FACTORS AFFECTING AVERAGE WEIGHT AND WEIGHT VARIATION OF COMPRESSED TABLETS

by

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A THESIS

submitted to

OREGON STATE UNIVERSITY

in partial fulfillment of
the requirements for the
degree of

MASTER OF SCIENCE

June 1962

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Date thesis is presented June 9, 1961

Typed by Gloria M. Merideth

ACKNOWLEDGMENT

Sincere appreciation is expressed to Dr. Ben F. Cooper for his guidance, criticism, helpful suggestions and encouragment, both during the study and in the preparation of this thesis.

Gratitude is also expressed to Dr. Jerome C. R. Li for his advice on the method of statistical analysis.

Thanks are also extended to Mr. Norman F. Billups and other colleagues at the School of Pharmacy for their valuable help and suggestions in preparation of the manuscript.

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INTRODUCTION

Definition and Origin

Tablets, the most widely used oral dosage form today, are a progressive development from two older dosage forms, powders and pills. Tablets are masses of solid medicinal substances compressed into various shapes. The modern era of tablets starts from the date of invention of the tablet machine by William Brockedon of England in 1843 (4, p. 1055). The evolution of the tablet machine from that date has passed through the various stages of mechanical development to present automatic machines capable of producing tablets at the rate of 1000 to 1500 per minute (6, p. 475).

The term "compressed tablets" was originated by John Wyeth and brother in the United States in 1877 (11, p. 82). Compressed tablets consist of a mixture of powdered ingredients formed into small or large granules, which are then compressed mechanically into a desired shape or size.

Popularity

The tremendous use of tablets as a dosage form for solid medicaments was evident in the early 1890's, when tablets were used for all diseases. The first official recognition of tablets was noted in U.S.P. IX in 1860. Only one monograph on poison tablets of corrosive mercuric chloride was mentioned. U.S.P. XVI (1960) contains monographs of 139 different tablets. A survey conducted in 1957 among all of the pharmaceutical dosage forms used in the United States indicated that 6.28% of the dosage forms were for solid medications (10, p. 49). Of these solid medications, tablets accounted for 65.9%.

Advantages and Disadvantages

The accuracy of dosage, ease in administration, convenience in handling, and ease in shipping and packaging are important factors for the increased use of tablets (14, p. 371). Because of the accuracy of dosage of the tablet, the trend in increased use of potent drugs has also increased the importance of tablets in industry as well as dispensing. In contrast to these major advantages, tablets have minor disadvantages. The manufacture of tablets is mostly

restricted to solid medicaments. Tablets of large size also have often been found difficult to administer by mouth.

Ingredients and Purpose

Making the tablet is not just a matter of compressing the powdered, crystalline or granular material into shape. Most drugs cannot be formed into a satisfactory tablet without preliminary treatment regardless of amount of pressure used during compression. Usually a formula must be devised which includes not only the active ingredient or ingredients but also a number of excipients, each selected to play a specific part in the manufacture and efficacy of the tablet. The excipients fulfill one or more of the following functions: dilution, cohesion, granulation, disintegration, lubrication, absorption, coloring and flavoring (4, p. 1056; 11, p. 82).

The diluent is a very important tablet excipient. If a single dose of the active ingredient incorporated into a tablet is too small in volume to permit the tablet to be compressed in the machine, an inert substance such as lactose, sucrose, starch, or kaolin is added to the formula to bring the tablet up to a convenient size and weight.

The cohesive is added to bind the powders together as granules and the granules together as tablets of desired hardness and size. Typical examples are gum acacia, gelatin and methylcellulose.

The granulating agent is a liquid such as water or alcohol used to moisten the dry powders for conversion into granules. Formation of granules promotes smooth and uniform flow into the die. The granulating agent often contains the cohesive.

The function of the disintegrating agent is to cause the tablet to break apart. Starch is the best and most used disintegrating agent.

Granules are compressed between the punch faces and the inside of the die. It is therefore necessary to introduce a lubricant to prevent adherence of the powder to the punches and die and to insure smooth ejection of the tablet from the die. Commonly used lubricants are talc, magnesium stearate and liquid petrolatum.

An absorbent is necessary when oils, tinctures, or fluid extracts are included in the formula for compressing the tablet. Certain diluents such as lactose and starch can act as absorbents.

The use of color is necessary when tablets of a

desired shade are required. Moreover, the use of color in tablets is often used as a means of identification. For psychological effect, certain drugs are available in different colored tablets.

When the drug used for the tablets is bitter or unpleasant in taste, flavors and essential oils may be added to produce a certain degree of palatability.

Methods of Manufacture

Compressed tablets are commonly prepared by three methods: direct compression, "slugging" or double compression, and wet granulation.

Direct compression consists of compressing crystalline granular substances directly to form a tablet. Only a few materials do not need preliminary treatment prior to the compression of the tablet. Examples include such materials as sodium and ammonium chloride, some iodides and bromides, methenamine and potassium permanganate. These substances are normally cohesive enough to bind under pressure and form satisfactory tablets.

Granulation by "slugging", known as dry granulation, consists of compressing the mixed powders into oversized tablets or "slugs". These are broken and

passed through a screen of suitable mesh and subsequently recompressed into tablets.

Wet granulation is the most commonly used process for the preparation of tablet granulations. Granulation is a process for converting materials to small granules, which flow freely and uniformly into the die for compression. It results in the reduction of specific surface area with an increase in density. Wet granulation consists of moistening the powder with a liquid or solution to produce a moist mass. The mass is then passed through a screen of proper mesh and the resulting granules are dried. Agents frequently used are aqueous solutions of sugar, gelatin, gums, dextrin, starch, and water, alcohol, glycerin, etc. Miller and Chavkin have reported the use of polyethylene glycol as a dry binding agent in tablet compression (16, p. 486).

Factors Affecting Average Weight and Weight Variation

Accuracy of dosage is an important requirement for the production of good tablets. This can be achieved by insuring proper and complete mixing of the components and maintaining a uniform weight of the compressed tablets. Producing a tablet of accurate and uniform weight necessitates the delivery of a constant volume of granulation into the die.

For the evaluation of average weight and weight variation of compressed tablets, all factors affecting average weight and weight variation should be studied together. The factors influencing the average weight and weight variation of compressed tablets include percentage composition of fines with granules, particle size of granules, physical and micromeritical properties of ingredients, diameter of punch and depth of die cavity, characteristics of particulates, and other factors as geometry of the hopper, speed of compression, and irregularity in pressure.

Fines and Lubricants

Any factor which influences the flow will influence the average weight and weight variation of the compressed tablets. Movement of the granulation inside the die is largely influenced by the lubricant during compression, while flow outside the die is largely influenced by the amount of fines with granules and granule size (7, p. 17). The lubricant plays the role for smoother operation and good appearance of the tablet. The distribution of particle size plays a role for uniform volumetric feeding of the die and thereby uniform weight of the tablet (4, p. 1056; 5, p. 466). It

has been found that the presence of a small amount of fines improves the flow rates of dry particulates. Schwartzkoff (7, p. 47) has shown that from 0 to 8 per cent fines will give optimum flow rates, depending upon the ratio of outlet-diameter to particle diameter. The use of a "glidiant" for increasing the flow rate has been reported (20, p. 263). Hammerness and Thompson have stated that fines have a measurable and uniform effect upon the flow of tablet granulations (8, p. 61). They have also stated that the addition of fines increased the rate of flow to an optimum level, after which the rate began to decrease. In studying the effect of lubricants and fines, Hammerness and Thompson concluded that lubricant and fines had synergistic actions on rate of flow. The role played by a small percentage of fines which have been found to improve the flow of particulates may be that of filling in the surface impressions of the larger particulates (7, p. 48). They also decrease the void fraction by going in between those granules in the die, thereby decreasing the weight variation. It is therefore necessary to study the effect of different percentages of fines with granules to determine the weight variation of the tablets.

