

A.6 WATER SOLUBILITY

1. METHOD

The methods described are based on the OECD Test Guideline (1).

1.1. INTRODUCTION

It is useful to have preliminary information on the structural formula, the vapour pressure, the dissociation constant and the hydrolysis (as a function of pH) of the substance to perform this test.

No single method is available to cover the whole range of solubilities in water.

The two test methods described below cover the whole range of solubilities but are not applicable to volatile substances:

-one which applies to essentially pure substances with low solubilities, ($< 10^{-2}$ grams per litre), and which are stable in water, referred to as the 'column elution method',

-the other which applies to essentially pure substances with higher solubilities ($> 10^{-2}$ grams per litre), and which are stable in water, referred to as the 'flask method'.

The water solubility of the test substance can be considerably affected by the presence of impurities.

1.2. DEFINITION AND UNITS

The solubility in water of a substance is specified by the saturation mass concentration of the substance in water at a given temperature. The solubility in water is specified in units of mass per volume of solution. The SI unit is kg/m^3 (grams per litre may also be used).

1.3. REFERENCE SUBSTANCES

Reference substances do not need to be employed in all cases when investigating a new substance. They should primarily serve to check the performance of the method from time to time and to allow comparison with results from other methods.

1.4. PRINCIPLE OF THE TEST METHOD

The approximate amount of the sample and the time necessary to achieve the saturation mass concentration should be determined in a simple preliminary test.

1.4.1. Column elution method

This method is based on the elution of a test substance with water from a micro-column which is charged with an inert support material, such as glass beads or sand, coated with an excess of test substance. The water solubility is determined when the mass concentration of the eluate is constant. This is shown by a concentration plateau as a function of time.

1.4.2. Flask method

In this method, the substance (solids must be pulverized) is dissolved in water at a temperature somewhat above the test temperature. When saturation is achieved the mixture is cooled and kept at the test temperature, stirring as long as necessary to reach equilibrium. Alternatively, the measurement can be performed directly at the test temperature, if it is assured by appropriate sampling that the saturation equilibrium is reached. Subsequently, the mass concentration of the substance in the aqueous solution, which must not contain any undissolved particles, is determined by a suitable analytical method.

1.5. QUALITY CRITERIA

1.5.1. Repeatability

For the column elution method, < 30 % may be obtainable; for the flask method, < 15 % should be observed.

1.5.2. Sensitivity

This depends upon the method of analysis, but mass concentration determinations down to 10^{-6} grams per litre can be determined.

1.6. DESCRIPTION OF THE METHOD

1.6.1. Test conditions

The test is preferably run at $20 \pm 0,5$ °C. If a temperature dependence is suspected in the solubility (> 3 % per °C), two other temperatures at least 10 °C above and below the initially chosen temperature should also be used. In this case, the temperature control should be $\pm 0,1$ °C. The chosen temperature should be kept constant in all relevant parts of the equipment.

1.6.2. Preliminary test

To approximately 0,1 g of the sample (solid substances must be pulverized) in a glass-stoppered 10 ml graduated cylinder, increasing volumes of distilled water at room temperature are added according to the steps shown in the table below:

0,1 g soluble in 'x' ml of water	0,1	0,5	1	2	10	100	>100
Approximative solubility (grams per litre)	>1000	1000 to 200	200 to 1000	100 to 50	50 to 10	10 to 1	<1

After each addition of the indicated amount of water, the mixture is shaken vigorously for 10 minutes and is visually checked for any undissolved parts of the sample. If, after addition of 10 ml of water, the sample or parts of it remain undissolved, the experiment has to be repeated in a 100 ml measuring cylinder with larger volumes of water. At lower solubilities the time required to dissolve a substance can be considerably longer (at least 24 h should be allowed). The approximate solubility is given in the table under that volume of added water in which complete dissolution of the sample occurs. If the substance is still apparently insoluble, more than 24 h should be allowed (96 h maximum), or further dilution should be undertaken to ascertain whether the column elution or flask solubility method should be used.

