Karl Fischer Volumetric Titration
Theory and Practice

Radiometer analytical

- when you need to be sure...

Table of contents

Introduction

Water content needs to be determined at all stages of the manufacturing process from raw materials to finished goods. The quality of the product depends on it. In products such as kerosene, transformer insulation oil or brake oil, the presence of unwanted moisture can have disastrous consequences.

In the pharmaceutical industry, it is essential to know the amount of water contained in the ingredients of a drug in order to correctly predict its lifetime, stability and effectiveness.

In the food industry, the water content of both raw materials and the finished foodstuff needs to be carefully monitored.

The technique most commonly used for these analyses because of its rapidity, accuracy and ease of use is Karl Fischer titration.

Thanks to its design and its titration algorithm, the **TIM550 Volumetric Karl Fischer Titrator** provides accurate results and clear sample information. An uncertainty calculation plug-in allowing all the measurement parameters to be taken into account is also available. Radiometer Analytical makes it easy for the user to comply with Quality Control requirements and follow Good Laboratory Practice.

The instrument is easy to program due to preset methods for titrations in the most common samples. The last calibration results of titrants, blanks and samples are stored. When used in conjunction with **TitraMaster 55** software, archiving of results and methods is limited only by available storage space.

Chemical reactions

The titration is based on the oxidation of sulphur dioxide by iodine in the presence of water. It is the same reaction as the iodometric titration of sulphur dioxide in water.

$$I_2 + SO_2 + 2H_2O \Leftrightarrow 2HI + H_2SO_4 \qquad (I)$$

In 1935, Karl Fischer published a description of “a new procedure for the titration of water” using the above reaction in an anhydrous nonaqueous solvent. However, in order to shift the equilibrium (I) to the right, it was necessary to neutralise the acids produced. Originally pyridine was used as the neutralising base. Later on, diethanolamine followed by imidazole were used as buffers.

Recent studies show that methanol, which is the most commonly used solvent, contributes in the reaction. The Karl Fischer titration can therefore be described by the two following reactions:

$CH_3OH + SO_2 + RN \Rightarrow [RNH]SO_3CH_3$ (II)

$H_2O + I_2 + [RNH]SO_3CH_3 + RN \rightarrow [RNH]SO_4CH_3 + 2[RNH]I$ (III)

(RN designates the base used)

pH considerations

The Karl Fischer reaction can only take place in a certain pH range between 5 and 7. In this pH range, the reaction remains constant. If the pH drops too low, end point attainment becomes sluggish or an end point will not be reached at all. If the pH is too high, side reactions occur making the titration non-stoichiometric. We can therefore say that errors occurring during a KF titration may be due to a change in the pH of the titration solvent.

The pH of the titration solvent can be tested using a combined pH electrode and a pH meter. The electrode is first calibrated with aqueous buffer solutions and afterwards the pH of the titration solvent is measured.

Note: do not place the pH electrode directly into the KF cell because excessive moisture will be introduced along with the electrode.

For further information, consult the users manuals of the main manufacturers of Karl Fischer reagents.

Volumetric titration

General remarks

Volumetric Karl Fischer titration requires the determination of the titre (t) of the Karl Fischer reagent. It is usually quoted in mg of water per ml of Karl Fischer reagent.

Modern reagents allow direct titration of water in the sample. The sample may be introduced directly into the KF cell or after an extraction or dissolution with a suitable solvent. The water concentration of the solvent must be determined previously in order to be subtracted from the sample analysis.

In the **TIM550 Volumetric Karl Fischer Titrator**, all these operations are simplified and the different results are accounted for automatically.

