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GRAVIMETRIC CHARACTERISATION OF THE SURFACE PROPERTIES OF A POROUS DRUG CARRIER

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Abstract

The gas adsorption method is the most common means to characterise the topology of solid surfaces with regard to its use as an adsorbent. Adsorption isotherms are determined advantageously using a vacuum microbalance: Thermogravimetric techniques allow the observation of sample degassing and its optimization. The dry mass is determined in situ, the mass of gas adsorbed is measured directly and different gases can be used without calibration. From the isotherm the pore size distributions, specific surface area, fractal dimension and density can be derived. Commercially available gravimetric sorption apparata and vacuum balances as well as software for data evaluation are reviewed in tables. The sorption analysis of an aluminum oxide is presented. The porous material was used as a matrix for a slow drug release.

Keywords: drug carrier, sorption analysis, topology of solid surface

The gravimetric method of sorption measurement

The gas adsorption method is the most common means to characterise the topology of a solid surface with regard to its use as an adsorbent or for heterogeneous chemical reactions. For this purpose adsorption isotherms are measured using a gaseous adsorptive which is weakly bonded (physisorbed) to the sample surface. Nitrogen adsorption at 77 K is the procedure mostly used and standardised by the IUPAC ISO and national institutions [1]. Adsorption of a gaseous sorptive can be measured volumetrically, gravimetrically, calorimetrically or by means of gas chromatographic techniques. Only the gravimetric method allows for the direct and independent determination of the three parameters of an adsorption isotherm: adsorbed amount, pressure and the constant temperature. From buoyancy of the sample its density can be evaluated. A feature of the gravimetric method is the possibility to control the cleaning of the

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sample by evaporating adsorbed layers from the surface. Therefore, sample preparation can be optimized and its damage by excessive temperature or to long degassing time can be minimised. In comparison to the volumetric method the sample bulb is connected to the vacuum pump by a wide orifice. At low pressures degassing is faster, more effective and contamination as a consequence of re-adsorption during cooling is avoided. This thermogravimetric procedure is, therefore, recommended by the IUPAC [2] even for volumetric measurements. After degassing, the sample is cooled down and thermostatted using liquid nitrogen. Than, starting from vacuum the gas pressure is increased stepwise or continuously and the adsorbed mass is recorded as a function of the pressure [3].

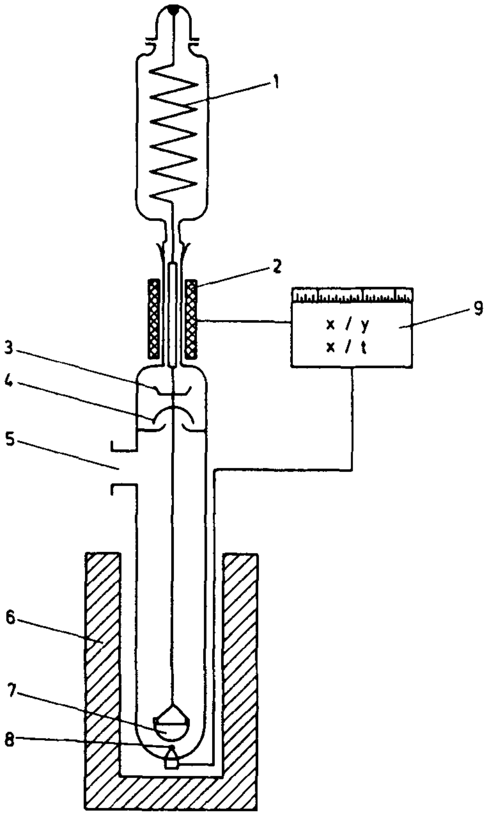

Fig. 1a Spring balance. 1 spring, 2 detector coil, 3,4 heat shields, 5 vacuum line, 6 thermostat, 7 sample pan, 8 thermocouple, 9 recorder

Sorption measuring apparatus

For sorption experiments microbalances are prefered in order to reduce temperature and buoyancy errors. Spring balances (Fig. 1a) are suitable for the use in a high vacuum on account of its simple design and the small amount of material needed. However, they exhibit only a little specific sensitivity (relation of sensitivity to sample mass). Most commonly electrodynamic compensating beam balances (Fig. 1b) are used. The symmetrical design allows for the compensation of some disturbances like buoyancy and thermo-molecular flow. In suspension balances (Fig. 1c) the sample is in a closed reaction tube separated from the balance and the environment and coupled via an electromagnet to the suspension part of an ordinary electrodynamic laboratory balance. Thus, the sample can be held in ultra high vacuum or treated in a corrosive atmosphere. Commercial balances, useful for sorption work are listed in Table 1.

