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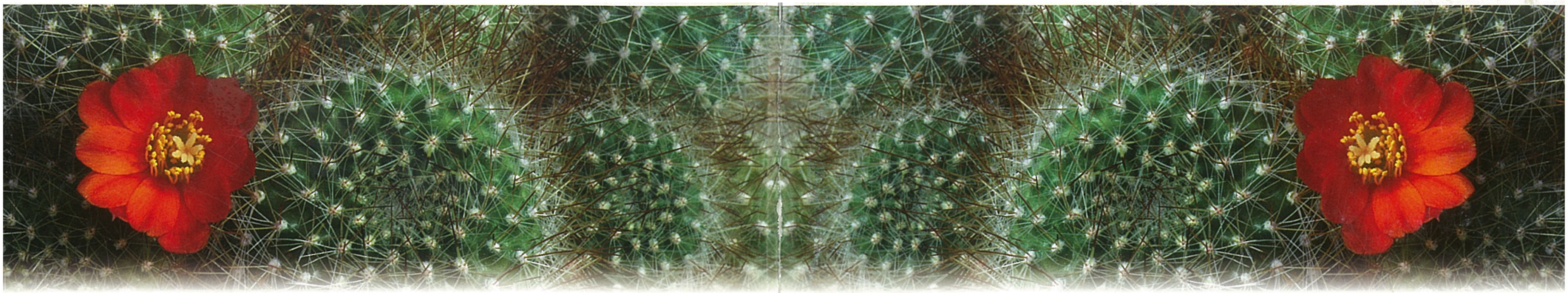
MOISTURE MEASUREMENT:
Karl Fischer Titrimetry

2nd Edition



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Preface

Since we published the first issue of this booklet in 1991, there have been only a handful of literature citations in which the term "Karl Fischer" has been used in the title of the article-notwithstanding the fact that the single most common test run in analytical labs today is moisture determination.

Given this insight, one might be tempted to conclude that there is nothing new in the world of Karl Fischer reagents or procedures, but we would beg to differ. In fact, the GFS commitment to Karl Fischer methodologies expanded to the point that we created a new staff position- Karl Fischer Reagents Product Manager-to ensure that GFS products and services are at the leading edge of the Karl Fischer Reagent Market.

This is very important for a test methodology that has endured since 1935. The refinements to the techniques that were described by John Mitchell, Jr. and Donald Milton Smith are still valuable for their insights into the workings of Karl Fischer reagent systems. We are also pleased to acknowledge the contributions of Alfred A. Schilt, Professor of Analytical Chemistry, Northern Illinois University, whose work laid the foundation for the publication of this expanded second edition of *Moisture Measurement by Karl Fischer Titrimetry.*

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Chapter I.
Introduction

Although water covers most of the earth's surface, we would put ourselves at grave risk if we took it for granted. In fact, the availability of pure water may be destined to become the dominant resource issue of the 21st century, much as was oil in the 20th century. However, for the scientist whose job it is to quantify moisture, its presence may not be a blessing, nor its absence a curse. The method by which it is measured, however, will frequently be critical.

To deal with water in any given system, we may need to view the quantity that is present in the context of a required optimum amount or a minimum acceptable level. Proper perspective can only be provided by accurate measurement of the amount or concentration of water present. The subject of this brief monograph concerns an important method of measurement-the Karl Fischer titration method.

The importance of this method is reflected in its inclusion in the ninth edition of *Reagent Chemicals,* the ultimate guide to analytical specifications and methods published by the American Chemical Society Committee on Analytical Reagents. This text devotes considerable space to the treatment of Karl Fischer methodologies, addressing both volumetric and coulometric procedures. Relevant topics include titration apparatus, electrometric endpoint determination, reagent preparation and standardization, and titration procedures.

The chemical literature abounds with different techniques and methods for the determination of water. This is largely a consequence of the complexities involved when water must be determined in so many different hosts and kinds of samples. Moreover, special methods are required for different concentrations, e.g. trace (parts per million) levels of water require unusually sensitive methods.

Essentially all real samples contain some moisture. If the sample is a liquid, a different technique is necessary than for a solid or a gas. Heterogeneous mixtures can be particularly troublesome. For solid samples, water theoretically can be present in six different modes:

- adsorbed
- absorbed
- imbibed
- occluded
- hydrated
- water of chemical combination

The tenacity by which water is held or incorporated by these different modes varies enormously, and so does the ease by which it can be detected or removed. Thus, many different methods are needed, in as much as none has proven adequate for all purposes and samples.

Of all the different methods available for the determination of water, the Karl Fischer method affords the greatest versatility and scope of application. It can even be employed for quantitative determination of certain organic as well as inorganic compounds by taking advantage of their reactivities whereby water is either liberated or consumed in a stoichiometric manner.

Described in 1935 by Karl Fischer,[1] a chemist employed by Edeleanu Gesellschaft, the reagent that now bears his name was composed of iodine, sulfur dioxide, pyridine and methanol. Its effectiveness, particularly for the determination of water in sulfur dioxide, was quite remarkable. Among the first to recognize the great potential of the reagent, Smith, Bryant and Mitchell, employed by E.I. du Pont de Nemours & Co. in Wilmington, Delaware, undertook further investigations of the reagent, measuring the stoichiometry of its reactions and developing new applications for it.[2] Their continuing work helped greatly to popularize both the use of the reagent and the name they gave to it, the Karl Fischer reagent. The well-known book entitled Aquametry by John Mitchell, Jr. and Donald Milton Smith

published in 1948 provided even greater impetus for widespread use of the Karl Fischer reagent. Now in its second edition,[3] this and other books[4-5] on the subject attest to the importance of the Karl Fischer reagent in chemical analysis. Other methods for determining water may also be of interest to the reader, so they are listed below. Details concerning these methods are available in a single source succinctly summarized by Mitchell and Smith:[6]

A. **Chemical methods:** include those based on reactions with acetyl chloride, acid anhydrides, lead tetraacetate, tertiary-butyl-o-vanadate, magnesium nitride, or calcium carbide.

B. **Gravimetric methods:** include use of oven drying, desiccation, thermogravimetry, freeze drying, absorption, or condensation.

C. **Thermal methods:** thermal conductivity, reaction, and differential thermal analysis methods.

D. **Spectral methods:** visible, ultraviolet, infrared, NMR, mass spec, microwave, and X-ray spectroscopy (see section 6.3 for the use of infrared methods to determine moisture content via dew point measurement).

E. **Separation methods:** measurement of water after separation by distillation, centrifugation, extraction, or chromatographically.

F. **Physical methods:** determination based upon measurement of turbidity, density, refractive index, vapor pressure, volume of gas liberated by reaction of water with various substances, dew point, freezing point, piezoelectric effect by sorbed mass of water, and other physical phenomena or properties influenced by moisture content.

G. **Radiochemical methods:** measurements based on isotope exchange reactions, neutron scattering, or beta and gamma-ray counting.

