TA Instruments

Thermal Analysis & Rheology

Thermal Analysis Application Brief

Improved Vitamin C Quality Through Moisture Analysis

Number TA-116

SUMMARY

Moisture content in pharmaceutical products is important because it affects long-term efficacy of the materials. Moisture evolution analysis (MEA) provides an easy method for determining ppm moisture levels in these products.

INTRODUCTION

The manufacturers and formulators of pure pharmaceuticals and excipients must be able to analyze their products for moisture level. Moisture content can markedly affect the stability, appearance, and quality of the final product (1). One such product in widespread use is ascorbic acid or Vitamin C. De la Vega found that when ascorbic acid is granulated with any substance containing even trace amounts of moisture, a considerable loss of ascorbic acid occurs, both during manufacture and subsequent storage (2). Blaugh and co-workers indicated that moisture greatly accelerated degradation of ascorbic acid and the formation of brown color (3).

Unfortunately, the moisture in ascorbic acid cannot be determined by the widely used Karl Fischer titration since the ascorbic acid itself is oxidized by the iodine to dehydroascorbic acid (4).

The TA Instruments 903 Moisture Evolution Analyzer can be used to quickly and accurately determine the amount of moisture in ascorbic acid either as the pure pharmaceutical or as formulated tablets. Such analyzers are widely used to determine moisture in pharmaceuticals, excipients (1), effervescent tablets, and lyophilized materials (5). Water levels as low as 10 µg/g can be routinely determined. With special care (e.g. dry box environment) levels of accuracies down to 1 µg/g are possible.

EXPERIMENTAL

The experimental conditions used depend to some extent upon the moisture level and the nature of any excipients present in the formulation. In the example given below, an over-the-counter Vitamin C dietary supplement tablet containing 2% moisture was analyzed.

Sample weight:	0.1 g (1/12 of a tablet)
Temperature:	125°C
Time:	30 min.

1. The sample is placed in a tared sample boat, is weighed, then placed in the instrument and analyzed under the conditions shown.

2. The "count" thus obtained is compared with a blank count previously obtained with no sample in the chamber, but otherwise identical conditions (including opening and closing of the sample chamber).

3. Using a calibration factor obtained by running a standard of known moisture content (e.g., sodium tungstate dihydrate), the water level in the sample is calculated using the equations given below.

CALCULATIONS

$$\text{Water level (\%)} = \frac{K(C_{sample} - C_{blank})}{W_{sample}}$$

$$K = \frac{F \times W_{std} \times 100}{C_{std} - C_{blank}}$$

Where:

C_{blank} = count obtained for blank
C_{sample} = count obtained for sample
C_{std} = count obtained for standard material
F = fraction of standard material attributable to water
K = calibration factor in milligram percent water per count (should be near 0.1)
W_{sample} = weight of sample in milligrams
W_{std} = weight of standard material in milligrams

RESULTS

Using the procedure described above, a standard deviation of ±0.03% (abs.) was obtained in a series of analyses performed on a sample analyzed to contain 2.1% (abs.) water.

The electrolytic cell used as a detector for the instrument is remarkably selective for water. There are no known positive or negative chemical interferents (i.e. substances which either chemically increase or decrease the indicated water level). Some glycols used in pharmaceutical formulations, dehydrate at elevated temperatures, however, and may provide higher than expected moisture readings. The major source of failure for the detector is the coating of its active surface by some organic material evolved from the sample. Evolution of corn syrup or other volatile excipients can markedly reduce the life of the detector. Detector deterioration is readily osbervable by running a blank and standard sample at regular intervals (e.g., once a shift). Deteriorated calls can be repeatedly regenerated using the simple procedure described in the Operator's Manual.

A number of excipients used in the formulation of Vitamin C tablets have been tested under temperature conditions described above and appear to be compatible with the analyses. Such excipients include calcium stearate, magnesium stearate, stearic acid, lactose, glucose, corn starch and talc.

The recommended calibration material is sodium tungstate dihydrate (F = 0.1092) which is stable to temperatures above 1000°C. Water itself (F = 1.000) can also be used in the microcapillary technique described in the Operator's Manual.

REFERENCES

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