OECD GUIDELINE FOR THE TESTING OF CHEMICALS

Adopted by the Council on 27th July 1995

Water Solubility

INTRODUCTION

1. This guideline is a revised version of the original Guideline 105 which was adopted in 1981. There are no differences of substance between the current version and that from 1981. Mainly the format has been changed. The revision was based on the EC method "Water Solubility" (1).

INITIAL CONSIDERATIONS

2. The water solubility of a substance can be considerably affected by the presence of impurities. This guideline addresses the determination of the solubility in water of essentially pure substances which are stable in water and not volatile. Before determining water solubility, it is useful to have some preliminary information on the substance, like structural formula, vapour pressure, dissociation constant and hydrolysis as a function of pH.

3. Two methods, the column elution method and the flask method which cover respectively solubilities below and above 10^{-2} g/l are described in this guideline. A simple preliminary test is also described. It allows to determine approximately the appropriate amount of sample to be used in the final test, as well as the time necessary to achieve saturation.

DEFINITIONS AND UNITS

4. The water solubility of a substance is the saturation mass concentration of the substance in water at a given temperature.

5. Water solubility is expressed in mass of solute per volume of solution. The SI unit is kg/m^3 but g/l is commonly used.

REFERENCE SUBSTANCES

6. Reference substances do not need to be employed when investigating a substance.

DESCRIPTION OF THE METHODS

Test conditions

7. The test is preferably run at 20 ± 0,5 °C. The chosen temperature should be kept constant in all relevant parts of the equipment.

Preliminary test

8. In a stepwise procedure, increasing volumes of water are added at room temperature to approximately 0.1 g of the sample (solid substances must be pulverized) in a 10 ml glass-stoppered measuring cylinder. After each addition of an amount of water, the mixture is shaken 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 is continued in a 100 ml measuring cylinder. The approximate solubility is given in Table 1 below under that volume of water in which complete dissolution of the sample occurs. When the solubility is low, a long time may be required to dissolve a substance and at least 24 hours should be allowed. If, after 24 hours, the substance is still not dissolved, more time (up to 96 hours) should be allowed or further dilution should be attempted to ascertain whether the column elution method or flask method should be used.

Table 1

ml of water for 0.1 g soluble	0.1	0.5	1	2	10	100	> 100
approximate solubility in g/l	> 1000	1000 to 200	200 to 100	100 to 50	50 to 10	10 to 1	< 1

Column elution method

Principle

9. 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, previously coated with an excess of the test substance (2). The water solubility is given by the mass concentration of the eluate when this has reached a plateau as a function of time.

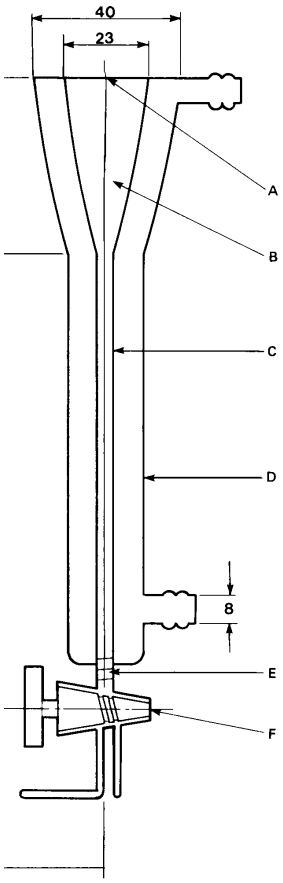
Apparatus

10. The apparatus consists of a microcolumn (Figure 1), maintained at constant temperature. It is connected either to a recirculating pump (Figure 2) or to a levelling vessel (Figure 3). The microcolumn contains an inert support held in place by a small plug of glasswool which also serves to filter out particles. Possible materials which can be employed for the support are glass beads, diatomaceous earth, or other inert materials.

11. The microcolumn shown in figure 1 is suitable for the set-up with recirculating pump. It has a head space providing for five bed volumes (discarded at the start of the experiment) and the volume of five samples (withdrawn for analysis during the experiment). Alternatively, the size can be reduced if water can be added to the system during the experiment to replace the initial five bed volumes removed with impurities. The column is connected with tubing made of an inert material to the recirculating pump, capable of delivering approximately 25 ml/h. The recirculating pump can be, for example, a peristaltic or membrane pump. Care must be taken that no contamination and/or adsorption occurs with the tube material.