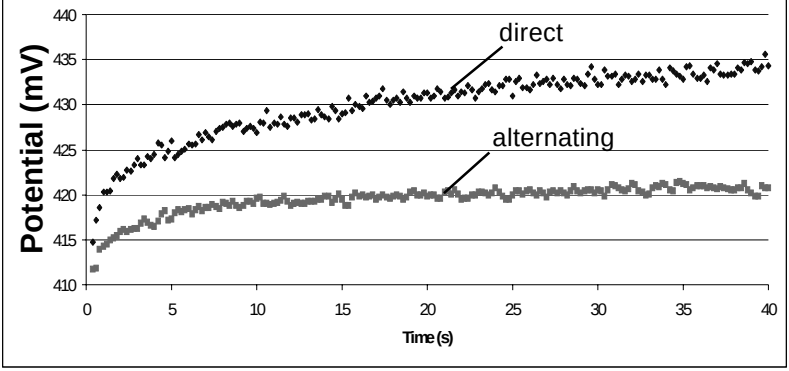
The volumetric titration of water allows the analysis of water concentrations between 0.1% and 100%. If an aliquot contains less than 1 mg of water, coulometric determination will result in a more accurate result. For reasons of precision, the titre of the titrant should be chosen so that the titration is completed with a titrant demand between 1 and 10 ml.

End point determination

The end point of the reaction is generally based on the detection of a slight excess of iodine which occurs when water is no longer present in the KF cell. The iodine excess can be indicated visually, photometrically or potentiometrically. The potentiometric method is the most common for the majority of titrators currently on the market. The method chosen by **Radiometer Analytical** in the **TIM550** uses a square wave alternating current. The electrode geometry, the signal amplitude and its frequency have been closely studied to obtain the best end point detection. Therefore, the user avoids the difficult choice of which polarisation current to use. The instrument does not operate with instantaneous potential values but uses half the difference between two consecutive measurements.

$$E = \left| \frac{E(t) - E(t-1)}{2} \right| \qquad \text{(IV)}$$

Figure 1



In a conventional system with dc current the electrodes are polarised, and become the site for reactions other than the reaction iodine to iodide. This leads to a drift in the potential difference between the electrodes and an end point that may be erroneous.

In figure 1, two curves for the same electrode are shown. Both have the same amplitude but one is with direct current whereas the other is with alternating current. It can be seen that with ac the potential is stabilised whereas with dc the potential increases, showing the appearance of reactions other than the reaction iodine to iodide.

The **TIM550** does not make a simple end point titration. The instrument controls the speed of reagent addition in order to maintain the indicating electrode potential at a constant value, thus an excess of iodine is never observed. This reaction control is achieved with a self-adapting PID algorithm[1]. The only input parameter is the maximum allowed speed that only depends on the reaction kinetics of the reagent used. Radiometer Analytical has tested most available reagents and the default value is valid for the most commonly used ones. The table below gives the maximum advised speed for the tested reagents.

Thanks to this principle, the TIM550 compensates the water introduced into the KF cell by determining a drift value which is subtracted during the titration. In this way more accurate results are obtained, especially for low water contents.

(1) PID: Proportional Integral Derivative

The working medium

Two types of reagents are available:

One-component reagents

One-component reagents contain all the reactants (iodine, sulphur dioxide and a base) dissolved in a suitable solvent. The working medium (i.e. the solvent required), can be freely chosen by the user depending on the dissolution properties of the sample to be investigated. The stoichiometry 1:1 of the Karl Fischer reaction is only fulfilled if there is more than 25% methanol in the reaction mixture. A methanol-free working medium can be used, however it is important to determine the titre of the KF reagent in the same working medium.

Two-component reagents

The solvent

The modern solvents available today present a high buffer and dissolution capacity. These solvents consist of sulphur dioxide, a base and methanol.

The main advantages of this solvents are:

- A more rapid titration due to better reaction kinetics. An advantage especially for the titration of large amounts of water.
- A better reproducibility, because the reaction environment is stable. The pH and the sulphur dioxide concentration remain constant.

For the titration of samples producing side reactions (aldehydes, ketones and silanols), it is necessary to use an appropriate solvent. Most reagent manufacturers include the letter **K** in the commercial name of such solvents.

