Developing and testing of a new balance for monitoring lyophilization in vials

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DEVELOPING AND TESTING OF A NEW BALANCE FOR MONITORING LYOPHILISATION IN VIALS

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Monitoring the lyophilisation process and promptly detect the end point of the primary drying phase is an important issue in order to preserve the product quality avoiding thermal damages. In this work we present an innovative balance able to weigh in line a group of vials having the same features of those of the batch. This is possible because the balance can be directly used in the vacuum chamber of the freeze-dryer without extracting samples from the drying chamber. The balance has been tested using it in a small production unit (Lyobeta, IMA-TELSTR) and comparing results with those obtained using other monitoring devices: thermocouples and DPE (non invasive monitoring method based on pressure rise tests).

Balance features

Design specifications

The balance prototype is composed of two measurement systems: one for the mass detection and one for the temperature measurement.

The mass system includes a load cell, a moving plate and a lifting system. During the mass measurement the lifting system rises the load cell, afterwards the vials are released over the shelf.

The temperature of the vials is measured by means of a Wireless Temperature Measurement System (WTMS). The WTMS circuit is located over the moving plate of the load cell. This prototype can measure up to three vials temperature by means of commercial thermocouples sensors.

The balance can measure the mass in a range between 100 – 200 g and can works inside the vacuum chamber where typically the temperature is set in a range between -40°C and +30°C.

It can tranfer data to a PC using a standard RS 232 interface. A special micro-controller system performs the acquisition of data and the control of the mechanical system.

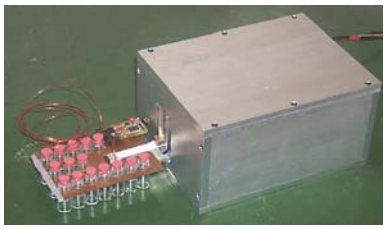

Figure 1. Balance equipment.

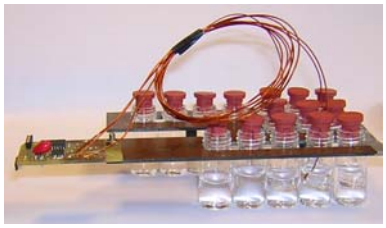

Figure 2. Load cell and wireless thermometer.

Figure 3. Lifting system.

Figure 4. Lifting system and load cell.

Figure 5. Balance positioned on a try in a batch of vials.

Figure 6. Balance positioned inside the vacuum chamber

Advantages of using this balance

- It is possible to measure the mass of a set of vials without extract any samples from the drying chamber
- The vials are monitored in line during the process and are exactly the same of the rest of the batch.
- The vials are almost always in contact with the heating shelf and they are lifted just during the mass measurement, therefore, the thermal exchange between glass vials and heating surface is not significantly modified
- The monitoring system based on the mass measurement is not invasive for the product and can be considered representative of the whole batch

Freeze-drying experiments

Experimental cycle

The experimental data have been obtained operating with Lyobeta (TELSTAR) freeze-drier. Samples were arranged on the shelf, surrounded by voids vials in order to minimise the effect of radiation. The vials of the batch were filled in with 1 ml of a 10% sucrose solution and partially sealed. The experiment showed in the following is carried out with a batch of 43 vials whereof 15 are on the balance brace. Product temperature has been monitored using both thermocouple sensors placed in contact with the bottom of the glass vials and DPE method. The recipe of freeze drying cycle is given in Table 1.

Figure 7. The pilot freeze-dryer used for experiments

Table1. Recipe of the experimental cycle

Phase	Duration	Temperature, K	Pressure, Pa
Freezing	2 h	-45	
Freezing	30 min	-45	
Vacuum			5
Primary Drying	2 h	-15	5
Primary Drying		-15	5

Results

The results showed in Figure 8 evidence a good agreement between th time evolution of the values of mass and of temperature. When the product temperature strongly increase, i.e. at the end of the primary drying, the monitored mass of the vials becomes almost constant. Therefore the end point of the primary drying phase can be detected b means of this balance.

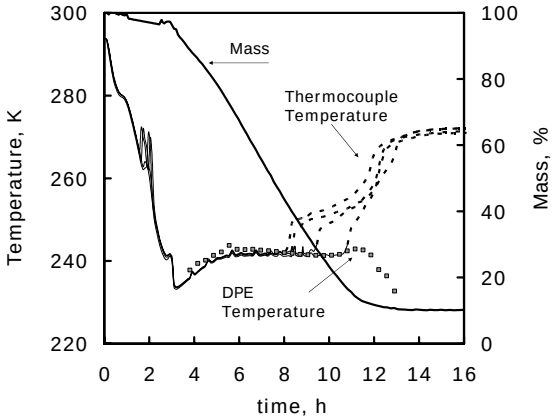

Figure 8. Time evolution of the temperature and of the mass values during the experimental cycle.

Acknowledments

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