Chapter II. Fundamental Chemistries

To determine water content in a sample, Fischer dissolved it in methanol and titrated with a solution consisting of 790 g (10 moles) of pyridine, 192 g (3 moles) of sulfur dioxide and 254 g (1 mole) of iodine dissolved in 5 liters of anhydrous methanol. The first appearance of unused iodine provided a sharp, reproducible endpoint. Fischer reported the stoichiometry of the reaction to be as follows:

$$I_2 + 2H_2O + SO_2 + 4py \rightarrow (py\,H)_2SO_4 + 2pyHI$$

Later, more detailed measurements by Smith, Bryant and Mitchell revealed that the reaction in methanol takes place in the following two distinct steps:

$$pyI_2 + pySO_2 + py + H_2O \rightarrow 2pyHI + pySO_3$$

$$pySO_3 + CH_3OH \rightarrow pyHSO_4CH_3$$

They also found that when chloroform or benzene was employed in place of methanol as solvent, a second mole of water is consumed as follows:

$$pySO_3 + H_2O \rightarrow pyH_2SO_4$$

Clearly, use of methanol as solvent affords improved stoichiometry: one mole of iodine consumes one rather than two moles of water, a factor of 2 in favor of sensitivity.

The following equations show the general Karl Fischer reaction in methanol, as currently accepted:

$$2\,CH_3OH + SO_2 \qquad CH_3SO_3^- + CH_3OH_2^+$$ *(Solvolysis)*

$$B + CH_3SO_3^- + CH_3OHt \qquad CH_3SO_3^-BH^+ + CH_3OH$$ *(Buffering)*

$$H_2O + I_2 + CH_3SO_3^-BH^+ + 2B \qquad CH_3SO_4^-BH^+ + 2\,BHI$$ *(Redox)*

(where B is a variable amine base)

2.1 Role of Solvent

The stoichiometry of the KF reaction is influenced by the nature of solvent employed. As seen by the reaction scheme above, sufficient methanol is required to favor formation of pyridinium methyl sulfite. If methanol is excluded from the Karl Fischer system, methyl sulfite cannot be formed, and the so-called Bunsen reaction will predominate:[1]

$$2\,H_2O + I_2 + SO_2 \qquad 21\text{-} + so/\text{-+} \quad 4H^+$$

Solvents other than methanol have been investigated for use in KF titrations.[2,7] Results for the most part confirm the importance of methanol. Inert solvents tend to give ill-defined stoichiometries. For example, the corresponding values (ratios) for pyridine, propylene carbonate, and dimethylformamide were found to be 1:1.09, 1:1.10, and 1:1.20, respectively. In some cases, these values may approach one mole of iodine per two moles of water (1:2).

One solvent other than methanol is notable in that it acts like methanol to ensure favorable stoichiometry but also provides much longer shelf life to the KF reagent.[8] The solvent is 2-methoxyethanol (Methyl Cellosolve®), and its stabilizing influence on KF reagent systems arises from its inertness in the type of side reaction that methanol tends to undergo, as described below in the section entitled Side Reactions.

2.2 Role of Pyridine and Other Bases

Various investigators have concluded that the role of pyridine is that of a buffer to maintain a favorable pH for the KF reaction. Cedergren[9] found that the reaction rate is independent of pyridine concentration and first order with respect to each of the other reactants: water, sulfur dioxide and iodine. Investigations by Verhoef and Barendrecht confirmed these rate results.[10] They found further that the log of the rate constant of the KF reaction increased linearly up to pH 5 and was constant (log K = 3.12) in the range from pH 5.5 - 8. Use of buffers other than pyridine, and of the same pH, gave the same reaction rate.

Suitable buffer substitutes for pyridine, some affording improved performance, include sodium acetate,[11-12] aliphatic amines (e.g. diethanolamine),[13] heterocyclic amines,[14] imidazole[15] and acyclic primary amines.[16] The pyridine-free WaterMark® reagents use combinations of these other amines, providing safety, performance and rapidity to your Karl Fischer titrations.

2.3 Side Reactions

Freshly prepared KF reagent suffers an initial rapid loss in titer (water equivalency), then a more gradual loss as a result of the reaction:

$$I_2 + SO_2 + 2CH_3OH + 3py \text{ -+ } 2pyHI + pyCH_3OSO_3CH_3$$

This reaction gives rise to formation of quaternary pyridinium methyl sulfate salt.[2] It is for this reason that the stabilized reagent containing Methyl Cellosolve®,[8] as well as the two-solution reagent,[17-18] have found wide acceptance. The pyridine-free one-component volumetric solutions still go through a titer loss, not only because of side reactions, but also because this system is very hygroscopic. The simple expedient of keeping at least one of the four ingredients apart from the others before use avoids the problem of short shelf-life and the need for standardization immediately before or after each use.

Parasitic reactions other than the above undoubtedly contribute also to the gradual diminution in strength of KF reagents with time, but these have not as yet been clearly elucidated. The complexity of the reagent mixture, the effects of possible impurities, and the varying influences of relative concentrations of ingredients and reaction products all contribute to the difficulty of identifying other possible parasitic reactions.

2.4 Interferences

Certain reactive substances can interfere in the KF determination of water. Samples known to contain such substances can be given special treatment, or special conditions can be employed to minimize or eliminate interferences. In general, substances that interfere are of three types: reductants that are oxidized by iodine, oxidants that are reduced by iodide, and substances that form water in reaction with components of the KF reagent or its reaction products. Reductants that interfere include:

- certain phenols such as hydroquinone and aminophenols (some of them can still be titrated by volumetric Karl Fischer, adding salicylic acid to the titration solvent)
- thiols (mercaptans) oxidize iodine as follows:

$$2\,\mathrm{RSH} + \mathrm{I_2} \longrightarrow \mathrm{RSSR} + 2\,\mathrm{HI}$$

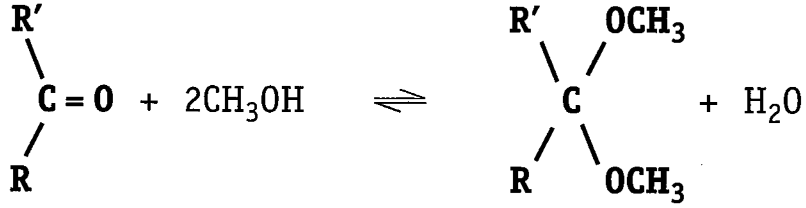
- thioacetate and thiosulfate

Because these reductants consume iodine, they cause high results in the Karl Fischer titration.

Oxidants that interfere are fewer in number. This is because KF reagents commonly contain a large excess of sulfur dioxide, which is capable of reducing many oxidants. Therefore the only oxidants that interfere, assuming sufficient sulfur dioxide is present, are those that fail to be reduced by sulfur dioxide but are strong enough to oxidize iodide to iodine. An example is sodium dichromate. Its presence causes low results in KF titrations, because any iodide formed in the titration will react with dichromate to form iodine to thus regenerate the titrant *in situ.* Potassium permanganate is a strong oxidant but it is relatively insoluble in methanol and does not interfere.

Substances that interfere by water-forming reactions include the following: esters, active carbonyl compounds, basic oxides and hydroxides, and inorganic carbonates.

Aldehydes and ketones react with methanol to form acetals and ketals:



Aldehydes are much more reactive than ketals. The longer the chain length of an aliphatic ketone, the lower its reactivity, and aromatic ketones are less reactive than aliphatic ones. The above reaction can be suppressed by using methanol-free Karl Fischer solvents and titrants.

For the other interfering compounds, proper choice of conditions and/or prior treatment (addition of a buffer) suffices in most applications to overcome interferences.

Chapter III
Karl Fischer Reagents

3.1 Types of Reagents

In addition to the conventional methanol-based reagent first introduced by Fischer, a number of different modified reagents have been proposed that afford advantages in special cases. Additional types include the two-component volumetric reagent and a new series of coulometric varieties. Many of the reagent compositions are patented or proprietary, and produced commercially at affordable prices, thereby minimizing the need for technicians to generate the reagents themselves. Handling and mixing of the odoriferous ingredients, complicated by possible health hazards and the need for anhydrous components and conditions, is a task not readily undertaken by the casual user.

