Powder Technology 334 (2018) 143–150

Contents lists available at ScienceDirect

Powder Technology

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

Novel drying of formulated naproxen sodium using microwave radiation: Characterization and energy comparison

Maha Al-Ali [a], Selvakannan Periasamy [b], Rajarathinam Parthasarathy [a,*]

[a] Chemical and Environmental Engineering, School of Engineering, RMIT University, Melbourne, Australia
[b] Applied Chemistry, School of Science, RMIT University, Melbourne, Australia

ARTICLE INFO

Article history:
Received 18 February 2018
Received in revised form 12 April 2018
Accepted 17 April 2018
Available online 19 April 2018

Keywords:
Microwave drying
Naproxen sodium
Conventional drying
Particle characterization
Energy

ABSTRACT

The extent of moisture content (MC) present in pharmaceutical formulations has a vital role in controlling the textural properties of the pellet, dispersion of active component and its dissolution kinetics. In particular, hydrophilic drugs such as naproxen sodium (NapS) tend to absorb moisture readily which necessitates the selection of a drying technique to ensure the preservation of drug's textural properties without compromising its pharmaceutical effect and release kinetics. In this paper, a novel drying process for naproxen sodium drug granules has been used successfully by employing microwave radiation technique and compared with other drying techniques. The major objective of the present work is to evaluate the effect of microwave drying technique in the removal of moisture from naproxen sodium and its impact on the textural properties of the final product of tablets powder. The pharmaceutical formulation is synthesized by mixing appropriate amounts of NapS, Poly (vinyl pyrrolidine), and microcrystalline cellulose and moisturized using deionized water to 10, 20 and 30 wt%. Four different drying methods namely vacuum drying (VD), freeze drying (FD), convective drying (CD) and microwave drying (MWD) are used to dry NapS wet granules. The rate of moisture removal and the energy requirement are found to be different for each drying process. The product of drying is also found to have different particle size, morphology, and crystallinity for each process. Among the four techniques, MWD is found to be highly efficient because of its rapid moisture removal which can be ascribed to the interaction of microwave with NapS that has a permanent dipole moment. The results of this work suggest that moisture content of NapS tablets could be reduced rapidly by microwave radiation technique, which has the potential of improving the energy efficiency of the drying process while preserving the textural properties of the drug formulation.

1. Introduction

Pharmaceutical powders are known to absorb moisture during various processing steps such as granulation, crystallization, spray drying and even during storage [1]. The absorbed moisture has undesirable impacts on drug's dissolution kinetics, microbial, physical, chemical and thermal stabilities, flow and medicinal properties, and textural properties such as hardness and compaction [2]. The absorbed moisture may also lead to the formation of new polymorphs of the drug, which also influence the dissolution rate, solubility and packing properties [1]. The incorporation of water molecules in the crystal structure of an organic compound has strong effects on its physical and chemical properties [3]. Dehydration of pharmaceutical products under ambient conditions does not remove the moisture completely, and the incomplete dehydration affects the pharmaceutical formulations negatively and produces different crystal forms of active drugs [4]. Therefore, drying is an important process in the preparation of pharmaceutical solids as it dictates the textural properties and characteristics of the dried product significantly [5]. Moreover, the operating conditions of the drying process also affect the product powder quality significantly [6]. The significance of the drying process becomes greater if pharmaceutical formulation consists any hydrophilic drugs because they tend to absorb more moisture than hydrophobic drugs.

Naproxen sodium is one of the most commonly used non-steroidal anti-inflammatory drugs. Naproxen sodium is a propionic acid derivative, which is widely used in a tablet form in the treatment of the osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. The sodium salt of naproxen increases its solubility in aqueous medium and enhances its uptake. Water absorbed by anhydrous naproxen sodium is known to transform its crystalline polymorphs due to the formation of various hydrates of the drug [1,7]. Any changes in the crystallinity and polymorphism of naproxen sodium can affect its bioavailability and physical stability [1,7]. The electrostatic interaction between water and dipole drugs such as naproxen sodium is very important because it influences the drug's biochemical reactions [8]. Therefore, it is essential to employ a drying process that can efficiently remove the total absorbed moisture without much change in the textural properties of the drug. A detailed

* Corresponding author.
E-mail address: rchrp@rmit.edu.au. (R. Parthasarathy).

https://doi.org/10.1016/j.powtec.2018.04.040
0032-5910/

study on the use of various drying techniques to dry naproxen sodium needs to be undertaken to understand any undesirable changes that may occur in the active properties of the drug due to the chosen technique thereby enabling us to choose the most suitable drying process.

In this work, we have chosen four different drying techniques to remove moisture from the pharmaceutical formulation containing naproxen sodium. Our study aims to investigate how each drying method influences the rate of moisture removal, crystallinity, and polymorphism of the drug. Convective drying (CD) using an oven, vacuum drying (VD), freeze drying (FD), and microwave drying (MWD) are the four drying methods chosen for the removal of moisture from naproxen sodium in this work.

