Influence of Formulation Components on Aerosolization Properties of Isoniazid Loaded Chitosan Microspheres

Aliasgar J. Kundawala\textsuperscript{a}, Vishnu A. Patel\textsuperscript{b}, Harsha V. Patel\textsuperscript{a}, Dhtaglaram Choudhary\textsuperscript{a}

\textsuperscript{a}Indukaka Ipcowala College of Pharmacy, New Vallabh Vidyanagar, Dist. Anand (Gujarat)-388 121, India
\textsuperscript{b}A. R. College of Pharmacy and G H Patel institute of Pharmacy, Vallabh Vidyanagar Dist. Anand (Gujarat)-388 120, India

ABSTRACT
The objective of the present study was to prepare microspheres with small size and good sphericity by spray drying technology using Isoniazid (INH) as model drug, chitosan as encapsulating polymer; lactose and L Leucine as bulking and dispersing agent respectively. Influence of formulation components on physical properties and aerosol performance were studied. The spray dried powders obtained were characterized for morphological characteristics, compatibility using scanning electron microscopy and Differential Scanning calorimetery respectively. Tapped density; bulk density and aerosol properties like Fine particle fraction, mass median aerodynamic diameter etc were also evaluated. The smooth microspheres with particle size ranging between 4 to 6 µm were obtained. The drug content of chitosan microspheres loaded with Isoniazid were in the range of 88 % to 108 %. The drug release studies showed that more than 90% of drug released from the chitosan microsphere matrix within one hour. The fine particle fraction observed between 55 to 67 % which indicate good lung deposition. Results of Fine particle fraction also revealed addition of L Leucine found to enhance powder dispersibility.

Keywords: Isoniazid, dry powder, L Leucine, Andersen cascade impactor, fin particle fraction.

INTRODUCTION
Inhalation therapy is widely employed to deliver drugs to the respiratory epithelium, predominately for the treatment of local disorders such as asthma and chronic obstructive pulmonary disease (COPD), although there is increasing interest in using pulmonary delivery for the administration of systemically-acting macromolecules like inhaled insulin. \textsuperscript{[1]} Pulmonary delivery systems have been widely applied in the treatment of pulmonary-related diseases to reduce side effects of systemic administration and enhance therapeutic effect for targeting delivery. Dry powders inhalers are increasingly used for the aerosol delivery of drug to lung. \textsuperscript{[2]} The development of antituberculosis formulation which can be delivered directly to the lung reduces the dose and frequency of administration resulting in less toxicity and improvement in patient compliance. Targeting the drug to the alveolar macrophage may improve the efficacy and potentially reduce the systemic toxicity of the drug. The high drug concentration localized in the lung may reduce the duration of treatment and prevent the multi-drug resistance of TB. Particulate characteristics such as density, particle size, morphology, surface charge and drug release crucially influence pulmonary delivery. Certain approaches have been employed to improve powder aerosolisation such as mixing the micronized drug with inert carrier particles or modification of particle morphology, particle surface roughness, particle porosity or powder density. \textsuperscript{[3-9]} Micronization of powder has been employed for preparation of respirable powders having particle size less than 5µm. Although strong interparticluate cohesion is a leading cause for poor powder flow property which directly affects aerosol properties. \textsuperscript{[10-11]} Spray-drying technology has potential to incorporate a range of excipients into the formulation to be spray-dried such as bulking agent and dispersibility enhancers (e.g. amino acids) \textsuperscript{[12-14]} to modify the aerosolisation characteristics of the resultant powder. In addition, spray-dried powders that exhibit sustained drug release properties may be generated through the inclusion of drug release modifiers such as hydroxypropyl cellulose, glyceryl behenate and polyactic acid poly lactides. \textsuperscript{[15-17]} The particle size of the microspheres prepared by the spray-drying method ranges from a few...
microns to several tens of microns and had a relatively narrow distribution.\[^{[18]}\] Chitosan (CS), a polysaccharide derived from deacetylation of the naturally occurring polymer chitin, is a promising excipient that can be employed in a wide range of applications, including sustained release preparations. Indeed, this compound has received considerable attention for the formulation of spray-dried powders for nasal drug delivery. It has also been studied for inhalation drug, due to its biodegradability, biocompatibility and low toxicity.\[^{[19-21]}\]