3.1.1 Single Solution KF Reagent

In the conventional KF method, the Karl Fischer reagent is employed as titrant to titrate the water content of a sample dissolved in methanol.

Different workers have used different concentrations and orders of mixing of ingredients in preparing the methanol-based KF reagent. The Mitchell and Smith procedure[3] has proven very satisfactory for their use and recommended for the interested reader. It provides a reagent having a water equivalency of about 3.5 mg/ml.

3.1.2 Two-Solution KF Reagent

To avoid the problem of gradual loss in strength brought about by slow side reactions (described in Chapter II), ingredients of the KF reagent are kept apart until the actual titration. The two-solution system consists of a titrant solution of iodine in methanol or other suitable solvent, and a second solution containing appropriate amine base, sulfur dioxide, and suitable hydroxy-containing solvent. The second solution is either used to dissolve the sample or added to a previously dissolved sample.

Use of the two-solution reagent affords the advantages that the titrant solution does not need to be aged before use, is less prone to absorb moisture on brief exposure to the atmosphere, and seldom requires re-standardization.

3.1.3 Coulometric KF Reagents

For coulometric titration of water based on the KF reaction, iodine is generated anodically in an electrolysis cell. The cell initially contains all the ingredients of the KF reagent except iodine; it also contains iodide in addition to the sample being titrated. The amount of water in the sample is directly proportional to the quantity of iodine generated by the anode.

Based on Faraday's Law of Electrolysis, the quantity of iodine generated is directly proportional to the quantity of electricity passed, this enabling the calculation of the amount of water in the contained sample.

Meyer and Boyd[19] employed "spent" KF reagent as coulometric electrolyte to titrate water automatically in an apparatus of their design. Their electrolyte was added to both anodic and cathodic compartments and consisted of conventional KF reagent to which was added an amount of water just sufficient to reduce the iodine content to iodide.

A number of patents claiming improvements in coulometric titrations have been granted for electrolyte compositions as well as for separate anode and cathode compartment compositions. Proprietary compositions are commercially available for coulometric KF titrations of special kinds of samples. These include WaterMark®(GFS Chemicals), Hydranal®-Coulomat (Riedel-deHaën®), Aquastar® (E. Merck, EMD Chemicals), Mitsubishi, and Fisher Scientific.

3.1.4 Modified KF Reagents

Numerous modified reagents have been recommended over the years for special applications with one or more advantages claimed for each. Brief summaries of some of these are given in the following paragraphs. An obvious advantage is provided by substitutes for pyridine that are odorless. Some examples are noted in Chapter II; others that have been tried include the following: N-ethylpiperidine and bipyridyl,[20] urea,[21] and mixtures of aminopyridine and dipyridyl compounds.[22]

Methyl Cellosolve® provides an advantage over methanol as solvent in KF reagents in that parasitic reactions are diminished so that shelf life is enhanced and the need for frequent restandardization is minimized. Such stabilized reagents are commercially available, e.g. WaterMark®/GFS Single Solution KF reagent which also incorporates an odorless buffer in place of pyridine.

Various KF reagent compositions have been explored in search of suitable reagents for titrimetric determination of water in active carbonyl compounds. For the most part these are based on the use of an alcohol or substance other than methanol to suppress or avoid ketal and acetal formation which is accompanied by water formation to give erroneously high results. Some of the more effective compositions contain one of the following in place of methanol: dimethylformamide,[23] a mixture of chloroform and an alkylene carbonate,[24] 2-chloroethanol,[25] and 2,2,2,-trifluoroethanol.[25] A comparative study of these and others has been reported by Scholz.[25] Reagents of this type are available commercially (e.g. from GFS Chemicals or Riedel-deHaën®).

A non-hygroscopic KF titrant/solvent system, patented by H. Dahms,[26] affords the advantage of eliminating drying tubes from burettes and the need for frequent restandardization. These xylene-based reagents can be used with all volumetric 2-component solvent systems. This is the most stable Karl Fischer titrant available today. Stable titrants of this kind are commercially available–for example WaterMark®/GFS Chemicals, with titer strengths of 5.0, 2.0, 1.0 and 0.5 mg/ml. The WaterMark® product line is the only one to offer a titrant as low as 0.5 mg/ml, for determinations of micro levels of water when the coulometric method is not available.

3.2 Standardization of KF Reagents

Standardization of a KF reagent is necessary in order to determine its water equivalency, i.e. the weight in mg of water that will react with exactly 1 mL of titrant. The process involves accurate measurement of the volume of titrant required to titrate an accurately weighed quantity of either water or a stable salt hydrate. To use plain water for standardization it is convenient to dispense it from a microsyringe. The weight of water delivered is found by accurately weighing the syringe immediately before and after dispensing the water directly into the titration vessel. Alternatively, water standards of known concentration are commercially available in w/w or w/v solutions. These standards are specially produced from dried industrial solvents and are typically standardized to NIST traceable water.

Calculation of water equivalency (WE) is made using the following equation:

$$\mathrm{WE} = \frac{\text{Weight of water in mg}}{\text{Volume of titrant required in mL}}$$

Note that the units of WE are mg H_2O/mL titrant. If a salt hydrate is used for standardization another relationship is used to calculate WE, likewise if a commercial water standard is used. These calculations are given below for each use.

3.2.1 Use of a Salt Hydrate

A commonly used substance for standardizing KF titrants is sodium tartrate dihydrate. Neuss and coworkers recommend it over a dozen other possibilities.[27] Its water content is 15.66% and constant in atmospheres of relative humidity 20 to 70 percent. One disadvantage is that it dissolves slowly in methanol, but dissolving time can be shortened significantly by using it in finely powdered form, or with the aid of a co-solvent. The following procedure is suitable for standardizing a KF titrant of WE = 2 - 5 mg water/mL using sodium tartrate dihydrate:

(1) Add 40 mL of dry methanol or suitable solvent to the titration vessel, e.g. a 100-ml volumetric flask. Titrate its water content with the titrant to be standardized, stopping at the first permanent brown color of iodine in the solution, or at the end-point found by the titrator. This step assures that the solvent is pre-titrated so that its moisture content is not a factor in the standardization.

(2) Accurately weigh a powdered sample of sodium tartrate dihydrate (about 0.5 g, weighed to the nearest 0.1 mg) and transfer it to the closed vessel containing the pre-titrated solvent. Stir until all of the powder dissolves. Titrate with the KF titrant to be standardized and record the volume required to titrate the weighed sample to the same end-point as before. Do not include in this volume the volume of titrant required for pre-titrating the solvent. This procedure should be performed a minimum of three times to ensure accuracy and follow good laboratory practice.

(3) Calculate the water equivalency of the KF titrant as follows:

$$\mathrm{WE} = \frac{(\text{mg of sodium tartrate dihydrate}) \times (0.1566)}{(\text{mL of KF titrant required})}$$

3.2.2 Use of Commercial Water Standards

Commercially available liquid water standards consist of water dissolved in an appropriate solvent or mixture of solvents. The WaterMark® water standards are methanol-free, and can be used for all applications including KF titrations involving aldehydes or ketones.

