

BENCHMARK TEST

COULOMETRY: HYDRANAL™ VS. REAGENT M

INTRODUCTION

Because of its selectivity and accuracy, Karl Fischer (KF) titration is the method of choice when determining water content.

For reliable results, particularly in coulometry, reagents must fulfill several requirements to measure low water content.

Water content or contamination is a cause for major concern in a large number of applications. Several methods are available to determine water content. A Karl Fischer (KF) coulometric titration is one of the most accurate methods. Unlike other techniques, the test is capable of measuring water levels as low as 1 ppm when used correctly in combination with the right reagents.

Coulometric KF titration is an in-situ method. The iodine required for the Karl Fischer reaction is generated electrochemically at the anode of the generator cell by oxidation of iodide present in the reagent. At the cathode, hydrogen is generated in parallel.

Iodine formation at the anode: $2I^- \rightarrow I_2 + 2e^-$

Hydrogen formation at the cathode: $2H^+ + 2e^- \rightarrow H_2$

The iodine reacts in the next step with existing water according to the Karl Fischer reaction:



As soon as no water is available, a small excess of iodine arises, which is recognized as the end point of the titration. Since the amount of titrated water is proportional to the total power consumption, the water content can be determined from the current required for the titration.

In order to achieve precise results, the Karl Fischer reagent must fulfill several requirements:

- 1) Fast titration and stable endpoint
- 2) Good water recovery* for different water quantities over a long operating time
- 3) Good buffering properties to stabilize the pH and ensure accuracy across sample types
- 4) High conductivity to titrate polar and unpolar samples
- 5) Low crystallization potential to avoid instrument damage
- 6) Long shelf-life to fulfill lab usage requirements

* as defined by industry regulations, such as European Pharmacopoeia

COMPARISON TESTS

All Hydranal tests have been performed with Hydranal-Coulomat AG as anolyte and Hydranal-Coulomat CG as catholyte.

All Reagent M tests have been performed with Reagent M as anolyte and as catholyte.

For details on how the comparison tests were carried out, see the methodology section of this paper.

SPEED OF TITRATION

Although it may look like the Karl Fisher titrator vessel is air-tight or moisture-tight, it is not so. Depending on how well the vessel is sealed there may be a little or a lot of background moisture interference. The moisture that infiltrates the titration cell is called drift. The drift cannot be eliminated but it can be measured and corrected from the test results. With an increase in titration time the negative influence of the drift correction on the accuracy of the results increases, too.

Therefore, for most accurate results, titration time should be short and the endpoint stable.

Fig. 1 and Fig. 2 show comparison of speed of titration of 100 µg and 1000 µg water when using Hydranal and Reagent M.

Hydranal results indicate a faster titration with a more stable endpoint.

A fast titration not only saves working time but also guarantees a proper drift correction and therefore very accurate results as evident in the following sections.

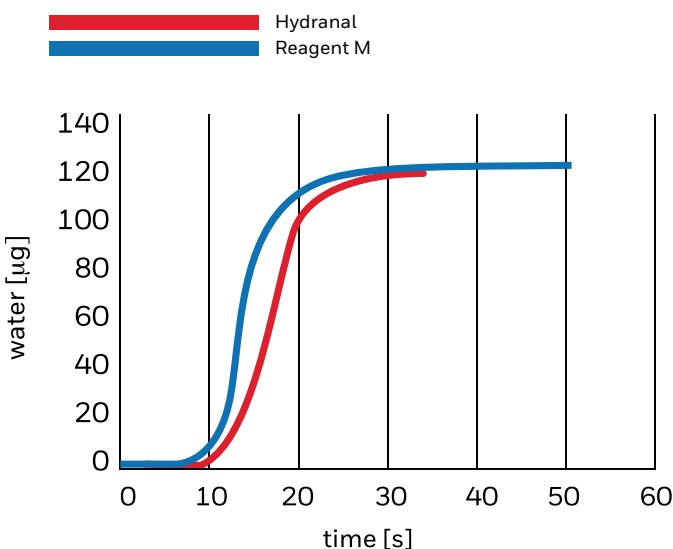


Fig. 1. The speed of titration of 100 µg water with Hydranal vs. Reagent M.