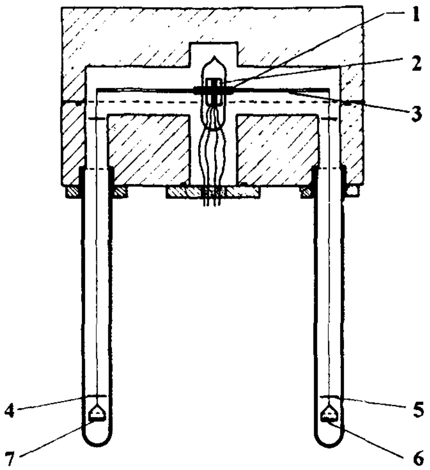

Fig. 1b Electrodynamic microbalance. 1 force coil, 2 magnet with coil, 3 quartz beam, 4,5 heat shields, 6 sample pan, 7 counterweight

A gravimetric sorption apparatus consists of balance, manometer, thermostat, furnace and vacuum pump, as shown schematically in Fig. 2. To produce a vacuum, a combination of a two-stage rotary vane pump may be combined with a diffusion pump and a cold trap or a turbo molecular pump. The gas supply is programmed stepwise or continuously by means of a metering valve. For pressure measurement, recording diaphragm or piezoelectric manometers are suitable. In case of the measurement of nitrogen isotherms the sample is thermostatted using a Dewar vessel filled with liquid nitrogen. The thermostat temperature should be recorded by means of a gas thermometer or a thermocou-

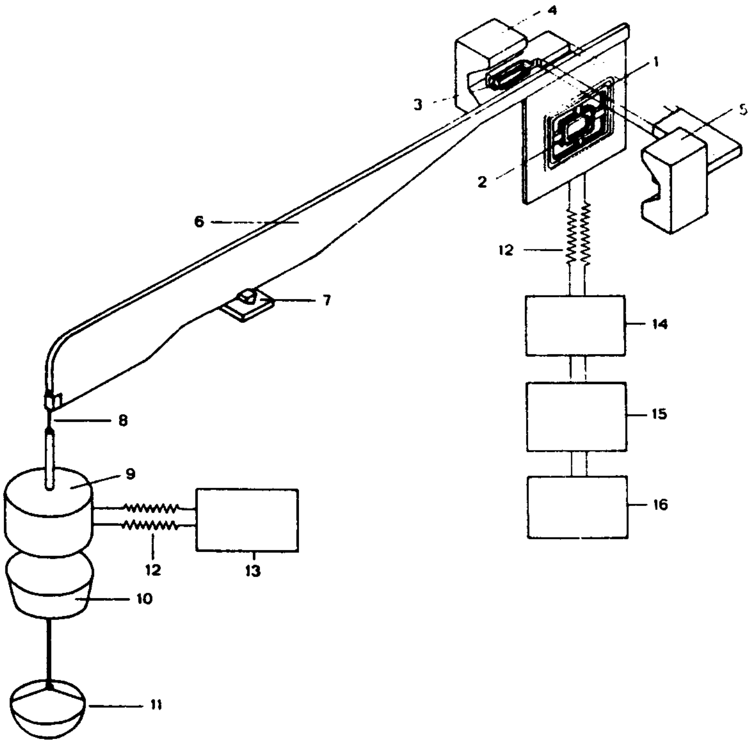

Fig. 1c Magnetic suspension balance. 1 balance force coil, 2 detector coil, 3 oscillator coil, 4, 5 magnets, 6 beam, 7 knife edge, 8 band suspension, 9 pending magnet, 10 suspension magnet, 11 sample pan