These water standards are available by weight (w/w–known weight of water per gram of standard solution) or by volume (w/v–known weight of water by volume of standard solution). Whenever possible, we recommend using water standards by weight. Use of an analytical balance will allow measurement of such standards with a precision of ± 0.0002 gram.

The standards come in single-use 5 mL ampules, and are injected via syringe into the titration cell. The syringe must be rigorously dried, and rinsed thoroughly with portions of the water standard from the ampule being used.

Protocol for water standards by weight: Pipet an approximate volume of 1 mL into the syringe. Weigh the full syringe. Inject the standard into the titrator and start the titration. Reweigh the syringe, and enter the mass of water (by difference) that corresponds to the mass of standard that was injected.

Protocol for water standards by volume: Pipet an *exact* volume of the standard in a calibrated syringe. Inject the sample into the titrator and enter the mass of water corresponding to the volume of the standard used.

Taking the example of the water standard by volume, calculation of the water equivalency of the KF titrant is as follows:

$$\mathrm{WE} = \frac{(\text{Volume of standard solution}) \times (\text{WE of standard solution})}{(\text{Volume of KF titrant required})}$$

3.3 Stability, Storage, and Safety

Different batches of KF reagent of the same formulation as well as those of differing compositions exhibit significant differences in their stabilities, measured in terms of loss in water equivalency with time. Much investigation and speculation has been devoted to elucidating causes of instability and discovering means for improving stability. Scholz[5] offers several hypothetical decomposition mechanisms but concludes that much remains to be learned.

Several important general findings about stability of KF reagents are summarized below:

(1) Conventional methanol-based single-solution KF reagents typically suffer rapid loss in water equivalency when first prepared and thence more gradual loss. Their use requires frequent standardization. Curiously, elevated temperature has little or no effect on the stability. Mitchell and Smith[28] report that the water equivalency of freshly prepared reagent is usually about 80% and in the course of a month falls to about 40% of theoretical, based on initial iodine content.

(2) Stabilized single-solution KF reagents also suffer some loss in water equivalency with time but much less than those that contain methanol. Such solutions need only occasional standardization, dictated by user experience. For single-solution KF reagents containing Methyl Cellosolve® in place of methanol, loss in water equivalency was originally reported at several percent per month.[8] Scholz[29] reported improved shelf life for reagents stored in glass ampules, but not as good as current technology, which can limit titer loss to under 1% per month in many cases. Some loss in strength undoubtedly results if the reagent is not adequately protected from ordinary moist air.

(3) Two-solution KF reagents exhibit long-term stability and require only occasional checking of water equivalency in the event that they may have been exposed to moisture from the atmosphere. Typically, iodine in methanol comprises one stable

solution, and the other contains suitable base and sulfur dioxide in methanol or similar solvent. Rather than mixing A and B just prior to use as a single solution, the sample is dissolved in B and titrated with A. This avoids the rapid initial loss in strength prevalent in freshly prepared single-solution KF reagent. The improved formulation of H. Dahms[26] substitutes for methanol and pyridine, extending stability and improving precision with a patented non-hygroscopic solvent system.

KF reagents are best stored in well sealed (ground glass or Teflon® stoppered) glass bottles, protected from air, moisture and sunlight. Methanol and other solvents used to dissolve samples for KF titration should be protected also. Dry methanol is especially prone to take up moisture.

Safety information is important in assessing possible health hazards in handling, storing and disposing of KF reagents. These reagents and their ingredients can be handled safely with proper laboratory procedures under competent supervision. Use and dispensing of the reagents should be done in well-ventilated areas or hoods.

As with all chemicals and formulations, the MSDS should be consulted prior to use of KF reagents and solvents.

Chapter IV.
Titration Methods and Equipment

Methods for performing KF titrations range from simple manual techniques to an automated, microprocessor controlled approach. Except for the crudest of these, all involve use of appropriate equipment to exclude atmospheric moisture from the titration system. Titration vessels, reservoirs, and titrant delivery units are fitted together with appropriate venting and protected by desiccant-filled drying tubes. The choice of automated over manual instruments is largely one of convenience over cost, except when dictated by a routine that requires processing large numbers of samples each day. The trade-offs to be considered when choosing between volumetric and coulometric methods have also been discussed elsewhere.[30]

The many different kinds of apparatus, instruments, and endpoint methods available to the user cannot be adequately covered in the space of this monograph; however, certain methods merit coverage here because of their popularity, practical advantages and general utility. These are described below.

4.1 Simple Manual Titration with Visual Endpoint Detection

The infrequent user of KF reagent may prefer not to invest in special titration vessels, burettes, and reservoirs. Ordinary glassware can be used with only a modest loss in precision provided that the glassware is dry and care is taken to minimize exposure of titrant and solvent solutions to the atmosphere. Glassware can be either oven dried or rinsed free of moisture with the solution to be contained. The simple expedient of covering the burette with an inverted test tube and use of a narrow long-neck flask (e.g. a 100-mL volumetric flask) with magnetic stirring for the sample solution helps to significantly minimize uptake of atmospheric moisture.

Exposure and titration times should also be kept to a minimum. Moreover, it is advisable to standardize the titrant immediately following or prior to titration of the sample, so as to achieve some compensation in errors common in both. It is important to limit this approach to samples that contain 50-250 mg of water, because relative error increases appreciably for smaller samples of lower moisture content.

Precision and accuracy are favored by use of a titration apparatus designed to guard against atmospheric moisture.

The titration procedure is essentially the same regardless of titration apparatus. A sample containing 50-250 mg of water is weighed or pipetted into the titration flask, a measured volume of dry methanol (pretitrated) or other appropriate solvent mixture (e.g. part B of a two-solution KF reagent) is added, and the mixture is titrated with KF titrant (when appropriate, the iodine in solvent component, part A, of the two-solution KF reagent). Magnetic stirring during titration is recommended. Titrant is added more slowly and in increasingly smaller increments as the visual endpoint is approached. The endpoint is taken at the first appearance in solution of a brown color that persists for at least 10 seconds. Visual detection of the endpoint color change from yellow to brown is considerably facilitated by viewing light transmitted through rather than reflected from the solution. Thus, illumination behind or below the titration vessel is appropriate. A yellow or daylight lamp also helps. Brief practice leads to easy recognition of endpoints. Agreement to within 0.05 mL between replicate endpoints is common. A titration blank should be carried out in the same way to determine the amount of titrant consumed by water in components added other than the sample. The net volume of titrant consumed by the sample is thus found by subtracting the blank from the sample result. The concentration of water in the weighed sample is calculated as follows:

$$\text{ppm Water} = \frac{(\text{WE of titrant})(\text{Net volume of titrant, mL})(1000)}{(\text{Weight of sample, g})}$$

and for a measured volume sample:

$$\text{ppm Water} = \frac{(\text{WE of titrant})(\text{Net volume of titrant, mL})(1000)}{(\text{Volume of sample, mL})(\text{Density of sample, g/mL})}$$

4.2 "Dead-Stop" (Biamperometric) Titration

For those who experience difficulty in perceiving color changes, especially when colored samples are to be titrated, electrometric endpoint methods are available. The most popular of these for KF titrations is the Willard and Fenwick technique[31] first applied to KF titration by Wernimont and Hopkinson.[32] A pair of platinum electrodes, sealed in the titration vessel and in contact with the solvent solution, are polarized by applying a voltage difference of approximately 100 mV. Very little or no current will flow through the solution between the two electrodes unless both electrodes are depolarized. Depolarization results in the case of the KF titration when both iodine and iodide are present. This first occurs just beyond the equivalence point in titration of water, i.e. when one drop or less of iodine-containing titrant has been added in excess of the amount required. Iodide, of course, is already present, having been formed as a product in the KF reaction. Thus the first appreciable deflection in a galvanometer or voltmeter (if potential drop is monitored) indicating passage of current is a signal to bring the titration to a stop, in effect a "dead-stop." Necessary instrumentation for this well-known method is available commercially and need not be described further here.

