

Influence the Distributions of Porosity on the Performance of Solubility Functions

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Abstract In this research , it was possible to include the porosity distribution factor among the factors affecting solubility instead of the surface area by developing a mathematical mode which based on equations Owtwald-Freundlich, Gibbs-Thomson and Kaptay's derivations which one of dependence on the surface area. Two sample of ammonium perchlorate were applied , the first sample at normal state, and the second model which had changes were made to the surfaces of the particles. The results of the porosity tests for them were found different. Conducting a mathematical analysis of the results and introducing the pore distribution variable. The surface area of the second model increased by (26%) in which the pore volume size between (30-4000) Å. The results indicate that the solubility increased in sample No. (2) by (12,28%) and this is due to the increase in the pore distribution in the second model. in this case the larger surface area in the porosity distribution is the reason for the resulting increase in the solubility value, by the noting of the mechanism dissolution process which adopted , that can provide an explanation for the increase in it. The idea of pore distribution can be applied to enhance the quality of drugs through depending it's on the amount of solubility which required in order to perform its function well. For this, the aim of this research was to draw attention to the challenges of solubility measurement and to present new techniques and detection methods that provide more accurate results by introduce the concept of pore size distribution to the particle instead of radii and surface area. It has been applied on ammonium perchlorate and determine the effective porosity distribution to obtain the best or required solubility based on the results obtained from studying the laboratory-wise and applying the results to mathematical models that are derived for.



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1. INTRODUCTION

Porosity is defined the fraction of the total volume that is taken of the material volume which is taken up by the pore space. The porosity of substance depends on several factors including: , 1) packing density , 2) the breadth of the particle size distribution (polydisperse and monodisperse) , 3) the shape of particles . Thus it is a single- value quantification of the amount of the space available to fluid with in specific body of substance .Also porosity is defined as the fraction of the bulk particles volume that not occupied by solid matter. Furthest the porosity can be expressed either as a percentage.[1]

Pores completely isolated from the external surface , not allowing the access of water or liquids in either liquid or vapors phase . they influence neither permeability nor the transport of liquids in materials but they do affect their density and mechanical and thermal properties. It can be divided into the following according to their shape :-

1-1- Calcification of pores

Pores can essentially be classified according to the their typology and size to.

a- Typology

- Closed pores
- Open pores

Pores connected with the external surface of the material and therefore accessible to liquid have direct bearing on deterioration phenomena . open pores permit the passage of fluids and retain wetting liquids by capillary action. They can be further dividing into dead-end or interconnected pores.(2)

b- Geometry

So the geometry pores is can also classified according to the shape of particle as:-

- Spherical pores;
- Basic pores,
- Dissolution pores,
- Shrinkage pores.

c- Size

Internal standards (IUPC) classify pores according to their radius :

- Microspores : radius < 0.01 nanometer,
- Mesopores : radius between 0.001 and 0.025 nanometer,
- Macropores : radius > 0.025 nanometer .

d- Volume of Pores

Three terms are exist

-Pore volume is the fraction of total volume of a solid occupied by pores.

-Apparent volume is the volume of solid including the space occupied by pores piece of material.

Real volume is defined the difference between apparent volume and pore volume.[3]

2-1 Deterioration of pores:

One of the main causes of substances decay are the interaction between liquid phase (β) and the pores structure. Liquid

adsorption can induce weathering on material phase (α) several ways;

- By chemical reaction (e.g. aggressive pollutants);
- By physical mechanism : through mechanical stress due to freeze/thaw cycle;
- By acting as transport medium for salts in dissolution and recrystallisation processes within the pore space;
- By providing an essential substrate for biological growth.[4]

The equation which has become widely accepted and is called today as the Ostwald–Freundlich equation. According to Google Scholar, more than 400 papers refer to this equation under this name. Its usage accelerated during the recent years, as follows from Fig. 1. Except the year of 1999, the yearly number of papers mentioning the Ostwald–Freundlich equation was below 10 before 2005, while it started to increase in an unexpected way during the last 5 years.[5]

