SHORT COMMUNICATIONS

DEVELOPMENT AND CHARACTERIZATION OF CANDESARTAN NANOCRYSTALS

ABSTRACT

Nanotechnology is the latest technology employed in pharmaceutical research. Candesartan is an antihypertensive drug belonging to the class of angiotensin II receptor blockers. Candesartan is slightly soluble in water and exists in crystalline form. Candesartan nanocrystals were prepared by the nanoprecipitation method to increase the dissolution rate. Pluronic F-68 and PVP K-30 were used as stabilizers. X-ray diffraction studies showed that the crystalline nature was restored. The SEM textures were found to have a cubic crystal shape. The zeta potential showed moderate stability. *In vitro* drug diffusion profiles showed a maximum drug release of up to 95.62%. No significant difference was observed from *in vitro* drug release study and drug content after stability studies. It was concluded that the optimized formulation increased the dissolution rate and was reproducible.

Keywords: Candesartan, nanocrystals, SEM, zeta potential, nanoprecipitation

INTRODUCTION

Candesartan is an antihypertensive drug belonging to the class of angiotensin II receptor blockers[1, 2]. The problem accompanying with this drug is poor solubility in water and availability in crystalline form. The formulation of nanocrystals leads to particle size reduction and thus leads to increase the surface area thereby increasing the dissolution rate. Nanocrystals are nanoparticles composed of 100% pure drug with very less concentration stabilizers, without any matrix material[3]. The purpose of this research studies were to develop and characterize candesartan nanocrystals to increase drug solubility[4].

MATERIALS AND METHODS

Candesartan drug gift sample was procured from Torrent Pharma, Gujarat. Polyvinyl pyrrolidone K-30 & Pluronic F-68 stabilizers were collected from Hi Media, Mumbai. Pre-formulation studies were carried out by using FTIR used for qualitative identification of substances either in pure form or in the form of mixture. FTIR study was carried out using Tensor 37 (Bruker Optics[5].) All the samples were run at (2θ) min^{-1} from 10° to 60° (2θ). The X-ray diffraction was performed using Smart Lab Diffractometer of Rigaku make. Formulation of candesartan nanocrystals was prepared by using nanoprecipitation method[4].

Evaluation of candesartan nanocrystals

A Brookhaven instrument was used to measure the particle size, polydispersity index and zetapotential of the nanocrystals (Particle size analyser, S90 plus)[6]. The polydispersity index, which ranges from 0.1 to 1.06, is a measure of particle homogeneity. SEM images of the prepared nanocrystals were examined using SEM[7] (Carl Zeiss FESEM model: Ultra 55 USA) at 10 KX and 100 KX magnifications. The zeta potential was calculated. The percent yield was calculated by comparing the weight of the final product after lyophilisation to the total weight of the drug and excipients used in nanocrystal preparation. A UV spectrophotometer set to 212.0 nm was used to determine the drug content. UV-Vis spectrophotometer at 212 nm with phosphate buffer pH 6.5 was used to analyse *in vitro* drug diffusion studies. Kinetics models were used to understand the drug diffusion data. All formulations were packed in small vials sealed with aluminium foil, stored in a refrigerator at 2-8 °C for 6 months and also kept at 30±2 °C with 65±5 % RH in stability chamber. Critical quality attributes such as *in vitro* drug diffusion studies and drug content were evaluated after stability studies.

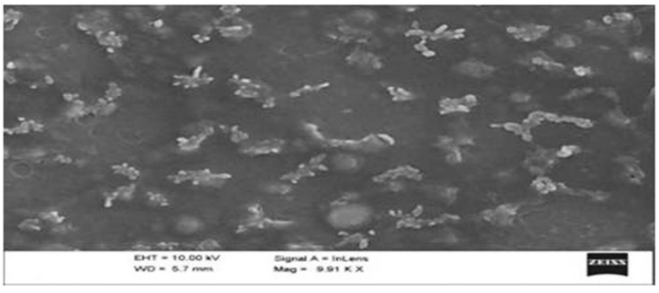

Fig. 1: SEM image of nanocrystals (F8) at magnification 9.91K X

RESULTS AND DISCUSSION

Candesartan has FT-IR peaks at 3049.48 cm^{-1} as a result of C-H aromatic stretching, 3398.87 cm^{-1} owing to

Table I: Physicochemical characterization of prepared formulations

Formulation code	Drug content %	% Yield	Particle size (nm)	Polydispersibility Index
F1	75.8±1.60	80.21	462.16	0.131
F2	79.13±1.3	90.65	224.23	0.215
F3	76.26±1.9	95.3	318.45	0.201
F4	67.46±1.8	82.72	335.51	10.175
F5	78.6±1.4	91.63	201.29	0.151
F6	72.13±1.3	86.26	197.75	0.127
F7	66.93±1.8	92.24	271.67	0.159
F8	82.33±0.7	96.52	151.02	0.129
F9	75.86±1.4	90.78	498.81	0.246

NH stretching, 3541.67 cm^{-1} due to O-H stretching, 1308.34 cm^{-1} as a result of C-N stretching, with stabilizers the same characteristic peaks as observed from the spectra. X-ray powder diffraction studies of the drug alone and with stabilizers have shown the sharpest crystalline peak. Nanocrystals size was found to be in the range of 151.02 to 498.81 nm. The PDI was found to be in the range of 0.127 to 0.246, as shown in Table I. SEM studies revealed that the nanocrystals were found to be needle type crystalline shape, as shown in Fig. 1. Zeta potential of Formulation F8 was found to be -42.47mV. The percentage yield was found to be in the range of 80.21 % to 96.52 %. Drug content was found in the range of 66.93 to 92.33%. Experiments on *in vitro* drug release profiles of pure drug and candesartan formulation, showed, that the maximum percentage of drug release was observed for F8. Drug release follows the zero order and Korsemeyer-Peppas model. The "n" values exhibits a non-fickian release pattern. No significant changes were observed after stability studies, which were executed under different conditions, i.e. 2-8 °C, 30±2 °C with 65±5 % RH for 6 months. It was clearly evident from the drug release profiles that the diffusion behaviour of formulation F8 was increased up to 95.62 % using nanoprecipitation method.

CONCLUSION

Candesartan nanocrystals (F8) successfully increased solubility by using the nanoprecipitation method. PVP K-30 and Pluronic F-68 acted as stabilizers. The prepared product was found to be simple to make, stable and reproducible.

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