Particle Size of Granules

The uniform and free flowing properties of granules have been discussed by many researchers. The major factors which affect the flow rate of granules are particle size, particle size distribution, particle shape, density of the particles and surface characteristics of the granulation (7, p. 47).

A study of the average weight and weight variation of compressed tablets related to particle size has been reported by Arambulo and Deardorff (2, p. 691; 3, p. 694). They concluded that the decrease or increase in the average weight and weight variation of tablets is related to the particle size used.

Solid particulates exhibit certain angular properties which have been found to be related to the manner in which they flow (7, p. 45). The three most important angular properties appear to be (1) the angle of internal friction, (2) the angle of repose, and (3) the angle of wall friction. Of these properties, the angle of repose is the most commonly measured and reported angular property. The frictional forces in a loose powder can be measured by the angle of repose. This is the maximum angle possible between the surface of pile of powder and the horizontal plane (13, p. 592).

Eino Nelson has studied the repose angle of sulfathiazole granulation as a function of the average particle size, the presence of lubricants, and the admixture of fines (17, p. 437). In general, the repose angle increased with decrease in particle size. He also concluded that addition of fines to coarse granulations caused a striking increase in the repose angle.

The correlation between punch size and granule size (with no indication about the fines) has been suggested by several investigators (19, p. 19; 14, p. 380). It should be emphasized that no original research has been reported to support these views.

Physical and Micromeritical Properties

Physical and micromeritical characteristics of particulates will influence the average weight and weight variation of the compressed tablets. Density, stickiness, and dustibility of the granulation are important factors. Hasegawa of Japan has studied the effect of various tablet formulations on the weight variation of the compressed tablets (9, p. 16). He found that no significant differences were recognized among the three tablet formulations used in this study.

Diameter of Punch and Depth of Die Cavity

Increase in punch size will increase the weight of the tablets. Thus, increase in weight of the tablets will ultimately lead to a numerical increase, but a percentage decrease, of weight variation of compressed tablets. Similar results can be obtained by increasing the depth of the die cavity also. In a study of these two factors, Hasegawa (9, p. 21) found that a decrease of the diameter of the punch increased the percentage weight variation of tablets quadratically.

Types of Machines

There are two main types of tableting machines used at the present time, the single punch and the rotary machines (6, p. 472). The single punch machine, as the name implies, contains only one station and has the capacity to produce from 50 to 100 tablets per minute (6, p. 472). The rotary machine is equipped with from 15 to 33 stations having the capacity to produce from 200 to 1500 tablets per minute (6, p. 472). Both the rotary and the single punch machines are used in industry and are capable of producing most of the standard size pharmaceutical tablets.

The principle of the two types of machines is similar. The granulation flows from the hopper into the feed shoe, then into the die where it is compressed between two punches to form the finished tablet.

A single punch machine is excellent for experimental work as it is possible to operate with a small amount of material. The main disadvantage of the single punch machine, as compared with a rotary type, is limited production. A rotary machine, in addition to greater production, is designed for smoother and quieter operation. A rotary machine compresses the tablet by a squeezing action from both sides. This type of compression and ejection is smoother than a single punch, where compression is made rapidly by a hammer-like blow of the upper punch.

In the rotary type, the granules are fed onto a moving plate with a device to scrape off the overfilled die which helps in uniform die fill. Some substances which do not flow easily into the die of a single punch type have been easily handled by the dies of the rotary type (6, p. 474).

Other Factors

Factors such as surface characteristics of granules, large variation in pressure, speed of compression, and geometry of hopper can influence the weight and weight variation of tablets. Effect of speed of compression on weight variations of a tablet has been evaluated by Hasegawa (9, p. 21). Hasegawa did not find any significant difference for the two different speeds which he selected. Any surface phenomenon which would promote difficulty in one particle sliding past another, as surface roughness or cohesiveness, would promote variable voidage. Thus, degree of surface roughness is an important consideration for flow property of dry solid particulates and thereby for weight variation of compressed tablets.

Experimental Design

Weight variation of compressed tablets is an indication of the accuracy and uniformity of dosage. Certain of the factors affecting weight variation and average weight were selected for comparative study while other factors were kept constant in the study.

The effects of the tablet base, punch size, percentage of fines and granule size on tablet weight

variation were evaluated. The evaluation consisted of accurately weighing each tablet in the order produced and analyzing the data statistically.

Lactose and sodium bicarbonate were selected for evaluation as tablet bases. For each base, three standard concave punch sizes were used: 3/8 inch, 4/8 inch and 5/8 inch. For each base and punch size, three fractions of granule sizes were prepared: 10-20 mesh, 20-30 mesh, and 30-40 mesh. For each tablet base, punch size and granule fraction, five percentages of fines were incorporated: 1%, 10%, 20%, 30% and 40%.

The overall plan for evaluation of these factors is shown in Figure I. Other factors affecting weight variation were controlled within the limits of experimental error.

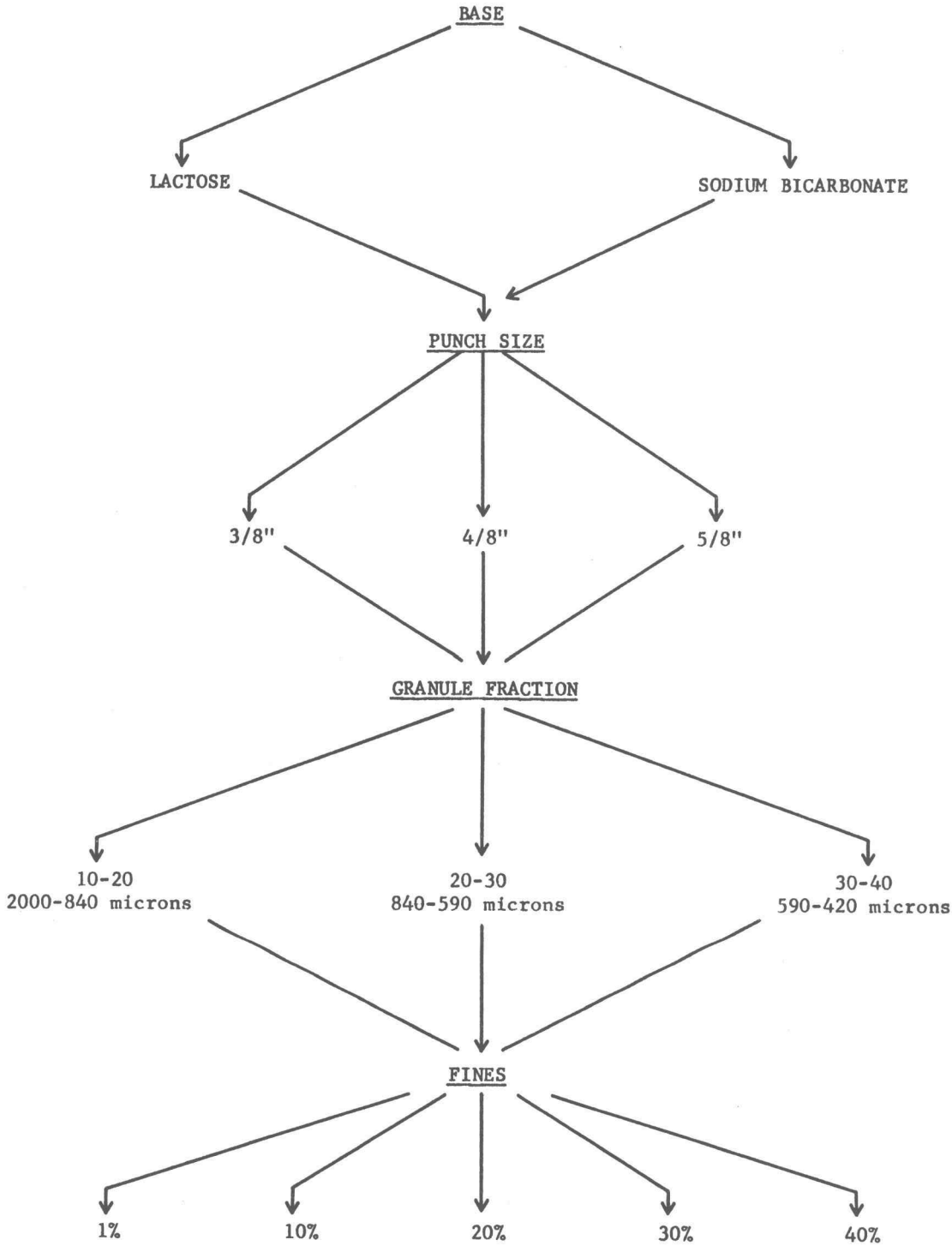
BASE
LACTOSE
SODIUM BICARBONATE
PUNCH SIZE
3/8"
4/8"
5/8"
GRANULE FRACTION
10-20
2000-840 microns
20-30
840-590 microns
30-40
590-420 microns
FINES
1%
10%
20%
30%
40%