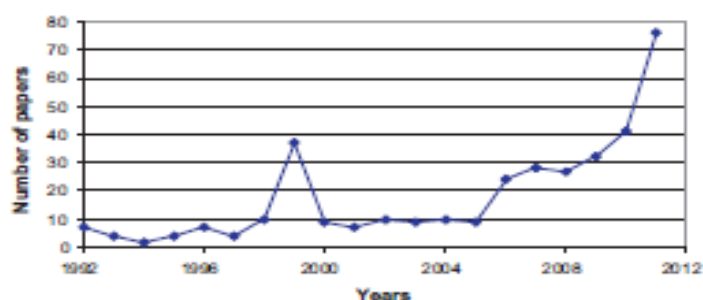


Fig. 1. The number of papers published yearly during the last 20 years, containing the expression "Ostwald–Freundlich" (according to Google Scholar, searched on 26 December, 2011).

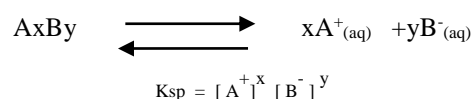
2. SOLUBILITY

Solubility is one of the most important physicochemical properties of a drug for the pharmaceutical industry. It can highly influence the absorption of a compound and consequently affect bioavailability [6]. Solubility is influenced by the lattice structure of a compound. Because of the different lattice energies, the dissolution requires more or less solvation energy.[7] Polymorphism is the ability of the compounds to exist in two or more crystalline structures, consequently it can affect their solubility or dissolution. [8] As a rule of thumb, the polymorph having the lower lattice-free energy is the more stable form and it has lower solubility while the one with higher energy is less stable but tends to dissolve faster and has higher solubility [9]. The topic received increasing attention in the past decades, as more and more cases with unexplored polymorphism caused serious safety problems.[10] Cases with the highest publicity. As the result, the discovery and investigation of possible polymorphs (i.e. polymorph screening) is now an inevitable requirement in drug development. Solubility difference of polymorphs will affect

the bioavailability/bioequivalence of a drug product if the solubility is the rate-limiting factor upon absorption (for BCS II and IV drugs).[11]

2-1- Solubility Equilibria

As we mentioned that the solubility properties is most important in drugs discovery, so low-solubility can lead to poor absorption and bioavailability after oral dosing, insufficient solubility for IV dosing, artificially low activity values or erroneous results in different biochemical and functional assays. Let the solubility of compound A_xB_y in the phase of (α) at the liquid phase of (β) then:



K_{sp} is the solubility product constant , so the dissolution of an ionic solid aqueous solution , then the equilibrium act the bellow of study state as;

$$Q < K_{sp} \quad \text{unsaturated solution} \quad \text{no precipitate}$$

$Q = K_{sp}$ saturated solution

$Q > K_{sp}$ supersaturated solution precipitate will form

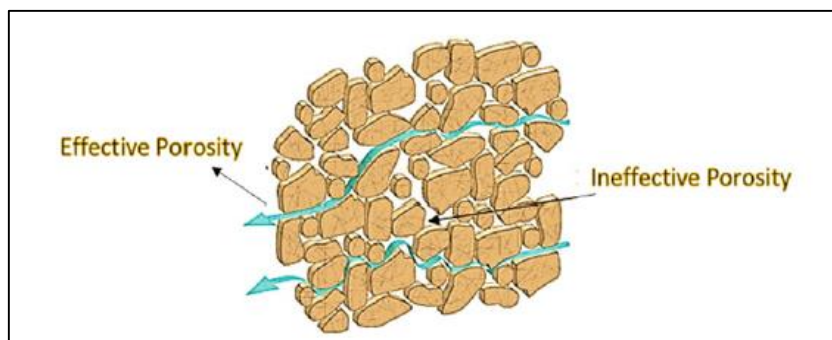
Low solubility is often associated with high plasma protein binding, slow tissue distribution, and drug-drug interactions. Increased time and resources are required with expensive formulations to develop a poorly soluble drug candidate. Concept use the shake-flask method for either kinetic or thermodynamic solubility depending on your preference.[12]

2-2- Effective , Ineffective and dual porosity

Tarek Al-Arbi was classified the types of porosity depend on their effectiveness and he put three types:

- **Effective porosity**

Fig. (2) shows the clean pore space and the effective porosity. Also shows the several types of clay distributions existing in reservoir rocks and their effect on reservoir porosity.



