Powder Technology 266 (2014) 388–395

Contents lists available at ScienceDirect

Powder Technology

journal homepage: www.elsevier.com/locate/powtec

Anti-hygroscopic effect of leucine on spray-dried herbal extract powders

Yue-Xing Chang, Jing-Jing Yang, Rui-Le Pan, Qi Chang, Yong-Hong Liao *

Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences & Peking Union Medical College, 151 Malianwa North Road, Haidian District, Beijing 100193, China

ARTICLE INFO

Article history:
Received 24 October 2013
Received in revised form 8 April 2014
Accepted 15 June 2014
Available online 8 July 2014

Keywords:
Anti-hygroscopic
Leucine
Spray-drying
Herbal extracts

ABSTRACT

The aim of this study was to investigate the anti-hygroscopic effect of l-leucine on the spray-dried powders of three Chinese herbal extracts, namely, Shuang-Huang-Lian (SHL), Mulberry leaves (ML) and *Lucid Ganoderma* (LG). The anti-hygroscopic effects were evaluated in terms of the ability to reduce the adherence to the spray-dryer, to increase the spray-drying yield, to enhance the flowability, to achieve anti-caking effect and to maintain the particle shape and the integrity against moisture stress. The results showed that the presence of leucine conferred to anti-hygroscopic effects on spray-dried SHL powders in a dose dependent manner. When the content of leucine was added to 10% (*w*/*w*) of spray-dried SHL, anti-hygroscopic effects appeared to reach a plateau with an increase in leucine content to 20% not leading to further significant improvement. In addition, the presence of 10% leucine to either ML or LG extracts also resulted in a similar anti-hygroscopic effect. The anti-hygroscopic effect conferred by leucine may be attributed to the enrichment of the excipient on the surface layer, which was indicated by the X-ray photoelectron spectroscopy, rather than the elevated glass transition temperature. The present study demonstrated that the addition of leucine in the feed solution may be a convenient means to achieve the anti-hygroscopicity of spray-dried herbal extract powders.

1. Introduction

Spray-drying has been widely utilized for the preparation of dried herbal extracts due to the high suitability for the continuous production of dry powders or granules from liquid feed in a single step [1–3]. However, many spray-dried herbal extracts, which are generally extracted by water or alcohols, can be hygroscopic and, as a consequence, such extracts may have problems during spray-drying or subsequent formulation processing [1]. The high hygroscopicity of the herbal extracts has been commonly attributed to the presence of the significant amounts of hydrophilic compounds including carbohydrates, glycosides, organic acids, phenolics, amino acids, proteins and so on [1,4].

Apart from the optimization of spray-drying parameters, the addition of excipients, also known as drying aids, to the feed solution is an important means to improve the properties of dried herbal extracts in the spray-drying process. Most commonly used excipients for spray drying of herbal products are high molecular weight carbohydrates such as starch, modified starches, dextrans, maltodextrins, solid corn syrups, gum arabic and cyclodextrins, as well as polymers and colloidal silicon dioxide (SiO_2) [3]. For example, incorporation of dextrans into two Chinese herbal extracts, *Radix ophiopogonis* and *Rhizoma polygonati*, was found to reduce the hygroscopicity of the spray-dried powders [5]. In addition, the combination of multi-excipients may confer to a better improvement in the physicochemical properties of spray-dried powders. Li et al. [6] have tested the effect of different excipients and their combinations on alleviating hygroscopicity and avoiding adherence to the walls during spray-drying. They found that the addition of a combination of SiO_2 and cyclodextrin to the feed solution of liquorice root extract brought about a superior improvement in spray-drying performance to any excipient alone. The role of these excipients in reducing the hygroscopicity of the herbal extract powders and wall adherence in spray-dryer has been assumed to be the ability to increase in the glass transition temperature (Tg) and the effect of the excipients on the Tg of the resultant herbal extracts is dependent on the amount of the excipients and follows the expanded Gordon-Taylor equation [5]. In other words, the anti-hygroscopic effect conferred by the excipients is mainly due to a dilution effect. As a result, the excipients generally require a large quantity (>50% *w*/*w*) to markedly increase Tg, leading to reduce the hygroscopicity of herbal extract powders.

Spray-dried herbal extract powders are generally used as intermediary products for the further preparation of pills, tablets, capsules, granulates and so on. However, many herbal products need to take a large number of tablets or capsules in order to achieve adequate therapeutic effects. To reduce the number of tablets or capsules for each dose, the quantity of excipients should be minimized. Therefore, more effective drying aids are desirable. L-leucine has been determined to be Generally Recognized as Safe (GRAS) by the FDA. In the literature, leucine has been utilized as spray-drying aids to improve the aerodynamic properties of the resultant particles for pulmonary drug delivery when present at an amount of as low as 10% *w*/*w* (e.g. [7,8]). The excipient has also

---

* Corresponding author. Tel./fax: +86 10 57833268.
E-mail address: yhliao@implad.ac.cn (Y.-H. Liao).

http://dx.doi.org/10.1016/j.powtec.2014.06.058
0032-5910/© 2014 Elsevier B.V. All rights reserved.

been found to improve the aerodynamic properties of spray-dried herbal extract, Shuang-Huang-Lian (SHL) [9], but the ability of this amino acid to enhance the spray-drying performance of herbal extracts has yet been established. Therefore, the objective of the present study was to investigate the anti-hygroscopic effects of leucine on the spray-dried herbal extract powders with a view to determining whether the presence of leucine at low amount (10% *w*/*w*) leads to improved spray-drying performance in terms of avoiding adherence to the walls, increasing the spray-drying yields and the anti-caking properties and flowability of the resultant powders. Three Chinese herbal extracts, Shuang-Huang-Lian, Mulberry leaves (ML) and *Lucid Ganoderma* (LG) extracts, have been selected as model herbal extracts for spray-drying in this study.