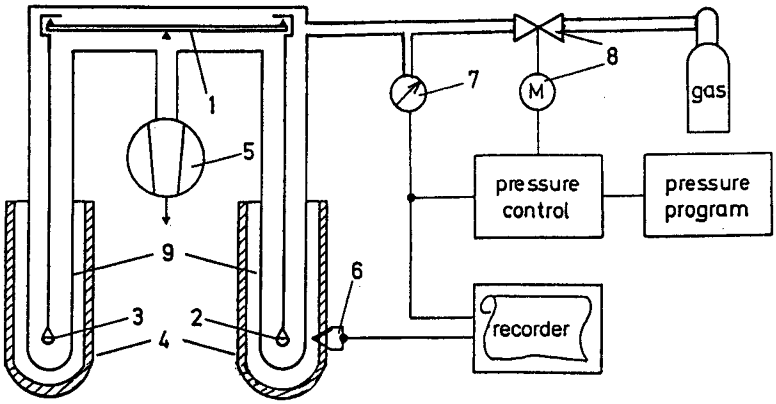

Fig. 2 Sorption apparatus. 1 balance, 2 sample, 3 counterweight, 4 thermostat (Dewar vessel with liquid nitrogen) or furnace, 5 vacuum pump, 6 thermocouple, 7 manometer, 8 metering valve

Table 1 Sorption balances and gravimetric sorption apparatus

Manufacturer	Model	Type	Sensor	Maximum load	Sensitivity
				g	μm
Cahn Instruments 16207 South	RG	unsymmetric beam	photo-electric	2.5	0.1
Carmenita road Cerritos,	RM 2	unsymmetric beam	photo-electric	5	5
CA 90701 USA	1000	symmetric beam	photo-electric	100	0.5
C. I. Electronics Brunel rd.	Mark 1	symmetric metal beam	photo-electric	0.5	5
Churchfields, (Salisbury, Wilts. GB.)	symmetric 2	photo- metal beam	5 electric	10	
Netzsch Gerätebau GmbH, Postfach 1460, D-95 100 Selb	TG suspension 449	magnetic dynamic	electro-	32	10
Rubotherm GmbH Auf dem Kalwes 151 D-44801 Bochum		magnetic suspension	electro-dynamic	5/25	2/10
Sartorius AG Weender Landstr.	4401	symmetric quartz beam	electro-dynamic	3	0.1
96-102 D-37070 Göttingen	4431	symmetric quartz beam	electro-dynamic	25	1
	4201	magnetic suspension	electro-dynamic	16	1
SETARAM, rue de l'Oratoire, F-69300 Caluire cedex	MTB 10-8	symmetric metal beam	electro-dynamic	10/100	0.4
DMT, Franz-Fischer- Weg 61, D-45307 Essen			Sartorius balance	25	1/10
Cahn Instruments (address above)	Ads.-kit	manual apparatus	Cahn RG balance	2.5	0.1
Hiden Analytical, 231 Europa bd. Gemini Business Park, GB- Warrington WA5 5TN	IGA	automatic apparatus	Cahn RG balance	2.5	0.1

ple because it depends on the atmospheric pressure and because oxygen from air is dissolved in the nitrogen during the measuring time. The temperature of the thermostat is conveyed to the sample by heat conduction through the gas and by radiation (in the high vacuum by radiation only). By means of metal screens fastened at the hangdown wire, the sample should be shielded from heat radiation of the balance casing, otherwise large temperature deviations can occur.