12. A schematic arrangement using a levelling vessel is shown in figure 3. In this arrangement the microcolumn is fitted with a one way stopcock. The connection to the levelling vessel consists of a ground glass joint and tubing made of an inert material. Theflow rate from the levelling vessel should be approximately 25 ml/h.

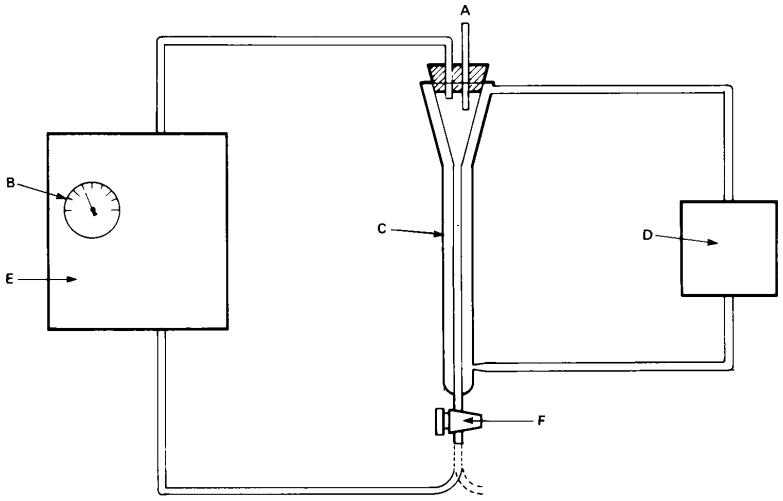
Figure 1



Dimensions in mm

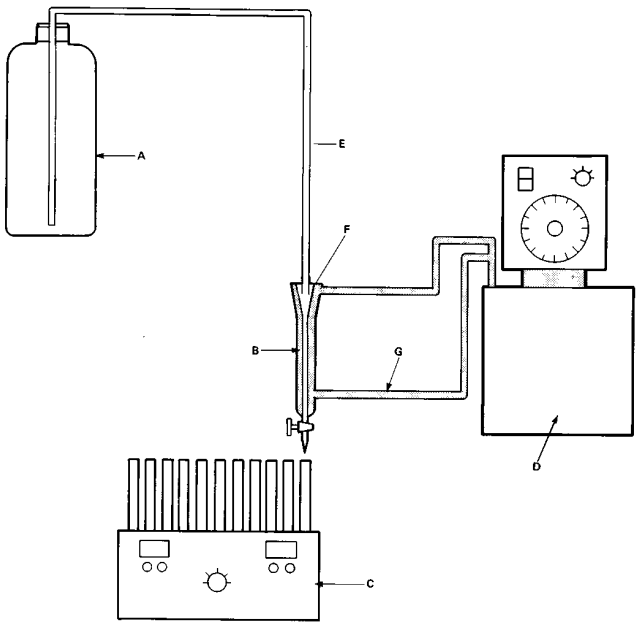
A. Connection for ground glass joint
B. Headspace
C. Interior 5
D. Exterior 19
E. Plug of glass wool
F. Stopcock

Figure 2



A. Atmospheric equilibration
B. Flowmeter
C. Microcolumn
D. Thermostatically controlled circulating pump
E. Recirculating pump
F. Two-way valve for sampling

Figure 3



A. Levelling vessel (e.g. 2.5 litres chemical flask)
B. Column
C. Fraction accumulator
D. Thermostat
E. Teflon tubing
F. Ground glass joint
G. Water line (between thermostat and column, inner diameter approximately 8 mm)

Loading of the support

13. Approximately 600 mg of support material is transferred to a 50 ml round-bottom flask. A suitable amount of test substance is dissolved in a volatile solvent of analytical reagent quality and an appropriate amount of this solution is added to the support material. The solvent is completely evaporated, e.g. using a rotary evaporator, as otherwise water saturation of the support will not be achieved during the elution step because of partitioning on the surface. The loaded support material is soaked for two hours in approximately 5 ml of water and the suspension is poured into the microcolumn. Alternatively, dry loaded support material may be poured into the water-filled microcolumn and two hours are allowed for equilibrating.