The titrant

The titrant consists of iodine dissolved in methanol. We often find that the titrant has three titres 1, 2 and 5 mg of water per ml titrant. Even if it is possible to perform a titration with more than one stroke of the burette piston, it should be avoided by an appropriate reagent titre and choice of sample size. This allows the titration time to be reduced and therefore improves the reproducibility.

As for two component reagents, the titration of samples producing side reactions (aldehydes, ketones and silanols), require an appropriate solvent.

The following table gives the recommended maximum speeds for given reagents and solvents. However, conditions may be modified with respect to the additives, solvents e.g. chloroform, or samples added.

Reagent	Solvent	Manufacturer	Recommended speed
HYDRANAL® -Composite 5	Methanol	Riedel-de Haën	150 %/min = 15 ml/min
HYDRANAL® -Composite 5K	HYDRANAL® -Solvent K	Riedel-de Haën	50 %/min = 5 ml/min
HYDRANAL® -Titrant 1	HYDRANAL® -Solvent	Riedel-de Haën	150 %/min = 15 ml/min
HYDRANAL® -Titrant 2	HYDRANAL® -Solvent	Riedel-de Haën	150 %/min = 15 ml/min
HYDRANAL® -Titrant 5	HYDRANAL® -Solvent	Riedel-de Haën	150 %/min = 15 ml/min
HYDRANAL® -Titrant 5	HYDRANAL® -Solvent CM	Riedel-de Haën	150 %/min = 15 ml/min
Karl Fischer Reagent T	Karl Fischer reagent S	Merck	150 %/min = 15 ml/min
Karl Fischer Reagent 2.5	Karl Fischer reagent S	Merck	150 %/min = 15 ml/min
Karl Fischer Reagent 5	Pyridine	Merck	50 %/min = 5 ml/min

Note:

If you are using an ethanol-based Karl Fischer solvent (example: E-Solvent), once a week, immerse the Pt-Pt electrode for 2 min. in a 10% v/v TritonX-100 solution. Then rinse with dry methanol and gently wipe. This treatment allows the electrode to recover full efficiency after a few minutes operation.

10% v/v TritonX-100 is available from reagent manufacturers or can be prepared by diluting 10 ml of TritonX-100 in 100 ml of deionised water.

If the titrator indicates an excess of iodine at the end of the titration, the burette speed should be halved. It is possible to adjust this speed later on (a speed below 50 %/min, i.e. 5 ml/min is rarely used). It should be remembered that the titration time is not necessarily proportional to the rate of reagent addition. It is recommended to adapt the addition rate so that it is proportional to the speed of the Karl Fischer chemical reaction. Increasing the speed may lead to a momentary excess of non reacted iodine which puts a stop to the reagent addition. The titrator must therefore wait until this excess has been consumed before continuing the addition.

Water determination using the TIM550

Using one or two component reagents, the titration comprises the following steps:

1) Filling the burette with titrant

Place the reagent bottle in the bottle holder (if mounted) and connect the suction tubing from titrant bottle to stopcock. Add desiccant to the absorption chamber mounted on the bottle. To prepare the titrant, use the TIM550 burette functions “Bottle exchange” or “New titrant”.

Note: replace the desiccant when saturated.

2) Filling the KF cell with solvent

Place the solvent bottle in the bottle holder (if mounted) and connect the tubing from the solvent bottle to the KF cell. Fill the desiccant tubes for KF cell and KF pump with an appropriate desiccant, e.g. silica gel.
Note: replace the desiccant when saturated.

Using the TIM550 solvent button, add between 30 and 40 ml of solvent to the titration cell. Radiometer Analytical has marked the KF cell to indicated the minimum level to which solvent must be added.

3) Mounting the waste bottle

Label and identify the waste bottle and place the bottle at the rear of the TIM550. Connect the tubings, KF cell to waste bottle and pump to waste bottle. Make sure that the tubing is correctly connected to the pump module. A bad connection could release liquid into the pneumatic module and cause severe damage. Use the waste button to empty the cell.