Fig(2) Diagram showing effective and ineffective porosity inside reservoir particle



Fig. (3) Diagram represent dual porosity model

2-3- Why is the solubility's measurement difficult ?

To the untrained eye, solubility determination seems simple and straight forward: Just measure the concentration of the compound in a saturated solution. The relative ease of performing solubility measurements has perhaps overshadowed the difficulty of correctly interpreting the results of such measurements and the consequences of poorly designed studies. There are numerous complications that can occur in the

- **Ineffective porosity (also called closed porosity)**

This porosity also called closed porosity, where the pores are isolated and no interconnected. Also, it's known as the part of the total volume where liquids or gases are exists but in which fluid flow can't efficiently occur includes the closed apertures

- **Dual porosity**

Known as dual porosity reservoirs because the fractured reservoirs have two dissimilar porosities, call matrix porosity, and fractures porosity. However, naturally fractured reservoirs comprise of asymmetrical fractures, they might be characterized by same homogeneous dual porosity systems. Dual porosity is defined also as a combination of primary, fracture and or vuggy mix where fluid flows are not simple shown Fig. (3).[13]

measurement of solubility, which could lead to unreliable results of diminished use in predicting the human absorption of drugs- Equilibration so the cause of that belong to:

- Time and Metastable Gel States;
- Poor Wettability;
- Formation of Aggregates and Micelles;
- Polymorphism and Amorphous States;

It's not just a number solubility reactions, being heterogeneous, are often slow to reach equilibrium. The classical techniques are generally slow and not easily adapted to the high-throughput needs of current drug discovery research. At the early stages of research, candidate compounds are not isolated in the crystalline form, but are stored as a stable solutions by add additives material. Consequently, solubility measurements need to be performed on samples introduced to buffer solutions .[14]

Equation (1) illustrated by Noyes and Whitney that proposed the static diffusion layer of thickness (δ) subjected to an equilibrium concentration (C_s) at the surface of an object in a mixing fluid. The dissolution occurs at steady state through diffusion across the diffusion layer. For a diffusion-limited system, the rate of dissolution is thus obtained by solving Fick's laws for the boundary conditions shown in Fig. 1, which yields the Nernst–Brunner law. [15]

$$\frac{dm}{dt} = \frac{DA}{\delta}(c_s - c). \quad \text{---- (1)}$$

In this law , dm/dt is the rate at which mass leaves the surface of the particle, D is the diffusivity, and A is the surface area of the solute exposed to the solvent.

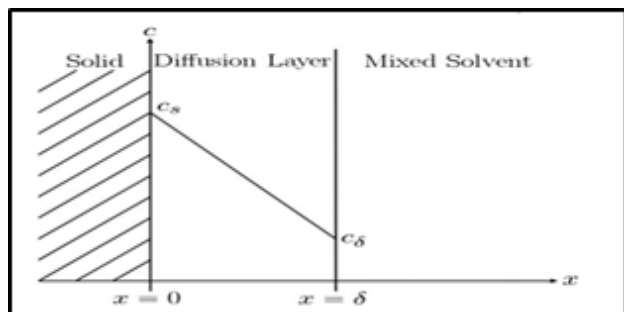


Fig. 2. Schematic of the diffusion layer proposed by Noyes and Whitney [9]. $x = 0$ represents the solid–liquid interface at the equilibrium concentration, C_s . The concentration in the diffusion layer drops to the solvent concentration, c_δ , at $x = \delta$, as shown by Brunner [16]

It is necessary to predict when handling with multiple phases, in this case should be evaluate with accuracy the Gibbs free energy of that multiphased system. The influence of interfaces on equilibrium (i.e. the interface curvature) has to be taken into account. This is the so called Gibbs–Thomson effect that

modifies the solubility limits given by equilibrium thermodynamics. Most of the time such effects are very small, but in some particular cases, like coarsening, the Gibbs–Thomson has been effect incorporated in the solubility limits.. During phase transformations, like precipitation or solidification, solubilisation processes such as nucleation, growth and coarsening depend strongly on interfacial effects, named Gibbs–Thomson effects fig(2). Based, on simple thermodynamics considerations, a formulation of the Gibbs–Thomson equation is proposed and different approximation solutions of this equation found in the literature are discussed.