Volumetric Karl Fischer titrators include: Metrohm/Brinkmann KFP Titrino 784; Mettler-Toledo DL31 and DL38;

Mitsubishi KF-100. These automated titrators work under the same principles but differ in their engineering and use.

Titrations following this method give excellent results. Users should be aware that the platinum electrodes of these systems can become coated with various substances (mostly oils and sugars) that interfere with the measurement process. If the electrodes are not clean, the end-point can be passed resulting in over-titration.

4.3 Coulometric Titration

Highly effective for microdeterminations and ideally suited for automation, it is obvious why coulometric titration has found popular application in the KF determination of water. Instead of adding iodine in standard solution from a burette, it is generated electrochemically in situ at an anode immersed in the solution to be titrated to which iodide as well as all the usual components of a KF reagent (save iodine) have been added. Applications of a direct current, under conditions of 100% net current efficiency to generate iodine, enables an electronic coulometer to serve the role of a burette. Thus the current-time integral necessary to produce a visual or electrometric endpoint is obtained as a number of "counts." The number of "counts" is directly proportional to the quantity of electricity required to generate the iodine which in turn is directly proportional to the amount of water in the sample.

An example of the sensitivity and time requirements of coulometric titration can be cited from the results of Karisson and Karrman[33] who found that determination of 0.100 mg of water required about 3 min. and 2.00 mg required about 12 min. Results obtained for organic solvent samples of 10-40 uL size exhibited excellent precision with standard deviations ranging from 0.2 to 0.5 ug of water.

Coulometric titrators, typically automated and microprocessor controlled, are commercially available: model 756 KF Coulometer by Brinkmann; the DL32 and DL39 from Mettler-Toledo; the MKC-510N and MKC-500 from KEM (Japan); the Photovolt Aquatest 2010; the CA-100 from Mitsubishi; Aquapal III from CSC Scientific, and others. Details on the operation of these instruments are available from their manufacturers.

A drying oven can be connected to most of these titrators. Some substances release their water only at high temperatures, or react with the Karl Fischer reagents, therefore their direct titration is not possible. Their moisture needs to be driven off in an oven at a temperature between 100 and 300 °C, and carried to the titration in a dry, inert gas.

4.4 Other Methods

Endpoint methods other than visual and biamperometric have been successfully employed in KF titrimetry. These include potentiometric,[34] photometric,[35] and thermometric[36] methods.

Automatic titrators, other than coulometric, are commercially available from various instrument makers, e.g. Radiometer, Brinkmann, and Mettler. Titrant delivery systems for these involve constant rate motor driven pumps or syringes in place of burettes. An electrometric endpoint signal terminates titrant delivery and initiates numerical display of elapsed time and thus volume of titrant delivered. Some even make the conversion to mg of water.

A recent innovation, although not a titrimetric method, is the application of flow injection analysis (FIA) to the determination of water using KF reagent. One of the great advantages of FIA is its capability of processing a large number of samples in a relatively short time.[37] Escott and Taylor[38] report determination of water in gasoline-alcohol blends at rates up to 60 samples/hr by FIA. They found that potentiometric served better than amperometric detection, providing a linear working range of 0 to 1500 ppm of water. Either methanol or methanol-xylene mixture was employed as carrier stream, into which samples were introduced via a 50 uL sample loop. The carrier stream was also continuously fed each part of a conventional two-solution KF reagent.

A general evaluation of the spectrophotometric determination of water by FIA using conventional single solution KF reagent as well as pyridine-free two-solution KF reagent was reported by Nordin-Anderson and Cedergren.[39] Very little interference effects were noticed for ketal-forming samples using the two-solution reagent, and none were evident using Hydranal® (Riedel-deHaën®).

Determination of water in organic solvents by FIA using biamperometric detection and two-solution pyridine-free KF reagent has been reported.[40] Response was linear in the concentration 0.03-0.11% water in methanol, ethanol, or isopropanol with methanol as carrier solvent.

Chapter V.
Sample Treatment and Handling

Every chemical analysis begins with the process of selecting an appropriate sample, i.e. one of convenient size that accurately represents the bulk material to be analyzed. Sampling is relatively simple for homogeneous materials but certainly not for heterogeneous mixtures, especially for solids of large and diverse particle sizes. Even though this brief chapter concerns the treatment rather than the selection of analytical samples, one should be reminded that analytical sampling is not a casual exercise but rather one which should be guided by statistical methods. For guidance one can consult one or more texts on statistical methods and specific sampling methods for various materials described in publications by the American Society for Testing and Materials, Association of Official Agricultural Chemists, American Oil Chemists' Society, etc.

For best results, samples should be pulled just prior to analysis. When this is not feasible, samples should be stored for as brief a period as possible. Obviously they need to be protected from moisture loss or gain from the atmosphere. For this purpose glass rather than plastic bottles are preferred, because the latter are not necessarily impervious to water vapor nor can they be as readily dried in an oven. Not all samples require scrupulously dried storage vessels. The need is most acute for samples that contain very little moisture. Air dried containers are suitable for ordinary hydrates or samples that contain moisture levels typically greater than 0.5%. To store homogeneous liquids, the container needs only to be rinsed with several small portions of the liquid sample before filling. A further concern about storage of any sample for water determination is the possibility that swings and changes in temperature might cause water in the samples to collect by condensation upon container walls. Liquid samples, of course, need only to be shaken well before removal from the container, but solid samples may not readily reabsorb water condensate on shaking. An area of uniform temperature should be provided for storage to avoid this problem.

Treatment of samples prior to determination of water depends upon the physical state and chemical nature of the sample. Need for special treatment arises if the sample is not readily soluble in methanol or a suitably inert solvent, or if it contains substances that will interfere in the determination. Gases require special treatment, particularly if their moisture content is very low.

5.1 Soluble Materials

Most liquids are sufficiently soluble in methanol or inert solvent such as xylene or chloroform to be titrated directly without need of special treatment. A liquid sample can be delivered into the titration vessel either by pipet or injection syringe that is pre-rinsed with sample rather than pre-dried. Weighing of liquid samples is more precise but, if not done quickly, one runs a greater risk of moisture gain or loss. Solid samples are weighed in closed, sometimes sealed, vessels and either introduced directly into the titration vessel or dissolved in a measured volume of appropriate solvent blank to calculate the needed correction. If the solid is transferred to a titration vessel that contains "pre-titrated" solvent, no blank is necessary.

5.2 Insoluble Solids

If only surface moisture is to be determined it is desirable that the solid sample not be soluble. For determination of total water, however, some method of liberating and collecting the water content of the sample must be employed. Methods involve extraction, distillation, or the use of an oven attachment common to today's titrators. The effectiveness of the method depends greatly upon the porosity of the solid and particle size. Thermal stability can also be a factor if decomposition is accompanied by liberation of water of chemical constitution.