4) Pre-titration

Pre-titration allows the removal of traces of water introduced with the solvent. It is only necessary if the stand by function is not used.

5) Sample introduction

The TIM550 is ready to start titrating when the message "Introduce sample" appears on the display. For two-component reagents, care must be taken to respect the quantity of water that can be analysed using the volume of solvent present in the KF cell. Please consult reagent manufacturer's instructions for use. In general, at least 5 mg/ml is allowed. With a newly filled KF cell, it is possible to titrate 5 x 35 = 175 mg of water.

6) Titrating the water

If "Autostart" has been activated, the titration will start as soon as the water in the sample is detected. Otherwise the titration will start as soon as the ✓ key is pressed.

The TIM550 constantly determines the speed of titrant addition which is adapted to the titration. The introduction or simple confirmation of the sample addition can be carried out by the operator in his own time. In fact, the titration may have finished before the sample amount is introduced. The TIM550 waits for the input of the sample amount before calculating the final result.

7) Result calculation

The TIM550 calculates the water content of the sample. The drift measured from titration start and if necessary the quantity of water introduced by the blank, the dilution factor etc... are also taken into account during calculations.

If the option has been unlocked and activated the TIM550 will also calculate the uncertainty of the measurement. These calculations comply with the following standard EN13005 (GUM)[1].

At the same time, the TIM550 will determine whether or not the result falls within the acceptance range specified by the user during programming. This allows the user to determine if the water content conforms to the specifications and if the result can be used for statistical purposes.

8) Solvent renewal

One-component reagents

It is possible to perform successive titrations in the same solvent. However, it is important to ensure that the methanol concentration is above 25% and that pH is maintained within the range 5 to 7.

Two-component reagents

Although it is advisable to renew the solvent after each analysis, successive titrations may be performed using the same solvent. Due to the fact that the quantity of sulphur dioxide present in the cell is limited, care must be taken to respect the

[1] GUM: Guide for the Expression of Uncertainty in Measurement, published by ISO, 1993

quantity of water that can be analysed using the volume of solvent present in the KF cell. For further information, consult the reagent manufacturer's instructions for use.

9) Restarting the titration using a new aliquot or return to the start of a menu

The KF titration cell will remain permanently on stand by i.e. ready for immediate use.

10) At the end of a series of titrations, the following statistical calculations are performed:

- Mean.
- Standard deviation or uncertainty (depending on the option chosen).

Use of an oven

The oven is necessary when:

- The solvent does not allow a sufficient dissolution of the sample.
- The sample interacts with the working medium.
- The sample inhibits the response of the indicating electrodes.

The preparation steps 1 to 4 for the titration are identical to the conventional method. Remember to pre-titrate the cell after having turned on the gas flow.

1. The TIM550 prompts you to weigh an "advised" amount of aliquot. The approximate value of this aliquot has been entered in the TIM550 beforehand.
2. Introduce the sample in the oven's cold zone.
3. Enter the "exact" amount of sample weighed.
4. The TIM550 will determine the drift value.
5. Move the sample to the oven's hot zone.
6. The titration will start automatically if the option “Autostart” has been selected. The TIM550 will display the result until the end of the titration.
7. Withdraw the sample from the oven.
8. Start a new titration with another aliquot or return to the menu. The cell will remain in stand by condition, i.e. ready for a new titration.
9. At the end of a series of titrations statistical calculations are performed.

The user is guided through all the stages in the titration by the TIM550's, clear and concise messages. In this way the quality of the analyses is optimised.

Good Laboratory Practice "GLP"

General remarks

Performing Karl Fischer Titrations is more demanding than other volumetric titrations. Thanks to the **TIM550,** the user is guided step-by-step to easily obtain reliable and reproducible results.

