Bull. Pharm. Sci., Assiut University
Vol. 10 Part 2, pp. 139 - 151 (1987).
Short Communication

EVALUATION OF READILY COMPRESSIBLE EXCIPIENTS USING AN INSTRUMENTED SINGLE PUNCH TABLET MACHINE

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ABSTRACT

The compression characteristics of eight different readily compressible excipients were studied using an instrumented single punch tablet machine. These excipients were chosen according to their nature as follows : LACTOSE for tableting (Merck), LACTOSE DMV and EMDEX being sugar in nature, STARCH 1500 and MALTODEXTRIN MD 02 being starch in nature, AVICEL PH 101 and ELCEMA P 100 being cellulose in nature in addition to EMCOMPRESS (dicalcium phosphate dihydrate). The application of the instrumented tablet machine offered a good sientific comparison for the compression characteristics of these tablet excipients.

INTRODUCTION

From about 30 years ago the research in the field of tablets was directed towards the detailed study of the compression course, which was divided into a number of partial processes. These studies needed the instrumentation of classical single punch tablet machines and more recently rotary tablet machines to create the possibility of measurement of the compressional and ejectional forces involved in the tableting operation.

The instrumentation of classical tablet machines enables the simultaneous recording of some or all of the following variables as a function of compression time :

a- The absolute force exerted by the upper punch.
b- The absolute force transmitted to the lower punch.
c- The force exerted on the die walls.
d- The force required for the ejection of the tablet.
e- The residual force after compression (tablet expansion).
f- The absolute displacement of the upper punch.
g- The absolute displacement of the lower punch.
h- The relative displacement of the upper punch during compression.

The interpretation of compaction data in tableting operations has received considerable attention in pharmaceutical literature during the four last decades. Initially powder compaction was quantitatively described by pressure/volume relationships, and subsquently by relating compaction pressure to tablet hardness. With the current widespread use of instrumented tablet machines, which monitor upper and lower punch pressures, radial die wall pressures and punch displacement, an extensive number of parameters are available for evaluating compaction mechanisms and comparing the compressibility of pharmaceutical powders.

One of the most direct means of comparing the tableting characteristics of powders is to plot tablet crushing strength versus mean compaction pressure[1] . Where the tablet crushing force is measured with a constant loading rate in tablet strength testing apparatuses and mean compaction pressure is given in case of single punch tablet machine.
by :

$$Pm = (Pa + Pb)/2$$

Where Pa is the maximum applied pressure by the top punch and Pb is the maximum transmitted pressure to the bottom punch.

The ratio (R) between the maximum transmitted pressure to the bottom punch and the maximum pressure applied by the top punch, was extensively used as indicator of force transmission through the powder bed. It was also utilized for comparison between different lubricants and excipients. It is given by the relation :

$$R = Pb/Pa$$

In addition, the ejection force that indicates the easiness of ejection of tablets, was found to provide a good estimation of the compressibility of powders. It is calculated from the following formula[2] :

$$EF\ \% = (2 \times EF \times 100 / (F\ max\ u.p. + F\ max\ 1.p.) \times A$$

Where EF is the measured ejection force.

F max u. p. is the maximal force at the level of the upper punch.

F max l. p. is the maximal force at the level of the lower punch.

A is the contact area between tablet and die during the ejection.

The effect of lubricant on the ejection force is a major parameter to be considered upon evaluation of lubricants.

It was found that powders with different packing characteristics and different elastic and plastic deformational properties would absorb different amounts of energy during compaction for equally applied pressures. Hence, it is more useful to correlate energy of compaction, rather than applied pressure, with tablet characteristics. Energy of compaction is obtained through plotting displacement of the upper punch versus the force transmitted to the lower punch[3].