14. The loading of the support material may cause problems, leading to erroneous results, e.g. when the test substance is deposited as an oil. These problems should be examined and the details reported.

Procedure using a recirculating pump

15. The flow through the column is started. It is recommended that a flow rate of approximately 25 ml/h, corresponding to 10 bed volumes per hour for the column described, be used. At least the first five bed volumes are discarded to remove water soluble impurities. Following this, the pump is allowed to run until equilibrium is established, as defined by five successive samples whose concentrations do not differ by more than ± 30% in a random fashion. These samples should be separated from each other by time intervals corresponding to the passage of at least ten bed volumes. Depending on the analytical method used, it may be preferable to establish a concentration/time curve to show that equilibrium is reached.

Procedure using a levelling vessel

16. Successive eluate fractions should be collected and analyzed by the chosen method. Fractions from the middle eluate range, where the concentrations are constant within ± 30% in at least five consecutive fractions, are used to determine the solubility.

Notes applicable to both procedures

17. Double distilled water is the preferred eluent. Deionized water with a resistivity above 10 megohms/cm and a total organic carbon content below 0.01% can also be used.

18. Under both procedures, a second run is performed at half the flow rate of the first. If the results of the two runs are in agreement, the test is satisfactory. If the measured solubility is higher with the lower flow rate, then the halving of the flow rate must continue until two successive runs give the same solubility.

19. Under both procedures, the fractions should be checked for the presence of colloidal matter by examination of the Tyndall effect. The presence of particles invalidates the test and the test should be repeated after improvement of the filtering action of the column.

20. The pH of each sample should be measured, preferably by using special indicator strips.

Flask method

Principle

21. 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. Alternatively, and if it is assured by appropriate sampling that the saturation equilibrium is reached, the measurement can be performed directly at the test temperature. 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 (3).

Apparatus

22. Following material is needed:

- normal laboratory glassware and instrumentation;
- a device for the agitation of solutions under controlled constant temperature;
- if required for emulsions, a centrifuge (preferably thermostatted); and
- analytical equipment.

Procedure

23. The quantity of test substance necessary to saturate the desired volume of water is estimated from the preliminary test. About five times that quantity is weighed into each of three glass vessels fitted with glass stoppers (e.g. centrifuge tubes, flasks). A volume of water, chosen in function of the analytical method and solubility range, is added to each vessel. The vessels are tightly stoppered and 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 thermostatted water bath. After one day, one of the vessels is 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 the 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 concentrations measured in at least the two last vessels do not differ by more than 15%, the test is satisfactory. If the results from vessels 1, 2 and 3 show a tendency of increasing values, the whole test should be repeated using longer equilibration times.

24. The test 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 concentrations measured.

25. The pH of each sample should be measured, preferably by using special indicator strips.

Analytical determinations

26. A substance-specific method is preferred since small amounts of soluble impurities can cause large errors in the measured solubility. Examples of such methods are: gas or liquid chromatography, titration, photometry, voltametry.

DATA AND REPORTING

Data

Column elution method

27. For each run, the mean value and standard deviation from at least five consecutive samples taken from the saturation plateau should be calculated. The mean values obtained from two tests with different flows should not differ by more than 30%.

Flask method

28. The individual results from each of the three flasks, which should not differ by more than 15%, are averaged.

Test Report

Column elution method

29. The test report must include the following information:

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

Flask method

30. The test report must include the following information:

- the results of the preliminary test;

- chemical identity and impurities (preliminary purification step, if any);
- 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 values for different flasks which were in agreement;
- the test temperature;
- the analytical method;
- evidence of any chemical instability of the substance during the test;
- all information relevant for the interpretation of the results, in particular with regard to impurities and physical state of the substance.

LITERATURE

(1) Official Journal of the European Communities L 383 A, 54-62 (1992)

(2) NF T 20-045 (AFNOR) (September 1985). 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) (September 1985). Chemical products for industrial use - Determination of water solubility of solids and liquids with high solubility - Flask method