$$\ln \left(\frac{S_c}{S_\infty} \right) = \gamma \Omega \frac{R_1^{-1} + R_2^{-1}}{kT} \quad \text{Gibbs-Thomson relation} \quad \text{---- (2)}$$

Where S_c is the solubility of a curved solid surface, S_∞ is the solubility of a flat surface, γ surface energy (tension), at reference surface. R_1 and R_2 are curved surfaces which can be described by two principal radii of curvature “ convex & concave of pore on surface.

let's go back to the early stages on the size dependence of solubility of solid particles in liquid solutions is due to Ostwald (1900). His derivation is based on the thermodynamics of Gibbs (1875–1878) and is applicable to the solubility of a spherical solid particle in a large liquid solution:

$$X^{\alpha}_{eq_r} = X^{\alpha}_{eq_\infty} (3\gamma v_m / rRT) \quad \text{--- (3)}$$

Where $X^{\alpha}_{eq_r}$ is the solubility of component A (mole fraction) in the form of a spherical, pure phase of radius r (m) in a given solution at temperature T (K) and at a fixed pressure, $X^{\alpha}_{eq_\infty}$ is the same of an infinitely large phase α , and $R = 8.3145$ J/(molK). Gibbs–Thomson pointed the effect that modifies the solubility limits given by equilibrium thermodynamics (phase). Most of the time such effects are very small, but in some particular cases, like nucleation or coarsening, the Gibbs–Thomson effect has to be incorporated in the solubility limits as we note that in equation (4)

$$X^{\alpha}_{eq_r} = X^{\alpha}_{eq_\infty} (2\gamma v_m / rRT) \quad \text{--- (4)}$$

In the case of multicomponent of ABC at equilibrium with phase β as $A_xB_yC_z \dots$. If X_A, X_B, X_C, \dots correct solubility limit as the matrix mole fraction surrounding the β phase, so equation (5) the generalized form of the Gibbs-Thomson is then:

$$\frac{2\gamma v_{at}^\beta}{r kT} (x + y + z + \dots) = x \ln \left(\frac{X_{A_r}}{X_{A_\infty}} \right) + y \ln \left(\frac{X_{B_r}}{X_{B_\infty}} \right) + z \ln \left(\frac{X_{C_r}}{X_{C_\infty}} \right) + \dots \quad \text{----- (5)}$$

where γ is the surface energy, $v_{\beta A}$ is the average atomic which linked with the radius r , T temp.

3-2 - Equilibrium between two phases

By assumed that the free energy is due to the bond energies between adjacent atoms, the determined the energy of a binary solution of n_A , A atoms and n_B , B atoms, then this solution is called α phase which written as follows of equation (6):

$$G^\alpha = n_A \left[G_A + kT \ln \left(\frac{n_A}{n_A + n_B} \right) \right] + n_B \left[G_B + kT \ln \left(\frac{n_B}{n_A + n_B} \right) \right] + \Omega \frac{n_A n_B}{n_A + n_B} \quad \text{---(6)}$$

where G_A , G_B are the molar free energies of pure A and pure B phase respectively, and $\Omega = z(H_{AA}/2 + H_{BB}/2 - H_{AB})$. H_{AA} , H_{BB} , H_{AB} are the A-A, B-B and A-B bond energies and (z) is the coordination number. if the (α) phase is in equilibrium with the β phase, transferring a small amount of A and B atoms from the α phase of composition X_{eq} to the β phase (composition X_p) will not change the global energy of the system.

It is very interesting to note that if the radius is equal to nucleation radius $r=R^*$, resulting from the classical nucleation theory, a direct comparison between the Gibbs-Thomson equation giving the driving force for nucleation gives $X_{eq} = X_0$ (X_0 is the matrix mole fraction of solute atoms). In that case, the driving force exactly compensate the surface force. The evaluation of the Gibbs-Thomson equation and the classical nucleation theory are fully consistent because they come out of the same thermodynamically approach and formalism.