Upon quantitating the tendency of materials to laminate or cap, Hiestand and co-workers[4] , have developed a direct test for assessing what they have termed B F P (brittle fracture propensity) which is defined as :

$$B\ F\ P = 0.5\ (T/To - 1)$$

and is obtained by performing a transverse compression test of a compact with and without a small hole in it, the tensile strengths being To and T respectively.

The extent of elastic deformation during compation was studied through the determination of percentage elastic recovery (E) defined by :

$$E = 100 \times (H-HC)/HC$$

Where Hc and H are the heights of the compact under pressure and after ejection respectively. Although this parameter does not provide a direct measurement of elastic deformation, it is useful as a measure of disruptive effects of elastic deformation.

Radial versus axial pressure cycle plots have received considerable attention in the literature. By employing pressure cycle plots, powders can be classified as having behaviour similar to a Mohr body, compacting by brittle fracture, or exhibiting a constant yield stress in shear, i.e. compacting by plastic flow. These pressure cycles have been employed as an indication of plastic flow during compaction[5]. The determination of residual die wall pressure gives an idea about the tendency of material to cap or laminate.

Another technique of analysing compression profiles was recently presented by Chilamkurti, et al[6,7].

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This technique involves plotting the area under the compression force-time curve (area, A) as a function of the maximum compression force (height, H). The slope of the relationship (or A : H ratio) could serve as a "compression finger print" for the formulation and be useful as a "trouble-shooting" tool and evaluating and classifying various pharmaceutical powders and systems[8] .

Celic and Travers[9] have proposed elastic recovery index (ERI) as a parameter to predict the compressional behaviour of the materials and to measure the disruptive effects of elastic expansion. This parameter is defined by :

$$ERI = ER/SM$$

where ER is elastic recovery of the compact on load release (corrected for punch recovery) and SM is the strain movement under a constant load. They suggested therefore, that if a material has a low ERI value then it may produce a good tablet.

An interesting thing in this last study is the use of computer as a means of measuring and recording of compression and displacement events. They passed the signals to the user port of a CBM Model 4032 microcomputer. The data were captured and stored into RAM (Random Access Memory) of the computer. Several programs were written to recall these data, read them into memory and print them in graphical form.

EXPERIMENTAL

Materials :

Eight direct compression excipients were used in this study :

- Lactose for tableting (Merck, West Germany).
- Lactose DMV (Zuid Nederlandse, Melkindustrie, N L).
- Avicel PH 101 (F M C corporation, American Viscose Division, Pennsylvania 19061, USA) : microcrystalline cellulose.

- Elcema P 100 (Degussa, West Germany) : microfine cellulose.
- Maltodextrin MD 02 (Roquette, France).
- Starch 1500 (Staley, USA) : corn starch in nature.
- Emdex (Ed. Mendell, USA) : spray crystallised dextrose maltose.
- Emcompress (Prolabo, France) : dicalcium phosphate dihydrate.
- Magnesium stearate (Prolabo, France) was used as a lubricant.

Equipment :

- A turbula T 2 A mixer (Basle, Switzerland).
- An instrumented single punch Korsch EK/0 tableting machine (Korsch, Berlin, West Germany) fitted with 12 mm flat punches and attached to a system of measurements and registration.
- An Erweka TBT hardness tester (Erweka Apparatbau, West Germany).

Methods :

1- Mixing :

The different excipients (used as received from the manufacturer) were mixed with 1 % magnesium stearate in a Turbula T 2 A mixer for 5 minutes at 25 r,p,m. as proposed by Stamm et al [10].

2- Preparation of the tablets :

Tablets were prepared using an instrumented Korsch EK/0 single punch tableting machine equipped with 12 mm flat punches. Batches, each of at least 100 tablets, were compressed. 4 different compression force levels were tried. The compression cycles of 10 tablets, in the middle of each batch were recorded by the aid of the UV recorder. From these records, the mean compaction pressure, the ejection force, the residual force and the force transmission index as well as the displacement of the upper punch were calculated.

