Study of the Porosity of Certain pharmaceutical Tablets using Mercury Intrusion Porosimeter

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Abstract:

Porosity and pore structure are important characteristics of pharmaceutical tablets, since they influence the physical properties, such as mechanical strength, density and disintegration time. This paper is an attempt to investigate the pore structure of four different paracetamol tablets based on mercury porosimetry. The intrusion volumes of mercury were used to calculate the pore diameter, pore volume and pore size distribution. The result obtained indicate that the variation of the pore volume in the tablets followed the sequence:- S.D.I. Iraq> Pharmacare,Dubai-U.A.E.> Bron and Burk(UK) London>Lark Laboratories(India), while the variation of surface area followed the sequence:-

S.D.I. Iraq> Lark Laboratories(India)> Pharmacare,Dubai-U.A.E. > Bron and Burk(UK) London

Key words:- Porosity, Pharmaceutical tablets, Mercury intrusion porosimeter, Pore size distribution

Introduction:

The most commonly used dosage form for pharmaceutical preparations is currently the tablet, available in various forms. They are manufactured by applying pressure to a powder bed, which compresses the powder into a coherent compact. The uniaxial compaction of a pharmaceutical powder results in an anisotropic and heterogeneous tablet with variations in such properties as density, porosity, and mechanical strength throughout the tablet. The tablet porosity of most materials is about 5 to 30%. This means that even at relatively high compaction pressures, tablets will rarely be non-porous [1-3].

Tablet properties such as mechanical strength and disintegration are in turn affected by the pore structure, (pore structure of tablet can be expressed in term of porosity and pore size distribution). It has been reported a linear relationship between porosity and the logarithm of the strength of tablets [4]. This suggests that tablets of low porosity will have high mechanical strength. Further, it has been suggested by Vromans et al [5] and de Boer et al [6] that an increase in the total pore surface area resulted in an increase in the tablet strength. Moreover, it was found an increase in tablet strength was related to a decrease in the volume of large pores and to a shift in the pore size distribution towards smaller pore diameter [7].

The disintegration time of a tablet can be affected by the pore structure and bonding structure within the tablet. A high porosity and the presence of large pores facilitate rapid water penetration into the tablet with a subsequent rupture of bonds, followed by disintegration of the tablet [8]. It

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has been proposed that the efficacy of disintegrate is dependent on tablet porosity [9,10]. A relatively low porosity was shown to be most effective for the action of a disintegrate since the swelling of the disintegrate particles would then exert more impact on the surrounding particles.

The porosity parameters of a tablet may be assessed by methods such as gas adsorption [11,12] or mercury porosimetry. The mercury porosimeter was used to measure the pore size distribution differences of tablets compressed from mixtures of sodium chloride and starch and tablets compressed after removal of the starch particles by burning [13]. It was found that the larger pores (>5μm) change, while the small pores stay constant in number and size and the median pore diameter in tablets compressed from the mixtures is higher than the median pore diameter in tablets compressed from the pure materials. Yn San Wu et al [14]. Proposed a method suitable for analyzing the pore size distribution quantitatively and for evaluating anisotropy in tablets. This was done by making scanning electron microscopic (SEM) images from different angles at different locations in the compact. These images were made binary with a two- means cluster algorithm (Isodata) after which the porosity could be calculated. In another proposed method [15], the images obtained with SEM for pharmaceutical tablet were analyzed and the pore size distribution in these images was determined with a technique referred to as a morphological sieve.

In the present work, the pore volume, pore diameter, pore area, and pore size distribution for four pharmaceutical- tablets have been measured using mercury intrusion porosimeter.

Materials and Methods:

The pore structure of the pharmaceutical tablets was determined by mercury intrusion porosimetry (Miceomertics, Model poresizer 9320,USA). Low pressure measurements were performed from 0 to30 psia, to measure pores with a diameter between 360 and 6μm.The pressures used for the high pressure measurements varied from 30 to 30000 psia, which correspond to pore diameters in the range of 6 to 0.006 μm.

The measurements were carried out as follows [16]:- On an analytical balance the tablet specimen to be examined was weighted and dried in vacuum oven at 120°C for overnight. After drying process, the specimen was transferred to the low pressure chamber and the measurements proceeded automatically recording the pressure (in pisa) and intrusion reading (in PF) (PF= Pico Farad). The same procedure was employed after the sample was transferred to the high pressure chamber. The duration time of the experiment lasted about five hours.

Four samples of pharmaceutical tablets have been used. These are different paracetamol tablets, which are manufactured in S.D.I. Iraq**,** Pharmacare Dubai-U.A.E., Bron and Burk (UK) London, Lark Laboratories (India), and obtained from the Iraqi market the tablets used in this study were cylindrical, had a diameter 13 mm, and a mass of approximately 500 mg.

