Spray dried oleanolic acid powder for pulmonary delivery

HKU PHARMACY

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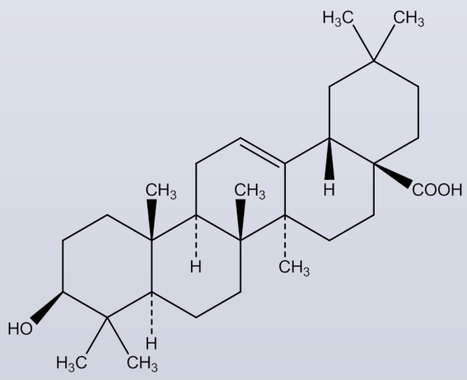
INTRODUCTION

- Oleanolic acid (OA), well known for its hepatoprotective effect [1], has been shown in vitro to be cytotoxic in A549 human non-small-cell lung cancer cell line [2]. Thus it may be potentially useful for lung cancer treatment. Being a BCS Class IV drug, it has low oral bioavailability [3]. Therefore, inhalation is the preferred route of administration for local delivery.

- The aim of this study is to develop an inhalable oleanolic acid dry powder formulation.



Molecular structure of OA

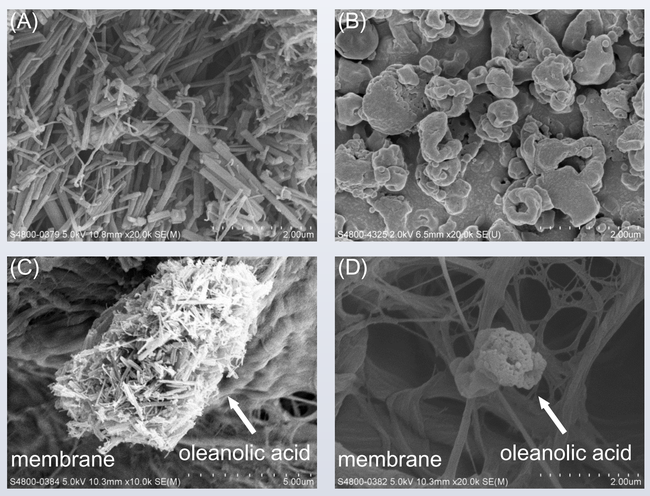
Methods

- OA was spray dried from an acetone solution using a Büchi B-290 Mini Spray Dryer. The spray dried powder was characterized and compared with raw OA.

- Particle morphology was observed by scanning electron microscopy (SEM), whereas aerodynamic performance was measured by dispersion from an Osmohaler™ into a Next Generation Impactor (NGI).

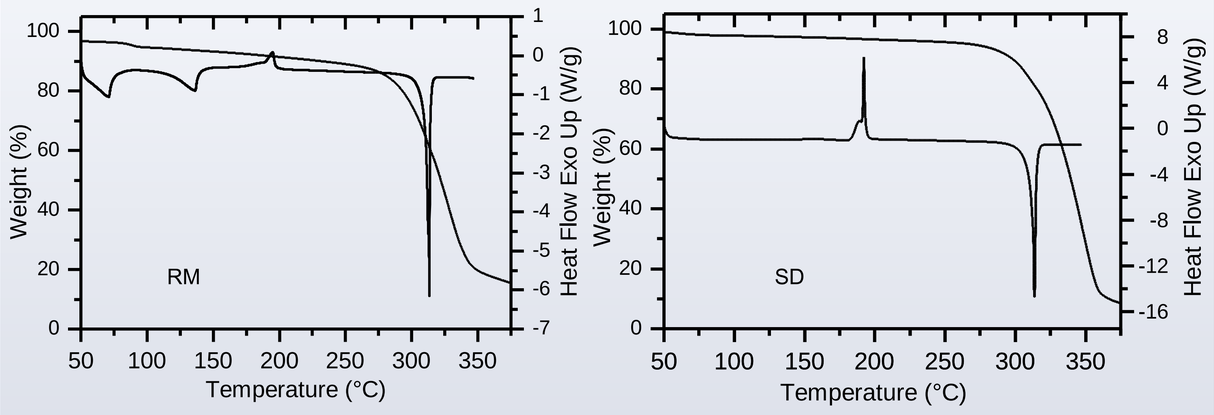
- The solid state of dry powders was studied by thermal analysis and X-ray powder diffraction.

