Karl Fischer Volumetric Titration
Theory and Practice
Guide to Reliable pH, Ion and Conductivity Measurements

This catalogue features a wide choice of electrodes for every application and budget: combined pH, glass or reference electrodes based on Red Rod or traditional technology, metal electrodes, ion-selective electrodes and conductivity cells.

It describes our range of buffers and standards for pH and conductivity measurements as well as electrode maintenance and filling solutions. You will also find practical advice on how to achieve reliable pH, ion and conductivity measurements.

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TitraLab titration systems brochure

TitraLab is a complete solution providing all the elements required to build titration workstations customised to individual applications: Titration Managers, sample changers, software, electrodes, solutions and accessories. Whether you are working in the pharmaceuticals, food, petrochemical, chemical or other industries you will appreciate the key features of our titration systems: accuracy, reliability and ease of use.

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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 their design and titration algorithm, Radiometer Analytical Karl Fischer Titrators provide accurate results and clear sample information. 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 dedicated PC 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.

$$I_2 + SO_2 + 2H_2O \leftrightarrow 2HI + H_2SO_4 \quad (I)$$

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:

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

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

(RN designates the base used)

Ethanol-based reagents have recently emerged. These have the advantage of being less toxic, offering more stable endpoints and faster kinetics.

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 Radiometer Analytical titrators 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.

Radiometer Analytical titrators allow the use of direct or alternating current. The indicating electrode geometry and frequency of the alternating signal have been optimised. The instrument does not operate with instantaneous potential values but uses half the difference between two consecutive measurements.

\[ E(t) = \frac{E(t) - E(t-1)}{2} \]  

(IV)

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 amplitude of the direct or alternating current and the value of the set point are modified according to the resistivity of the reactive medium. Radiometer Analytical titrators offer more than 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.

The working medium

The 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. For methanol-based reagents, 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.

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

The main advantages of these 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.

\(^{(1)}\) PID: Proportional Integral Derivative
Note:
If you are using an ethanol-based Karl Fischer solvent (example: E-Solvent) and you have difficulties balancing your cell, you may need to immerse the Pt-Pt electrode for 2 min. in a 10% v/v TritonX-100 solution once a week. 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.

The titrant
The titrant consists of iodine dissolved in methanol or ethanol. 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.

The titration of samples producing side reactions (aldehydes, ketones and silanols) requires 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.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Solvent</th>
<th>Manufacturer</th>
<th>Recommended speed</th>
<th>Recommended current</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYDRANAL®-Composit 5</td>
<td>Methanol</td>
<td>Riedel-de-Hahn</td>
<td>150 %/min = 15 ml/min</td>
<td>AC 50 µA</td>
</tr>
<tr>
<td>HYDRANAL®-Composit 5K</td>
<td>HYDRANAL®-Solvent K</td>
<td>Riedel-de-Hahn</td>
<td>50 %/min = 15 ml/min</td>
<td>AC 50 µA</td>
</tr>
<tr>
<td>HYDRANAL®-Titrant 1</td>
<td>HYDRANAL®-Solvent</td>
<td>Riedel-de-Hahn</td>
<td>150 %/min = 15 ml/min</td>
<td>AC 50 µA</td>
</tr>
<tr>
<td>HYDRANAL®-Titrant 2</td>
<td>HYDRANAL®-Solvent</td>
<td>Riedel-de-Hahn</td>
<td>150 %/min = 15 ml/min</td>
<td>AC 50 µA</td>
</tr>
<tr>
<td>HYDRANAL®-Titrant 5</td>
<td>HYDRANAL®-Solvent CM</td>
<td>Riedel-de-Hahn</td>
<td>150 %/min = 15 ml/min</td>
<td>AC 50 µA</td>
</tr>
<tr>
<td>HYDRANAL®-Titrant 5 E</td>
<td>HYDRANAL®-Solvent E</td>
<td>Riedel-de-Hahn</td>
<td>15 ml/min</td>
<td>AC 20 µA</td>
</tr>
<tr>
<td>HYDRANAL®-Titrant 2 E</td>
<td>HYDRANAL®-Solvent E</td>
<td>Riedel-de-Hahn</td>
<td>15 ml/min</td>
<td>AC 20 µA</td>
</tr>
<tr>
<td>HYDRANAL®-Composolver E</td>
<td>Ethanol</td>
<td>Riedel-de-Hahn</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Karl Fischer Réagent T</td>
<td>Karl Fischer reagent T</td>
<td>Merck</td>
<td>150 %/min = 15 ml/min</td>
<td>AC 50 µA</td>
</tr>
<tr>
<td>Karl Fischer Réagent 2,5</td>
<td>Karl Fischer reagent 2,5</td>
<td>Merck</td>
<td>150 %/min = 15 ml/min</td>
<td>AC 50 µA</td>
</tr>
<tr>
<td>Karl Fischer Réagent 5</td>
<td>Pyridine</td>
<td>Merck</td>
<td>50 %/min = 5 ml/min</td>
<td>AC 50 µA</td>
</tr>
</tbody>
</table>

If the titrator indicates an excess of iodine at the end of the titration, the burette speed should be halved (a speed below 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 reagent addition.

Water determination using Radiometer Analytical titrators

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 titrator 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. Start the pump then using the titrator solvent button, add between 30 and 40 ml of solvent to the titration cell. Radiometer Analytical has marked the KF cell to indicate 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 titrator. 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. Start the pump then 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 titrator is ready to start titrating when the message “Introduce sample” appears on the display.

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 titrator 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 titrator waits for the input of the sample amount before calculating the final result.

7) Result calculation
The titrator 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.

At the same time, the titrator 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
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.

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 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.

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. Use a specific method based on the preprogrammed «Oven KF method».

Remember to pre-titrated the cell after having turned on the gas flow.

1. The titrator prompts you to weigh an «advised» amount of aliquot. The approximate value of this aliquot has been entered in the titrator beforehand.
2. Introduce the sample in the oven’s cold zone.
3. Enter the «exact» amount of sample weighed.
4. The titrator 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 titrator 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 titrator’s, clear and concise messages. In this way the quality of the analyses is optimised.
Performing Karl Fischer titrations is more demanding than other volumetric titrations. Radiometer Analytical titrators guide the user step-by-step to ensure reliable and reproducible results are obtained every time.

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 titrator measures the effect of ambient humidity during conditioning so that the KF cell is ready for immediate use.

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. Start the pump then press the emptying button. When the cell is empty, release the button then stop the pump. To add solvent, start the pump then hold the solvent button down until the solvent reaches the level marked on the cell.

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 and indicating electrode

The delivery tip should be placed after the indicating electrode following the direction of rotation of the stirrer.

The burette

Most manufacturers titrant and solvent bottles can be connected directly to Radiometer Analytical titrators 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 titrator alerts the operator when a calibration is necessary. The calibration interval is entered by the operator during programming. In the same way, when using dedicated PC software, it is possible 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.

Use of dedicated PC software allows unlimited archiving of results and data and lets you consult your results and methods at all times. As many as 7 titrators can be connected via a standard RS232C serial port.

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 titrator 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 titrator 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 titrator includes specific QC parameter setting together with High-Low alarms to help operators make the right choice in reviewing results.
70 years of excellence in electrochemistry

- pH - Redox - ISE
- Conductivity
- Titration
- Polarography
- Voltammetry and EIS

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