Results and Discussion:

The pores of solid materials can be characterized by measuring the pore volume, pore diameter, and pore volume or pore area distributions The mercury porosimetry method for measuring is well known and documented [17,18]. It is provides the

widest range of measurable pore radius (from 2nm to 10^5 nm), but the method is suffer from complexity of the equipment and toxicity of mercury.

Table (1) shows a typical pore size distribution data form and pore area distribution data form for paracetamol tablet S.D.I. Iraq

Table (1) pore size and pore area distribution data form for paracetamol tablet S.D.I. Iraq

Pressure Psia	Pore size/um D	Intrusion Reading pF	Cumulative Por volume cc/gm	Average Pressure psia	Incremental Pore volume cc/gm	Average Pore size um	cumulative Pore area m^2/gm
0.8	225	70.86	-----	------	----	----	----
1.2	150	70.77	0.00410	1	-----	180	0.000091
2.2	81.8	70.74	0.00547	1.7	0.00136	105.9	0.000206
3.5	51.4	70.72	0.00638	2.85	0.00091	63.15	0.000404
4.5	40	70.71	0.00684	4	0.00046	45	0.000608
5.6	32.1	70.70	0.00729	5.05	0.00045	35.69	0.000819
6.6	27.27	70.69	0.00775	6.1	0.00046	29.5	0.001051
7.7	23.37	70.68	0.00821	7.15	0.00046	25.17	0.001304
10.1	17.8	70.66	0.00912	8.9	0.00091	20.22	0.001804
11.4	15.8	70.64	0.01003	10.75	0.00088	16.74	0.00239
12.3	14.6	70.63	0.0104	11.85	0.00037	15.20	0.00273
13.3	13.5	70.62	0.0109	12.8	0.0005	14.06	0.00310
13.6	13.2	70.62	0.0109	13.45	0.000	13.4	0.00325
13.8	13.04	70.61	0.0114	13.7	0.0005	13.13	0.00347
58	3.1	76.93	0.0114	----	----	----	----
249	0.72	76.22	0.0437	153.5	0.0323	1.17	0.1494
332	0.54	74.86	0.1058	290.5	0.0621	0.62	0.6825
830	0.21	73.94	0.1477	581	0.0419	0.31	1.906
2533	0.07	73.86	0.1511	1681.5	0.0034	0.12	5.0366
4548	0.04	73.83	0.1528	3540.5	0.0017	0.051	11.984
6477	0.027	73.81	0.1537	5512.5	0.009	0.032	19.2125
6750	0.0266	73.80	0.1541	6613.5	0.00093	0.027	22.82
6785	0.0265	73.80	0.1541	6767.5	0.0004	0.026	23.71

The technique is based on the mercury property to behave as non-wetting liquid with a lot of solid materials, as results of this property mercury penetrates through the open pores of a solid sample under an increasing pressure. The pore diameter is inversely proportional to the applied pressure according to a relation proposed by the Washburn equation[17,18];

$$D = -4\gamma Cos\theta / p$$

Where D= The pore diameter, in units of micrometer.

γ= The surface tension of mercury.

θ= The contact angle between mercury and solid containing the pores.

p= The pressure in pound per square inch.

It was assumed that the surface tension of mercury was 480 dynes cm^{-1} and the contact angle of mercury with the materials was assumed to be 140° in all cases.

Converting intrusion meter readings to pore volumes requires, first, calculating cumulative changes in capacitance are there multiplied by the conversion factor (pentameter

constant) supplied for the penetrometer (and a units conversion factor) to give the cumulative pore volume. Cumulative pore volumes per gram of sample are obtained by dividing by the weight of the sample.

The total pore surface area obtained by assuming that all the pores are cylindrical capillaries. Then the pore surface area (A) for each diameter increment is simply related to incremental pore volume (V) and the average pore diameter (D) by the equation[19] : A= 4V/ D

The cumulative surface area for each point is the sum of these for all preceding points.The experimental values obtained for pore volume, pore area , and medium pore diameter on the four different pharmucential tablets are summarized in Table(2).