There are number of advantages to developing sustained release formulation using chitosan for pulmonary drug delivery, given that chitosan not only act release modifier but also possess a mucoadhesive properties. Chitosan microspheres are most widely studied drug delivery systems for the controlled release of drugs viz. antibiotics, anti-hypertensive agents, anti-cancer agents, anti-inflammatory agents, proteins, peptide drugs and vaccines.\[^{[22]}\]

The purpose of the present study was to prepare chitosan microspheres by spray drying technique using L Leucine as a dispersing agent. Formulation factors were investigated for physical properties such as particle size, surface morphology and densities of chitosan microspheres. The influences of various particulate parameters were investigated in relation to aerosol performance and in-vitro drug release characteristics. The aim was to prepare chitosan microspheres loaded with Isoniazid as pulmonary delivery system which might enhance efficacy of Isoniazid for local antitubercular activity.

**MATERIAL AND METHODS**

Isoniazid was obtained as a gift sample from Strides Acrolab, low molecular weight Chitosan was generously provided by C E Roeper GmbH, Hamburg, and Germany. α, mono lactose was received as gratis sample from Meggle, Wasserburg GmbH and Co, Germany. L Leucine was purchased from Loba Chemicals India. All Other chemicals and solvents used were of analytical grade.

**Preparation of spray dried microspheres**

Microspheres were prepared by spray dried technique. In brief, 1% w/v Chitosan solution was prepared by dissolving chitosan in 300ml of 1% acetic acid solution at 50°C by mechanical stirring. Isoniazid alone or in combination with lactose and L Leucine was dissolved in previously prepared and filtered chitosan solution. After adjusting the pH at 5, the drug chitosan solutions was stirred mechanically at 500 rpm for 20 minutes and then spray dried by LabUltima spray drier (LU-222 advanced. Mumbai, India) with standard 0.7 mm nozzle. The spray drying conditions such as inlet temperature, outlet temperature, pump rate, pressure and aspirator setting were kept at 140°C, 70-80°C, 5 ml/min, 3 kg/cm² and 45 m³/hr respectively.

**Characterization of microspheres**

**Spray dried yield and drug content**

The yield of spray dried product was identified as the percentage of anticipated yields. 10 mg of drug loaded chitosan microspheres were dissolved in 50 ml of 0.1 N HCl. The solution was then passed through 0.22 µm membrane filter (VWR international) and then the drug content was assayed by measuring the absorbance at 264 nm after suitable dilution using UV spectrophotometer. The experiment was carried out in triplicate (n=3) and loading efficiencies were calculated according to following formula,

\[
\text{Loading Efficiency} = \left( \frac{\text{calculated drug content/ theoretical drug content}}{100} \right)
\]

**Scanning electron microscopy**

Surface morphology of spray dried chitosan microspheres were obtained by using scanning electron microscope (ESEM TMP with EDAX, Philips, and Holland). Spray dried powders were mounted onto separate, adhesive coated 12.5 mm diameter aluminum stubs. Excess powder was removed by tapping the stubs sharply and then gently blowing a jet of particle free compressed gas across each. The specimens were examined using EDAX SEM. The SEM was operated at high vacuum with accelerating voltage of 5KV and specimen working distance of 12mm.

**Differential scanning calorimetric characterization**

Differential scanning calorimetry pattern of the samples were obtained using Differential scanning calorimeter (DSC-PYRIS-1, Perkin Elmer,USA). Each sample was heated from 30 to 300°C at scanning rate of 10°C /min. DSC analysis were carried out on blank and drug loaded chitosan microspheres. A physical mixture of the blank microspheres and the pure drug was used as control.

**Particle Size**

The particle size of the spray dried powder was measured by laser diffraction (HELOS particle size analyzer vibro/rodos dry dispersion system: Sympatec gmbh system partikel technik, Clausthal Zelerfeld, Germany). Approximately 100 mg of each powder was used to achieve the required obscuration of 5%, and each sample was measured in triplicate. The data were expressed as the volume weighted mean particle size.