The simplest extraction procedure is one that can be carried out in the titration vessel with an appropriate solvent (e.g. methanol, pyridine, dimethylformamide, or ethylene glycol), stirring, and sometimes at elevated temperature. Finely divided powders may require only a few minutes extraction time if they are sufficiently porous. Longer times are more often the rule, but extraction is not always completely effective, especially for impervious solids, even when carried out by refluxing in special apparatus. Of course, certain types of samples have to be extracted in separate vessels or at least removed from the titration vessel prior to titration of the extract because they would otherwise interfere in the titration. Also one needs to take precautions against possible loss or gain in moisture when solids must be pulverized to facilitate complete extraction.

Examples of substances that typically require use of an extraction procedure prior to moisture determination include grains, flours, powdered milk, cheese, wood, and cotton.

Distillation or volatilization methods are less commonly used than extraction for determination of moisture in insoluble compounds. Commercial systems that incorporate oven heating and inert gas sweeping to determine moisture by KF titration in plastics and other insoluble matter are available from manufacturers, including Mettler, Brinkmann, Photovolt, and Mitsubishi. Azeotropic distillation has been employed in conjunction with the KF determination of moisture in coffee and coffee products.[41] A volatilization method using a stream of dry nitrogen to sweep the water vapor from a heated sample into a KF reagent gave more accurate results than extraction with methanol in determination of moisture in electrical insulating paper.[42] ASTM method D789-81 for the determination of moisture in nylon materials involves heating the sample at 180-260°C to volatilize its water content which, after condensing in a cold trap, is titrated with KF reagent.

5.3 Gases

To determine moisture in gases, a measured amount of the gas is caused to pass through an absorber that physically or chemically retains water. The absorber can be a dry solvent, KF reagent, desiccant, or cold trap. A liquid of low vapor pressure is preferred to keep evaporation loss to a minimum, particularly if a large volume of gas must be passed to accumulate sufficient water for accurate measurement. Ethylene glycol therefore is sometimes also employed in mixture with other solvent or KF reagent absorber. The amount of water retained is then determined by titration with KF reagent or with a standard solution of water in methanol if KF reagent was employed as absorber. Coulometric titration is particularly effective for this purpose because of its high precision and the low level of moisture in most gases. Use of dilute KF reagent to achieve the same purpose is less precise, and complicated by the difficulty of excluding extraneous moisture from solvent and reagents.

The moisture content of a gas can also be determined by measuring the volume of the gas at a given pressure and temperature that must be passed through a measured volume of standard KF solution in order to consume the iodine. In effect, the moist gas serves as the titrant to be standardized in a gasometric titration, the endpoint being marked by a change in color from brown to yellow.

Suitable apparatus for gas analysis is available commercially. Gas flow is regulated by a valve and monitored by a flowmeter to constant flow between 100 to 500 mL/min. After purging with hot, dry nitrogen to remove any moisture from the glass tubing and absorption/titration cell, the volume of gas sampled is calculated as the product of flow rate and time. A volumetric flowmeter can also be used to measure total volume passed. It should be installed at the end of the line with a drying tube or tower between it and the absorption/titration cell to protect the cell from back diffusion of moisture from the flowmeter.

Chapter VI.
Applications

Attesting to its effectiveness, the KF method for determination of water enjoys widespread use in a great many different applications. These are classified and summarized briefly in this Chapter. Procedural details are omitted for brevity, but literature references are included to identify sources of specific information.

6.1 Moisture or Hydrate Water in Simple Substances

6.1.1 Inorganic Compounds

Inadequate solubility in appropriate titration media is a commonly encountered problem when inorganic substances are to be analyzed. Recourse to extraction or distillation, as described in Chapter V, is necessary in many cases. Some substances may also react with the Karl Fischer reagent itself, or with the reaction product.

Water in inorganic salts can be found as water of crystallization, included water, and adherent moisture. It is better to dissolve the inorganic salt completely to determine total water (including water of crystallization).

If a hydrate does not dissolve in pure methanol, one can try adding formamide to the titration solvent (up to 50% formamide). Other techniques, such as fine milling, or titration at elevated temperature can assist in dissolving an inorganic salt.

Salts of inorganic acids that are sufficiently soluble to enable titration of their total water content include the following diverse illustrative examples: sodium bisulfate, aluminum chloride, mercurous nitrate, ferrous sulfate, boron trifluoride, manganese ammonium phosphate, potassium ferrocyanide, ruthenium sulfide, ammonium perchlorate, cesium iodide, and sodium chloride.[43] High purity metal salts such as those used in discharge lamps can be analyzed for traces of water, hydroxide and oxide by coulometric KF titration.[44]

Carbonates and bicarbonates react with KF reagents by oxidation of iodide formed by the KF reaction; water is formed which is then also titrated. Water content of these compounds is best determined titrimetrically after isolation by extraction or volatilization.

Oxides and hydroxides react with KF reagent to yield water, according to reactions such as the following shown for silver oxide:

$$Ag_2O + 2\,HI \rightarrow 2\,AgI + H_2O$$

Although the reactions are stoichiometric they are not always rapid or complete. It is thus not always possible to distinguish between water content and water generated in reaction. Very insoluble oxides, such as ferric and aluminum oxide, do not react, so their surface adsorbed water can be measured by KF titration.

Acids and acidic gases should be treated with excess pyridine or other suitable buffer (e.g. WaterMark® Buffer Solution, Cat. No. 1615) prior to titration to prevent water formation attending esterification of methanol, and to avoid adverse acidity. Water has been determined in the following: sulfur dioxide,[1] hydrogen chloride,[45-46] hydrogen fluoride,[47] and sulfamic, sulfuric and nitric acids.[48] For the determination of moisture in sulfuric acid monohydrate and its mixtures with ammonium acid fluoride, a modified KF reagent in which methanol is replaced with dimethylformamide has been described.[49] Amperometric titration yielded results with relative errors of 6-11% for samples containing 1.5 to 7.5% water.

Among other specific applications of the KF method was the determination of water in desiccants such as calcium chloride, silica gel, Fuller's earth, alumina, and Drierite®.[1, 50]

6.1.2 Organic Compounds

The KF method proves particularly advantageous in comparison to other methods when applied to determination of water in compounds that are volatile, thermally unstable, or susceptible to hydrolysis. For example, esters, lactones and carbamates are best analyzed for moisture by KF titration.

False endpoints are occasionally encountered when nearly anhydrous liquid samples are titrated to determine their water content. Mitchell and Smith[3] point out that false endpoints are associated with insolubility of one or more reaction products, notably pyridine hydroiodide, in the liquid being titrated. They assert that this problem can be avoided easily by "the addition of an inert solvent, such as methanol, in which both the sample and the reaction products are soluble." A suitable solvent for this purpose is GFS General Purpose KF Solvent (Cat. Item # 1610).

A complete list of organic compounds for which the KF method has proven satisfactory for determination of water content is too long to include here; instead, applicable classes of compounds that present no particular difficulty are listed below:

CLASSIFICATION OF APPLICABLE ORGANIC COMPOUNDS

Acetals
Acid anhydrides
Acyl halides
Aldehydes, stable
Alkaloids
Amides
Amines, weak base
Amino acids
Amino alcohols
Anilides
Aromatic hydrocarbons
Azo compounds
Carbamates
Carboxylic acids

Hydrocarbons, saturated
Hydroperoxides
Hydroxamic acids
Imines
Isocyanates
Isothiocyanates
Ketones, stable
Lactams
Lactones
Nitriles
Nitro compounds
Nitroso compounds
Oximes
Peroxides (not acyl)

CLASSIFICATION OF APPLICABLE ORGANIC COMPOUNDS
(CONTINUED)

Cyanohydrins
Cyanic acid derivatives
Disulfides
Ester
Ethers
Ethylenic hydrocarbons
Halides
Phenols
Proteins
Purines
Sulfides
Sulfonic acid
Thiocyanates
Thio esters

Not included in the above listing, the following compounds have not proven applicable as yet because they react with iodine under conditions required for the KF titration, and no means of inhibiting their interferences is known: ascorbic acid, diacylperoxides, peracids, and quinone. For these compounds, titration at low temperature can suppress or slow down the side reactions. The titration vessel can be placed in an ice bath, or in a dry ice/methanol mixture to achieve a lower temperature.