Each of the above dryings methods involves a different drying mechanism, which eventually affects the particle aggregation, crystallinity, and other textural properties. VD and FD remove water at low temperature and liquid nitrogen temperature, respectively. In the case of CD, the moisture is removed slowly by using higher temperatures. In MWD, the radiation is absorbed by water and the polar drug, and consequently heating occurs at molecular levels. In VD, the removal of moisture is achieved by lowering its boiling point under vacuum so that it can be removed under milder conditions [9,10]. In this case, the main characteristics and properties of pharmaceutical compounds are preserved, and any thermal degradation is avoided [9]. In FD, the moisture from the pharmaceuticals is removed by shrinking or toughening. This method is known to enhance the properties of biopharmaceutical products in terms of high bioavailability, stability, and dissolution rate with less damage to the dried drug [11–14]. In CD, which is the most common method of drying, heat is transferred from the hot air to the pharmaceuticals by convection which enhances the removal of moisture [15]. Each of the above drying techniques has some disadvantages. Although VD and FD use low temperature to remove the moisture, they involve a long drying time [15], and they are expensive and energy intensive [16]. The CD consumes a significant amount of energy especially at the later stage of drying [17]. In contrast, MWD is an environmentally friendly technique, which uses a lower amount of energy and requires a very short residence time in comparison to the other drying methods. In MWD, heating by microwave is governed by the interaction between the electromagnetic field of the microwave and the dielectric properties of the materials [18]. According to literature, MWD is more effective than the CD and VD [17]. Although MWD has been used in the drying of various pharmaceuticals, its effectiveness has not been tested yet in the drying of naproxen sodium and therefore, it becomes the primary objective of the current study. Moreover, most of the successful applications of MWD in drying pharmaceuticals used hybrid systems by combining one or more of the conventional drying techniques with microwave technique [19]. In this study, however, microwave technique was used without combining it with other conventional drying methods to dry naproxen sodium at various moisture contents. The current study also aims to compare the performance of the four drying above techniques in removing the moisture from naproxen sodium. The dried product was subjected to powder X-ray diffraction, Fourier transform infrared spectroscopy (FTIR), and scanning electron microscope (SEM) to evaluate the performances of the four drying methods. This paper presents the details of the experimental techniques and the results. It also evaluates the efficiency of the four drying techniques using the amount of moisture removed per unit energy input. The results of this study show that microwave radiation can be used to dry naproxen sodium efficiently without altering the textural properties of the drug significantly.

2. Materials and method

2.1. Materials

The key materials used in our experiments were 1) naproxen sodium powder (NapS), (*S*) 6 methoxy α methyl 2 naphthaleneacetic acid, CAS: 26159-34-2; purity (titration by $HClO_4$): 98.0–102.0%. 2) Microcrystalline cellulose powder (MCC) (CAS: 9004-34-6). 3) Povidone powder (PVP), Polyvinylpyrrolidone (CAS: 9003-39-8). All these chemicals were purchased from Sigma–Aldrich and used as per the quality requirements of the American Pharmacopeia, USP 9. Deionized water was used as the solvent to moisturize the drug powder.

2.2. Methods

2.2.1. Formulation and wet granulation processes

Naproxen sodium drug formulation consists of 50 wt% NapS as an active pharmaceutical ingredient (API), 40 wt% microcrystalline cellulose (MCC) as a binder and 10 wt% Povidone (PVP) as a filler [4]. The drug powder (DP) mixture was prepared manually at ambient conditions and was divided into four parts. Three parts, each consisting of 40 g DP, were wetted using deionized water (the granulation solvent) and the remaining 20 g was kept as reference material to compare its characteristics with those of dried granules.

In the wet granulation process, three batches of DP (each weighing 40 g) were moisturized manually to obtain wet powder samples containing approximately 10, 20 and 30 wt% water. Each batch of the wet powder was remixed in a planetary centrifugal mixer (non-Vacuum Thinky Mixer: ARE-310) at a speed of 500 rpm for 5 min to ensure homogeneous dispersion of NapS. The granules were then grounded manually using mortar and pestle, and the resulting mixture was stored in a desiccator. Table 1 shows the details of the three samples of moisturized drug granules and their expected crystal form.

2.2.2. Drying Techniques

Each batch of wet granules containing 40 g NapS was divided into four equal parts containing 10 g each, and they were dried using microwave drying, vacuum drying, freeze drying and convective drying. Each drying technique involved different operating conditions as shown in Table 2.

2.2.2.1. Freeze drying technique. A CPERON model freeze dryer was used to dry the wet granules. Each sample was placed in a cylindrical container of 90 mm diameter in a refrigerator at −19 °C and kept overnight. Consequently, samples were placed in the freeze dryer operating at −55 °C and 30 mTorr (0.004 kPa) vacuum pressure for 6 h. The dried samples were grounded using mortar and pestle manually, and the resulting samples were used for the determination of the moisture content and characterization using XRD, SEM, and FTIR.

2.2.2.2. Vacuum drying technique. The wet granules were placed on a flat plate of 90 mm diameter and placed inside the vacuum dryer. The vacuum dryer was operated at a temperature of 60 °C and a pressure of 20 in Hg (67.7 kPa) over a period of 200 min. The dried samples were collected, grounded, tested for the moisture content, and characterized by the same instruments as above.

2.2.2.3. Convective drying technique. Convective drying was carried out using Barnstead Thermolyne 1400 furnace operating at 100 °C and atmospheric pressure for 60 min by placing the samples on a flat glass plate of 90 mm diameter. Testing and characterization of dried samples were carried out similar to those mentioned above for other drying techniques.

2.2.2.4. Microwave drying technique. An accelerated microwave reaction system with dimensions 635 × 508 × 584.2 mm (CEM Corporation-MARS5, USA) with 2.45 GHz frequency and variable output power was used for MWD. The system had a turntable to increase the drying efficiency and reduce the reflected radiation on the magnetron by absorbing some of the microwave power [20]. For drying, the drug sample weighing 10 g was placed on a 90 mm flat glass plate and the plate was placed on the turntable inside the microwave system cavity. The microwave was operated at atmospheric pressure and 70 °C for 4.8