Table (2) The porosity parameter of the different type of tablets

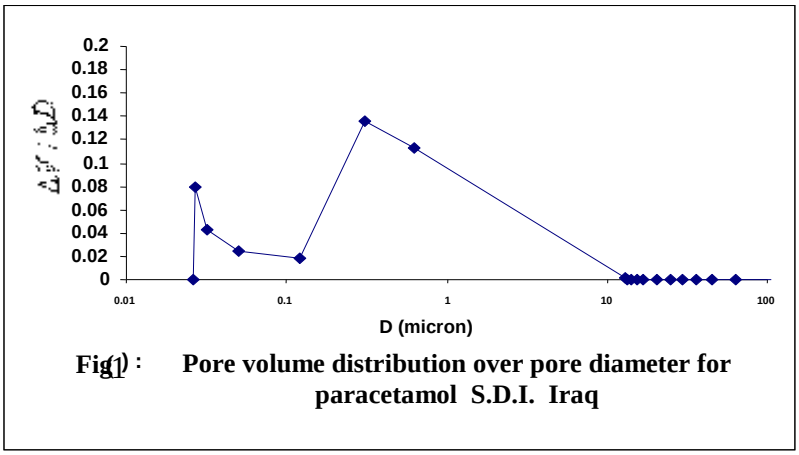
Type of Tablet	Pore volume cc/gm	Pore area m^2/gm	Median pore diameter /µm
S.D.I. Iraq	0.1541	23.710	0.310
Bron and Burk (UK) London	0.0752	11.545	0.455
Lark Laboratories (India)	0.0684	14.325	0.019
Pharmacare,Dubai-U.A.E.	0.0892	13.215	0.027

The value of D on the distribution curve corresponding to the maximum value of ΔV/ΔD is termed the median pore diameter and also called the most abundant pore diameter.

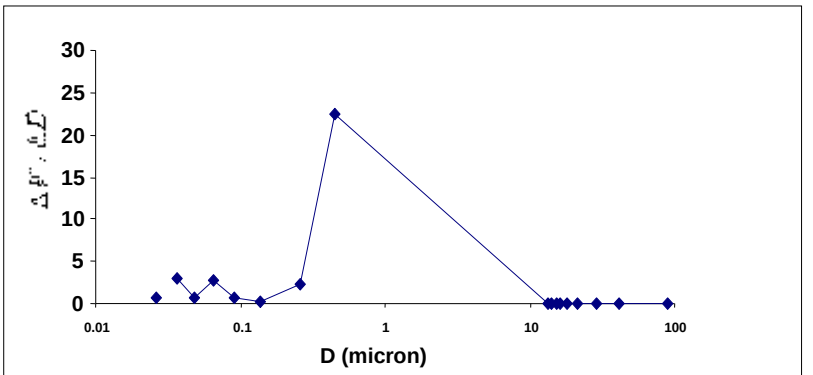
The differential pore size distributions were estimated from the plot ΔV/ΔD against D. The values ΔV/ΔD and D obtained were tabulated in Table (3) and illustrated in figs (1-4).

Table (3) the data of pore size distributions for the three types of tablets

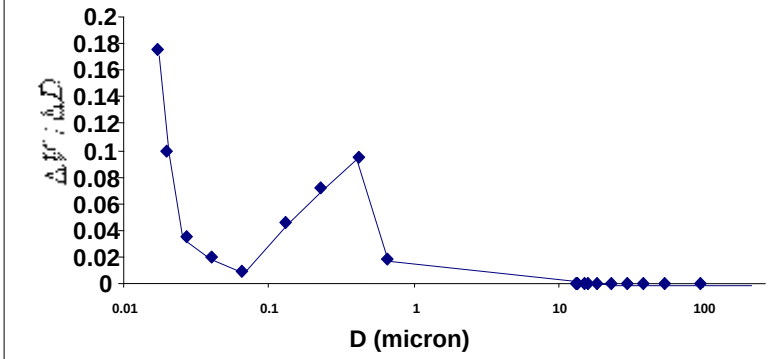
S.D.I. Iraq		Bron and Burk (UK) London		Lark Laboratories (India)		Pharmacare,Dubai-U.A.E.	
ΔV/ΔD	**D**	**ΔV/ΔD**	**D**	**ΔV/ΔD**	**D**	**ΔV/ΔD**	**D**
0.0000184	105.9	0.0000038	88.61	0.000004	95.32	0.0000126	112.5
0.0000212	63.15	0.0000072	41.31	0	52.99	0.0000292	63.97
0.0000253	45	0	28.52	0.0000337	38.62	0.0000573	47.40
0.0000478	35.6	0.0000487	21.54	0.0000538	29.7	0.0000435	35.69
0.0000754	29.5	0	18.34	0.000072	23.04	0.0000441	25.73
0.0001062	25.17	0	16.23	0	18.26	0.0001602	19.80
0.0001838	20.22	0.000327	15.21	0.000215	16.02	0.0001492	16.65
0.0002528	16.74	0	14.03	0.000544	15.14	0.000282	15.09
0.0002402	15.2	0.000448	13.28	0.000539	14.25	0.000521	14.13
0.000439	14.06	22.545	0.455	0.000645	13.49	0.000710	13.44
0.000	13.4	2.3067	0.256	0	13.19	0.00134	13.09
0.001852	13.13	0.23926	0.139	0.0182	0.51	0.0221	1.07
0.11291	0.62	0.6869	0.092	0.0941	0.325	0.0575	0.59
0.1352	0.31	2.778	0.0646	0.07124	0.204	0.0571	0.35
0.01789	0.12	0.667	0.0485	0.04583	0.12	0.003267	0.20
0.02464	0.051	3	0.0364	0.00875	0.064	0.01264	0.128
0.0434	0.032	-1.75	0.0298	0.02	0.04	0.021	0.058
0.08	0.027	0.75	0.0261	0.0354	0.027	0.0404	0.035
0.000	0.026			0.1	0.022	0.063	0.027
				0.1724	0.0191		



