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SciVerse ScienceDirect

Procedia Engineering 42 (2012) 644 – 650

Procedia Engineering

www.elsevier.com/locate/procedia

20th International Congress of Chemical and Process Engineering CHISA 2012
25 – 29 August 2012, Prague, Czech Republic

Evaluation of functional characteristics of lactose by inverse gas chromatography

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Abstract

The work was focused on the analysis of different batches of the common pharmaceutical excipient lactose using inverse gas chromatography (IGC). Several batches of amorphous (spray dried) and crystalline form of lactose were studied. Surface properties represented by the surface energy and specific (acid-base) interactions between probes and analyzed samples shows batch variations and significant differences between manufacturers and technological processes. The second part of this work was focused on effect of relative humidity and temperature on stability of lactose. The variations of surface energy and specific interactions over time were studied. The changes in surface properties of two batches of lactose- amorphous and crystalline caused by higher relative humidity were measured by IGC. From measured values are obvious different chemical and physical properties of both lactose forms. Negative effect of higher temperature and air humidity lead to changes in surface energy and mainly rapid changes of electron-acceptor and electron-donor surface sites. Lactose monohydrate shows dramatic decrease in the surface energy and in the strength of electron-accepting sites on the contrary of spray dried where the acidity of surface increased.

Keywords: Inverse gas chromatography; lactose monohydrate; spray dried lactose; increased humidity

1. Introduction

At the present, lactose is one of the most common excipients used in the pharmaceutical industry. It is particularly suitable in terms of minimum interaction with active ingredients and the other excipients,

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doi:10.1016/j.proeng.2012.07.457

good availability and low costs. Over a long period lactose is primarily used in the pharmaceutical industry as excipient in the formulation of drugs, which is closely related to its relatively low sweetness, high stability, low hygroscopicity, low costs, good availability and safety and numerous applications in drug formulations. It covers a wide range of applications such as in the direct compaction, wet granulation and micronization to the devices of inhalational drugs [1].

Lactose exists in multiple forms, which have different properties, while some forms are more suitable for processing in certain formulations. A selection of the correct form of lactose in the formulation of drugs is very important. Mainly the reproducibility of the particle properties, which are required for the manufacture of consistent tablets, has to be kept [2].

There are several techniques and methods of lactose production, and there are significant differences between lactoses produced by different technological processes. E.g. spray drying forms amorphous lactose, by milling and sieving is formed crystalline one. Therefore, the prediction of long-term behaviour of lactose is very important characteristic of different types of lactose.

Lactose monohydrate is widely used as an excipient in processes where granulation and drying occur. It is often used for the production of the inhalational devices, which must be finely milled. Lactose acts here as a carrier of micronized drug and helps in transfer to the lungs. For direct compression an appropriate form of lactose appears to be α-lactose monohydrate containing a small amount of anhydrous lactose. It is used as the excipient in smaller quantities and dosage forms where granulation in the production is not required. Because α-lactose monohydrate is the cheapest form of lactose commercially available, it is also the most widely used.

Amorphous lactose prepared by spray drying technique has good flow and binding properties due to its high sphericity of agglomerates. Commonly it is combined with microcrystalline cellulose and is used as the excipient in the process of direct stamping [3].

A wide range of the methods for the analysis of lactose is known. In laboratory and also in the industrial scale are commonly used: differential scanning calorimetry, X-ray diffraction and IR spectroscopy. The method used in this work is the inverse gas chromatography (IGC). Application of IGC has been recently expanding into several disciplines. It is suitable for analyzing the properties of solids and its advantage consists in easy pretreatment of the investigated material. IGC allows the measurement of values of some complicated measurable characteristics of pharmaceutical materials, such as surface energy of powders, acid-base and polar properties of the surface [4]. These properties influence behaviour and technological processing of the materials.

This work is focused on the functional characteristics of lactose, which can be observed by differences in crystallinity of each batch manufactured by the same or a different technique, or even another manufacturer. The results can determine whether a transition to another form of lactose occurred, and how its properties are affected.

For characterization of lactose IGC method was used, through which it can be evaluated the surface properties of pharmaceutical powders. As a result, the effects of external environment can be examined. For example the influence of humidity on changes in surface properties and thus the structure and composition changes of the sample can be determined. One of the indicators of surface properties is the surface free energy. Its measurement by IGC compared with conventional methods is very simple, reproducible, and particularly non-destructive.

IGC is carried out in the infinite dilution, in which any adsorbed molecule is theoretically not in such proximity to other molecules adsorbed on surface, to allow their interaction [5]. The adsorbed molecules are basically isolated and the interaction cannot occur in the vapor phase, on the surface, or between desorbed and adsorbed molecules. There is a lack of interaction, which means that the parts of the sample with the highest surface energy are preferable to those with lower energy. Therefore, there is the assumption that IGC analyzes preferably sites of high energy and retrieves the value of dispersive surface