1.6.3. Column elution method

1.6.3.1. Support material, solvent and eluent

The support material for the column elution method should be inert. Possible materials which can be employed are glass beads and sand. A suitable volatile solvent of analytical reagent quality should be used to apply the test substance to the support material. Water which has been double distilled in glass or quartz apparatus should be employed as the eluent.

Note:

Water directly from an organic ion exchanger must not be used.

1.6.3.2. Loading of the support

Approximately 600 mg of support material is weighed and transferred to a 50 ml round-bottom flask.

A suitable, weighed amount of test substance is dissolved in the chosen solvent. An appropriate amount of this solution is added to the support material. The solvent must be completely evaporated, e.g. in a rotary evaporator; otherwise water saturation of the support is not achieved due to partition effects on the surface of the support material.

The loading of support material may cause problems (erroneous results) if the test substance is deposited as an oil or a different crystal phase. The problem should be examined experimentally and the details reported.

The loaded support material is allowed to soak for about two hours in approximately 5 ml of water, and then the suspension is added to the microcolumn. Alternatively, dry loaded support material may be poured into the microcolumn, which has been filled with water, and then equilibrated for approximately two hours.

Test procedure:

The elution of the substance from the support material can be carried out in one of two different ways:

-recirculating pump (see figure 1),

-levelling vessel (see figure 4).

1.6.3.3. Column elution method with recirculating pump

Apparatus

A schematic arrangement of a typical system is presented in figure 1. A suitable microcolumn is shown in figure 2, although any size is acceptable, provided it meets the criteria for reproducibility and sensitivity. The column should provide for a headspace of at least five bed volumes of water and be able to hold a minimum of five samples. Alternatively, the size can be reduced if make-up solvent is employed to replace the initial five bed volumes removed with impurities.

The column should be connected to a recirculating pump capable of controlling flows of approximately 25 ml/h. The pump is connected with polytetrafluoroethylene (P.T.F.E.) and/ or glass connections. The column and pump, when assembled, should have provision for sampling the effluent and equilibrating the headspace at atmospheric pressure. The column material is supported with a small (5 mm) plug of glass wool, which also serves to filter out particles. The recirculating pump can be, for example, a peristaltic pump or a membrane pump (care must be taken that no contamination and/or absorption occurs with the tube material).

Measurement procedure

The flow through the column is started. It is recommended that a flow rate of approximately 25 ml/hr be used (this corresponds to 10 bed volumes/hr for the column described). The first five bed volumes (minimum) are discarded to remove water-soluble impurities. Following this, the recirculating pump is allowed to run until equilibration is established, as defined by five successive samples whose concentrations do not differ by more than $\pm 30\%$ in a random fashion. These samples should be separated from each other by time intervals corresponding to the passage of at least 10 bed volumes of the eluent.

1.6.3.4. Column elution method with levelling vessel

Apparatus (see figures 4 and 3)

Levelling vessel: The connection to the levelling vessel is made by using a ground glass joint which is connected by PTFE tubing. It is recommended that a flow rate of approximately 25 ml/hr be used. Successive eluate fractions should be collected and analyzed by the chosen method.

Measurement procedure

Those fractions from the middle eluate range where the concentrations are constant ($\pm 30\%$) in at least five consecutive fractions are used to determine the solubility in water.

In both cases (using a recirculating pump or a levelling vessel), a second run is to be performed at half the flow rate of the first. If the results of the two runs are in agreement, the test is satisfactory; if there is a higher apparent solubility with the lower flow rate, then the halving of the flow rate must continue until two successive runs give the same solubility.

In both cases (using a recirculating pump or a levelling vessel) the fractions should be checked for the presence of colloidal matter by examination for the Tyndall effect (light scattering). Presence of such particles invalidates the results, and the test should be repeated with improvements in the filtering action of the column.

The pH of each sample should be recorded. A second run should be performed at the same temperature.

1.6.4. Flask method

1.6.4.1. Apparatus

For the flask method the following material is needed:

- normal laboratory glassware and instrumentation,
- a device suitable for the agitation of solutions under controlled constant temperatures,
- a centrifuge (preferably thermostated), if required with emulsions, and
- equipment for analytical determination.