Figure 1.

EXPERIMENTAL

All drugs and chemicals used in this study were USP or NF quality (1, p. 1-531; 21, p. 1-1148). All sieves and mesh numbers conformed to the U.S.P. equivalent series (21, p. 932).

Tablet Base

Two bases used for this study were prepared as follows:

Base A:	Sodium bicarbonate	100 Gm.
	Corn starch.	10 Gm.
Base B:	Lactose.	100 Gm.
	Corn starch.	10 Gm.

Each base was mixed thoroughly and passed through #40 mesh sieve to break up lumps.

Granulation

Wet granulation process was used throughout the study. In both bases 10% gum acacia solution, prepared as below, was used as granulating and cohesive agent.

Gum acacia.	10 Gm.
Water to make	100 Gm.

Each tablet base was moistened with measured and necessary amount of gum acacia solution, until the whole

mass became damp and could be broken into lumps. The whole mass was then passed through #6 mesh sieve onto trays and trays were placed in drier for 24 hours at 45° C.

The dry granules were then passed through #10 mesh sieve, #20 mesh sieve, #30 mesh sieve and #40 mesh sieve by hand. The whole amount was then classified into the following three fractions of granules of required amounts for tabletting:

10-20 fractions: The granules which passed through #10 mesh sieve and retained by #20 mesh sieve.

20-30 fractions: The granules which passed through #20 mesh sieve and retained by #30 mesh sieve.

30-40 fractions: The granules which passed through #30 mesh sieve and retained by #40 mesh sieve.

Percentage of Fines

Five different composition of fines were combined with each fraction of granules as listed below. The fines used were #60 mesh and above. One per cent magnesium stearate was used as lubricant for all

compositions. The magnesium stearate was included in the percentage of fines.

1% fines: 1 part of magnesium stearate.

10% fines: 1 part of magnesium stearate.
9 parts of sodium bicarbonate for Base A, or lactose for Base B.

20% fines: 1 part of magnesium stearate.
19 parts of sodium bicarbonate for Base A, and lactose for Base B.

30% fines: 1 part of magnesium stearate.
29 parts of sodium bicarbonate for Base A, or lactose for Base B.

40% fines: 1 part of magnesium stearate.
39 parts of sodium bicarbonate for Base A, or lactose for Base B.

The final composition of each tablet formulation consisted of:

Magnesium stearate, fine powder . . . . . 1 part
Sodium bicarbonate or lactose, fine powder. x parts
Fraction of granules, to make . . . . . 100 parts

The quantity of sodium bicarbonate or lactose as fines was varied according to percentage of fines desired.

Each tablet formulation was mixed thoroughly by rolling on paper and compressed immediately. Five percentages of fines were combined with each of the three fractions of granules for two bases, resulting in (5 x 3 x 2 = 30) different tablet formulations. Each tablet formulation was compressed with three different punch sizes, resulting in (30 x 3 = 90) batches of compressed tablets.

Tabletting and Sampling

A Stokes model E single punch tablet machine was used for the study. Three standard concave punch sizes selected for study were 3/8 inch, 4/8 inch, and 5/8 inch. The depth of die cavity was kept constant for each punch and base separately. The machine was adjusted to a fixed pressure which produced a tablet hardness of 8 Strong Cobb Units*. Speed of compression was kept constant at sixty tablets per minute. Approximately 100 Gms. of each tablet formulation was fed into the hopper and compressed into tablets. The compressed tablets were collected in the order punched. For each

*A Strong Cobb Unit is an arbitrary unit obtained from the reading on a Strong Cobb tablet hardness tester and is approximately equal to a pressure of 1.6 kg exerted against the tablet (15, p. 85).

batch of tablets, the first five tablets were discarded and the next fifty tablets were examined and weighed. The average weights and statistical interpretations were drawn from these samples of fifty tablets for the ninety batches.

During the compression it was found that sodium bicarbonate tablets containing 40% fines often capped, while no capping was found in 40% fines composition of lactose. It was noted that excessive fines of lactose had a tendency to stick to paper, hopper and punch. It was also noted that 40% fines composition of sodium bicarbonate flowed well through hopper to die and compression was easily done, but in lactose it was found that 40% fines composition sometimes flowed with difficulty from hopper to die and often a small amount of powder came out of the die on ejection without compression into tablet form.

Repose Angle

The repose angle of each tablet formulation was measured by a modified method similar to that described by Train (22, p. 928). The apparatus (Figure I) consisted of a smooth glass funnel having an inside diameter of 15.2 cm. on upperside and a tip of 1.1 cm. inside diameter. A circular glass dish of 9 cm. diameter

with edges 1.5 cm. high was placed beneath the funnel a distance of 3 cm. from the tip. The tip of the funnel was closed by one hand and the funnel was filled with a sample of the tablet formulation. Then the hand was taken off and the formulation was allowed to drop in the dish. When the conical pile in the dish reached the tip of the funnel, the funnel was raised slowly by a mechanical screw until the height of the pile was the maximum possible. The height of the pile was measured by pointing a metal tip on the top of the pile and then removing the pile and measuring the distance from the edge of the dish to the metal tip point. The process was repeated three times for each composition. The average of three readings was used to calculate the repose angle, according to the following formula:

$$\phi = \tan^{-1} \frac{H}{\frac{1}{2} R}$$ where H is height of pile and

R is diameter of circular dish.