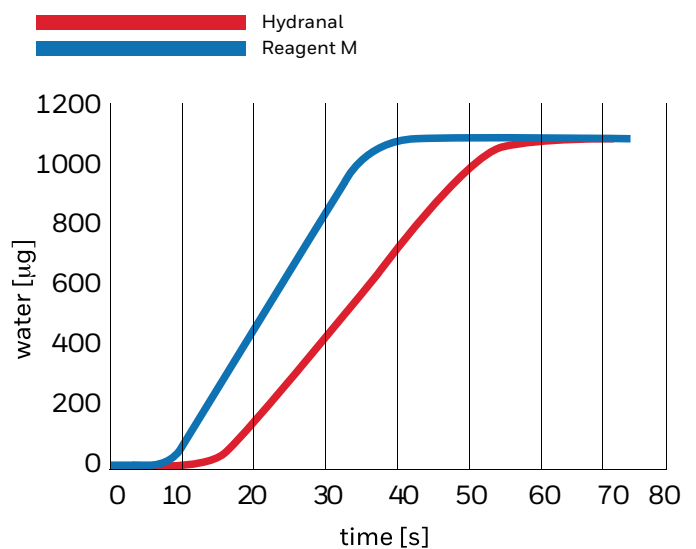


Fig. 2. The speed of titration of 1000 µg water with Hydranal vs. Reagent M.

WATER RECOVERY

Some operators use the Karl Fischer water determination method daily while other users do so sparingly. Regardless of the type of operator the accuracy of the titration reagent should be stable over a long period of time.

To check if the titrator and/or the reagent is working properly, certified water standards with a defined amount of water are introduced into the titration cell. This known amount of water that was added should then be found (recovered) in the titration. If it is not, then there could be a problem.

The recovery of 100 µg water and 1000 µg water was compared by titrating the corresponding water standards with Hydranal and Reagent M over a period of three days. Five titrations were performed each day.

According to the European Pharmacopoeia (Ph. Eur.), recovery for 100 µg water should be within 90.0-110.0% and for 1000 µg water - within 97.5-102.5% of the actual water content. Standard deviation should be below 2.5% in all cases.

The results show that both water recovery and standard deviation with Hydranal are well within the acceptable range of the European Pharmacopoeia for both 100 µg and 1000 µg water on all days, thereby ensuring accurate and stable results. However, with Reagent M both standard deviation and water recovery exceed the acceptable range on Day 1 and Day 3 respectively for 100 µg water. In the case of 1000 µg water, water recovery with Reagent M is already on the borderline on the second day.

Table 1. Average recovery of five titrations. 100 µg water was titrated with Hydranal and Reagent M over a period of three days. Titrations were performed with Hydranal-Water Standard 0.1.

100 µg H ₂ O			
	Day 1	Day 2	Day 3
Hydranal			
Av. recovery [%]	102.1	105.6	105.0
Std. dev.	0.6	2.3	1.6
Reagent M			
Av. recovery [%]	107.4	106.9	113.7
Std. dev.	3.2	0.7	1.6

Table 2. Average recovery of five titrations. 1000 µg water was titrated with Hydranal and Reagent M over a period of three days. Titrations were performed with Hydranal-Water Standard 1.0.

1000 µg H ₂ O			
	Day 1	Day 2	Day 3
Hydranal			
Av. recovery [%]	100.3	100.4	100.4
Std. dev.	0.2	0.1	0.4
Reagent M			
Av. recovery [%]	101.0	102.4	102.5
Std. dev.	0.3	0.2	1.5

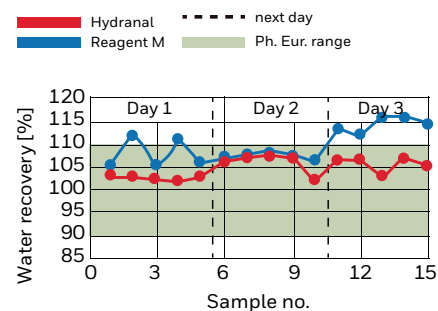


Fig. 3. Recovery of the titration of 100 µg water with Hydranal vs. Reagent M over a period of three days. Five titrations were performed each day with Hydranal-Water Standard 0.1.

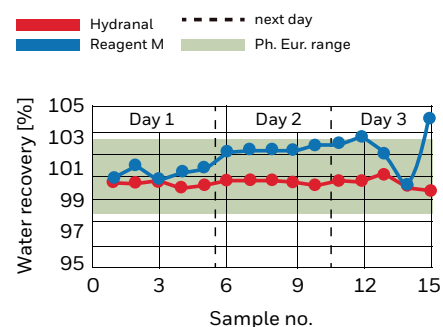


Fig. 4. Recovery of the titration of 1000 µg water with Hydranal vs. Reagent M over a period of three days. Five titrations were performed each day with Hydranal-Water Standard 1.0.