**Powder density and aerodynamic diameter**

The poured density of the spray dried powder was determined by pouring known mass of powder (0.5g) under gravity into a calibrated measuring cylinder and recording the volume occupied by the powder. The tapped density of spray dried powder was determined by volume measurement of tapped mass until no further change a in the powder volume was observed. Measurement was performed in triplicate. Carr’s index values for each spray dried powder were derived from poured density data, according to following equation.

\[
\text{Carr’s Index} = \left( \frac{1 - (\text{bulk density / Tapped density})}{100} \right)
\]

The Carr’s index values gives an indication of powder flow; a value less than 25% indicate a fluid flow, where as values greater than 25% indicates a cohesive powder.\[^{[23]}\]

Theoretical estimation of the particle primarily aerodynamic diameter \(d_{ae}\) was derived from the sizing \((d_{50})\) and tapped density data \((\rho)\) according to following equation.\[^{[24]}\]

\[
d_{ae} = d \sqrt{\frac{\rho}{\rho_1}} \quad \text{Where } \rho_1 = 1 \text{ g cm}^{-3}
\]

**In vitro drug release studies**

Dissolution testing was performed on a USP Type II tablet dissolution test apparatus (VEEGO) at a stirring speed of 150 rpm. A dialysis membrane (Himedia, LA 401) was cut into equal pieces of about 5 cm × 3 cm and pre-treated as suggested by the manufacturer. Microspheres (20 mg) were accurately weighed out on the pre-treated dialysis membrane and sealed with clips. The pouch thus formed was attached to the paddles of the apparatus using cotton threads over the clips. 900 ml of phosphate-buffered saline at pH of 7.4 was used as a dissolution medium to ensure sink conditions. Samples were withdrawn for analysis at specified time intervals and assessed for Isoniazid content by UV
spectroscopy (Shimadzu UV-1700, Japan) at 265 nm. Each dissolution experiment was performed in triplicate (n=3).

Characterization of Aerosol Performance

*In vitro* aerosolization properties of spray dried powders were investigated by using Andersen cascade impactor with preseparator (Graseby-Andersen, Atlanta, GA, USA) operating at air flow rate of 60 L/min. A size 2, HPMC capsules were obtained from Cipla Ltd, Mumbai. The capsules were filled dry chitosan microspheres equivalent to 10 mg of isoniazid. Ten capsules were shot for each impaction at inspiration rate of with 60 L/min for an inhalation time of 10 seconds. The powder deposited in induction port, preseparator, individual impaction plates and remaining in capsule and inhaler device was recovered by immersing each part in 0.1 N HCl. Drug concentration was determined by UV spectrophotometer (Shimadzu Corporation, Japan) after suitable dilutions by immersing each part in 0.1 N HCl. Drug concentration was determined by UV spectrophotometer (Shimadzu Corporation, Japan) after suitable dilutions.

For each sample *Emitted Dose (ED)*, *Fine Particle Fraction* (FFP), experimental Mass Median Aerodynamic Diameter (MMADae) and Geometric Standard Deviation (GSD) was calculated. The emitted dose (ED) defined as the percentage of total loaded powder mass exiting the capsule. The fine particle fraction (FPF), which is the total percentage deposition at stages 2–7 of the cascade impactor, was used to evaluate the aerosol performance. A higher fine particle fraction deposition is thought to indicate a higher in vitro aerosol performance. The mass median aerodynamic diameter (MMADae) of the powders was also derived, defined as the particle size at the 50% mark of a plot of cumulative fraction vs. effective cut-off diameter. The geometric standard deviations (GSD) were obtained by the square root of the particle size at 84% cumulative divided by the 16% cumulative.

RESULT AND DISCUSSION

Preparation of chitosan microspheres

The micro encapsulation technique used for production of entrapped drug particles is usually efficient not only for modification of drug release rate but also for temporary isolation of the active compound from surrounding environment. To optimize these functions, chitosan was used for encapsulation of drug as well as the particulate carrier for pulmonary delivery of Isoniazid. Chitosan is currently receiving a great deal of interest in pharmaceutical industry. Spray drying technique is a well known process which is used to produce dry powders, granules or agglomerates from the drug excipients prepared as suspension, emulsion or solutions. [23] The chitosan microspheres produced by spray drying method showed good narrow size distribution ranging from 4.27 µm to 6.01 µm. Since Isoniazid is a very water soluble drug the attempt was made to control the drug release from the chitosan matrix. The L Leucine was used as antiadherant to improve the aerosol dispersion of chitosan microspheres. α-mono lactose was used as bulk forming agent.

