SUMMARY

Optimizing the Spray-Drying Parameters of a Formulation of Nanoparticles-In-Microparticles System (NiMS) of Acetazolamide

Introduction

In recent years, significant consideration has been focused on the expansion of novel drug delivery systems (NDDS). The reasons behind the development of NDDS include drug delivery to the site of action without any significant immunogenicity reactions, biological inactivation, or the potential side effect to the critical tissues, such as liver, lungs, bone marrow, kidney, etc. The main goal in developing NDDS is to advance the therapeutic efficacy and safety of existing drugs by altering the biodistribution pattern of the drugs, reducing the amount and frequency of dosing.

Objective

In the present study, the goal was to formulate Nanoparticles-in-Microparticles System (NiMS) of Acetazolamide (ACZ) by spray drying, and the objective behind the study was to investigate the effect of spray-drying parameters, i.e., inlet temperature and feed rpm on the percentage yield, entrapment efficiency, loading capacity, and particle size.

Experimental Methods

In the current research, NiMS were prepared using the ionic gelation method. In this method, chitosan (0.5% w/v) was dissolved in 0.3% v/v glacial acetic acid. 500 mg of the ACZ was dissolved in it. The solution of sodium tripolyphosphate (NaTPP) (0.2% w/v) was prepared in distilled water. The NaTPP solution (32 to 50 ml) was added to the chitosan solution (70 to 100 ml) dropwise stirring continuously. The suspension was spray dried (JISL, Navi Mumbai) at a feed rate (30, 50, and 80 rpm) and at specified temperature (50°C, 100°C, and 160°C) to get the free-flowing powder. The aspirator blower capacity was 118 Nm^3/hr, and the nozzle size was 0.7 mm with auto deblocking device. To study the effect of various formulation variables, NiMS were prepared as shown in Table 1. In the current research, using Agilent Technologies 1200 series, Germany [Quaternary pump, a stainless-steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (3 μm), UV detector dual wavelength]. HPLC analysis was performed utilizing the parameter as shown in Table 2.10 Initially, the column was washed with a mixture of acetonitrile and methanol with varying flow rate for half an hour and decreasing ratio of methanol. After that, the column was saturated with 1.0 ml/min of flow rate for 30 mins and mobile phase. After that, the standard drug dilution samples (5 μl) were injected and run for 10 min. The drug retention time was found between 1.5 to 2.0 min.

Table 1. Formulation of NiMS (NiMS-1 to NiMS-5)

Batch No.	Inlet Temperature (°C)	Feed rpm	Chitosan (ml)	NaTPP (ml)
NiMS-1	100	50	70	32
NiMS-2	100	30	100	50
NiMS-3	160	80	70	32
NiMS-4	50	30	70	32
NiMS-5	160	30	100	50

Results and Discussion

The spray drying technique was used for the conversion of suspensions into solid particles (nanoparticles/microparticles) and no additional drying adjuvant was needed. Sodium tripolyphosphate (NaTPP) is an anion that can form cross-linkage involving ionic interactions between the TPP molecules (negatively charged) and amino group (positively charged) of chitosan. The opalescence indicated the development of particles with a size range of nanoparticles to microparticles with the incorporation of ion TPP to chitosan solution. In spray drying, there are various factors that affect the formulated product, such as inlet temperature, outlet temperature, feed rpm, feed concentration, aspirator rate, nozzle size, etc. Out of these factors, inlet temperature and feed rpm of spray dryer were selected to evaluate and the analysis of entrapment efficiency, loading capacity, percentage yield and particle size of all five formulations were carried out and are tabulated in Table 2. It has been observed that the NiMS-5 have the highest percentage yield (25.8%) with highest entrapment efficiency (17.94%), highest loading capacity (33.2%) and with a smallest particle size of 763 nm. Figure 1 shows the SEM of the NiMS-5 of spray-dried powder. It was found that the particles were of irregular shapes, typically in the range of 2.5 to 3.5 μm. The irregular particles may be attributed. In Figure 2, DSC analysis of NiMS-5 suggested that the entrapment of the nano and microparticles and spray-drying generate a noticeable crystallinity of ACZ and confers a nearly amorphous state to this drug.

Table 2. Characterization of NiMS (NiMS-1 to NiMS-5)

Batch No.	Entrapment Efficiency (%)	Loading Capacity (%)	Percentage Yield (%)	Particle Size (nm)
NiMS-1	4.15±0.03	15.02±0.06	14.54±0.07	1639.7±4.32
NiMS-2	12.68±0.02	24.54±0.04	17.55±0.06	1613.9±7.87
NiMS-3	1.05±0.05	14.69±0.02	10.65±0.05	1908.1±5.12
NiMS-4	1.18±0.03	14.98±0.02	12.02±0.06	3642.03±7.16
NiMS-5	17.94±0.01	33.20±0.01	25.80±0.02	763.66±5.13

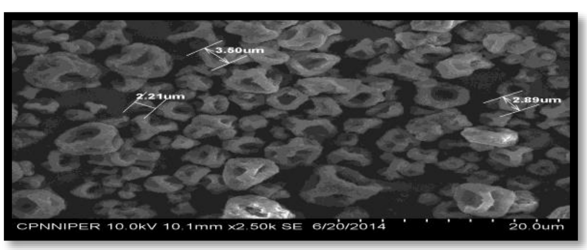

Figure 1. SEM of NiMS-5

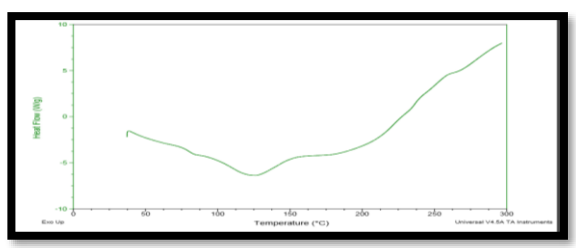

Figure 2. DSC of NiMS-5

Conclusion

It has been concluded that the formulation with higher inlet temperature and lower feed rpm resulted in maximum percentage yield along with entrapment efficiency, loading capacity, and smallest particle size.

Bibliography

1. Li, F.Q., *et al.*, Int J Nanomed, Vol. 6 (1), pg 897, 2011.
2. Pirooznia, N., *et al.*, Int J Pharm, Vol 77, pg 183, 2012.