RESULTS



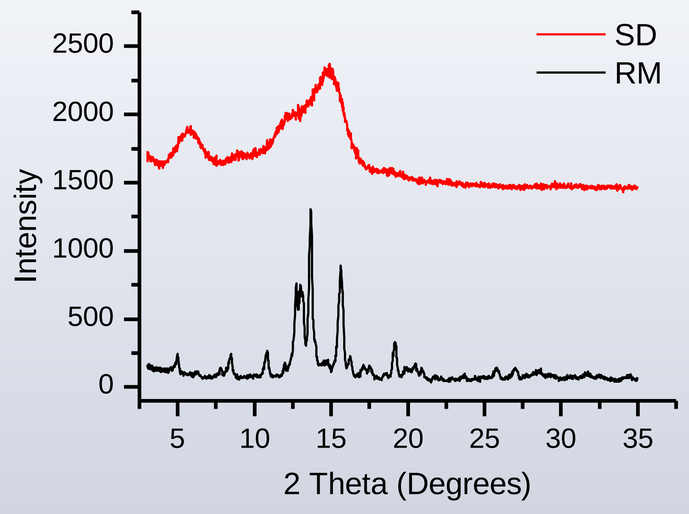
SEM pictures of raw (A, C) and spray dried (B, D) OA particles before (A, B) and after (C, D) dispersion.

- Raw OA particles were needle-like, while the spray dried ones were corrugated spherical of 0.5–3 μm in diameter.
- After dispersion, spray dried OA could be dispersed into primary particles while the raw material seriously agglomerates.

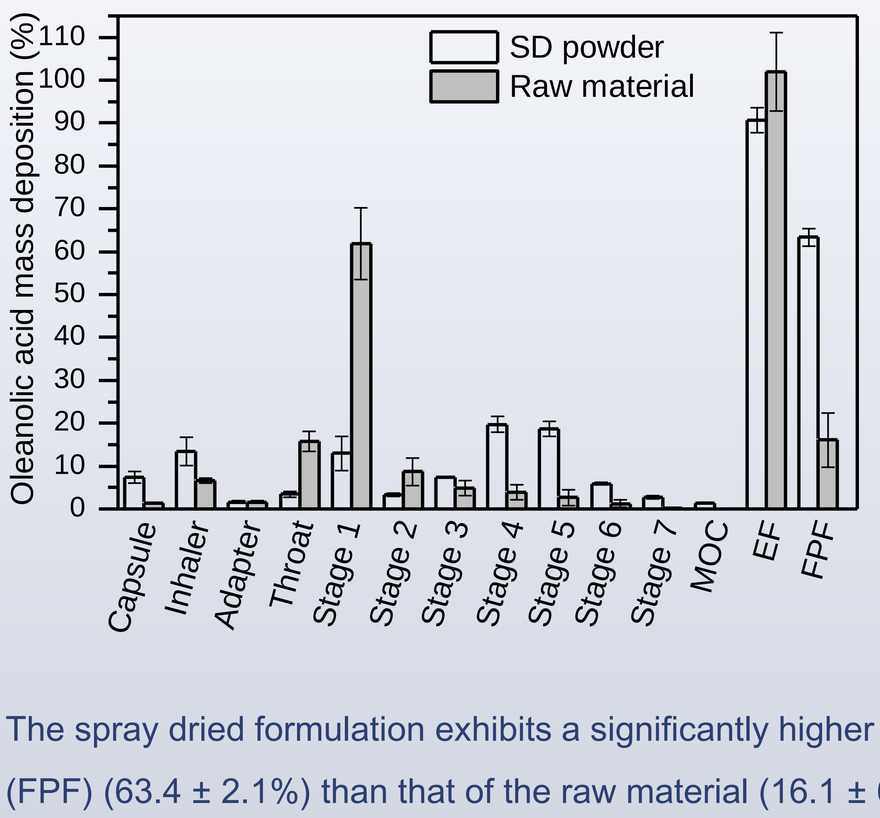


Thermal analysis

- For the SD, the exothermic process was observed at around 190 °C followed by endothermic process at around 310 °C with concomitant weight loss.



- The XRPD pattern of the RM showed crystalline peaks.
- The SD exhibited halo pattern suggesting extremely low crystallinity nearly amorphous.



Aerodynamic properties

The spray dried formulation exhibits a significantly higher fine particle fraction (FPF) (63.4 ± 2.1%) than that of the raw material (16.1 ± 6.3%), indicating an enhanced dispersion efficiency.

CONCLUSION

An OA dry powder formulation was successfully prepared by spray drying. It showed excellent aerosol performance (63% FPF) and may be useful for pulmonary delivery.

References

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(2) Liu, Q.; Liu, H.; Zhang, L.; Guo, T.; Wang, P.; Geng, M.; Li, Y. European Journal of Medicinal Chemistry 2013, 64, 1.
(3) Tong, H. H.; Wu, H. B.; Zheng, Y.; Xi, J.; Chow, A. H.; Chan, C. K. International journal of pharmaceutics 2008, 355, 195.