APPLICATION NOTE

Pharmaceuticals – TGA-DSC-MS

Thermal Characterization of Testosterone by TGA-DSC-MS: Implications for Drying, Melting, and Processing

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Introduction

Testosterone is a steroidal active substance whose thermal behavior is highly relevant for drying, storage, formulation, and thermal processing. Even small amounts of residual moisture or residual solvent can influence crystallinity, melting behavior, powder handling, and thermal stability. Therefore, a combined TGA-DSC measurement with simultaneous mass spectrometric analysis of the gases evolved is particularly suitable for comprehensive characterization. This approach makes it possible to distinguish between volatile release, melting, and chemical decomposition and thus provides valuable information for process optimization and quality control.

Measurement Conditions

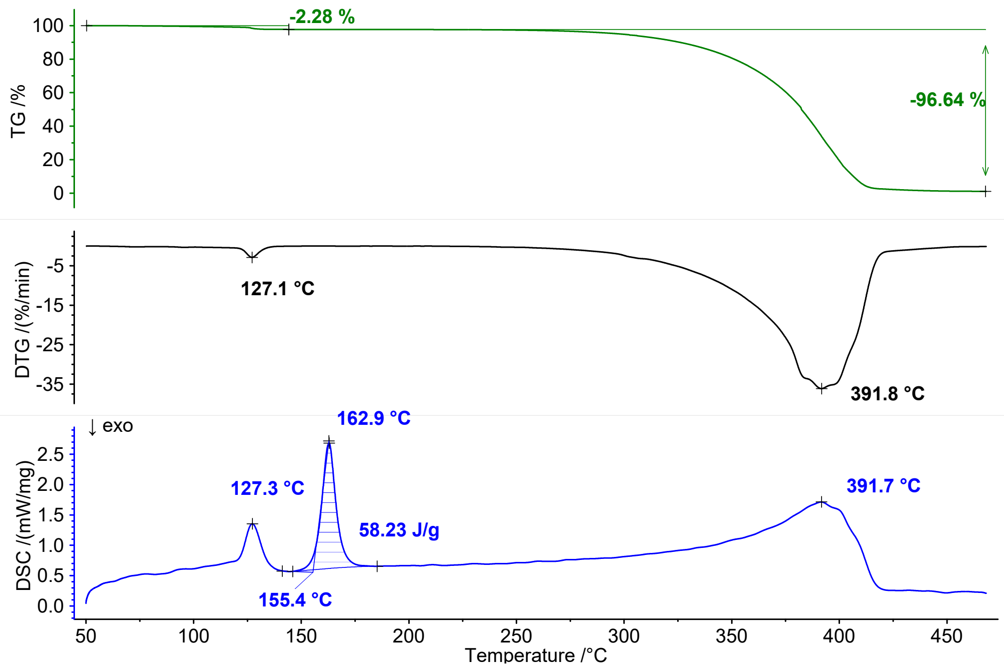
The measurement conditions are detailed in Table 1.

Table 1 Measurement conditions for STA

Instrument	STA *Aëolos*®
Sample	Testosterone
Sample mass	10 mg
Temperature range	30°C to 500°C
Heating rate	20 K/min
Atmosphere	Nitrogen, 70 ml/min
Crucible	Pt with pierced lid

Results and Discussion

Figure 1 shows the TGA, DTG, and DSC curves of testosterone.



1 TGA-DSC measurement on testerone, recorded in a nitrogen atmosphere.

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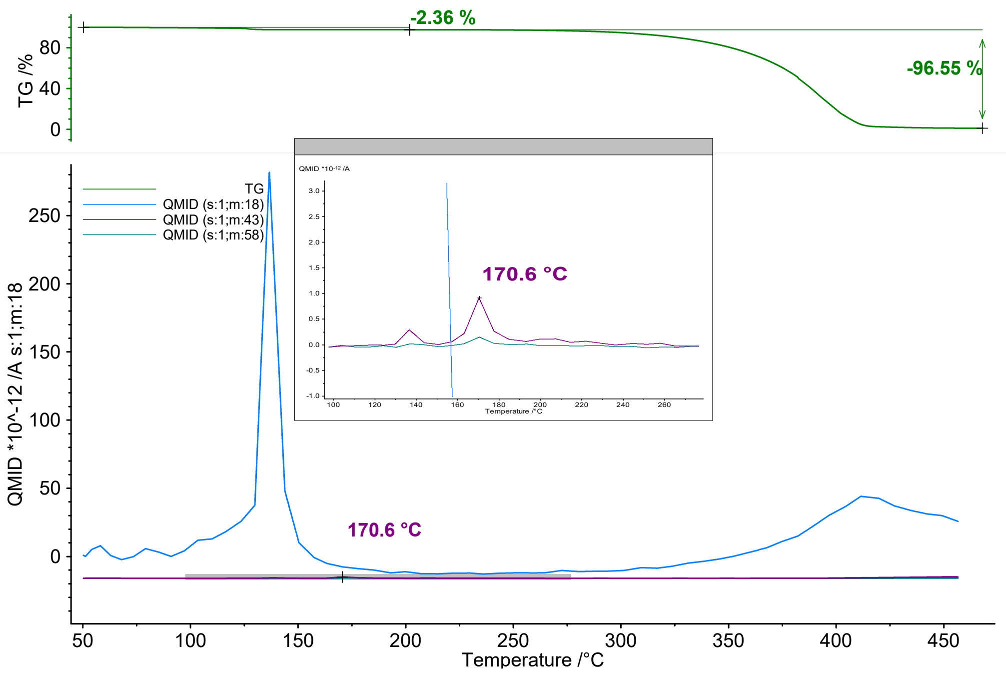
In the low-temperature range between room temperature and approximately 130°C, a small mass loss of 2.3% with a DTG peak at 127°C is observed. This behavior can be attributed to the release of residual humidity and weakly bound volatile species. The DSC signal simultaneously exhibits an endothermic effect with a peak temperature of 127°C. These events indicate desorption or dehydration-related processes prior to the main phase transition. Such information is important because even small amounts of residual humidity may influence storage stability, powder flow, and the reproducibility of downstream processing.