1.6.4.2. Measurement procedure

The quantity of material necessary to saturate the desired volume of water is estimated from the preliminary test. The volume of water required will depend on the analytical method and the solubility range. About five times the quantity of material determined above is weighed into each of three glass vessels fitted with glass stoppers (e.g. centrifuge tubes, flasks). The chosen volume of water is added to each vessel, and the vessels are tightly stoppered. The closed vessels are then agitated at 30 °C. (A shaking or stirring device capable of operating at constant temperature should be used, e.g. magnetic stirring in a thermostatically controlled water bath). After one day, one of the vessels is removed and re-equilibrated for 24 hours at the test temperature with occasional shaking. The contents of the vessel are then centrifuged at the test temperature, and the concentration of test substance in the clear aqueous phase is determined by a suitable analytical method. The other two flasks are treated similarly after initial equilibration at 30 °C for two and three days, respectively. If the concentration results from at least the last two vessels agree with the required reproducibility, the test is satisfactory. The whole test should be repeated, using longer equilibration times, if the results from vessels 1, 2 and 3 show a tendency to increasing values.

The measurement procedure can also be performed without preincubation at 30 °C. In order to estimate the rate of establishment of the saturation equilibrium, samples are taken until the stirring time no longer influences the concentration of the test solution.

The pH of each sample should be recorded.

1.6.5. Analysis

A substance-specific analytical method is preferred for these determinations, since small amounts of soluble impurities can cause large errors in the measured solubility. Examples of such methods are: gas or liquid chromatography, titration methods, photometric methods, voltammetric methods.

2. DATA

2.1. COLUMN ELUTION METHOD

The mean value from at least five consecutive samples taken from the saturation plateau should be calculated for each run, as should the standard deviation. The results should be given in units of mass per volume of solution.

The means calculated on two tests using different flows are compared and should have a repeatability of less than 30 %.

2.2. FLASK METHOD

The individual results should be given for each of the three flasks and those results deemed to be constant (repeatability of less than 15 %) should be averaged and given in units of mass per volume of solution. This may require the reversion of mass units to volume units, using the density when the solubility is very high (> 100 grams per litre).

3. REPORTING

3.1. COLUMN ELUTION METHOD

The test report shall, if possible, include the following information:

- the results of the preliminary test,
- precise specification of the substance (identity and impurities),
- the individual concentrations, flow rates and pH of each sample,
- the means and standard deviations from at least five samples from the saturation plateau of each run,
- the average of the two successive, acceptable runs,
- the temperature of the water during the saturation process,
- the method of analysis employed,
- the nature of the support material employed,
- loading of support material,
- solvent used,
- evidence of any chemical instability of the substance during the test and the method used,
- all information relevant for the interpretation of the results, especially with regard to impurities and physical state of the substance.

3.2. FLASK METHOD

The test report shall, if possible, include the following information:

- the results of the preliminary test,
- precise specification of the substance (identity and impurities),
- the individual analytical determinations and the average where more than one value was determined for each flask,
- the pH of each sample,

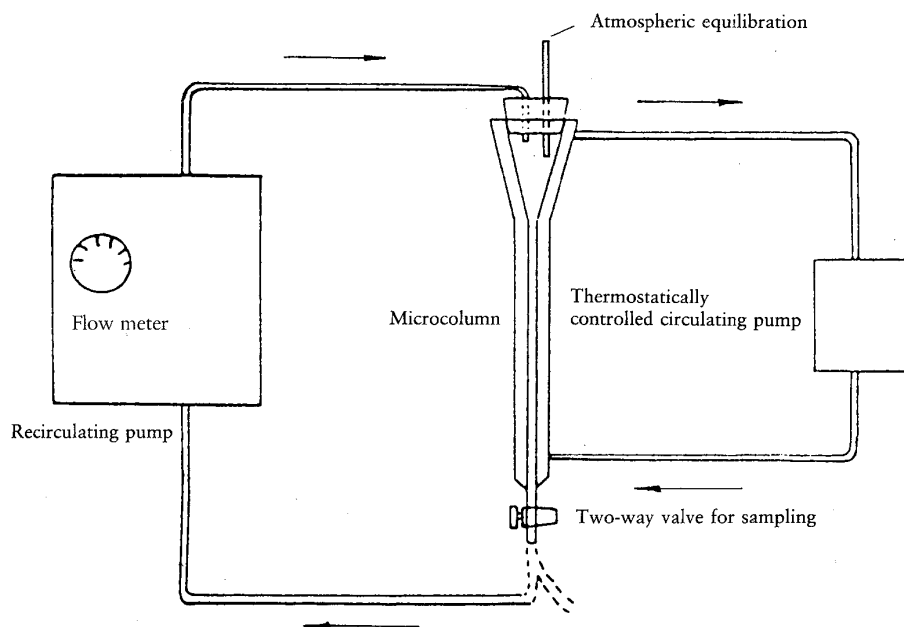
- the average of the value for the different flasks which were in agreement,
- the test temperature,
- the analytical method employed,
- evidence of any chemical instability of the substance during the test and the method used,
- all information relevant for the interpretation of the results, especially with regard to impurities and physical state of the substance.