3- Hardness :

The hardness of 10 tablets of each batch was determined using an Erweka hardness tester. The mean value was calculated in each case.

RESULTS AND DISCUSSIONS

The instrumented single punch tablet machine was used to compare the compression characteristics of the eight direct compression excipients in order to evaluate these excipients and their value as carriers in direct compression tableting and to explore the role of an instrumented tablet machine in this domain.

Table 1 shows the compression characteristics of the studied direct compression excipients. This table gives the very simple parameters obtained using an instrumented tablet machine and which represent a very useful base of comparison amomg the studied excipients. Calculating the mean compression pressure gives the compressional force requirements of the different excipients to form reasonable tablets. The lower these requirements the better the excipient because this explains the easiness with which tablets are compressed, the less energy input and the long life of the machine. From the table, it could be seen that the excipients which are cellulose in nature (AVICEL and ELCEMA) are more easily compressed than the other studied excipients followed by those which are starch in nature and at last come those which are LACTOSE in nature.

The residual force percentages give an idea on the expansion of tablets after compession which may have a disruptive effect on the tablets and may lead to capping[11-14]. The lower the residual force the better the tableting properties of the excipient in question. EMDEX, EMCOMPRESS,MALTODEXTRIN MD 02 and AVICEL PH 101 were found to be better than LACTOSE Merck, STARCH 1500, LACTOSE DMV or ELCEMA with respect to the residual force.

The ejection force indicates the easiness with which excipients could be compressed into tablets. In addition it can give an idea about the compressibility of excipients. It can be affected by the type, mode of incorporation, particle size, proportion and time of mixing of lubricant. Utilizing the same lubricant in the same condition, the lower the ejection force the better the excipient. STARCH 1500, MALTODEXTRIN MD 02, ELCEMA P 100 and AVICEL PH 101 showed lesser ejection force percentages than LACTOSE Merck, LACTOSE DMV, EMDEX or EMCOMPRESS.

The R value, as an indicator of force transmission within the compact, was extensivly used for comparison of excipients and lubricants. The higher the value of R the better the excipient or the lubricant in consideration, MALTODEXTRIN MD 02 showed the highest R value among the studied excipients while, LACTOSE Merck showed the least value in this respect.

All the studied vehicles gave rise to sound tablets with reasonable hardness values. The compressional force required for the compression of tablets having hardness of 6 kg (Erweka) were calculated to facilitate the comparison between the excipients. AVICEL PH 101 needed the least force while, LACTOSE DMV showed the highest force requirements. A descending sequence of excipients in this respect can be deduced from Table 1 as follows : LACTOSE EMV > LACTOSE Merck > EMCOMPRESS > EMDEX > MALTODEXTRIN MD 02 > ELCEMA P 100 > STARCH 1500 > AVICEL PH 101. This indicates the superiority of microcrystalline cellulose among the studied vehicles .

Figure 1 demonstrates the pressure hardness profiles of EMDEX, LACTOSE Merck and LACTOSE DMV being the three sugar in nature. The pressure hardness profile is used as a parameter of excipient compressibility. The figure indicates the superiority of EMDEX over the two other excipients.

Figure 2 shows the pressure hardness profile of AVICEL PH 101, ELCEMA P 100, MALTODEXTRIN MD 02 and STARCH 1500 being all of disintegrating properties. AVICEL PH 101 showed the best compressibility among those vehicles.

Figure 3 shows the pressure hardness profile of EMDEX, LACTOSE Merck and EMCOMPRESS. EMDEX showed also its superiority among these three excipients. It's worth mentioning that these figures were plotted using the least square method (four points) and the corresponding correlation coefficients are indicated in the figures.

So, it can be concluded that :

An instrumented tablet machine is very useful as a mean of preformulation studies in tableting.

It offers many facilities for a better comprehention of the process of tablet compression and for a good scientific comparison of the compression characteristics of different tablet ingredients.