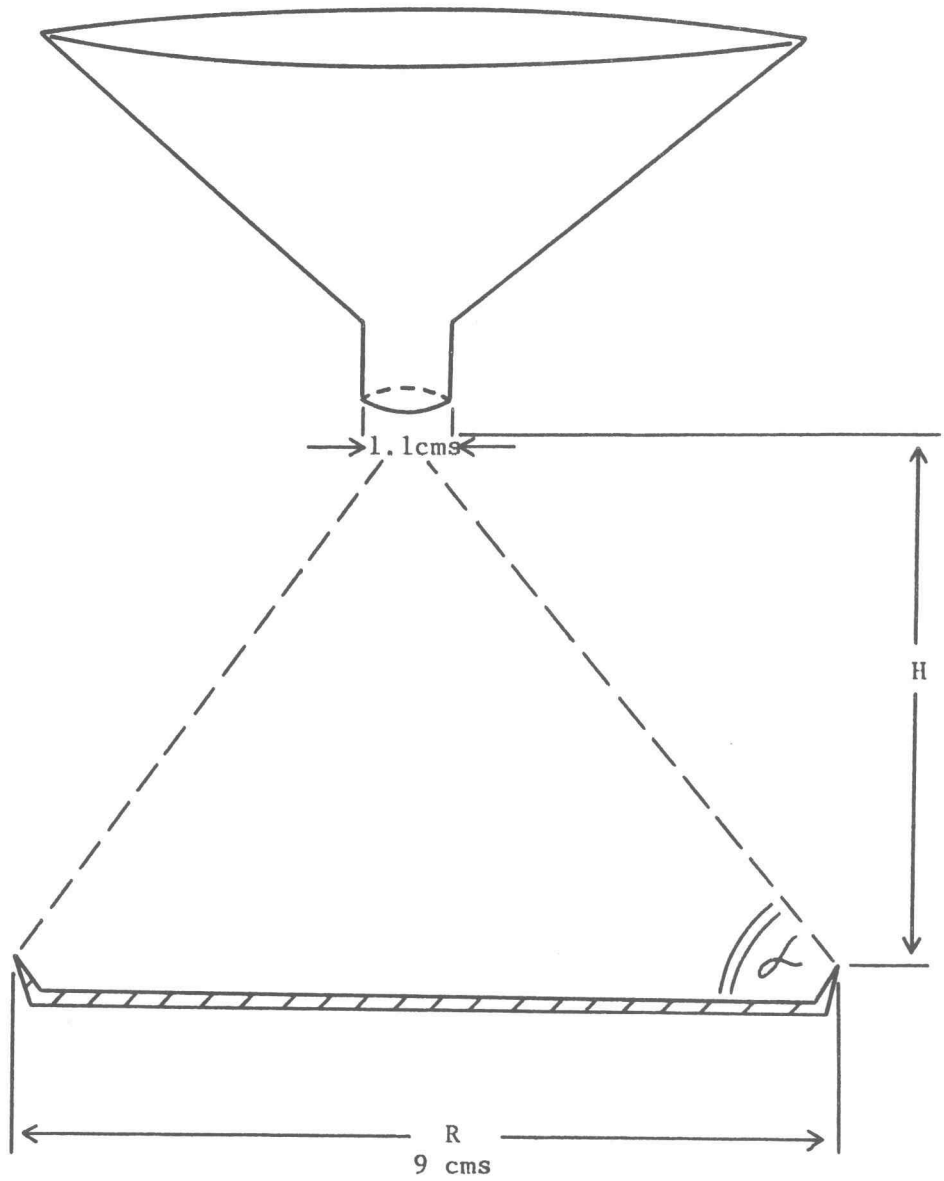

Figure II. Method of Measuring Repose Angle.

RESULTS AND DISCUSSION

Average Weight of Tablets

Table 1 shows the average weight of each sample of fifty tablets for the ninety batches. Graphs of average weight against the percentage of fines for each fraction, punch size and base are shown in Figures III to VIII.

The graphs show that in sodium bicarbonate base, the average weights of tablets increased as the percentage of fines increased, regardless of granule size or punch size. No maximum was obtained in sodium bicarbonate graphs and the average weight was increasing even at 40% fines composition.

In lactose base it was concluded that the average weights of tablets increased as percentage of fines increased, reached a maximum at 30% fines composition and then leveled off or declined at 40% fines composition. This effect was found in all fraction of granules and all punch sizes, except in 10-20 fraction of 4/8 inch punch size.

These different results in lactose base and sodium bicarbonate base indicated that fines played an important role for increase or decrease in average weight of the tablets.

Table 1

Average Weight in Milligrams

Punch Size	Fines	Sodium Bicarbonate Base 10-20 Fraction	Sodium Bicarbonate Base 20-30 Fraction	Sodium Bicarbonate Base 30-40 Fraction	Lactose Base 10-20 Fraction	Lactose Base 20-30 Fraction	Lactose Base 30-40 Fraction
3/8 In.	1%	484.9	530.9	521.6	370.2	418.0	442.4
	10%	514.2	551.1	551.2	393.0	443.8	462.1
	20%	569.8	603.4	571.9	433.3	480.9	492.7
	30%	626.7	661.5	655.0	466.3	499.6	497.5
	40%	688.6	722.8	713.0	460.1	499.3	462.3
4/8 In.	1%	907.8	995.6	1002.2	680.6	795.0	816.0
	10%	944.9	1057.7	1046.6	744.5	849.7	868.1
	20%	1048.4	1178.0	1182.9	813.2	921.8	911.5
	30%	1105.4	1274.5	1297.4	822.4	943.4	917.5
	40%	1313.2	1389.0	1383.5	872.4	926.5	895.6
5/8 In.	1%	1406.2	1480.8	1500.8	974.2	1114.6	1143.0
	10%	1532.9	1564.4	1589.6	1012.7	1212.6	1190.8
	20%	1664.4	1729.2	1753.8	1078.9	1242.5	1203.3
	30%	1796.8	1898.6	1864.1	1080.7	1259.7	1214.8
	40%	1977.3	2025.4	2043.6	1035.4	1179.4	1116.5

For each batch the fifty tablets were weighed in order punched. The average weight of those fifty tablets was calculated.

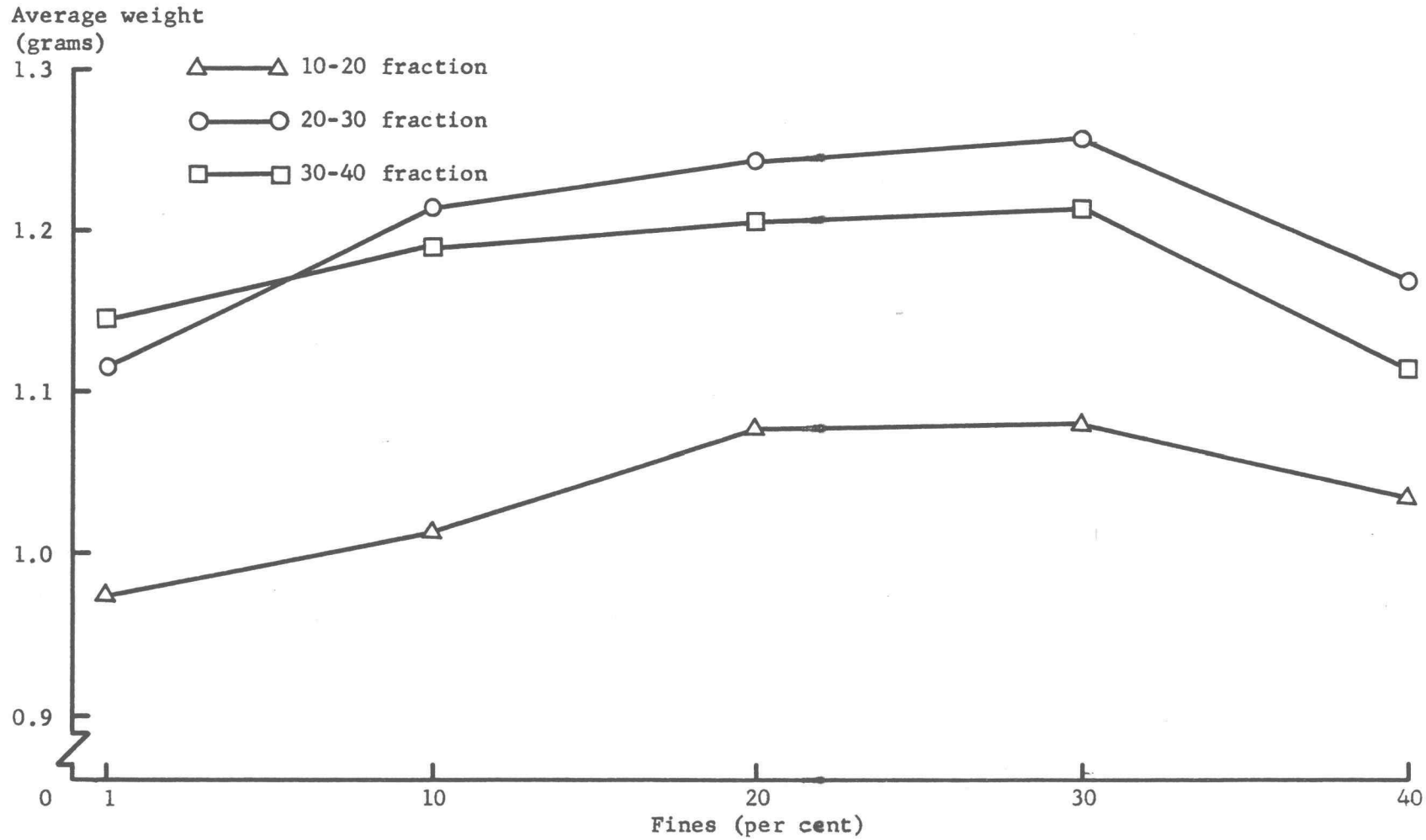

Figure III. 5/8 Inch Punch, Lactose Base.