Some types of organic compounds can react with one or more KF reagent components other than iodine, but their interference can be easily avoided by prior treatment of the sample or by suitable adjustment in the KF reagent composition. Examples of each such type are cited below together with one or more comments concerning the necessary modification to avoid interference.

Aldehydes and Ketones

Carbonyl compounds can react with methanol to form an acetal or ketal and water which causes high results or may even preclude reaching the end-point of the titration. The amount of water generated is dependent on the extent and rate of the reaction and thus the time required to complete the titration. Special conditions or techniques are therefore necessary to determine water content of active carbonyl compounds. The most commonly used approach is to eliminate methanol from the KF reagent, replacing it with either an inert solvent or a much slower reacting alcohol. Various non-methanol compositions have been recommended, some patented. Substitutes for methanol include dimethylformamide,[51] pyridine,[32] isopropanol or butyl alcohol,[52] propylene glycol and pyridine,[53] 2-methoxyethanol, ethylene glycol, a mixture of chloroform and propylene carbonate,[54] and 2-chloroethanol or trifluoroethanol.[25] It is important to know that the course of the titration with these solvents is slower, and can be very sluggish. It is also recommended to increase the end-point potential (read by the electrode) from 100 mV (default value) to 120-125 mV.

Some carbonyl compounds that do not interfere in the conventional KF titration using methanol are the following: formaldehyde, 2-furaldehyde, chloral, sugars, benzil, benzoin, benzophenone, diisopropyl ketone, dibenzylacetone, and quinalizarin.

Amines

Strong bases adversely affect the KF method. If not neutralized they cause high results, even total endpoint failure. Amines with pK_B values less than 8 should be neutralized with an appropriate acid prior to KF titration. Of the various acids recommended, salicylic or benzoic acid afford the advantage that they do not readily undergo esterification in methanol-containing solutions. Esterification, of course, generates water and leads to high results. A methanolic solution of benzoic or salicylic acid can be employed for neutralization whereupon cooling to minimize esterification is unnecessary. Acetic acid is unsuitable because it esterifies too rapidly. It is still not possible to reach a stable end-point with certain amines such as aniline, toluidine, aminophenol, and certain diamines.

Hydrazine Salts

Hydrazine and its derivatives react mole for mole with iodine of KF reagent when dissolved in methanol and titrated. This is true also of their hydrochloride salts. Curiously, the sulfuric acid salt of hydrazine is unreactive and its water content can be measured by KF titration without interference. Thus, to prevent iodine consumption by hydrazine or its derivatives it is appropriate to employ sulfuric acid, or other strong acid such as dichloroacetic acid or boron trifluoride in glacial acetic acid, to neutralize the free base prior to the KF titration. Hydrochloride salts can be prepared for titration quite simply by first dissolving them in glacial acetic acid, but the free bases require more exact neutralization to minimize excess strong acid.[55]

Mercaptans (Thiols)

Unlike other components containing sulfur, mercaptans present some difficulties when it comes to KF titration. Iodine oxidizes mercaptans to disulfides according to the following reaction:

$$2\,RSH + I_2 \longrightarrow RSSR + 2HI$$

Different techniques for the KF titration have been investigated. Avoidance of iodine consumption by mercaptans in a KF titration can be achieved by converting the mercaptan to an inactive addition compound, using an olefin such as isooctene, acrylonitrile, or N-ethylmaleimide. The procedure using isooctene or mixed octenes, described by Mitchell and Smith,[56] employs acetic acid and boron trifluoride as catalyst. Unfortunately, under these conditions any alcohol in the sample will tend to interfere by esterification to form water. The addition reaction between mercaptan and either acrylonitrile or N-ethylmaleimide is carried out in the presence of pyridine as catalyst and is not accompanied by interference from alcohols. Furthermore, unlike the addition of octene, these reactions go to completion at room temperature.

Another simple method is to dissolve the mercaptan sample with formamide in the titration vessel. The sulfide group is then oxidized upon the addition of iodine solution (GFS Item #1616, the 5 mg/ml methanol-based titrant). KF solvent (Item #1610) is then added to the titration vessel through a syringe, and the titration can be performed using the titrant (Item #1616). This method requires water determination of the KF solvent that was added to the titration vessel to allow correction of the final result.

Francis and Persing[57] report satisfactory results for the determination of a few ppm to several percent water in straight chain C_2 to C_{12} thiols using either acrylonitrile or N-ethylmaleimide. The procedure for 1-octanethiol is as follows: 20 mL of dry methanol, 5 mL of KF buffer, and 1 gm of N-ethylmaleimide are added to the titration vessel, and titrated for water with GFS one-component reagent (Item # 1600 or 1601). Sample of 1-octanethiol (approx. 0.5 gm) is then added. Wait at least five minutes for the conversion of mercaptan to go to completion, then titrate using the one-component reagent.

Thioacids

These behave like mercaptans and consume iodine if not inactivated prior to KF titration. The method of Francis and Persing, described above, is reported to be effective for their inactivation and moisture determination.

Thiourea and Substituted Thioureas

Untreated, these also consume iodine as evidenced by high results and slowly fading endpoints in KF titration of their water content. Mitchell and Smith recommended use of olefin-boron trifluoride reagent to inactivate thiourea or thiobenzanilide prior to KF titration.[58] Presumably, the method of Francis and Persing (see above) should also be effective.

6.2 Moisture in Foodstuffs

Many uncertainties and limitations are associated with the use of oven drying, vacuum drying, or azeotropic distillation applied to moisture determination in foods and beverages. Reproducible results are difficult to obtain and not always reliable. Most foods are complex materials that contain more than one volatile component, decompose on heating, and incorporate water not only at surfaces but in cells and capillaries. Time and temperature as well as the state of subdivision of the sample greatly influence results. For such reasons the KF method became the method of choice for determining water in foodstuffs. One problem limiting more widespread use has been sluggish endpoints, caused by slow release of water from cells and capillaries in certain foodstuffs. Cellular water needs to be extracted before titration is feasible. This introduces a slow step and some additional risk of contamination from external moisture.

Zurcher and Hadorn recommend the technique of titration at elevated temperature for substances that otherwise give sluggish endpoints.[59-60] In effect, this combines extraction with titration and eliminates the need for a separate extraction and additional apparatus. They successfully titrated at elevated temperatures the water content of some 100 food products.[61] Pyridine-free KF reagent is especially appropriate for elevated temperature titrations to avoid the objectionable odor of pyridine.

Foods that do not dissolve in appropriately inert solvents require extraction or prolonged contact with methanol, formamide, or other solvent prior to titration. Many need to be ground, pulverized, or chopped to reduce particle size in order to facilitate extraction of their water content. Extraction time and temperature depend upon the sample and vary from a few minutes to several or more hours, from ambient to solvent boiling point. Detailed procedures are given below for a few of the more common foodstuffs.