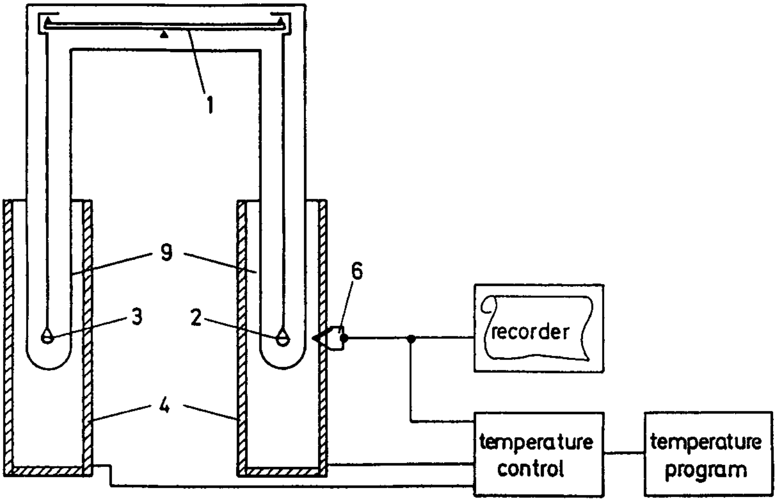

Fig. 3 Thermogravimetric apparatus. For designation see Fig. 2

The extension of a thermogravimetric (Fig. 3) apparatus for sorption measurements provides difficulties because of the sturdy TGA apparata which are mostly designed for this task. An adsorption apparatus, however, allows for thermogravimetric measurements simply by addition of a controlled furnace. Whereas a large choice of thermogravimetric apparata are on the market, only one automatic computer-controlled sorption measuring apparatus is commercially available [4], besides of adsorption kits as ancillary equipment for manual operation [5].

Evaluation data

From the sorption isotherm the specific surface area, the fractal dimension and the pore size distribution can be calculated [6]. For such calculations commercial software is available (Table 2). The calculation of the specific surface area is based on the idea to cover the surface with a complete monolayer of an adsorbate and to determine the required adsorbed mass, the surface covered by one molecule being known from independent measurements. For the measurements physisorbing gases like nitrogen or noble gases are used or, in special cases, water vapour. Because the forces binding the adsorbate molecules at the surface are of the same magnitude as those responsible for condensation, the weakly bound molecules start to form multilayers before the monolayer is complete. It is necessary, therefore, to calculate a fictive monolayer using an isotherm equation. The mostly applied two-parameter equation of Brunauer, Emmett and Teller (BET) is standardised on an international basis [7]. This equation is based on a simple adsorption model which assumes that on a surface an indefinite number of layers can be adsorbed. This, however, is not possible in porous materials. For a more precise analysis we prefer the three-parameter BET-equation or the equation of Aranovich [8, 9]. To calculate the pore size distribution in the mesopore range and the micropore volume several methods are available.

Table 2 Software to calculate surface properties from absorption data

Name	Manufacturer	Specialities
ASAP 2000	Micromeritics, Hammfelddamn 10, D-4 1460 Neuss	control of volumetric apparatus
DEN-AR-MAT	Ströhlein, Girmeskrezstr. 55, D-4 1564 Kaarst	control of volumetric apparatus
DIAPOR	Institute for Physical Chemistry, Russian Academy of Sciences, Leninski Pr. 31, SU-117915 Moscow	calculation of fractality [10]
IGAsoft	Hiden Analytical, 231 Europa bd. Gemini Business Park, GB-Warrington WA5 5TN	control of gravimetric apparatus
MILESTONE	Fisons Instruments, Peter-Sander-Str. 43, D-55252 Mainz-Kastel	control of volumetric apparatus [11]
FSORB	Géomécanique, 212 av. Paul Doumer, F-92508 Rueil Malmaison Cedex	control of volumetric apparatus
OMNISORP	Coulter Electronics, Gahlingspfad 53, D-47803 Krefeld	control of volumetric apparatus
PM	Porous Materials, Cornell Industry Research Park, Ithaca N. Y. 14850, USA	control of volumetric apparatus
QUANTA-CHROME	Quantachrome, 6 Aeral way, Syosset N. Y. 11791, USA	control of volumetric apparatus
RT-LineTrace	H. Reichert, Binger Str. 17, D-55437 Ober-Hilbersheim	calculation of two-dimensional functions [12]

The results of the above methods depend on the size of the sorptive molecules used. Thus, the obtained data are doubtful when measured with nitrogen and applied for organic drug molecules. Therefore, the characterisation of the surface should be supplemented by the surface fractal dimension, a parameter which characterises the self-similarity of the surface over a wide range. In contrast to the pore size distribution the fractal dimension is a measure of the roughness and thus, gives additional information of the surface morphology. We apply the thermodynamic method [13] in which the surface fractal dimension is determined from the isotherm in the region of capillary condensation.