And from another viewpoint, the dissolution occurs as steady state put under the study during how the diffusion phenomena case as through diffusion the solid phase with liquid solute phase across a layer which called diffusion layer. For a diffusion-limited system, the rate of dissolution is thus obtained by solving Fick's laws for the boundary conditions shown in Fig.1. yields the Nernst-Brunner law which is in formulating the theories, Nernst and Brunner, assumed that the process at the surface proceeds much faster than the transport process and that a linear concentration gradient is confined to the layer of solution adhering to solid surface. [7,8]:

In order to address the issue of solubility especially when working is in the pharmaceutical field, it must first be defined, the solubility of a substance can be broadly defined as maximum amount of the substance that dissolution a specified volume of solvent. However, it is important to understand that the solubility of the compound can be vary drastically depending on the condition of the solvent (temp & PH) and the physicochemical properties of the compound (eg ionization and crystalline). These critical factors need to be considered during data that will be useful in the progression of compounds through the discovery and development stages.

The functional meaning and concept of solubility also differ for drug discovery scientist and development scientist and can sometimes be a source of mist understanding. In drug discovery, solubility assays are often to use to priorities hit selection, to flag compounds with potential liabilities and validate hits by comparing the dose response values of compounds with their apparent solubility values during lead optimization. in development the formation and solid state properties of the compound are the key area to be addressed with solubility assays.

4-2- Ostwald-Freundlich equation and its derivatives

the derivation of Ostwald (1900) was depended on solubility of solid particles in liquid solutions which based on the thermodynamics of Gibbs (1875-1878) and is applicable to the solubility of a spherical solid particle in a large liquid solution, which also called today as the Ostwald-Freundlich equation:

$$x_{A(\beta)} = x_{A(\beta)}^0 \cdot \exp \left(\frac{3 \cdot V_{A(\alpha)}^0 \cdot \sigma_{\alpha/\beta}^0}{R \cdot T \cdot r_\alpha} \right) \quad \text{--- (7)}$$

where $x_{A(\beta)}$ is the solubility of component A (mole fraction) in the form of a spherical, pure phase of radius r (m) in a given solution at temperature T (K) and at a fixed pressure p (Pa), $x_{A(\beta)}^0$ is the same of an infinitely large phase, $\sigma_{\alpha/\beta}^0$ is the interfacial energy (J/m²) between the two phases (supposed to be size independent), $V_{A(\alpha)}^0$ is the molar volume (m³/mol) of the pure phase $A(\alpha)$, and $R = 8.3145$ J/(molK), the universal gas constant.

Using the analogy of the Kelvin equation (under the name Thomson, 1871), the Ostwald equation was quite soon corrected by Freundlich (1909) as:

$$x_{A(\beta)} = x_{A(\beta)}^0 \cdot \exp \left(\frac{2 \cdot V_{A(\alpha)}^0 \cdot \sigma_{\alpha/\beta}^0}{R \cdot T \cdot r_\alpha} \right) \quad \text{---(8)}$$

One can see that Eqs.(8) and (9) differ from each other only by a numerical coefficient. However, behind this small qualitative difference, a quantitative difference between different approaches are hidden, as recently shown by Kaptay (2012) for the vapor pressure of small droplets.[12]

In a binary system containing solvent atoms (A) and solute atoms (B), β -phase particles of pure B exist in equilibrium with the surrounding A-rich α -phase at the equilibrium concentration of B in A, that is, at the solubility limit, c_s . It is well-known that the equilibrium concentration of B atoms in the vicinity of β -phase particles increases with decreasing size

of the β -phase particles [17]. In limit of ideal solutions, the relationship between solubility and particle size is given by the Ostwald–Freundlich equation, which is a special case of the Gibbs–Thomson effect [18]:

$$\frac{c_1}{c_2} = \exp \left[2\gamma_{sl} \frac{V_c}{RT} \left(\frac{1}{r_1} - \frac{1}{r_2} \right) \right] \quad (10)$$

where c_1 is the solubility of a spherical particle with radius, r_1 , and c_2 is the solubility of a spherical particle with radius, r_2 . For a large radius, r_2 , the interface between the particle and solvent is comparatively flat, so $c_2 \approx c_s^\infty$, where c_s^∞ is the solubility of a flat surface, i.e., $r = \infty$, and thus

$$\hat{c}_s = \frac{c_s}{c_s^\infty} = \exp \left(\frac{2\gamma_{sl}V_c}{rRT} \right) \quad (11)$$

where \hat{c}_s is the normalized solubility limit. This equation is analogous to equilibrium vapor pressure of a liquid droplet suspended in a gas of the same substance [18], which leads to analogous evaporation kinetics.