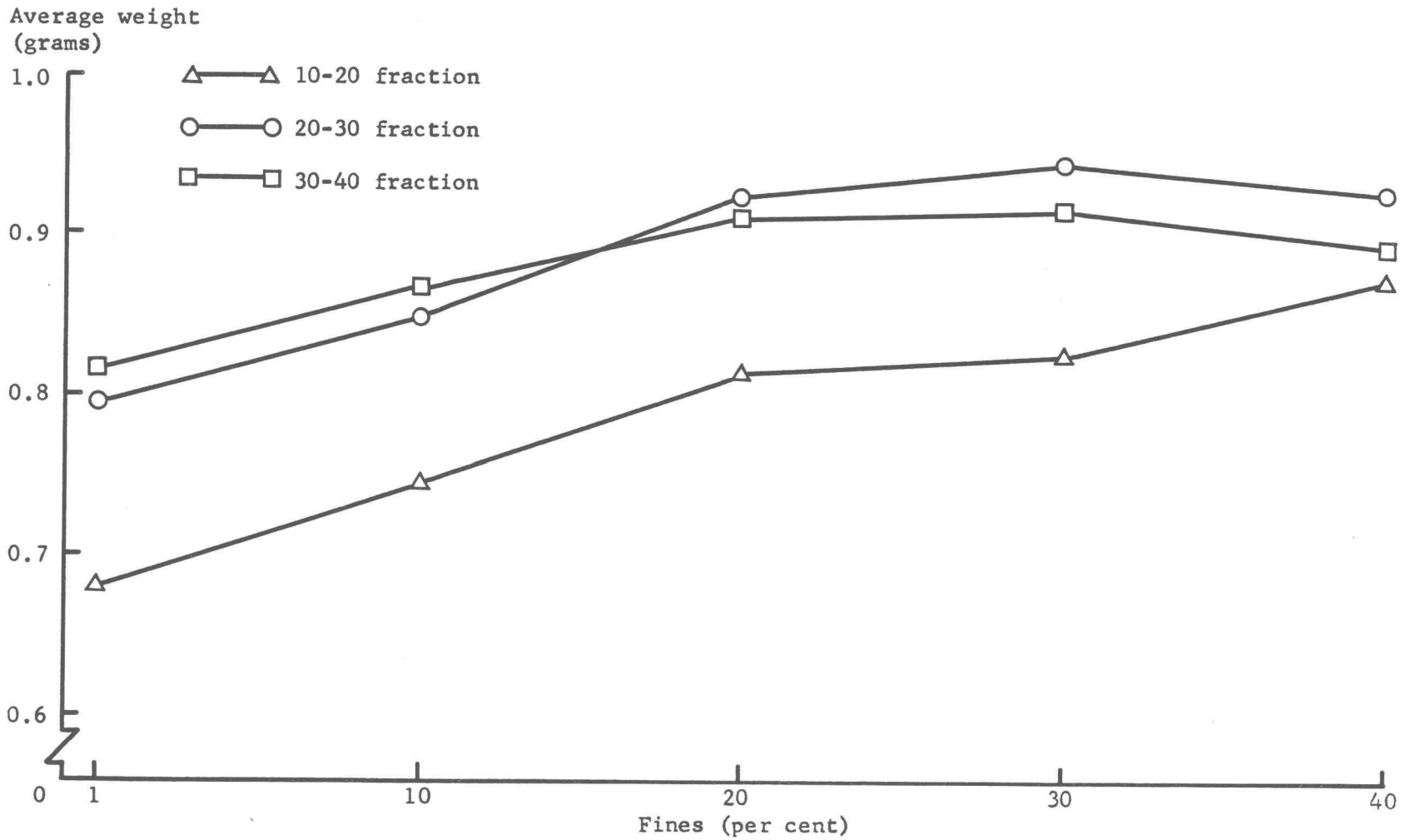

Figure IV. 4/8 Inch Punch, Lactose Base.

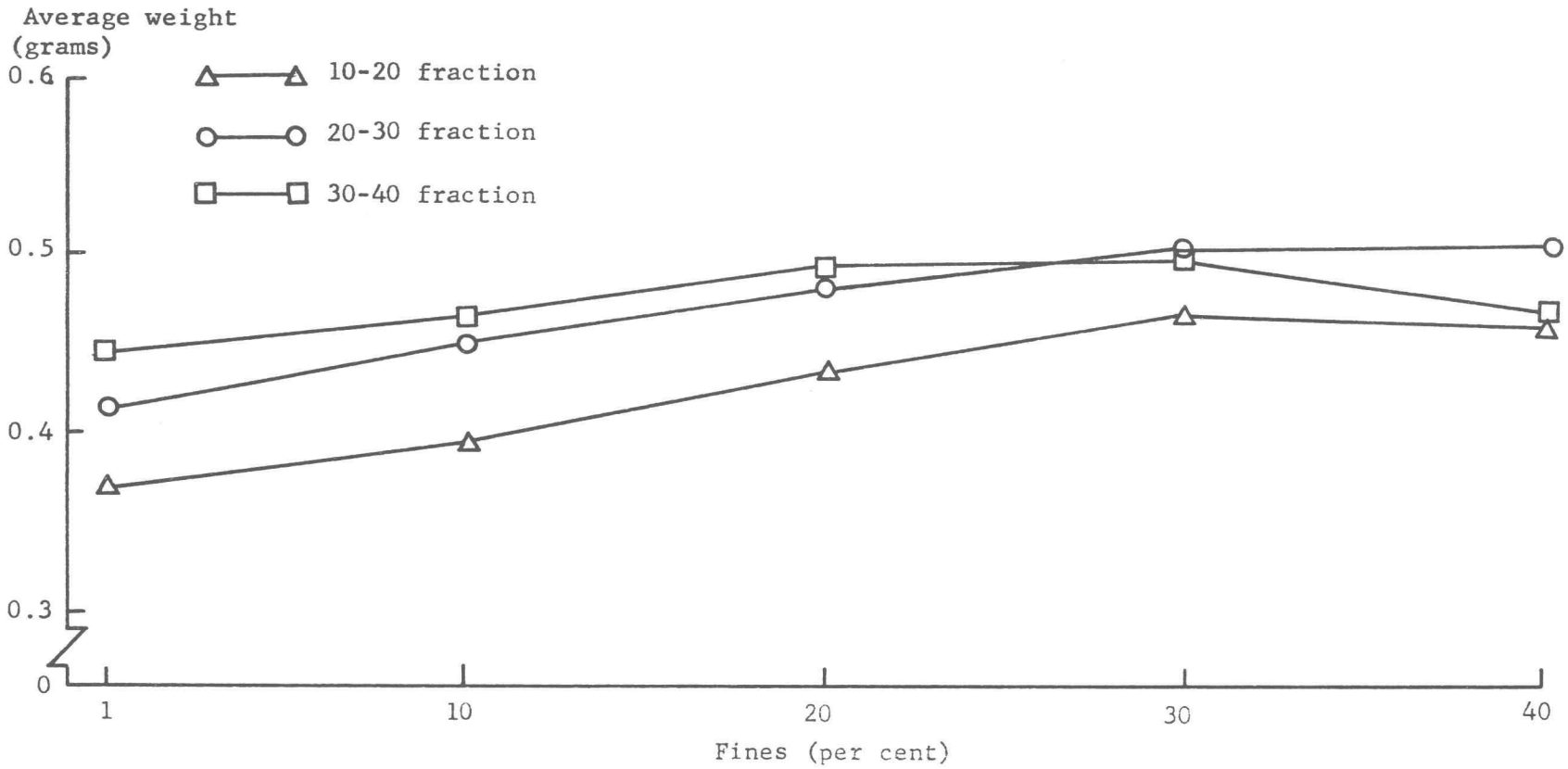

Figure V. 3/8 Inch Punch, Lactose Base.