BUFFERING CAPACITY

Many samples analyzed by Karl Fischer titration can act as proton donors (e.g. R-COOH, R-NH₄⁺, R₃N·HCl, H₃O⁺) or as proton acceptors (e.g. R₃N, RNH₂, R₂NH, NH₃, ClO₄⁻) and are thus able to shift the pH value of the reagent. Even a small change in the pH value can have a serious impact on the accuracy of the results and hence a good KF reagent needs to be able to buffer the impact of pH changes.

The acid/base buffering capacity of Hydranal and Reagent M was compared by changing the pH in the titration cell and checking the water recovery with Hydranal-Water Standard 1.0. Results are shown on Fig. 5.

On one hand, if a basic sample is introduced into the titration vessel, then the pH value of the reagents increases and on the other hand, if an acidic sample is added, then the pH value decreases. If the reagent is not adequately buffered, shifts in the pH value very quickly lead to glaring errors. For example, if a basic sample is introduced to Reagent M and its pH is shifted from the initial value of 5.3 to 7, this results in increased water recovery of over 150%, out of the acceptable range (see Fig. 5). In contrast, if Hydranal is used and the pH is shifted from its original value of 6.2 to any value between 4.2 and 7.5 the recovery is maintained at ~100%, because this reagent is well buffered and provides correct results over a wide pH range.

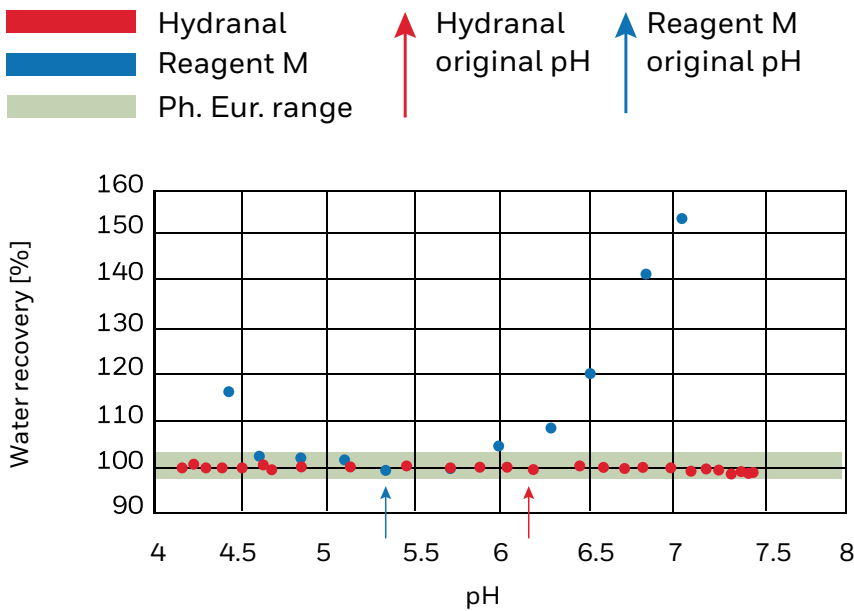


Fig. 5. Recovery of 1000 µg water with Hydranal and Reagent M at different pH values.

CONDUCTIVITY

Hydranal is observed to have a higher conductivity than that of Reagent M (see Fig. 6). This is particularly useful when titrating unpolar samples such as hexane and chloroform as they tend to sharply decrease reagent conductivity and the titration process can come to a standstill. As a result of its lower conductivity, 100 mL Reagent M can only titrate 20 mL of hexane, whereas the same amount of Hydranal is able to titrate 30 mL of hexane (see Fig. 7).