Spray dried yield and drug content

The spray dried yield of chitosan microspheres (yield, drug loading and encapsulation efficiency) loaded with the drug is presented in the Table 1. The yield percentage of the spray dried chitosan microspheres ranged from 16.4 ± 1.3 to 36.8 ± 2.5 %. The addition of lactose and L Leucine in combination helped in getting higher yield by increasing the total content of mixture for spray drying. The chitosan microsphere yield without the bulking and dispersing agent ranged between 16.4 ± 1.3 to 26.1 ± 2.1 %. The relative lower yields were due to both the low quantity of the feed and the fact that the structure of the apparatus made it impossible to collect the smallest and lightest particles.

Table 1: Composition and characterization of spray dried chitosan microspheres (n=3)

<table>
<thead>
<tr>
<th>Dry powders</th>
<th>Drug % w/w</th>
<th>Chitosan % w/w</th>
<th>L Leucine (mg)</th>
<th>Lactose (mg)</th>
<th>% Yield</th>
<th>% Loading Efficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.20</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>16.4 ± 1.3</td>
<td>89.97 ± 2.86</td>
</tr>
<tr>
<td>F2</td>
<td>0.30</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>18.3 ± 1.7</td>
<td>95.32 ± 2.19</td>
</tr>
<tr>
<td>F3</td>
<td>0.40</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>23.8 ± 2.2</td>
<td>94.44 ± 2.01</td>
</tr>
<tr>
<td>F4</td>
<td>0.50</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>26.1 ± 2.1</td>
<td>92.90 ± 2.01</td>
</tr>
<tr>
<td>F5</td>
<td>0.50</td>
<td>-</td>
<td>- 500</td>
<td>-</td>
<td>29.8 ± 1.9</td>
<td>107.23 ± 2.58</td>
</tr>
<tr>
<td>F6</td>
<td>0.50</td>
<td>500</td>
<td>-</td>
<td>-</td>
<td>30.7 ± 1.1</td>
<td>89.53 ± 1.96</td>
</tr>
<tr>
<td>F7</td>
<td>0.50</td>
<td>250 250</td>
<td>-</td>
<td>-</td>
<td>34.9 ± 1.5</td>
<td>88.56 ± 2.24</td>
</tr>
<tr>
<td>F8</td>
<td>0.50</td>
<td>335 165</td>
<td>-</td>
<td>-</td>
<td>33.8 ± 3.1</td>
<td>87.34 ± 2.12</td>
</tr>
<tr>
<td>F9</td>
<td>0.50</td>
<td>375 125</td>
<td>-</td>
<td>-</td>
<td>36.8 ± 2.5</td>
<td>88.11 ± 2.81</td>
</tr>
<tr>
<td>F10</td>
<td>0.50</td>
<td>400 100</td>
<td>-</td>
<td>-</td>
<td>36.5 ± 3.3</td>
<td>93.62 ± 2.80</td>
</tr>
</tbody>
</table>

Table 2: Aerosol properties of spray dried chitosan microspheres (n=3)

<table>
<thead>
<tr>
<th>Dry powders</th>
<th>Particle size D50 g/ml</th>
<th>Tapped density g/ml</th>
<th>Carr’s index %</th>
<th>MMADae µ</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>5.65 ± 0.31</td>
<td>0.294 ± 0.02</td>
<td>42.2</td>
<td>3.06 ± 0.16</td>
</tr>
<tr>
<td>F2</td>
<td>5.80 ± 0.29</td>
<td>0.245 ± 0.01</td>
<td>47.3</td>
<td>2.87 ± 0.14</td>
</tr>
<tr>
<td>F3</td>
<td>6.01 ± 0.52</td>
<td>0.230 ± 0.02</td>
<td>45.4</td>
<td>2.88 ± 0.21</td>
</tr>
<tr>
<td>F4</td>
<td>6.21 ± 0.43</td>
<td>0.289 ± 0.02</td>
<td>42.6</td>
<td>2.80 ± 0.23</td>
</tr>
<tr>
<td>F5</td>
<td>4.58 ± 0.11</td>
<td>0.409 ± 0.03</td>
<td>39.5</td>
<td>2.45 ± 0.06</td>
</tr>
<tr>
<td>F6</td>
<td>4.87 ± 0.24</td>
<td>0.288 ± 0.03</td>
<td>31.2</td>
<td>2.06 ± 0.15</td>
</tr>
<tr>
<td>F7</td>
<td>5.46 ± 0.42</td>
<td>0.271 ± 0.02</td>
<td>36.1</td>
<td>2.42 ± 0.24</td>
</tr>
<tr>
<td>F8</td>
<td>4.45 ± 0.31</td>
<td>0.241 ± 0.03</td>
<td>34.9</td>
<td>2.18 ± 0.27</td>
</tr>
<tr>
<td>F9</td>
<td>4.40 ± 0.26</td>
<td>0.238 ± 0.04</td>
<td>36.2</td>
<td>2.14 ± 0.19</td>
</tr>
<tr>
<td>F10</td>
<td>4.27 ± 1.21</td>
<td>0.196 ± 0.08</td>
<td>32.3</td>
<td>2.08 ± 0.59</td>
</tr>
</tbody>
</table>