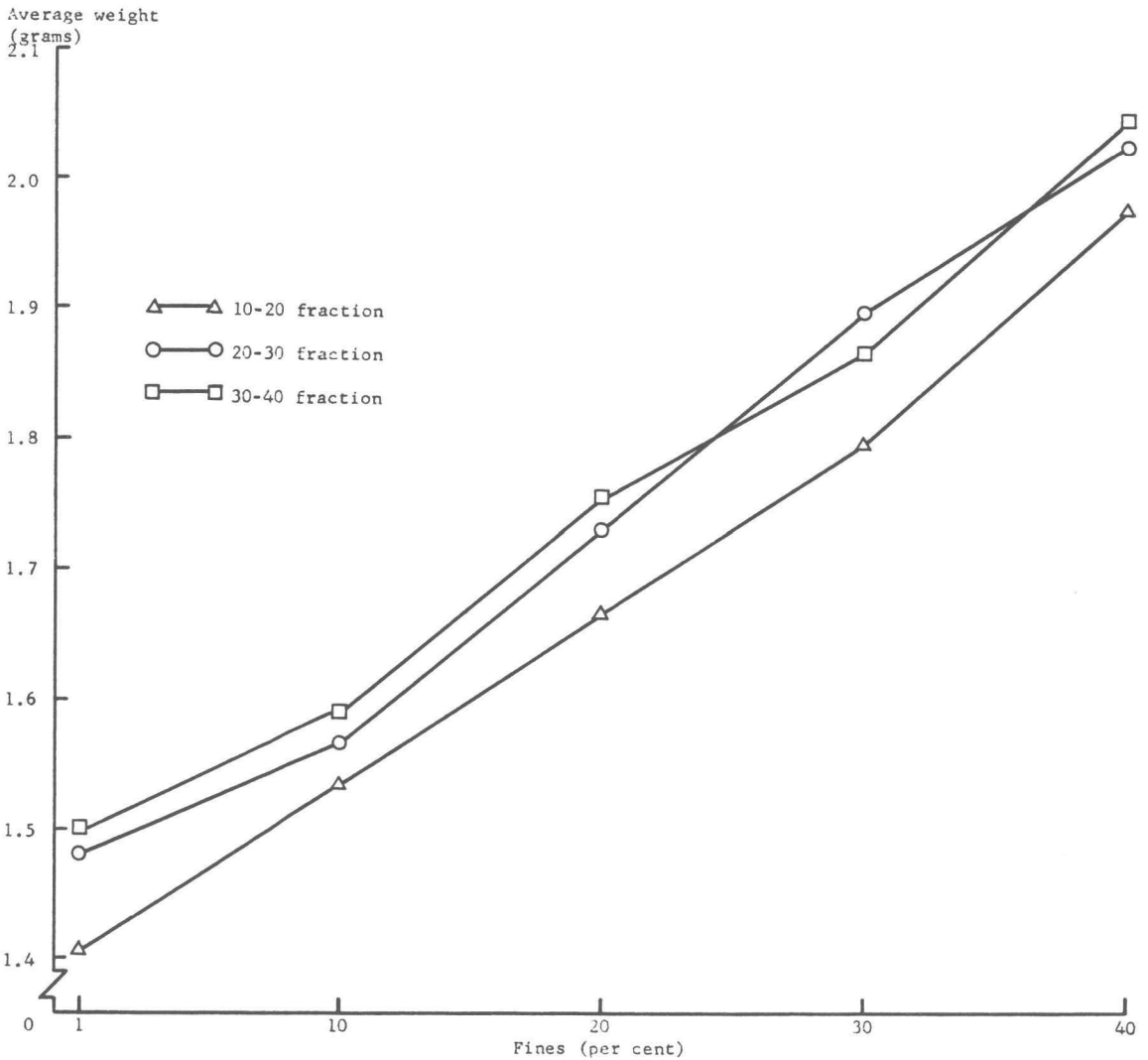

Figure VI. 5/8 Inch Punch, Sodium Bicarbonate Base.