The main difficulties of a Karl Fischer titration are:

- The omnipresence of water in the atmosphere. Leakage of water and vapour in the cell during the titration will lead to an erroneous result. **Radiometer Analytical** has designed a titration stand which is easy to use and ensures operation without contact with the external atmosphere. An electronically driven pump allows addition of solvent and emptying of the cell without any leakage. The user should inspect the desiccant tubes regularly and replace the desiccant when saturated.
- Side reactions will be detrimental to the accuracy of the titration. For example, the reaction with iodine (ketones and aldehydes) or reactions which inhibit the response of the indicating electrodes. In the first case, a specific reagent should be used to reduce the influence of these side reactions and in the latter, an oven is required.

The KF titration cell

It is recommended to always leave the cell on stand by, i.e. the TIM550 measures the effect of ambient humidity during conditioning so that the KF cell is ready for immediate use. Automatic cell conditioning reduces downtime while continuous and intelligent cell volume monitoring prevents overflowing.

The built-in electronically driven pump assures the draining of the KF cell. In this way, exchanges with ambient humidity as well as solvent handling are avoided. A simple key press is all it takes to start the pump. The time delay of the pump has been calculated so that it corresponds to a cell being filled with a solvent such as methanol. If cell emptying is too fast the user can interrupt the procedure and if insufficient the procedure can be repeated.

The **TIM550** permanently monitors the level of liquid in the KF cell to prevent overflowing. It considers by calculation that zero liquid remains each time the cell is emptied. Care should be taken to always empty the cell completely, in order to preserve this monitoring function. This ensures optimal conditions for the Karl Fischer reaction.

The KF titration cell should be completely disassembled if not being used for longer periods of time. The parts should be washed in methanol and then dried. The parts can also be dried in an oven. The temperature of the oven must not exceed 50°C. Higher temperatures are not recommended as this can lead to deformation of plastic parts.

Stirring speed

The stirring speed should be selected to ensure a rapid mixing of the reagent added, without introducing an excessive amount of air into the solution. Insufficient stirring can easily lead to an over-titration whereas excessive stirring may disturb the response of the electrodes.

Delivery tip

The delivery tip should be centred above the stirrer to ensure a rapid distribution of the reagent added.

Platinum electrode

The indicator electrodes should be near the cell walls to ensure sufficiently adequate contact with the titration medium.

The burette

Most manufacturers titrant and solvent bottles can be connected directly to the **TIM550** using the bottle stoppers supplied.

The burette should be equipped with an absorption chamber filled with silica gel or a molecular sieve for H_2O absorption. This will preserve the titre of the titrant and limit titrant consumption during the pre-titration of the solvent.

GLP

Even with all the precautions taken in order to preserve the titre of the KF reagent, it is recommended to perform a calibration at regular intervals. The **TIM550** alerts the operator when a calibration is necessary. The calibration interval is entered by the operator during the programming of the TIM550. In the same way, users of TitraMaster 55 software are able to enter a KF titre expiry date during programming of the KF reagent library. The operator will then be prompted when it is time to replace the KF reagent.

As many as 15 TIM550's can be connected to a single PC via the Windows® based TitraMaster 55 PC software. One standard RS232C serial port is all you need. TitraMaster 55 allows unlimited archiving of results and data, and lets you consult your results and methods at all times.

Safety

A ventilation hood is advisable, particularly if a titrant containing pyridine is used. Please note that, almost all KF titrants and solvents used are inflammable and toxic.

Result calculations

The TIM550 automatically calculates the water content of the sample in the chosen units. The drift measured from the start of the titration, the quantity of water introduced by the solvent and the dilution parameters are also taken into account during calculations. If a series of measurements is performed, the TIM550 will calculate the mean value, the standard deviation and the uncertainty on the mean value.

The user is able to accept or refuse the last result obtained and check the impact it might have on the mean result. A rejected result will remain in the GLP table with the indication “rejected”.

Finally, the TIM550 includes specific QC parameter setting together with High-Low alarms to help operators make the right choice in reviewing results.

D61T001 • Printed by Radiometer Analytical SAS • France • 2004-04D