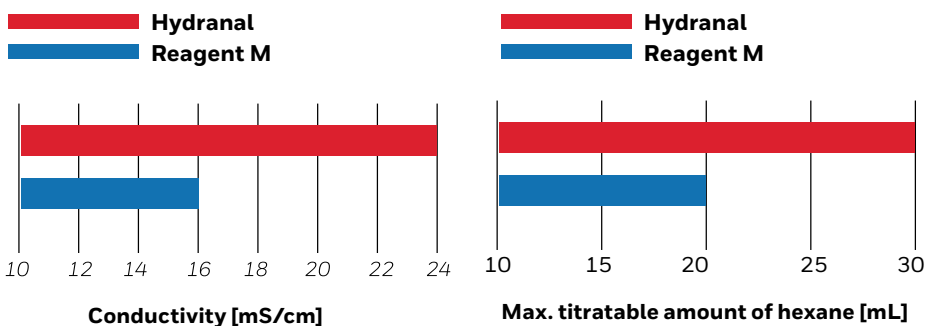


Fig. 6. Conductivity of Hydranal and Reagent M as analyte.

Fig. 7. Maximum titratable amount of hexane in 100 mL Hydranal and in 100 mL Reagent M.

CRYSTALLIZATION

Crystal formation in the connection tubes and/or in the dosing unit can cause serious damage to the titration device and expensive consequences for the end-user. Additionally, crystallization on the bottle neck can lead to reagent contamination. After using the bottles for five fillings of the titration cell, in the case of Hydranal the bottle neck was still clean (Fig. 8). However, Reagent M was contaminated with crystals as visible on its bottle neck (Fig. 9).

The most negative impact arises from crystal formation inside the reagent, e.g. in the anodic or cathodic chamber (see Fig. 10 and 11). Here the precipitations may disturb the proper work of the indication and/or generator electrode that would compromise the titration accuracy. Fig. 10 shows crystals from Reagent M in the cathodic compartment and blackened generator electrode due to impurities in Reagent M. The generator electrode must be then cleaned up with hot conc. nitric acid which is both very time consuming and dangerous.

Hydranal™ reagents are developed to suppress the crystallization process. Even after evaporating to 30% of its initial volume, Hydranal-Coulomat AG still does not form crystals, whereas Reagent M visibly crystallizes (see Fig. 12).



Fig. 8. Hydranal-Coulomat AG bottle neck after five titration cell fillings. Crystallization is suppressed.



Fig. 9. Bottle neck of Reagent M after five titration cell fillings. Reagent M crystallizes very fast and contaminates the bottle neck.



Fig. 10. Crystals from Reagent M in the cathodic compartment. Generator electrode can sometimes turn black due to impurities in Reagent M.

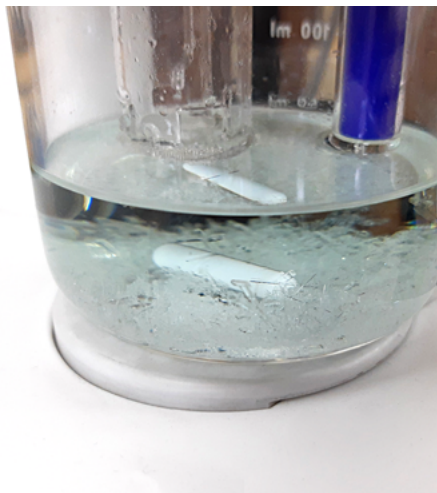


Fig. 11. Crystallization of Reagent M in the anodic chamber after one week. The crystals are very difficult to dissolve.

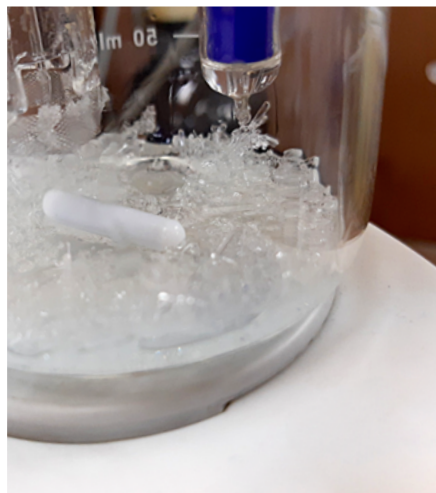


Fig.12. Hydranal-Coulomat AG (left) and Reagent M (right) after four days in open vials.

SHELF LIFE

All Hydranal coulometric reagents have a shelf life of five years, whereas Reagent M expires after three years per its CoA.