3. Derivation of case study of solubility

3-1- Equilibrium between two phases

Let (α) is a pour phase of component (A) with (β - phase) Of component (B), firstly by returning to the equation (1) of the rate of dissolution to reach the relation of solubility of the binary solution. As it is known that when the surface area increases the solubility , so the amount of solubility (S) is directly proportional to the surface area ϕ , and let us point that the surface area β -phase consist of multi- of pores sizes (P) (porosity) , then:

$$S \propto \phi$$

And solubility is expressed the amount of β mass which loss over a period of time:

$$\begin{aligned} S &\propto \frac{dm_\beta}{dt} \\ S &\propto \left(\frac{m dm_\beta}{tdt} \right) (\phi) \\ S &= k \left(\frac{m dm_\beta}{tdt} \right) (\phi) \quad (1a) \end{aligned} \quad (12)$$

Where k is constant, $m\beta$ is the dissolution in the mass of compound (B) at $t(dt)$ time.

$\phi = \sum M$ (where $\sum M$ is summation of pore size of the compound B),

$\sum M$ act the total of both of the porosity distributions on the surface of the compound . In this scope M_a , M_b ,,, M_n are the porosity which install as required by the pore distribution of the compound.

$$\phi \equiv (M\beta_1) + (M\beta_2) + \dots + M_n \quad (2a) \quad (13)$$

Now we can put the surface of porosity distribution (M) instead of the surface area(ϕ) , and the equation (12) become :

$$\begin{aligned} S &= (k) [m dm_\beta / t dt] \\ S t dt &= (k) m dm_\beta \\ S \beta_1 \int_0^{t_n} t dt &= k \int_{a_1}^{a_2} (M\beta_1) dM\beta_1 \\ S \beta_2 \int_0^{t_n} t dt &= k \int_{b_1}^{b_2} (M\beta_2) dM\beta_2 \\ S \beta_n \int_0^{t_n} t dt &= k \int_{n_1}^{n_2} (Mn) dM\beta_n \\ \frac{1}{2} (S \beta_1) t^2 &= k \left[\frac{1}{2} (M\beta_1)^2 \right]_{a_1}^{a_2} \\ \frac{1}{2} (S \beta_2) t^2 &= k \left[\frac{1}{2} (M\beta_2)^2 \right]_{b_1}^{b_2} \\ \frac{1}{2} (S \beta_n) t^2 &= k \left[\frac{1}{2} (M\beta_n)^2 \right]_{n_1}^{n_2} \end{aligned}$$

Where $a_1, a_2, b_1, b_2, \dots, n_1, n_2$ are numerical values of pore size
 S act $S \beta_1 + S \beta_2 + \dots + S \beta_n$
 $S = k \{ [(a_2)^2 - (a_1)^2] + [(b_2)^2 - (b_1)^2] + \dots + [(n_2)^2 - (n_1)^2] \} / t^2 \quad (3a) \quad (14)$

The equation (2) Gibbs – Thomson relation we note that the magnitudes of (γ , V_c , r , R and T) are constant so k is :-

$$\begin{aligned} k &= \exp \left(\gamma V_c / rRT \right) \quad (15) \\ \text{substituted the equation (15) in the (14)} \\ S &= \exp \left(\gamma V_c / rRT \right) \{ [(a_2)^2 - (a_1)^2] + [(b_2)^2 - (b_1)^2] + \dots + [(n_2)^2 - (n_1)^2] \} / t^2 \quad (16) \end{aligned}$$

4. RESULTS

We performed the determination of porosity and pore distribution on ammonium perchlorate, which possesses certain properties that were measured with a device mercury porosimetry . In this research, two models were taken, the first in its normal state without undergoing any change in the surfaces of the crystals, and the second model was a change in the surface of the particles in terms of porosity, pore distribution, and surface area.

