uvođenja ovih tehnika, kao dopunskih, u analizi stabilnosti lekova.

DSC ispitivanje uzoraka Loratadin praha pokazuje da nema razlike u temperaturi topljenja u zavisnosti od temperature, odnosno atmosfere u kojoj su uzorci kondicionirani (133,4-133,8^{o}C). U uzorcima Loratadin tableta temperatura topljenja (130,0-131,6^{o}C) je snižena u odnosu na temperaturu koja odgovara Loratadin prahu, jer su prisutne i pomoćne supstance, koje se ponašaju kao primese, pa samim tim snižavaju temperaturu topljenja Loratadina. Druga dva endotermna pika koja se javljaju potiču od drugih komponenata. Oblik TGA termograma Loratadin tableta je stepenast, zavisi od pomoćnih komponenti koje ulaze u sastav tableta. Kako se koja komponenta razgrađuje, tako dolazi do gubitka mase koji odgovara udelu te jedne ili više komponenata koji se razgrađuju na toj temperaturi. Kod Loratadin praha kriva gubitka mase ima jedan nagli pad, i skoro se sav uzorak razgradi na 500 ^{o}C. Atmosfera kondicioniranja uzoraka nema nikakav uticaj na rezultate dobijene TGA analizama. S obzirom da vrednosti temperatura topljenja, kao i gubitaka mase na određenim temperaturama, i odgovarajući oblici krivih termograma, nisu zavisili od atmosfere kondicioniranja, termijske metodele su pokazale dobru stabilnost Loratadin praha, kao i Loratadin tableta. Rezultati ovih ispitivanja su potvrđeni praćenjem sadržaja aktivne materije u svim ispitivanim uzorcima, metodom visoko efikasne tečne hromatografije (HPLC).

THERMAL ANALYSIS IN STABILITY EXAMINATIONS OF LORATADIN PELLETS

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Active substance, Loratadin (4-(8-Chloro-5,6-dihydro-11*H*-benzo-[5,6] cyclohepta-[1,2-b]pyridin-ylidene)-1-piperidinecarboxylic acid ethyl ester), and drug Loratadin pellets (antihistamine), were aged for three months at: 4, 40, 50 i 60 ^{o}C, in the sorroundings of: nitrogen, air and pure oxigen. Stress conditions, (temperature, as well as various surroundings), were chosen in such way to accelerate the degradation process, respectively to found the influence of surrounding on the degradation processes. Aged samples were analysed by thermal methods, by differencijal scanning calorimetric (DSC) and thermogravimetric (TGA) methods, with the aim of introducing this technics, as additional, in drug stability analysis.

DSC examinations of Loratadin powder samples pointed out the independance of the melting temperatures (Tm) from the aging temperatures and surroundings (133,4 - 133,8^{o}C). The samples of Loratadin pellets have lower Tm (130,0 - 131,6 ^{o}C) comparing to Tm of Loratadin powder, becouse of the presence of additional components. They act as impurities decreasing the Tm of Loratadin powder. The additional two endothermic peaks originate from other components. Neither the temperature nor the surrounding of aging have the influence on Tm of the tabllet samples. The shape of TGA thermogram of Loratadin tabllets has few mild weight losts, depending of the constituents of the composition. Particular weight lost on the certain temperature corresponds to the weight percents of the ingredient which decompose on that temperature. The shape of Loratadin powder TGA thermogram has one sudden weight lost and almost whole sample is decomposed at 500 ^{o}C. The surrounding of aging has no influence on obtained TGA data.

Regarding that the values of melting temperatures, weight lost on particular temperatures, and corresponding shapes of the curves, were independent of the surroundings, thermal methods have pointed out the good stability of Loratadin powder, as well as Loratadin pellets. The results of this examinations were confirmed by high performance liqued chromatography (HPLC). The content of active substance in aged samples prove good stability of Loratadin powder, as well as Loratadin pellets.