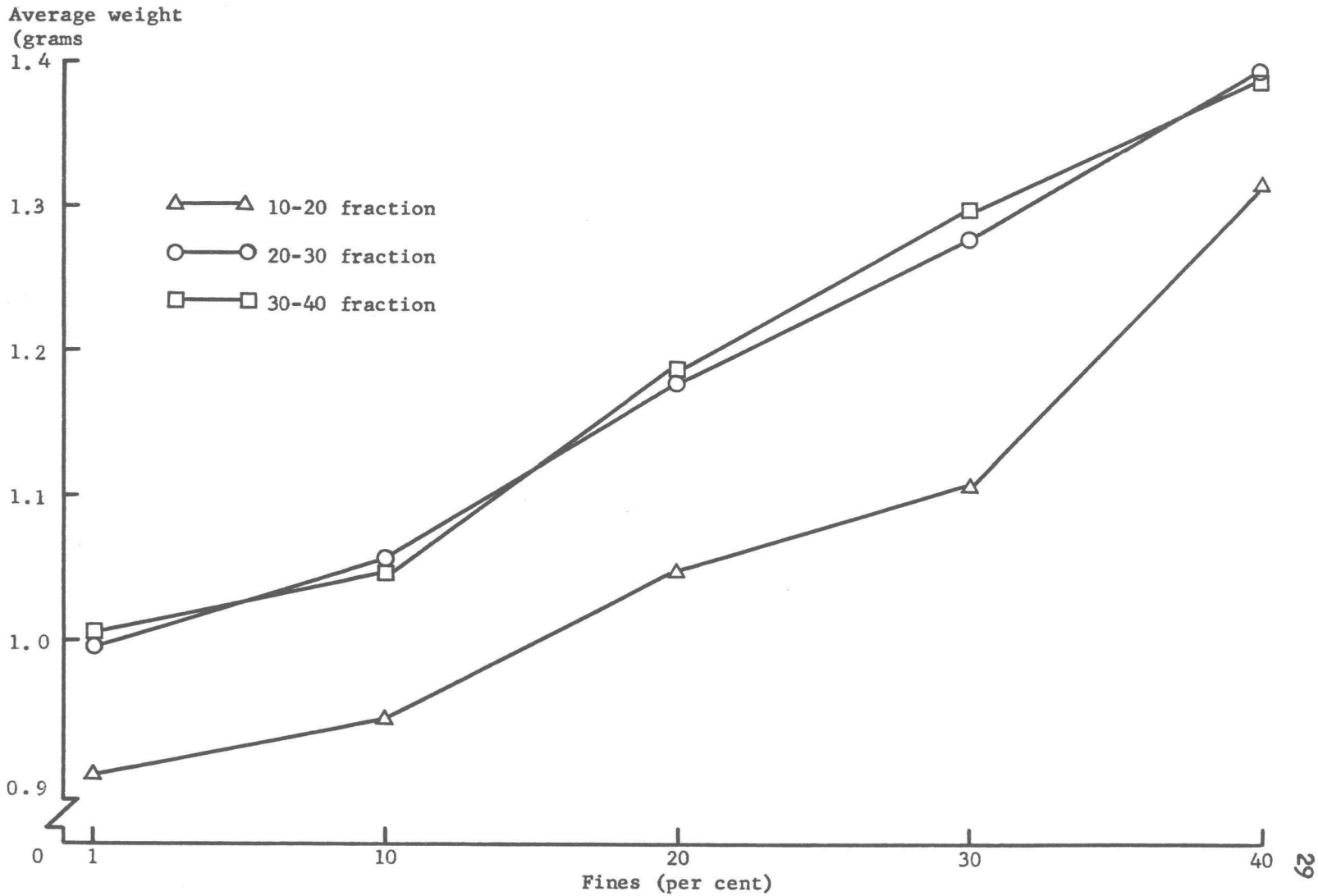

Figure VII. 4/8 Inch Punch, Sodium Bicarbonate Base.

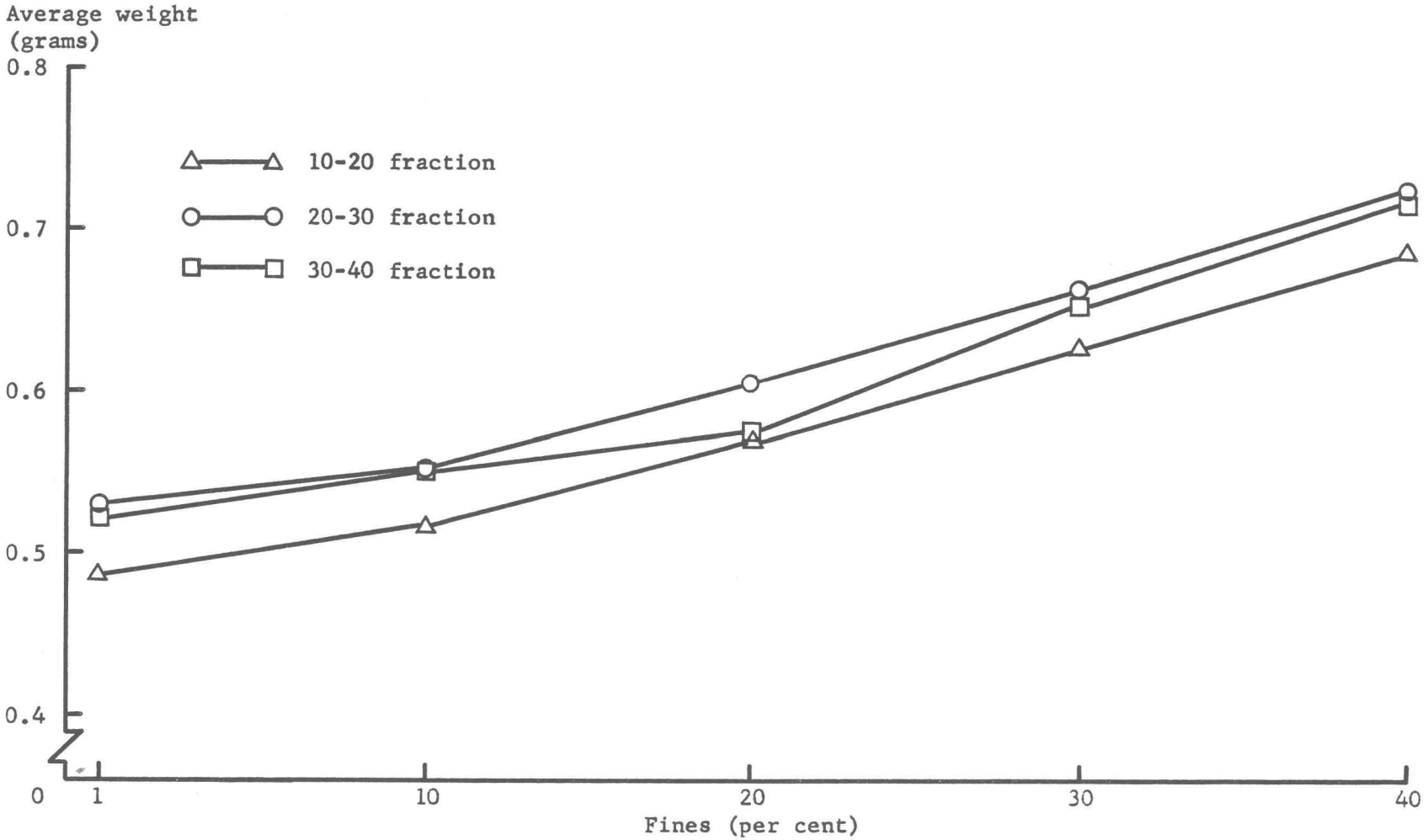

Figure VIII. 3/8 Inch Punch, Sodium Bicarbonate Base.

Volumetric feeding of the die (and therefore tablet weight) can be affected in two ways: (1) by increasing or decreasing the rate of flow of the material from the hopper to die and (2) by increasing or decreasing the void fraction.

The rate of flow of the lactose base from the hopper to die was hindered by the sticking of fines to the hopper. This stickiness may have been due to electrostatic charges, which increased as the percentage of fines increased, resulting in a leveling off of average weight at 30%. Sodium bicarbonate was relatively unaffected by this property. Another factor which may have influenced the flow rate of lactose compared to sodium bicarbonate was lower density, resulting in smaller flow rate when subjected to gravitational forces.

Increase or decrease in void fraction largely depends on the surface characteristics of the granules and granule size. If the granule size and surface characteristics of granules for the two bases were similar, then only different percentages of fines used with granules would give a comparative increase or decrease the void fraction.

Thus, increase in average weight up to 30% fines in lactose and 40% fines in sodium bicarbonate was largely

due to decreased void fraction and increased flow of material.

The decrease in average weight of 40% fines compositions of lactose base was due to the decreased flow of material. This might be due to electrostatic charges and low density of fines of lactose.

The sodium bicarbonate base containing 40% fines gave no difficulty in compression or flow through the hopper into the shoe. Even 60% fines compositions were compressed successfully. However, it was found that 30% fines composition and above gave capped tablets occasionally.

No capping was observed in lactose tablets, even at 40% fines composition, but sometimes it was difficult to compress the tablets of 40% fines compositions. This difficulty was due to the electrostatic property of lactose fines, resulting in adherence to papers, walls of hopper and faces of punches.

Thus, it could be said for sodium bicarbonate base that decrease in void fraction and increase in flow of material acted synergistically for increase in average weight of the compressed tablets. In lactose base, decrease in void fraction was more important up to 30% fines composition and then for 40% fines composition

decrease in flow of material was more responsible for decrease in average weight of the compressed tablets.

Visual analysis of Figures III to VIII shows that the average tablet weight increased as the granule size decreased from 10-20 mesh to 20-30 mesh (i.e. from 2000-840 microns to 840-590 microns). No such apparent difference was noted between 20-30 and 30-40 fractions (i.e. from 840-590 microns to 590-420 microns). This is true for all percentages of fines. One reason for this difference was the big difference in micron size of the granules. Another reason was the void fraction due to granule size as increase in granule size increases void fraction.

Based on the above observations, it was concluded that increase or decrease in average weight of compressed tablets was largely influenced by the percentage of fines and characteristics of fines used with granules and granule size.

Weight Variations

Each batch of fifty tablets was weighed in the order punched. The fifty weights were considered as observations for each sample and the sample variances were calculated and tabulated as shown in Table 2.