1-4- Below we list the extracted results that will be applied throughout the research:-

First sample

- Sample weight 0.230 gm
- Bulk density 1.9367 gm/cm³
- Bulk Sample volume (v) 0.119 Cm³
- Total pore surface 15.18 m² / gm
- Pore volume in pores greater than 40000 A ... 0.0017 cm³ / gm
- Pore volume in pores between 30-40000 A ... 0.00368 cm³ / gm
- Pore volume in pores less than 30 A 0.0132 cm³ / gm

Second sample

- Sample weight 0.2154 gm
- Bulk density 1.8014 gm/cm³

- Bulk Sample volume (v) 0.1196 Cm^3
- Total pore surface20.66 m^2 / gm
- Pore volume in pores greater than 40000 Å. 0.00 cm^3 / gm
- Pore volume in pores between 30-40000 Å ... 0.0464 cm^3 / gm
- Pore volume in pores less than 30 Å 0.0056 cm^3 / gm
- Total pore volume intruded ... 0.052 cm^3 / gm

2-4- Results Application

By application the results in the math model (equation 16), the surface area of the second sample increased than the first sample by (26%) in which the pore volume size between (30-4000) Å. Then the results indicate that the solubility increased in sample No. 2 by (12.28%) and this is due to the increase in the pore distribution in the second sample.

5. DISCUSSION

A - for point the Mechanism the solubility process when the solute substance (phase α) comes into contact with a solvent liquid (phase β) then the liquid begins to penetrate into the pores of the phase (β) , In this case, a new phase ($\alpha\beta$) will be created in which the two phases are in a state of mixing. This phase requires study by developing scientific hypotheses, then the steps of solidity process are:-

- After a period of time, the new phase ($\alpha\beta$) will reach a saturated state, and we would like to call it the relative saturation state (RSS). Then the solubility process will be slow down and approaches to zero.

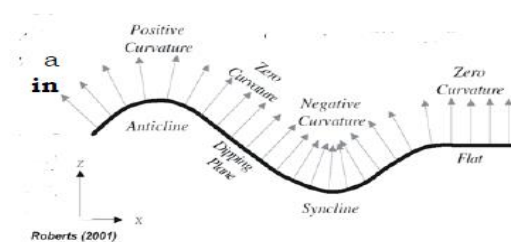
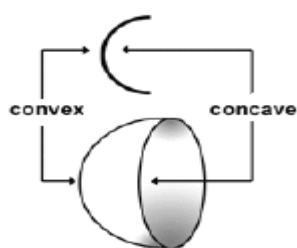
- Now the process of osmosis and diffusion begins, in which the solute molecules of solute in the ($\alpha\beta$ phase) move from higher to lower concentration. Thus, the concentration of the $\alpha\beta$ phase begins to decrease as a result of its contact with the solute phase. This step are depended on the pressure of osmosis.

- The third step will be begins the solubility process by transfer the molecules of the solute to (α phase) and then between the concentration in the phase ($\alpha\beta$) reaches a state of relative (RSS). Then both process repeat until the solubility is complete.

B - the results illustrated that the difference between surface area and pore size distributions which found that the best pore size distribution for the material in order to perform its solubility function and in this case We can obtain the required solubility and we found high in the solubility of second sample.

C -The outer surface of the crystals usually consists of pores, and these pores are either convex or concave, as in the figure (3), which also consist of different sizes , the pores have different radii. In most cases, these pores have irregular shapes which shows how effective the crystal surface is toward dissolution, so it is not possible to take this into consideration to obtain solubility as accurately when inserting the radii of either crystals or pores. Also, relying on surface area to determine effective solubility is not accurate, as each substance has a specific pore size that is effective in terms of solubility.

D - Introducing the concept of the size distribution of pores is the most accurate because by applying the equations (14&16) the best pore size will be identified in which the solubility is the best possible or is the required value.



*Fig (3) illustrate the curvature in two dimensions**

6. CONCLUSIONS

The characterization of pore space is a vital and fruitful aspect of material's investigation's Physical, chemical, and biological which influences acting on the substances constituents of the ammonium perchlorate determine the form and development of pores, whose character in turn profoundly influences the nature and behavior on solubility.

Ammonium perchlorate porosity is fairly well standardized in definition and measurement techniques. Pore size distribution, however, is not obvious how to define, much less to measure. Yet it is central to topics like macropores, aggregation, fractures. Pore distribution size plays a key role in various proposed means of quantifying the structure of partials. It also has a major practical role in the prediction of properties of solubility. New pore distribution size concepts have a relationships to solubility phenomena are likely to remain a

major emphasis in the study of drugs ,assuming that was investigated i ammonium perchlorate is definitely a key to solid of pharmaceutical materials when dealing with solubility.