Table 3: Summary of aerosol deposition data of spray dried chitosan microspheres of selected formulations (n=3)

<table>
<thead>
<tr>
<th>Dry powders</th>
<th>Emitted dose (ED) %</th>
<th>FPF</th>
<th>MMADae (µ)</th>
<th>MMADae (µ)</th>
<th>GSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>F4</td>
<td>84.6</td>
<td>54.83</td>
<td>2.80 ± 0.23</td>
<td>3.85</td>
<td>2.44</td>
</tr>
<tr>
<td>F5</td>
<td>92.1</td>
<td>59.81</td>
<td>2.45 ± 0.06</td>
<td>3.64</td>
<td>2.29</td>
</tr>
<tr>
<td>F6</td>
<td>93.3</td>
<td>61.12</td>
<td>3.11 ± 0.15</td>
<td>3.48</td>
<td>2.80</td>
</tr>
<tr>
<td>F7</td>
<td>93.7</td>
<td>65.44</td>
<td>2.42 ± 0.21</td>
<td>3.44</td>
<td>2.59</td>
</tr>
<tr>
<td>F10</td>
<td>94.2</td>
<td>66.52</td>
<td>2.08 ± 0.59</td>
<td>2.71</td>
<td>1.92</td>
</tr>
</tbody>
</table>

*FPF = fine particle fraction, MMADae = theoretical mass median aerodynamic diameter, MMADae = Mass median aerodynamic diameter and GSD = Geometrical standard deviation*

The % yield of spray dried microspheres was found to be increased when the drug concentration increased from 20 to 50% w/w. Analysis of Isoniazid content of the spray dried powder indicated that the drug loading ranged from 88.56 ± 2.24 to 107.23 ± 5.88. However, slight yellowing of the
chitosan powders was observed on storage; this may be due to acid hydrolysis of lactose into glucose monosaccharide by residual acetic acid. \[27\]

**Fig. 1:** Scanning electron micrograph of A) blank chitosan microspheres without additives B) drug loaded chitosan microspheres without additives C) chitosan microspheres with L Leucine and Lactose combination (ratio 4:1)

**Scanning electron microscopy [SEM]**

Scanning electron microscopy was used to visualize the particle diameter, structural and surface morphology of the spray dried powder. Photomicrograph of chitosan loaded drug particles showed regular spherical particle with a diameter less than 10µm. The unloaded chitosan microspheres had comparatively smooth surface to drug loaded microspheres as shown in Fig. 1(A). The chitosan microspheres loaded with Isoniazid exhibited smooth with irregular depression. The aggregation of chitosan microspheres was also observed in micrograph that may be the result of drying conditions in spray drying process as seen in Fig. 1(B, C). The optical microscopy at 100 X also indicates the aggregation formation of chitosan microspheres as shown in Fig. 5.

**Differential scanning calorimetric characterization**

DSC thermograms of pure drug, chitosan microspheres and physical mixture, D1, D2 and D3 shown in Fig. 2, these result indicate that the pure drug D1 has shown endothermic peak at 173.27°C, which is due to the melting of drug. The thermograms of D2 has shown a slightly lesser intense peak at 172.197°C, the peak may be concentration dependent as it was in a physical mixture. A broad peak at 125°C in the thermogram of D3 is because loss of associated water. However, sharp peak has not appeared at 173°C in thermogram D3 indicating the drug was in amorphous and complex form with the polymer, chitosan.