6.2.1 Carbohydrates

Saccharose

To measure adherent moisture: working medium – 80% chloroform/20% methanol. To measure total water: working medium – 50% formamide/50% methanol (dissolve the sample completely). For both methods, titrate with GFS Item #1600 or #1601.

Other Carbohydrates

If the sample does not dissolve in methanol, use a mixture of formamide / methanol, with a maximum of 50% formamide. Titration can also be carried out at temperatures up to 50°C.

6.2.2 Fats and Other Fatty Products

Chloroform is often used as co-solvent for better solubility of fatty products. GFS offers a chloroform-based solvent for these applications (Item #2978).

The titration of most oils is straightforward. Margarine and butter should be made homogeneous before titration.

6.2.3 Milk and Other Dairy Products

Milk and liquid creams can be titrated without difficulties. A one-component or two-component volumetric reagent can be used, along with a methanol-based solvent.

Yogurt can be analyzed the same way, after being made homogeneous.

References to specific literature for moisture determination in each type of foodstuff is included in the following list:

MOISTURE DETERMINATION OF FOODSTUFFS

Butter[62]
Bread and pastries[61,63]
Catsup[62]

MOISTURE DETERMINATION OF FOODSTUFFS
(CONTINUED)

Cereals and cereal product[62,64]
Coffee[62,63]
Cocoa and chocolate[63,65,66,67,68]
Cottonseed[69]
Dairy products[70,71]
Eggs[61,72]
Fats and oils[61,63,73,74,75]
Flour (oat, wheat and soy)[62,64,76,77,78]
Fruit, dried[64]
Fruit, jams[62]
Grains[64,79,80]
Hops[71]
Meat and meat products[61]
Milk and milk products[61,64,82]
Molasses[83,84,85,86]
Nuts[61,63]
Noodles, pasta[63,73]
Orange juice concentrate[62]
Protein materials[61,63,87]
Soy protein[77]
Starches (corn, wheat, potato)[64,72,73,88,89,90]
Sugars and confectionary products[61,63,64,72,73,91,92,93,94,95,96,97,98,99,100]
Vegetables, dehydrated[72,77,101,102,103,104]
Yeast[62]

6.3 Moisture in Pharmaceuticals and Biological Materials

Karl Fischer has been widely used in the pharmaceutical industry for the determination of water content of chemicals used in medicines.

The U.S. Pharmacopeia recommends a solution comprising 670 mL methanol, 270 mL pyridine, 125 gm iodine, and sulfur dioxide. As this specific formulation is not commercially available, the use of commercially available pyridine-free reagents is permitted as long as procedures of the U.S.P. are being followed.

The following list identifies materials and references to methods for determining moisture content in pharmaceutical and biological materials:

Alkaloids[105]
Animal tissues and blood[106]
Blood[107,108]
Drugs and drug extracts[105,109,110]
Feces[111]
Medicinal chemicals and ointments[112,113,114]
Penicillins[115,116]
Tobacco smoke condensate[117]

The importance of moisture measurement technologies in the qualification of biological products and freeze-dried vaccines regulated by the U.S. FDA was underscored in a recent report.[118] Meeting residual moisture specifications is essential to ensure product potency and stability throughout the product's licensed shelf life.

This report is notable in that it confirmed correlation between two standard moisture determination techniques, Thermogravimetry and Coulometric Karl Fischer titration, and with Vapor Pressure methodology, wherein the moisture present in the head space of a vial is determined as a function of the Ideal Gas Law.

The data demonstrated the accuracy of both the Karl Fischer and the TG residual moisture values, as well as the precision of the vapor pressure measurement, which consistently detects small increases in head space moisture. This method uses an electro-optical dew point measurement to obtain the moisture content, via the photo-detection of infrared light to the point that the light beam is interrupted by condensation on the vial wall surface. The temperature at which this occurs can be converted to pressure, and the micrograms of water subsequently calculated.

6.4 Moisture in Commercial Products

A diverse array of products can be analyzed for water by the Karl Fischer method. Even though it is not possible to cite every known application, the following list identifies the many kinds of materials for which KF techniques can be applied; literature references are cited by number.

Antifreeze, glycol-based[119]
Cotton and textiles[120,121,122]
Dry Cleaners[123]
Epoxy resin powders[124]
Explosives[4,125,126,127,128,129,130]
Ion-exchange resins[131,132,133,134,135,136,137]
Lacquer solvents[138,139]
Lubricants, oils and greases[140,141,142]
Naval stores, pine products[143,144]
Nitrocellulose[145,146]
Nylon[147,148,149,150,151,152,153,154]
Paints and varnishes[155,156]
Paper[157]
Pesticides[158]
Plastics and polymers[159,160,161,162,163]
Plastic molding powders[164,165]
Rubber, GRS[166]
Shellac[130,167]
Silage[168]
Soaps and detergents[109,119,169]
Wood[121]
Woodpulp and sawdust[129,130,170]

6.5 Functional Group Determinations

Mitchell and Smith have devised and described procedures for quantitative determination of various reactive substances based upon either consumption or generation of water in suitable chemical reactions. Using the KF titration method to determine the water provides an indirect method for determining the reactive substance. Methods for the following are given in their important treatise:[3]

Acid anhydrides
Acetyl chlorides
Alcohols, aliphatic and alicyclic
Amines, primary
Amino alcohols
Carbonyl compounds
Carboxylic acids
Esters
Nitriles
Peroxides
Phenols
Silanols
Oxygen and hydrogen in metals

Chapter VII.
Reagents For KF Titrations

The WaterMark® reagents for Karl Fischer titrimetry emerged from the research of Harold Dahms in the 1970's;[26] the patented results of his work in this area included the composition of pyridine-free KF reagents now offered by GFS.

We invite you to review the current line of GFS Karl Fischer Reagents using the link on the GFS web site – www.gfschemicals.com. The wide range of KF formulations include:

- Two-component volumetric systems
- Non-hygroscopic titrants
- Single solution volumetric reagents
- CFC-free coulometric reagents
- Chloroform-free reagents
- Diaphragmless cell reagents
- New products from ongoing R&D

The volumetric product group includes single and two-component reagents. The coulometric product group includes vessel (anode reagent) and generator (cathode reagent) solutions for general applications, water determination in aldehydes/ketones, and diaphragmless vessel solution. A reagent package for coulometers is available as a kit (item #1611) and consists of vessel, generator and neutralizer solutions.

Several solvent selections are also available, as well as a WaterMark® Buffer solution that contains sulfur dioxide along with buffering agents that allow it to be used directly in the titration vessel.

The GFS web site will also be routinely updated with new reagent developments. At the time of publication of this book, our internal R&D had recently produced the CFC-free coulometric vessel solution, a 1 mg/ml single component reagent for volumetric titration of low water content samples, and a selection of solvents specifically designed for the analysis of oils, waxes and sugars.

All Karl Fischer products that were previously available in a one-liter size are also available in the one-liter 45 mm European bottle, which readily adapts to Mettler and Brinkmann instruments. A bottle adapter that accommodates the small-mouth standard U.S. made one-liter bottles is also available from GFS.

GFS also offers a significant line of pyridine-based Karl Fischer Reagents for applications requiring that methodology. Please consult the current GFS catalog or the GFS web site for more information. The web site includes a table that cross-references many GFS Karl Fischer reagents with products offered by other suppliers.

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