A theoretical framework was developed to predict the dissolution kinetics of spherical particles ranging in size from the Angstrom to the more the scale of Angstrom. By using the Noyes–Whitney , Nernst–Brunner law , Gibbs–Thomson equation and Ostwald–Freundlich equation , concepts, the dissolving process was assumed to be surrounded by a static layer of solution as like immigration the molecules or molecules leaves the surface layer of ammonium perchlorate , with a smooth concentration gradient that drops from the equilibrium concentration at the solid–liquid interface to the concentration in the well-mixed dissolution medium. The assumption of constant solubility was relaxed by incorporating the Ostwald–Freundlich relation, and our changing from the surface area of the dissolving solute to pore size distribution was accounted for.

The resulting relationship is a new relation as put assume in equation (12) and , by dependent on the loss of amount of the

layer surface in time then using pore size distribution in place of surface area that it is clear in the equation (16).so, the “solubility factor” is to modify of the total dissolution time and identified to establish a correction for that dissolution time through dependence on the pore size and using the mathematic model in equation (16).

This review, albeit brief, points towards the complexity in understanding and predicting solubility-related processes. These include dissolution, solubilization /aggregation, pH-, counterion - and buffer strength effects on solubility, and the impact of substance and co-crystal formation on dissolution, solubility and supersaturation. And inter the concept of the pore distribution in this research. The debate around how consistent data can we achieve from solubility assays and to what extent the data can be used to model and predict, such as, pH-dependence ,surface area , pore size and porous distributions , solubilization tendencies in different solvents will continue . A platform for such a vibrant discussion which will spur new ideas is the upcoming in researches where these topics will be further explored.

REFERENCES

- [1] Ernesto Borrelli / Laboratory Handbook porosity / ICCROM Vol 1, 199.
- [2] TORRACA G., porous building materials , Rama, ICCROM , 1988 pp 11-17.
- [3] IUPAC Manual of Symbols and Terminology, Appendix Chemistry ,31,587,1977
- [4] B “Characterization of pore structure for interpretation of moister transport “ in THIEL , M.J. [ed] conversation of stone and other material . Proccedings of the international RILEM/UNESCO Congress , Paris . 29 June-I July 1993 ,London , E & F N, SPON , 1993 ,pp , 155-162.
- [5] R. Eyjolfsson, Pharmazie, 2002, 57, 347–348.
- [6] G. L. Amidon, H. Lennerna’s, V. P. Shah and J. R. Crison, Pharm. Res., 1995, 12, 413–420.
- [7] A. Avdeef, Absorption and Drug Development: Solubility, Permeability, and Charge State, 2012.
- [8] T. L. Threlfall, Analyst, 1995, 120, 2435–2460.
- [9] H. G. Brittain, Polymorphism in Pharmaceutical Solids, 2ndedn, 2016.
- [10] P. A. Pangarkar, A. M. Tayade, S. G. Uttarwar and
- [11] R. S. Wanare, Int. J. Pharm. Technol., 2013, 5, 2374–2402.
- [12] G. Kaptay, On the size and shape dependence of the solubility of nano-particles in solutions , International Journal of Pharmaceutics, 430 (2012) 253-257
- [13] Tarek Al-Arbi Omar Ganat, Fundamentals of Reservoir Rock Properties, January 2022
- [14] Solubility, Permeability, and Charge State Second Edition A JOHN WILEY & SONS, INC., PUBLICATION ALEX AVDEEF in-ADME Research.
- [15] A.A. Noyes, W.R. Whitney, The rate of solution of solid substances in their own solutions, J. Am. Chem. Soc. 19 (1897) 930–934.

- [16] David R. Ely a , R. Edwin García b , Markus Thommes , Ostwald–Freundlich diffusion-limited dissolution kinetics of nanoparticles .
- [17] R.W. Balluffi, S.M. Allen, C.W. Carter, Kinetics of Materials, Wiley-Interscience, 2005
- [18] W. Wu, G.H. Nancollas, A new understanding of the relationship between solubility and particle size, J. Solut. Chem. 27 (1998) 521–531