**Fig. 2:** DSC thermogram of pure drug [D1], physical mixture with chitosan [D2] and chitosan microspheres [D3]

**Particle size analysis**

Laser diffraction data related to particle size analysis are presented in Table 2. The particle size of each spray dried powders was less than 10 µm and showed \(D_{50}\) values for smallest to largest particle ranging from 4.27± 1.21 µm to 6.21 ± 0.43µm. It is interesting to note that the larger sized particles may be resulted due to the higher chitosan concentration i.e. 1% w/v employed and secondly may be due to the powder aggregation. The aggregation was confirmed from SEM micrographs, where chitosan microspheres found to show aggregation of particles. The particles were seemed to be below <5 µm. as seen in Fig. 1(B, C). The result of optical microscopy and SEM also support for the larger particle size due to aggregation of
formulation resulted in faster dissolution greater than 90% Isoniazid showed some resistance to release. All the very fast within 5 minutes. Chitosan microspheres loaded powder dissolution testing was used to provide dissolution profile pure drug and the spray-dried chitosan microspheres. The Isoniazid as pure drug found to get into the dissolution medium. The faster drug release also attributes towards the small diffusion path. Several investigators dealing with lower to higher molecular weight chitosan reported that increasing the amount of chitosan and molecular weight increases the thickness of this diffusion layer, resulting in greater retention of drug release. In our studies, we maintained a constant amount of chitosan in the formulations i.e. 1 % w/v chitosan concentration.

Aerosol performance of spray dried powder

Five selected formulations (F4- F8) were studied for emitted dose (ED), Fine Particle fraction (FPF) and Mass median Aerodynamic Diameter (MMAD ae) using Andersen Cascade Impactor (ACI). The data are displayed in Table 3. All the powders showed high emitted dose greater than 90% except the formulation F4 (84%). The high dispersibility is clearly a reflection of inclusion of L Leucine as a dispersibility enhancer. The ACI mass deposition pattern for all the formulations under test is shown in Fig. 4. The small fraction of deposition in device and throat region suggests good deposition at central region of lung. The capsule and device retention was found to be comparatively higher for formulation F4. The result showed FPF was found to be increasing as the ratio of L Leucine to lactose changed from 1:1 to 4:1. The FPF and emitted dose was increased from 54 to 67 %; and 84 to 95 % respectively. For formulation F10 the % FPF (66.52 %) was marginally higher than the F4 (54.83 %). The improvement of FPF may be result of firstly, reduction in the capsule and device retention and/or secondly due to increase in the powder dispersibility, that is, the amount of fine particles in the aerosol cloud per emitted dose; which is probably because of combined role of their spherical shape, weak Vander Waals forces between them. Higher mass deposition at stage 1- 4 indicated good deposition in central to lower region of lung. This result suggests possibility of delivering fairly large proportion of drug gets deposited to the central region of the lung. The MMAD ae for spray-dried powders were in the range of 3.41 µm to 3.85 µm was slight higher in line with the theoretical estimates of MMAD, ranged between 2.08 µm to 3.15 µm. This was in common with opinions of other investigators who have noted that aerosolisation of spray-dried powders can result in MMAD values much greater than the theoretical estimates of aerodynamic diameter derived from powder density and physical diameter. This behavior may be result of aggregation of particles during aerosolisation or aggregated particles. The difference MMAD, and MMAD ae value indicative of partial individual behavior of spray dried powders rather than particle aggregates during aerosolisation. This may be due to the high proportion of L Leucine in these powders. L Leucine is a particularly hydrophobic amino acid. It’s surfactant like properties may causes L Leucine to migrate to the droplet surface during the rapid drying phase in spray-drying, and hence influence the surface characteristics of the resultant particle, resulting in highly dispersible particles that display optimal aerosolization properties. In addition, researchers have shown that chitosan can enhance the dispersibility of spray-dried powders, and it is feasible
the chitosan is not only acting as a drug release modifier, but also modifies the surface of the particles, decreasing interparticulate cohesion and thereby improving powder dispersibility. These studies on spray dried chitosan microspheres demonstrate that it is possible to generate highly respirable powders that exhibit good aerosolisation properties. It is possible to produce good spherical particles with size less than 10µm with spray drying technique, suitable for inhalation. Incorporation of larger dose is also possible with suitable carrier like chitosan. The chitosan microspheres loaded with Isoniazid was found to possess effective fine particle fraction as well as lower impaction loss and device retention. In our study the incorporation of dispersing agents, L Leucine in different concentration improves the aerosol performance of chitosan microspheres. These spray dried microspheres would be predicted to deposit predominantly in the central and peripheral regions of the lung following inhalation, with minimal oropharyngeal deposition and maximizing the lung deposition efficiency.

REFERENCES