Cellulose based excipients (AVICEL PH 101 and ELCEMA P 100) showed better compression characteristics than starches, sugars or dicalcium phosphate dihydrate (EMCOMPRESS).

EMDEX showed good compression characteristics with excellent force transmission index (R).

The two studied LACTOSES showed the worst compression characteristics among the examined excipients especially LACTOSE FOR tableting (Merck) as it showed the highest residual force, the highest ejection force, and the least R values.

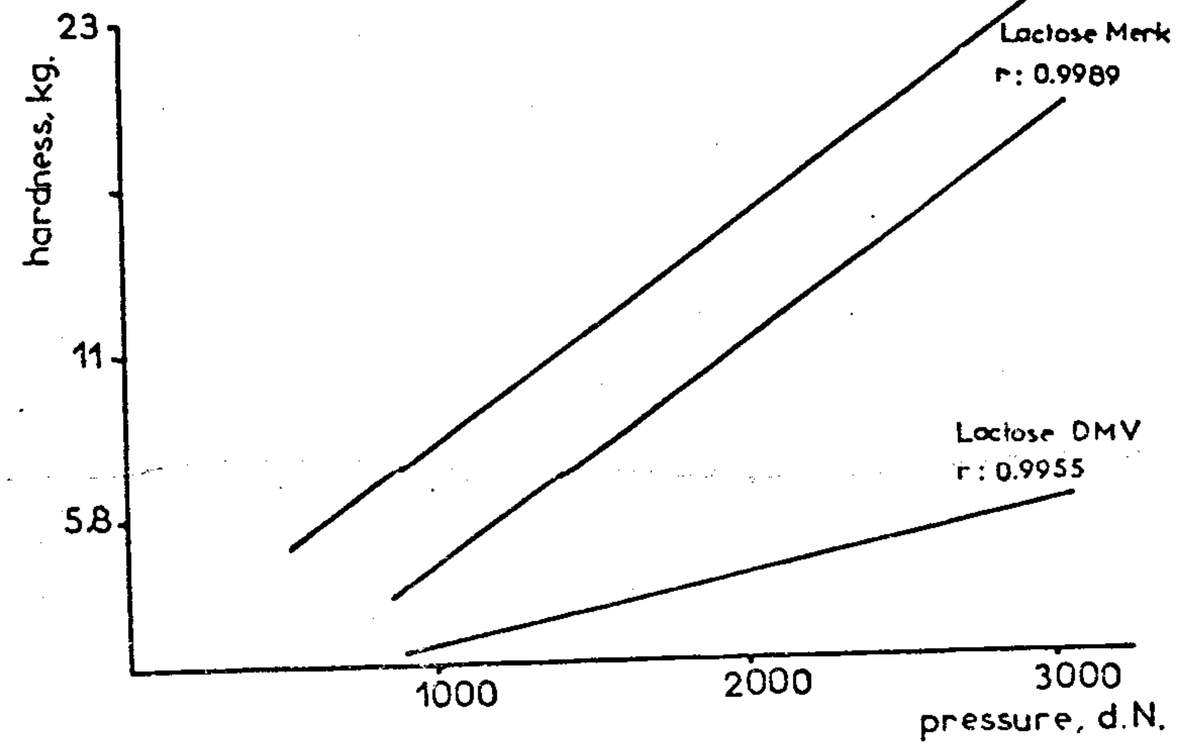

Figure 1: Pressure Hardness Profiles of sugar based direct compression excipients.