A pronounced endothermic DSC peak appears with an extrapolated onset temperature of 155°C, which corresponds well to the melting point reported in literature. The melting enthalpy amounted to 58 J/g. This signal is assigned to the melting of testosterone and represents the main physical phase transition of the substance. The well-defined peak shape indicates a distinct melting process. Knowledge of the melting temperature is essential for the design of thermal processing steps. Thermal degradation started above 250 °C and was complete at about 450°C. The DTG peak was found at 392°C.

The evolved gas analysis shown in Figure 2 provides important additional information on the nature of the mass-loss events. The ion trace of m/z 18 shows a clear signal with a maximum at about 137°C, which is assigned to the release of water. This confirms that the low-temperature mass loss seen in the TGA curve is at least partly caused by residual humidity. In addition, the ion traces of m/z 43 and m/z 58 exhibit a distinct maximum at around 171°C, indicating the release of traces of acetone as soon as the sample is molten. This suggests the presence of residual solvent, likely originating from synthesis, purification, or crystallization.



2 TGA curve related to ion traces m/z 18, m/z 43 and m/z 58.

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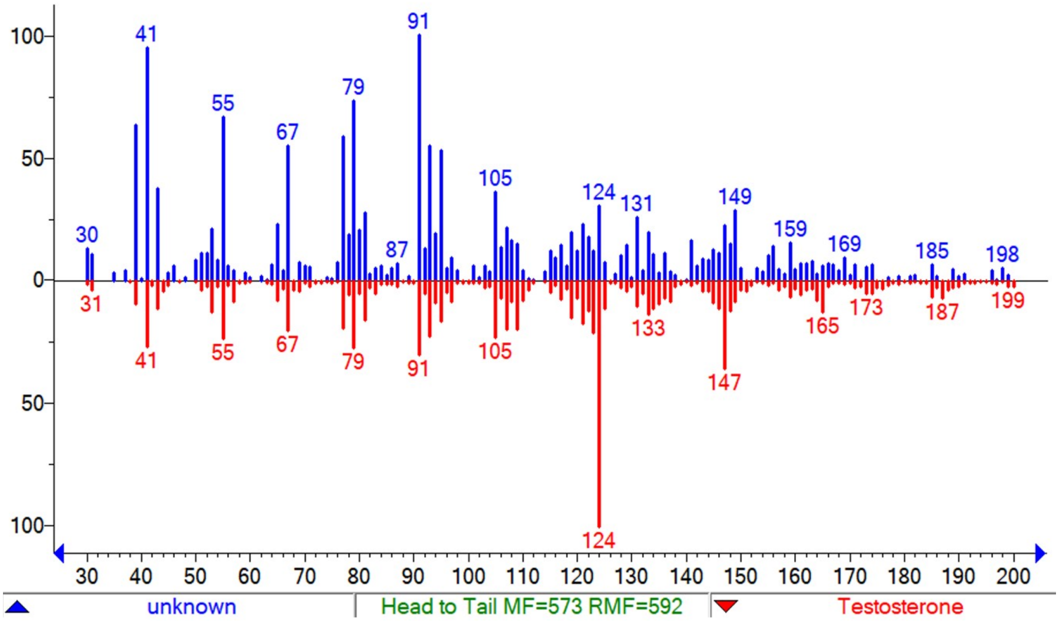

3 Measured MS spectrum at 374°C compared to the library spectrum of testosterone.

The measured MS spectrum at 374°C is depicted in Figure 3 and shows some similarities to the library spectrum of testosterone. This finding suggests partial decomposition and partial evaporation of testosterone during thermal treatment. Upon pyrolysis, probably several different decomposition products are simultaneously released as a mixture.

Conclusion

The measurement demonstrates that a combined TGA-DSC approach, ideally supplemented by evolved gas analysis, is essential for reliable assessment of the material's thermal behavior. Only this combination allows the clear differentiation between physical transitions such as drying and melting and chemical degradation processes. Without MS coupling, these low-level mass loss events could be detected by TGA, but their chemical origin could not be identified with the same level of confidence. These results provide an important basis for optimizing drying, storage, and thermal processing conditions for testosterone.

This thermal characterization of the melting behavior of testosterone provides valuable information for assessing its physical stability in transdermal dosage forms. The data obtained support the development of robust formulations and enable the evaluation of potential recrystallization processes that may impair drug release and, consequently, product efficacy. Preventing crystallization is essential to ensure both bioavailability of the active pharmaceutical ingredient and long-term adhesion performance of transdermal patches during storage and use.

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