NANOPARTICULATE AEROSOL MANUFACTURING PROCESS

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Introduction

Asthma is a chronic disease affecting the lungs by inflaming and narrowing the airways which causes serious symptoms that affect people's daily life like shortness of breath, wheezing, chest tightness, and coughing. A very common way of application of the aerosols is called Metered Dose Inhalers (MDIs). The MDIs can be either in a solution form or in a suspension dosage form which micronised drug particles be homogenised by dissolved or dispersed with excipients as surfactants, co-solvents etc. and a liquefied gas. The solution or suspension formulation can be stored in a container which must be strong enough to resist the pressure of the liquefied gas and be inhaled through a dose measured valve to the lungs.

In each actuation of the aerosol product, doses should be satified the spesifications in terms of dose uniformity in its shelf life that are claimed by the manufacturer and also satisfy the specified parameters which are defined by the authorised regulations as EMEA, FDA etc.

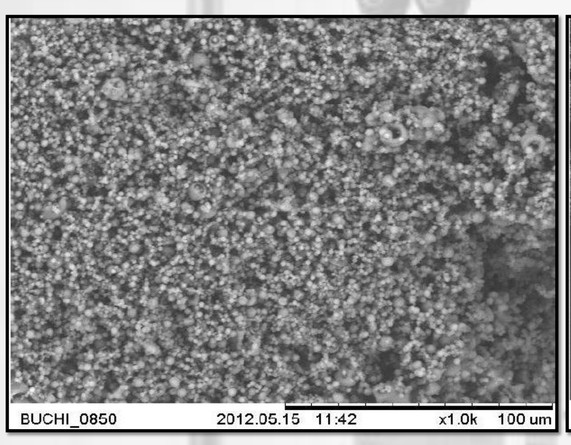
Micronised drug particles for MDI products of aerosol asthma drugs on the market tends to be acculumated on the inner surface of containers, or valve components during their shelf lifes. These micronised particles can also undergo moisture initiated instability where water can promote chemical instability and particle adhesion/cohesion differences in these formulations. This reduces the target quantity in every actuated dose during usage. Also the lumps that are formed because of the moisture sensitivity reduce the shelf life and also the quality of use.

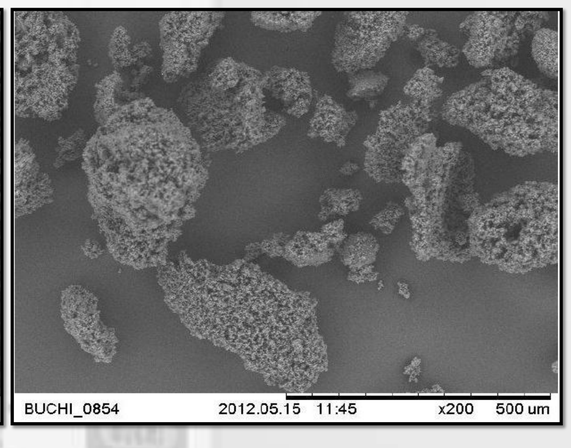
Experimental

The formulation is comprising a nanoparticulate pharmaceutical composition -solid concentration between 0.1 % - 0.5 %- at least one active pharmaceutical ingredient or salt or solvate, at least one propellant or propellant mixture, at least one polymer or polymer combination which has moleculer weight of 190-70000 g/mol.

Formulation trials have been done for these nanoparticulate aerosol formulations in order to obtain desired particle size and morphology which are < 0.5 µm and spherical, respectively.

Spray drying feasibility results of different polymers and their different ratios were compared and encapsulation of active substance in these shell material have been investigated. Sample concentrations were used in 2.5 % - 5 % (as weight basis). Solution or suspension were prepared in water and mixed by mechanical mixer before spraying through the nozzles.





Results & Discussion

Nano spray-drying method encapsulates successfully active ingredient with polymer/ polymer combinations which increases the moisture and gas barrier properties while increasing surface area of dispersed particles in liquefied gas. This leads to improvements on the chemical instability resulted from the moisture in the structure and more cohesive forces which enhances the uniformity of the composition.

Active ingredient were mixed with polymer or polymer combinations in different ratios. A yield of 70-75% is attained with the use of spheric particles with the size between 0,6 and 4 micron. For the process optimization, particle size reduction obtained by the reduction of the sample concentration. In a very small concentrations as 0.1 - 0.5 %, little particles are produced. The lowest particle size with Nano Spray Dryer B-90 is about 300 nm.

Conclusion

While we were devoloping a new aerosol formulation, suprisingly, we founded that if the formulation have specific parameters in terms of particles size distribution rate or morphology which affects obtainable surface area and moisture absorbtion profiles, the resulted formulation have greater suspension stability in its life-time use while comparing its former specifications. This maintains the linear dose uniformity profile for the finished product during patient use and ensures the suspension stability, prevents aggregation.

References

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