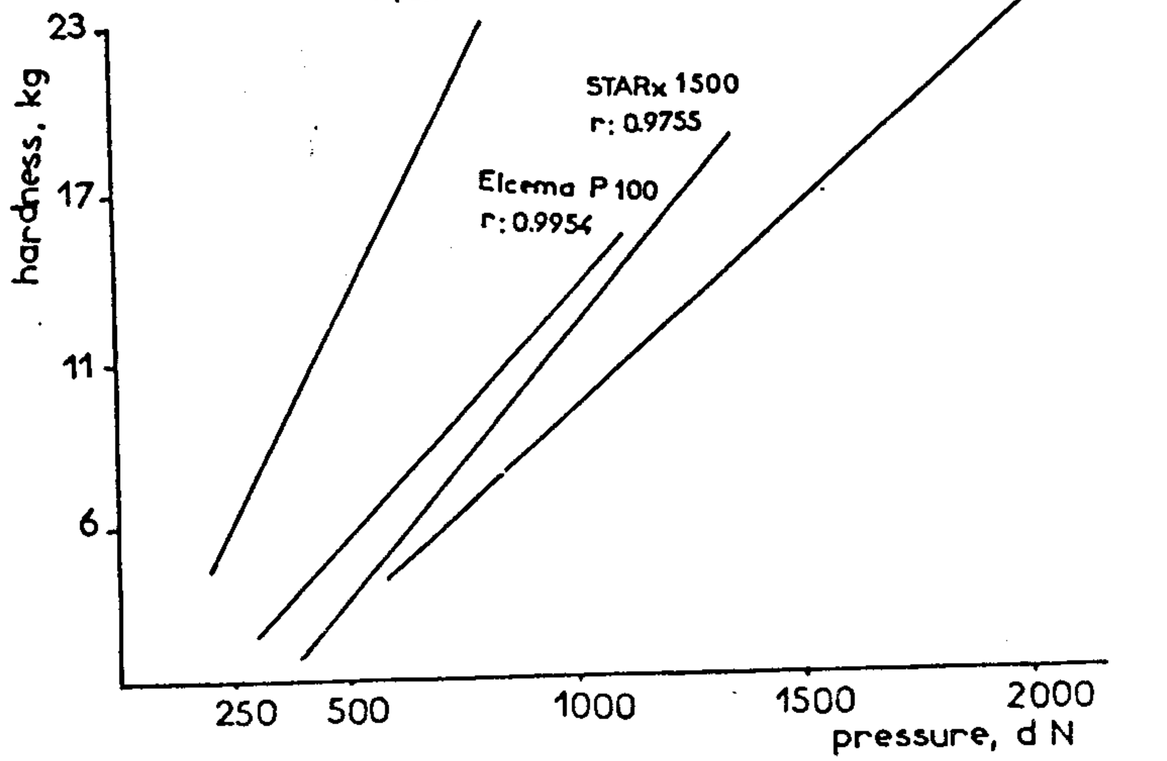

Figure 2: Pressure Hardness Profiles of cellulose or starch based direct compression excipients.