4. REFERENCES

- (1) OECD, Paris, 1981, Test Guideline 105, Decision of the Council C(81) 30 final.
- (2) NF T 20-045 (AFNOR) (Sept. 85). Chemical products for industrial use -Determination of water solubility of solids and liquids with low solubility -Column elution method
- (3) NF T 20-046 (AFNOR) (Sept. 85). Chemical products for industrial use -Determination of water solubility of solids and liquids with high solubility -Flask method

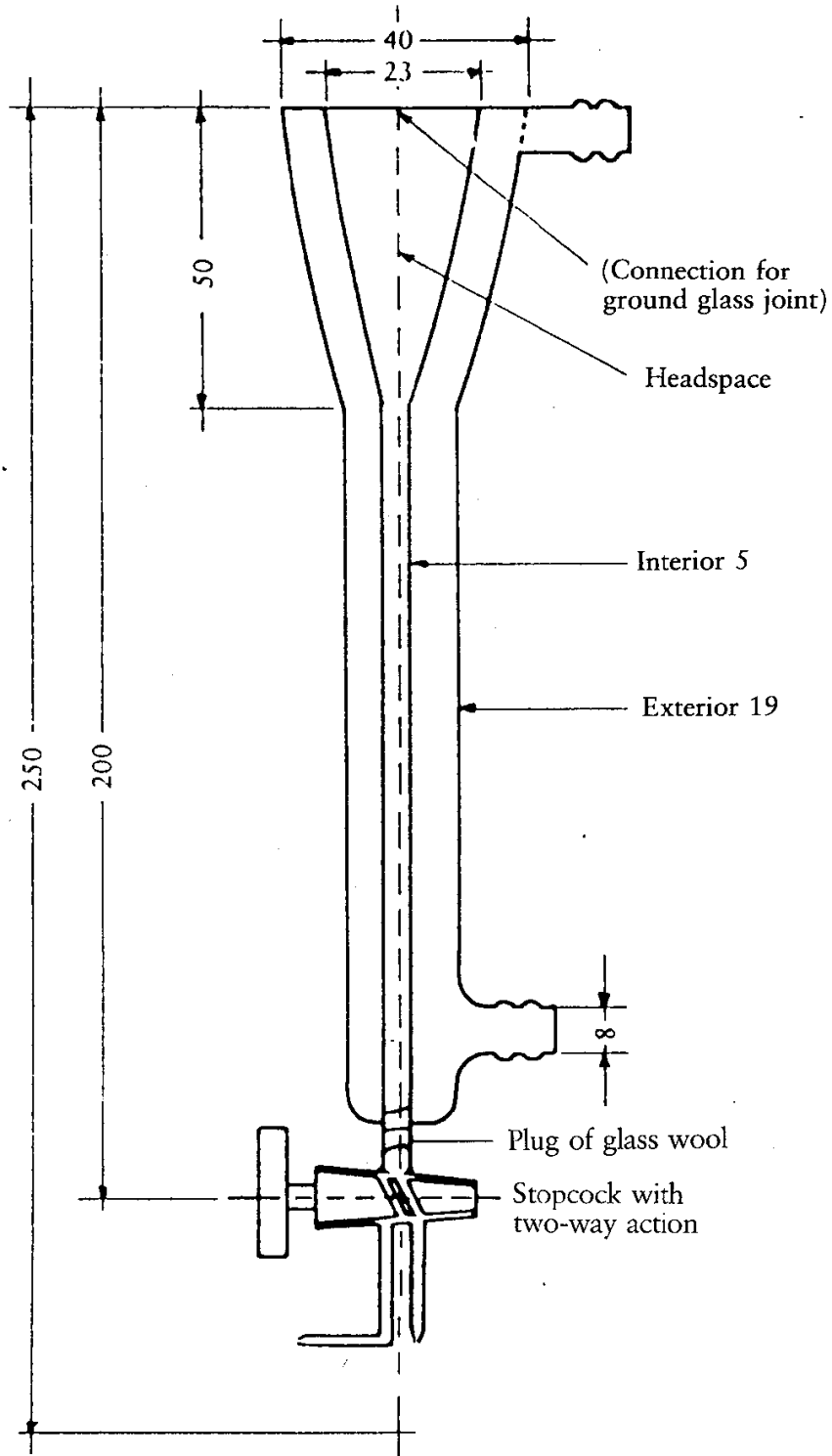
Appendix

Figure 1
Column elution method with recirculating pump



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Figure 2
A typical microcolumn
(All dimensions in millimetres)