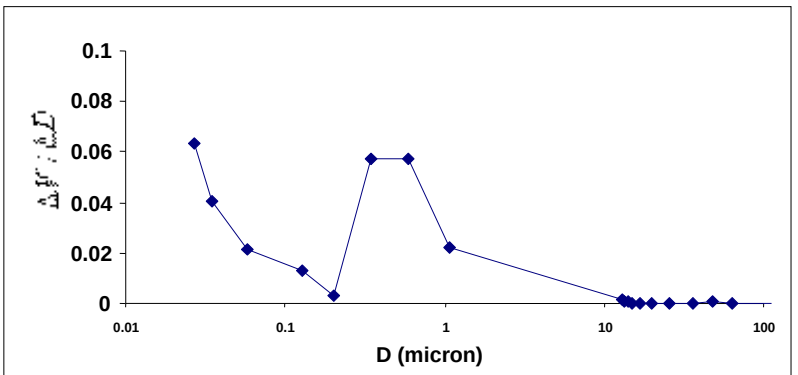
Fig(1) : Pore volume distribution over pore diameter for paracetamol S.D.I. Iraq



Fig(2) :Pore volume distribution over pore diameter for paracetamol tablet Bron and Burk (UK) London



Fig(3) : Pore volume distribution over pore diameter for paracetamol tablet Lark Laboratories (India)



Fig(4) : Pore volume distribution over pore diameter for paracetamol tablet Pharmacare,Dubai-U.A.E.

The results of tablts of Table (2) and figs (1-4) indicated the following :-

1-The highest pore volume is (0.1541cc / gm) obtained on (S.D.I. Iraq tablet) and the pore volume of the four tablets varied in an order that may be arranged in sequence as

S.D.I. Iraq> Pharmacare,Dubai-U.A.E.> Bron and Burk(UK) London>Lark Laboratories(India)

2-The highest pore area is (23.71m^2/ gm) obtained on (S.D.I. Iraq tablet) and the pore area of the four tablets varied in an order that may be arranged in sequence as

S.D.I. Iraq> Lark Laboratories (India)> Pharmacare,Dubai-U.A.E. > Bron and Burk(UK) London

3-The mesopores (defined as 2-50 nm) are exist in (Pharmacare,Dubai-U.A.E.) and (Lark Laboratories (India)) , while the (S.D.I. Iraq) and (Bron and Burk(UK) London) tablets contain only macro pores.This indicate that the tablet strength of the (Pharmacare, Dubai -U.A.E.) and(Lark Laboratories (India)) tablets was higher than the (S.D.I. Iraq) and (Bron and Burk(UK) London) , but the disintegration time was increased on (Pharmacare,Dubai-U.A.E.) and (Lark Laboratories(India)) tablet ,while on (S.D.I. Iraq) and (Bron and Burk(UK) London) tablet was decreased (6,8).

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دراسة مسامية بعض حبات الدواء بأستخدام مقياس المسامية الزئبقي

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الكلمات المفتاحية: المسامية- حبات الدواء- مقياس المسامية الزئبقي- اقطار المسام بالنسبة الى حجمها

الخلاصة:

تعتبر المسامية وشكل المسام من الصفات المهمة لحبات الدواء ، حيث انها ذات تأثير كبير على الصفات الفيزيائية ، كالكثافة والصلادة الميكانيكية وزمن الذوبان (التحلل) لتلك الحبات. في هذا البحث تمت محاولة للتحري وقياس المسامية الموجودة في أربعة أنواع من حبات الباراسيتول المتوفرة في الأسواق العراقية، وذلك بأستخدام مقياس المسامية الزئبقي. تم استخدام حجم الزئبق النافذ لحساب كل من حجم المسام وقطرها ومساحتها السطحية بالأضافة الى معرفة توزيع أقطار المسام بالنسبة الى حجمها. وقد دلت النتائج المستحصلة على أن حجم المسام في حبات الدواء المستخدمة في الدراسة تتبع النسق التالي :-

S.D.I. Iraq> Pharmacare,Dubai-U.A.E.> Bron and Burk(UK) London>Lark Laboratories(India)

بينما كانت مساحة السطح تتبع النسق التالي :-

S.D.I. Iraq> Lark Laboratories(India)> Pharmacare,Dubai-U.A.E. > Bron and Burk(UK) London