2. Experimental

2.1. Materials

L-leucine was obtained by Alfa Aescar (Heysham, Lancashire, UK). Cyclodextrins and colloidal silicon dioxide were purchased from Beijing Chemical Works (Beijing, China), respectively. Shuang-Huang-Lian extracts were prepared according to the preparation protocol required in Ministerial Standard-WS3-B-2104-96 [9], whereas Mulberry leaves (ML) and *Lucid Ganoderma* (LG) extracts were kindly gifted by Botanic Century (Beijing, China). Water was purified by reverse osmosis systems (Millipore, Ireland). All other reagents and solvents were supplied by Beijing Chemical Works (Beijing, China).

2.2. Spray-drying of herbal extracts

Herbal extracts were spray-dried using a Buchi B-290 mini spray dryer consisting of a high-performance cyclone and a two-fluid atomizer with a nozzle diameter of 1.5 mm (Flawil, Switzerland) after the preparation of drug and excipient solution, and spray-dried particles were obtained in the collection jar of the spray dryer. The spray-drying yield was calculated as the ratio between the sum of the added solids and the collected powders, expressed in percentage. The extract and excipient solutions were prepared by dissolving in purified water. For the spray-drying of herbal extract, the total solid amount in the feed was maintained at 2.50 g, and the spray-drying parameters were as follows: solute concentration at 10 mg/ml, the inlet temperature at 100 °C for the SHL extract, 150 °C for the ML extract and 120 °C for the LG extract, the atomization pressure at 600 L/h; the feed rate at 10% (3.75 ml/min), and the aspirator rate at 100% (40 m^3/h).

2.3. Water vapor sorption–desorption isotherms

The water vapor sorption–desorption isotherms of spray-dried herbal extracts were obtained using Hydrosorb-1000 vapor adsorption analyzer (Quantachrome Instruments, America) at 298 K in a relative pressure (P/P_0, $P_0 =$ saturation vapor pressure) range from 0.1 to 0.9. Briefly, an aliquot of approximately 100 mg of spray-dried powders was accurately measured and uniformly transferred to the test tubes. The proportion of moisture absorption (PMA) was defined to the percentage of increased weight in the original weight of the samples, and the formula was as follows:

$$PMA(\%) = \frac{\Delta W}{W_1} \times 100\% \quad (1)$$

In the equation, PMA (%) was the percentage of moisture absorption, and W_1 was the original weight of the powders, ΔW was the value of the increased weight of the powders. The water sorption–desorption isotherms were obtained when RH was regarded as *x* axis and the PMA (%) as *y* axis.

2.4. The morphology of spray-dried powders

The morphology of powders before and after the adsorption and desorption was investigated using a scanning electron microscope (SEM) (JSM-6510LV, JEOL, Japan) at 15 kV. Prior to SEM imaging, agglomerates were ground with a pestle and powders were fixed onto the metal stakes with the electric adhesive tapes and coated with a film of gold powders using Auto Fine Coater (JFC-1600, JEOL, Japan).

2.5. Water content and thermal analysis

Water content was determined using thermo gravimetric analyzer (TGA Q50, TA, USA). Approximately 5 mg samples were placed in aluminum pans, and data were collected between 20 °C and 200 °C at a heating rate of 10 °C/min.

Thermal analysis was analyzed using a differential scanning calorimeter (DSC Q200, TA, USA). Approximately 5 mg of sample was placed in an aluminum pan, and data were collected between 20 °C and 300 °C at a heating rate of 10 °C/min.

2.6. Density measurements

A 5-ml cylinder was used in the bulk density determination of spray-dried particles. The container was filled with accurately weighed particles, and the top was leveled. The bulk density was calculated as the ratio of the mass to the volume of the sample without any external force or taping. The tap density was determined using the same sample for the bulk density, but the volume was taken for calculations after taping. The taping is performed manually, in a vertical manner from a distance of approximately 5 cm onto a level bench top surface, for up to 500 strokes until the volume no longer changed. Measurements were performed in triplicate.

2.7. X-ray powder diffraction (XRD)

Powder crystallinity was assessed by XRD. The samples were analyzed using a Philips XRD system consisting of a PW 1710 control unit, PW 1820 goniometer and PW 1830 generator (Netherlands). CuKα radiation (45 kV, 100 mA, with the wavelengths Kα1 of 0.154060 nm, Kα2 of 0.154443 nm and a Kα1/Kα2 intensity ratio of 0.5) was used. The XRD patterns were recorded at diffraction angles from 3° to 70° in 2θ using a step size of 0.02° and a scan speed of 0.004° 2θ/s.

2.8. X-ray photoelectron spectroscopy (XPS)

The particle surface was analyzed with a XPS (ESCA Lab 250, Thermo Scientific Corporation, USA) with nonmonochromatic 300 W AlKα radiation. Pass energy for the narrow scan is 30 eV. The base pressure was about 6.5×10^{-10} mbar. The binding energies were referenced to the C1s line at 284.8 eV from alkyl or adventious carbon. The elements O (total of all orbitals), C (1s orbital), and N (1s orbital) were used for the elemental analysis. The data was obtained with the processing software of Thermo Avantage 4.15.

3. Results and discussion

3.1. Preparation of spray-dried herbal extracts

SHL extract was known to be hygroscopic and the high hygroscopicity led to not only low spray-drying yield but also difficulty in further formulation processing due to the stickiness and poor flowability of the spray-dried powders [10,11]. In the present study, the addition of leucine was found to improve spray-drying performance of SHL in a dose dependent manner (Table 1). Visually, with increasing the leucine content in the feed solution, the amount of powders adhering to the equipment walls was found to apparently decrease. As a result, the