Characterisation of porous alumina

In the course of development of a drug with sustained release several aluminium oxides were precipitated by water from aluminumisopropylate [14] un-

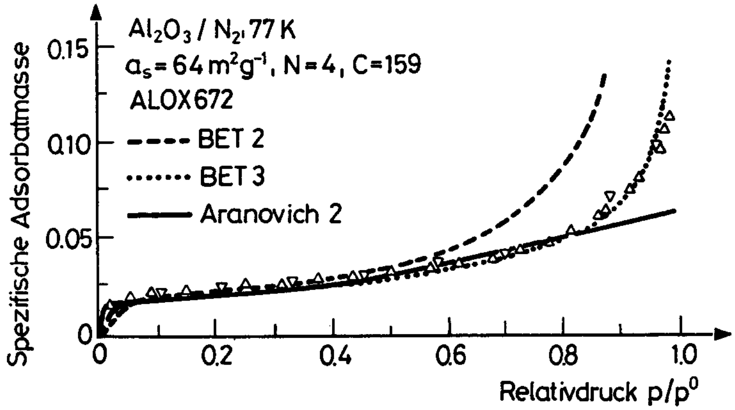

Fig. 4 Nitrogen adsorption isotherm at 77 K at aluminum oxide

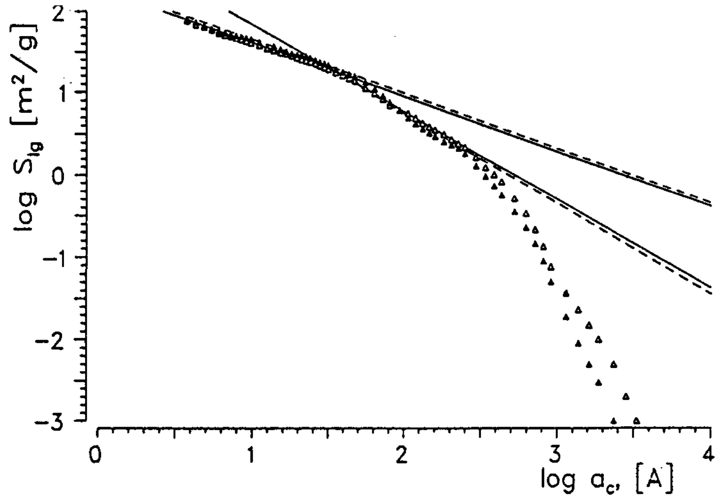

Fig. 5. Calculation of the surface fractal dimension

der various conditions. In this way highly dispersed and porous powders were obtained. The isotherm and its approximation by the BET and the Aranovich equation, respectively, is depicted in Fig. 4. The fractal analysis of the surface roughness has been provided by means of the thermodynamic method. The results are presented in Fig. 5. The values of the surface fractal dimension, d_{fs}, and the limits of fractality, a_{min} and a_{max},, have been obtained by using the linear regression of the adsorbate surface area, S_{lg}, *vs.* mean radius of curvature, a_c, in the double-logarithmic plot. Both, the adsorption -Δ- and the desorption branch -Δ- of nitrogen adsorption isotherm have been used. We observed two regions of fractality: In the range of about 1 to 4 nm we calculated a surface fractal dimension of 2.72–2.73 both from the adsorption and from the desorption branch. For the adsorption branch in the range of 4 to 28 nm and for the desorption branch in the range of 4 to 23 nm we calculated a value of 3. This, however, cannot be accepted as a real surface fractal dimension but characterises the surface in the pores of the sample to be extremely rough and disordered.

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Zusammenfassung — Die Gasadsorptionsmethode ist das weitverbreitetste Mittel zur Charakterisierung der Topologie von Feststoffoberflächen in Bezug auf die Verwendung als Adsorbens. Adsorptionsisothermen werden vorteilhafterweise unter Verwendung einer Vakuum-Mikrowaage ermittelt: Thermogravimetrische Techniken erlauben die Verfolgung der Probenentgasung und deren Optimierung. Die Trockenmasse wird in situ bestimmt, die Masse des adsorbierten Gases wird direkt gemessen und ohne Kalibrierung können verschiedene Gase verwendet werden. Anhand der Isothermen können Porengrößenverteilung, spezifische Oberfläche, Fraktaldimension und Dichte hergeleitet werden. In Tabellen wird ein Überblick über handelsübliche gravimetrische Sorptionsgeräte und Vakuumwaagen als auch über die Software zur Datenauswertung gegeben. Darstellung findet die Sorptionsanalyse eines Aluminiumoxides. Dieses poröse Material wurde als Matrix für eine langsame Wirkstofffreisetzung benutzt.