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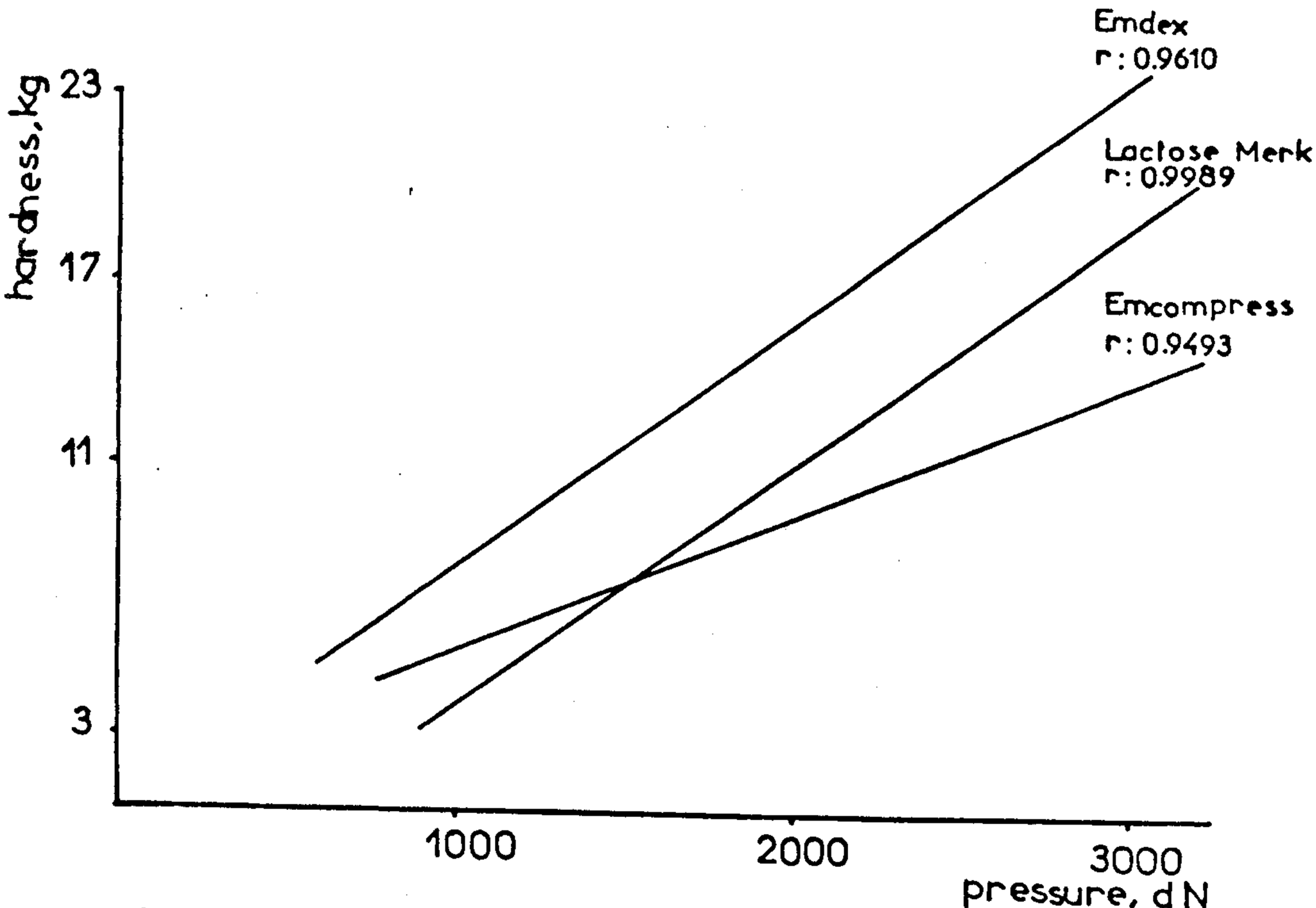

Figure 3 : Pressure Hardness Profiles of Emdex, Lactose Merk, and Emcompress.

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تقويم بعض الصواغات سهلة الكبس باستعمال ماكينة كبس أقراص أحاديـــــة الصياغ ومجهـــزة آليـــا .

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الملخـــــص

تمت دراسة صـفات الكبس لثمان صواغات مختلفة باستعمال ماكينـــة كبس أقراص أحادية الصباغ ومجهزه اليا . وتم اختيار هذة الصواغات طبقـــا لطبيعتها كما يلى : ـ

سكر اللبن لصياغة الاقراص (انتاج مـــيرك) وسكر البن دم ف والامدكـــس الذين لهم طبيعة سكرية ، النشا ١٥٠٠ والمالتودكسترين م د ٢٠ اللذان لهـــما طبيعة نشوية ، السيل ب هـ ١٠١ السيماب ١٠٠ وطبيعتها سلسيلوزية بالاضافة الى الامكمبرس .

ولقد وجد أن استعمال ماكينة كبس أقراص المجهزه آليا أتاح عمل مقارنة علمية لصفات كبس هذة الصواغات المستخدمه فى صناعة الاقراص .

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received in 11/5/87 & accepted in 25/12/87