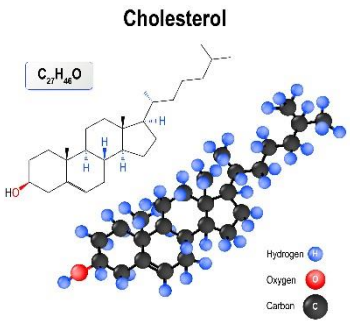

Differential Scanning Calorimeter

Thermal analysis of Cholesterol

Chip-DSC 100

Introduction

The pharmaceutical industries develop tons of drugs and natural products as therapeutics for various diseases. All these products undergo a very strict quality control program and usually are characterized very well before they are used in any kind of therapy. Among the characterization methods, there are also a couple of calorimetric experiments that can be very useful for quality control, solubility prediction or analysis of composition.

Methods

Using a DSC for analyzing pharmaceutical products is a more or less common technique. In this application, the new Chip-DSC was used for measurements of dry cholesterol powder to check melting and phase transition behavior. This test is useful to control the substance purity before it is used for the preparation of tablets.

The DSC signal in general is generated by heating a sample containing pan and an empty reference pan with the same heat source and subtracting the heat flow signals of the two pans from each other, resulting in endothermic or exothermic peaks if the sample shows thermal effects.

The Chip-DSC sensors integrates all essential parts of DSC in a small chip. The chip-arrangement comprises the heater and temperature sensor in a chemically inert ceramic arrangement with metallic heater and temperature sensor. Therefore, the Chip-DSC allows very fast heating and cooling rates combined with high resolution and accuracy as well as reproducibility.

The result of a DSC measurement can be used as a fingerprint model for substance identification in quality control but can also be used to determine enthalpies of effects like phase transitions.

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Table 1. Experimental Conditions

Instrument	Chip-DSC 100 with Peltier cooling
Heating rate	10 K/min
Sample Mass	7 mg
Sample Pan	Aluminum pan
Purge Gas	Nitrogen

Results

Cholesterol is a polycyclic alcohol. It belongs to the group of steroids and lipids. A common mistake is to consider cholesterol as fat which it is definitely not, even if it is an isoprenoid and therefore has a very lipophilic character.

In human body, cholesterol is produced by biosynthesis and used as a main component of the cell membrane as well as a raw material for synthesis of hormones and transmitters. Some diseases can cause a higher or lower cholesterol level which can lead to severe damage. Being such an important biomolecule, cholesterol is used in drug production and research very frequently and can be synthesized chemically.

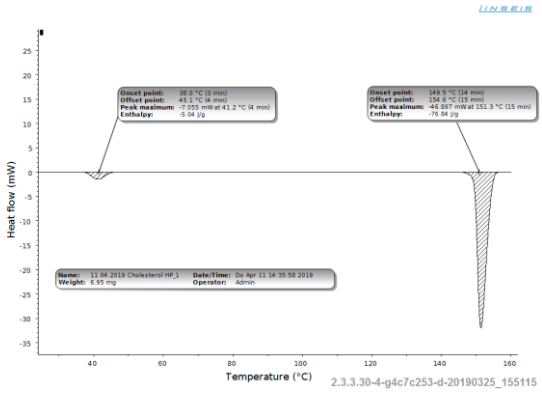

Fig.1 DSC Heat Flow curve of dry cholesterol, with solid phase transition at 38°C and melting at 149°C.

Figure 1 shows the DSC profile of dry cholesterol that was measured from 0 °C up to 160 °C with a linear heating rate of 10 K/min using a Chip-DSC with Peltier cooler. The building Peltier cooler is a very useful attachment reaching a minimum temperature of 0 °C. It avoids external cooling by an intracooler or liquid nitrogen.

The first effect that can be observed is the endothermic solid phase transition at 38 °C that occurs only if the cholesterol sample is completely water free. Therefore, it can be used as an indicator of substance purity.

The second effect is the endothermic melting peak at 149 °C. The melting enthalpy and melting temperature can give additional information about substance purity in quality control and can also be used as a tool to identify the substance in general of drug identification.

Experimental

The sample was obtained from a pharmaceutical laboratory as pure, dry sample. Samples were used as provided and measured directly using a Chip-DSC 100 with Peltier cooler. The sample has been cooled to 0 °C in the instrument before it was measured. The detailed experimental setup is given in table 1.

Summary

The Chip-DSC technique with its short measurement time can be a useful method for quality control to investigate purity and composition of drugs and pre-drugs like the dry cholesterol that was used in this application. The phase transition of cholesterol indicates if it is dry or has seen humidity and the melting onset and enthalpy can provide further information about purity and effects like aging, oxidation or reactions during storage and transport.