WATER CONTENT DETERMINATION IN HYGROSCOPIC POWDER PHARMACEUTICAL PRODUCTS USING KARL FISCHER COULOMETER WITH OVEN

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INTRODUCTION

Water content determination in pharmaceutical products is important in order to demonstrate compliance with pharmacopoeial requirements [1]. Also, water content determination has a direct influence on stability and quality of the pharmaceutical products.

One of the techniques that can be used to quantitatively determine the water content in powder pharmaceutical samples is coulometric determination of water content using Karl Fischer (KF) method. The measurement takes place in a measuring cell consisting of a generator electrode (anode) and a platinum electrode (cathode). During the passage of electric current through the measuring cell filled with electrolyte, iodide ions from the electrolyte solution are oxidized at the anode into iodine, which quantitatively reacts with the water present in the sample. The end of the reaction is determined voltammetrically by measuring the voltage between the double platinum electrode, which is significantly reduced by the presence of free iodine [1,2].

Water content determination in hygroscopic powder samples can be challenging. The combination of Karl Fischer coulometer with oven, coulometric Karl Fischer titration and the use of isolator with controlled relative humidity condition, can greatly facilitate the water content determination in samples where this is difficult.

This paper shows how handling of hygroscopic powder samples can affect the accuracy and precision of the method for water content determination.

MATERIALS AND INSTRUMENTS

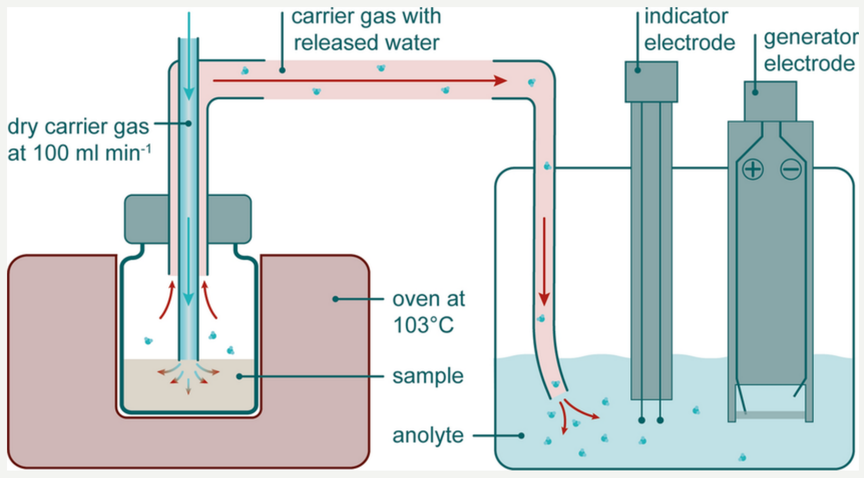
Hygroscopic powder pharmaceutical product

Karl Fischer vials

Isolator with controlled relative humidity condition

Karl Fischer coulometer with oven

METHOD



Anode: $2I^- \longrightarrow I_2 + 2e^-$

Figure 1. Design of an oven and measuring cell for coulometric Karl Fischer titration

ANALYTICAL RESULTS

Table 1. Precision results of the method for water content determination in hygroscopic pharmaceutical product

	ANALYST 1		ANALYST 2	
	Sample weight/mg	Water content in sample / %	Sample weight/mg	Water content in sample / %
n°1	99.45	3.5852	99.11	3.5913
n°2	101.96	3.5889	97.06	3.5829
n°3	104.93	3.6051	102.35	3.5833
n°4	99.13	3.6120	98.34	3.5980
n°5	100.15	3.6109	100.18	3.5946
n°6	105.09	3.6361	103.06	3.6004
RSD / %	N/A	**1**	N/A	**0**

Table 2. Accuracy results of the method for water content determination in hygroscopic pharmaceutical product

Accuracy - recovery	Sample weight /g	H_2O added/ µg	H_2O found/ µg	Water content in standard/%	Water content in sample/%	Recovery/%	Average recovery/%
Level 1 (80 %)	0.06349	3212.59	3295.3	5.0747	3.2953	100.29	**100.3**
	0.06359	3217.65	3301.7	5.0767	3.3017	100.33	
	0.06346	3211.08	3297.7	5.0808	3.2977	100.41	
Level 2 (100 %)	0.07913	4003.98	4096.4	5.0840	4.0964	100.48	**100.6**
	0.07931	4013.09	4113.6	5.0942	4.1136	100.68	
	0.07959	4027.25	4121.4	5.0861	4.1214	100.52	
Level 3 (120 %)	0.09553	4833.82	4947.3	5.1020	4.9473	100.83	**100.5**
	0.09555	4834.83	4919.9	5.0722	4.9199	100.24	
	0.09542	4828.25	4919.6	5.0788	4.9196	100-37	

Using an isolator with controlled humidity condition for sample weighing can affect on the accuracy and precision of the method for water content determination.

CONCLUSION

Karl Fischer reaction can be used in coulometric water content determination. This method is used for low water content determinations in the samples. During this study, it is shown how important is to understand properties of the sample that is analyzed. If the sample is hygroscopic powder with a low water content, manipulation of that kind of sample can significantly affect the obtained result of the water content. Therefore, it is proved that using an isolator with controlled humidity condition together with KF coulometer with oven, it is possible to determine the water content in hygroscopic powder samples with high precision and accuracy as shown in Table 1. and Table 2.

LITERATURE

[1] United States Pharmacopeia (2024) General Chapter, ⟨921⟩ Water Determination
[2] Metrohm Monograph 8.026.5013 - Water Determination by Karl Fischer Titration

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