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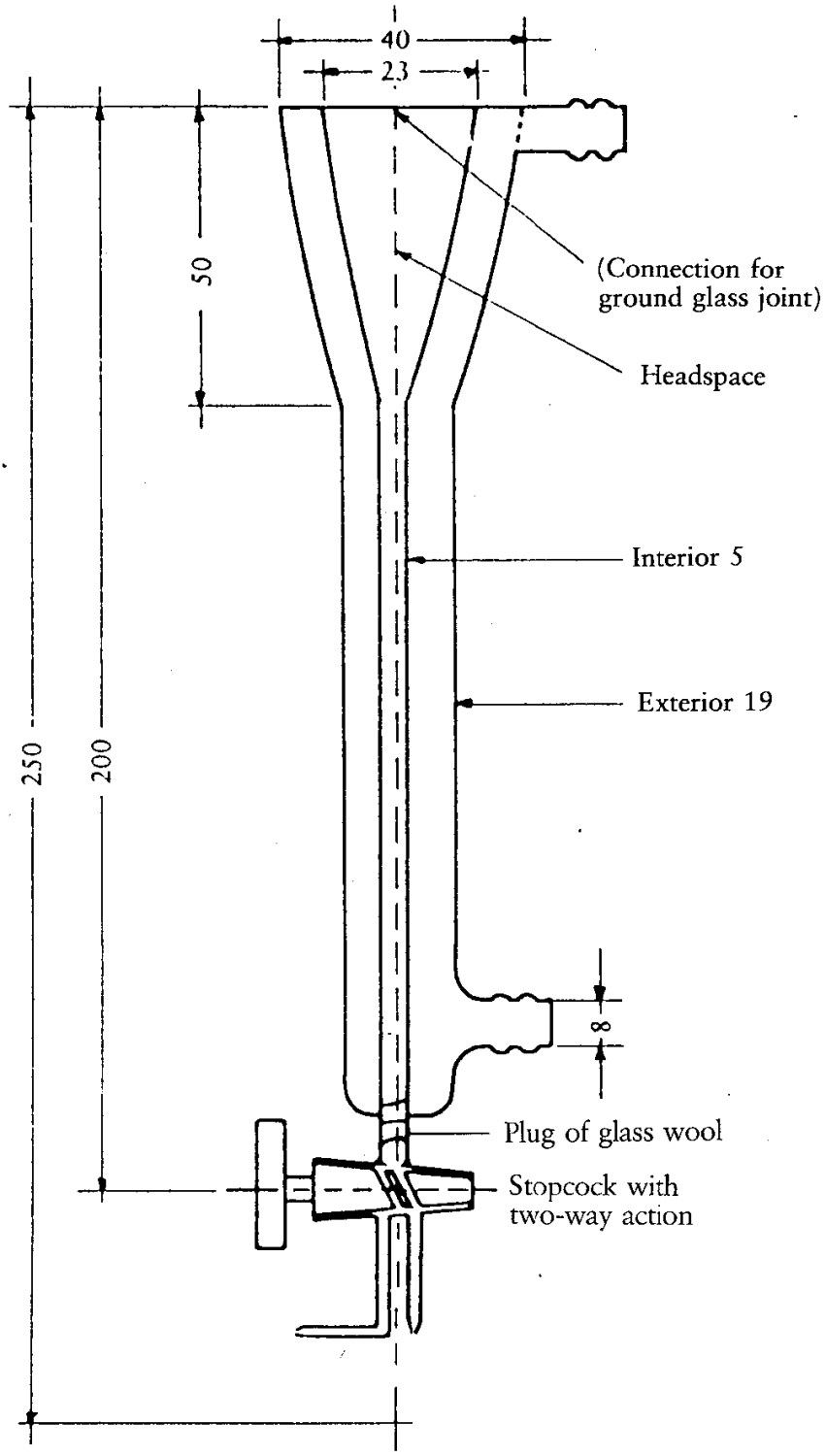
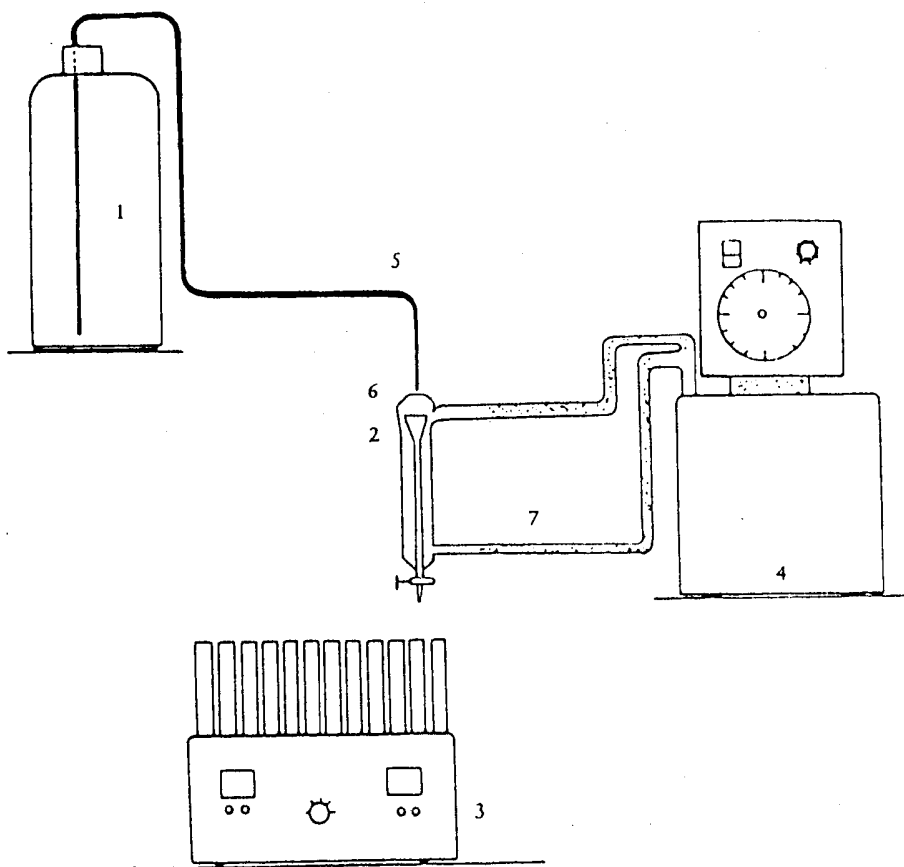


Figure 4

Column elution method with levelling vessel



- 1 = Levelling vessel (e.g. 2,5 litre flask)
- 2 = Column (see figure 3)
- 3 = Fraction collector
- 4 = Thermostat
- 5 = Teflon tubing
- 6 = Ground glass joint
- 7 = Water line (between thermostat and column, inner diameter: approximately 8 mm)