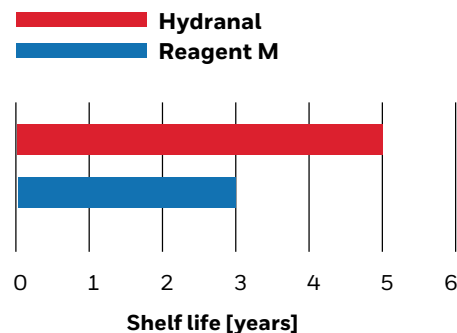


Fig. 13. Shelf life of Hydranal and Reagent M.

TEST METHODOLOGY

Reagents: All Hydranal tests have been performed with 100 mL 34836 Hydranal-Coulomat AG as anolyte and 5 mL 34840 Hydranal-Coulomat CG as catholyte. All Reagent M tests have been performed with 100 mL Reagent M as anolyte and 5 mL Reagent M as catholyte.

Titration device: Metrohm 852 Titrando, coulometric cell with diaphragm.

Lab conditions: Relative Humidity 62-74%, Temperature 25-26°C.

All titrations were started after reaching a low and stable drift value. Drift correction was turned on.

Special Notes on Water Recovery

For the recovery tests 34828 Hydranal-Water Standard 1.0 and 34847 Hydranal-Water Standard 0.1 were used. 34828 Hydranal-Water Standard 1.0 was handled in a 10 mL glass gas-tight syringe (81620 HAMILTON 10 mL Model 1010 TLL) and 34847 Hydranal-Water Standard 0.1 was handled in a 5 mL glass gas-tight syringe (81520 HAMILTON 5 mL Model 1005 TLL), with 120 mm long metal hub needles (7748-07 HAMILTON, point 4, gauge 21).

To meet different end-user conditioning procedures, between Day 1 and Day 2 the titration cell was left in conditioning mode. Between Day 2 and Day 3 the titration device was turned off and the conditioning mode was started again prior to the measurements. The different procedures did not impact the conditioning performance of the reagents.

Special Notes on Buffering Capacity

To decrease the pH value of the reagents, a concentrated methanolic solution of 37865 Hydranal-Salicylic Acid was used. For increasing the pH value, neat 4-methylmorpholine (67870, Sigma-Aldrich) was added portion wise to the titration cell. Since pH measurement is difficult in a non-aqueous KF titration vessel, the related pH values were measured under aqueous conditions outside the titration vessel in a 150 mL beaker. 1 mL acid/base portions were added to a mixture of 25 mL anolyte + 25 mL Hydranal-Methanol dry + 5 mL deionized water.

The pH impact on the water recovery was tested in the titration vessel filled with 100 mL anolyte and 5 mL catholyte and successive addition of 4 mL portions of acid/base to the anolyte solution. After each addition, water recovery was tested by adding 1 g portion of 34828 Hydranal-Water Standard 1.0.

All tests were carried out by the Hydranal Application Lab in Shanghai, China and have been supervised and approved by the Hydranal Center of Excellence in Seelze, Germany.

TITRATION PARAMETERS

Polarization current	10 μ A
Gen. current	auto
EP	50 mV
Dynamics	70 mV
Max. rate	max. μ g/min
Min. rate	15 μ g/min
Extraction time	15 s
Rel. stop Drift	5 μ g/min
Stirring speed	8
Start Drift	20 μ g/min
Drift correction	auto
Stop time	off
Stability time	15 s
Pause	0 s

CONCLUSION

While Hydranal performed well across all comparison tests, we found deficits in Reagent M that lead to incorrect results, slower titration and dangerous cleaning conditions. Importantly, these deficits become more prominent with use resulting in increased lab errors, time and cost.

Unfortunately, users often don't notice these deficits and the errors they lead to since these can be within acceptable standard deviations. For example, as we observed in a titration of 100 µg water, while the standard deviation was within an acceptable range (below 2.5%) the measured water content was outside of the Ph. Eur. range.

Furthermore, as we see performance (water recovery and crystallization) is impacted over time, competitive products need to be replaced much more frequently. Since coulometry is a cumulative method of using a reagent in the titration vessel for multiple samples for as long as possible, this is a huge drawback. Not only does this result in an increased cost of reagents but also more time & effort to change and maintain titration equipment.

The composition of Hydranal ensures high conductivity and exceptional buffering properties to stabilize KF stoichiometry. Correct results are achieved over a long period of time for different water quantities. The ingredients do not undergo side reactions on the electrodes and suppress crystal formation. This ensures quick and easy cleaning of the titration cell and saves valuable working time and cost. Hydranal fulfills all requirements for an ideally functioning KF reagent.

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