Table 2

Punch Size	Fines	Sample Variance (S^2)* in Mg.^{2} Sodium Bicarbonate Base 10-20 Fraction	20-30 Fraction	30-40 Fraction	Lactose Base 10-20 Fraction	20-30 Fraction	30-40 Fraction
3/8 in.	1%	84.56	8.04	3.39	81.89	11.10	2.87
	10%	178.22	82.37	33.40	160.73	10.86	7.71
	20%	535.47	213.60	426.50	93.40	42.20	17.06
	30%	2411.52	760.52	110.96	115.69	28.24	7.86
	40%	624.00	212.81	203.49	357.22	22.27	38.17
4/8 in.	1%	166.12	20.52	16.01	117.32	14.87	4.95
	10%	1247.54	150.66	860.82	341.56	33.23	30.83
	20%	3694.60	1162.94	955.36	346.81	207.95	30.90
	30%	3996.32	1033.99	950.45	413.89	41.93	58.63
	40%	18429.61	1622.34	741.35	509.47	82.51	476.87
5/8 in.	1%	375.81	43.26	30.27	294.99	24.10	9.39
	10%	326.94	2294.92	1166.08	487.34	186.28	381.76
	20%	4251.23	8184.16	763.47	557.01	212.65	86.00
	30%	20416.89	1178.22	2049.81	1212.08	168.90	26.53
	40%	1917.25	3675.48	968.03	6979.23	2460.99	3150.69

*Each sample consisted of fifty tablets and variance of that sample was calculated according to the following formula:

$$S^2 = \frac{\leq y^2 - \frac{(\leq y)^2}{n}}{n-1}$$

where y stands for observation, i.e. weight of tablet in milligrams and n stands for sample size, which is equal to fifty for all samples.

The chi square (x^2) test for testing the homogeneity of variances was carried out. Bartlett's method was used for this purpose (23, p. 194). The statistic used in testing the hypothesis that k population variances are equal was:

$$x^2 = \frac{2.3026\ (D-C)}{1 - \frac{A-B}{3(k-1)}} \quad \text{with } k-1 \text{ d.f.}$$

where D-C was the difference between the pooled d.f. log S^2 and sum of d.f. log S^2, A-B was the difference between sum of 1/d.f. and pooled 1/d.f., and k was number of samples.

This was a one tail test. If the k sample variances were equal, D = C and the chi square value was equal to zero. If the sample variances were very much different from one another, the chi square value would be large and the hypothesis that the population variances were equal may be rejected.

Each composition within fraction was considered as a sample and k samples were the number of compositions (five) in each fraction. Thus, for each fraction, the x^2 test was carried out separately. The hypothesis that the variances were equal was tested for all fractions and for all punch sizes. The x^2 values obtained are given in Table 3. The results were significant. Thus, it was concluded that different percentages of fines gave

Table 3

x^2 values (with 4 degrees of freedom) for each fraction having percentage of fines as k samples

Base	Punch	x^2 Values 10-20 Fraction	20-30 Fraction	30-40 Fraction	Critical Region	Conclusion
Lactose	3/8"	38.530	33.226	88.240	$x^2 > 13.276$ at 1% significance level with 4 d.f.	Hypothesis is rejected. Results are significant.
	4/8"	25.3190	96.164	225.474		
	5/8"	175.105	260.727	437.332		
Sodium bicarbonate	3/8"	149.847	187.717	215.12	$x^2 > 13.276$ at 1% significance level with 4 d.f.	Hypothesis is rejected. Results are significant.
	4/8"	208.409	193.648	142.472		
	5/8"	265.740	211.833	141.252		

Table 4

x^2 values (with 2 degrees of freedom) for each punch having granule fractions as k samples

Base	Punch	x^2 Values	Critical Region	Conclusion
Lactose	3/8"	93.166	$x^2 > 9.210$ at 1% significance level with 2 d.f.	Hypothesis is rejected. Results are significant.
	4/8"	79.384		
	5/8"	48.063		
Sodium bicarbonate	3/8"	2.448	$x^2 > 9.210$ at 1% significance level with 2 d.f.	Hypothesis is accepted. Results are not significant.
	4/8"	3.644		
	5/8"	1.515		

significantly different weight variations of compressed tablets. One per cent fines gave the least weight variation.

Then each fraction was considered as a sample and the three granules fractions (10-20, 20-30 and 30-40) were considered as k samples. In this case, all the compositions of fines in each fraction were considered as one sample of 250 observations. The x^2 test was performed for each punch size separately. The results are given in Table 4.

The results were found significant in lactose base and were found non-significant in sodium bicarbonate base. It was concluded that granule size had a significant effect on weight variation in lactose base, but not in sodium bicarbonate base. Least weight variation occurred in 30-40 fraction (neglecting variation of 40% fines).

From the results in Table 2, it was concluded that 1% fines composition with all granule sizes gave less weight variation than 10%, 20%, 30% or 40% fines composition in same fraction. Similar results were obtained in all fractions and all punch sizes and both bases.

It was also concluded that 1% fines composition of 30-40 fraction gave less weight variation than 20-30 fraction and 1% fines composition of 20-30 fraction gave less weight variation than 1% fines composition of 10-20 fraction, regardless of punch size.

Also 1% fines composition of all fractions in 3/8" punch size gave less weight variation than 4/8" punch size and 1% fine composition of all fractions of 4/8" punch size gave less weight variation than 5/8" punch size.

Results also indicated that as the percentage of fines increased the weight variation increased, reached a maximum, in some cases, at 30% fines composition and in some cases at 40% fines compositions.

The results in Table 2 also showed that in 3/8" punch size, 10% fines in 30-40 fraction gave less variation than 1% fines composition in 10-20 fraction of same punch size, in lactose as well as sodium bicarbonate base.

In lactose base, the results of weight variation were found significantly different among the fractions (Table 4). The 30-40 fraction in all punch sizes gave less weight variation than 10-20 fraction in all punch sizes. The results in Table 2 also showed that all percentages through 30% fines composition in 30-40 fraction gave less variation than 1% fines composition in 10-20 fraction in lactose base, regardless of punch size.

No such significant differences could be calculated in sodium bicarbonate base, indicating that it was not

the granule size but the use of fines of these two bases that had played roles in differentiating them.

Repose Angle

The repose angle was measured for all compositions of fines and fractions of granules. The results obtained are shown in Table 5 and Figure IX. It was found that repose angle decreased as granule size decreased, while increase in percentage of fines resulted in increase in repose angle.

A comparison of the data for repose angle with the data for weight variation (Table 1) showed similar trends, i.e. repose angle and weight variation generally decreased as granule size decreased, and repose angle and weight variation generally increased as the percentage of fines was increased. Therefore, it was concluded that granulations with small repose angles generally had small weight variations and granulations with large repose angles had large weight variations.

Table 5

REPOSE ANGLE*

Fines	Sodium Bicarbonate Base 10-20 Fraction	Sodium Bicarbonate Base 20-30 Fraction	Sodium Bicarbonate Base 30-40 Fraction	Lactose Base 10-20 Fraction	Lactose Base 20-30 Fraction	Lactose Base 30-40 Fraction
1%	42°-07'	42°-00	39°-56	41°-10'	38°-32'	40°-55'
10%	42°-28'	41°-02	39°-56	43°-15'	40°-48'	42°-55'
20%	42°-28'	42°-00	40°-18'	46°-45'	44°-02'	44°-41'
30%	43°-02'	42°-55	41°-18	48°-28'	47°-03'	45°-50'
40%	44°-22'	43°-29	43°-01'	48°-25'	49°-13'	48°-1'

*Average of three readings was used to compute repose angle by the following formula:

$$\phi = \tan^{-1} \frac{H}{\frac{1}{2} R}$$ where H is height of pile and R is diameter of circular dish

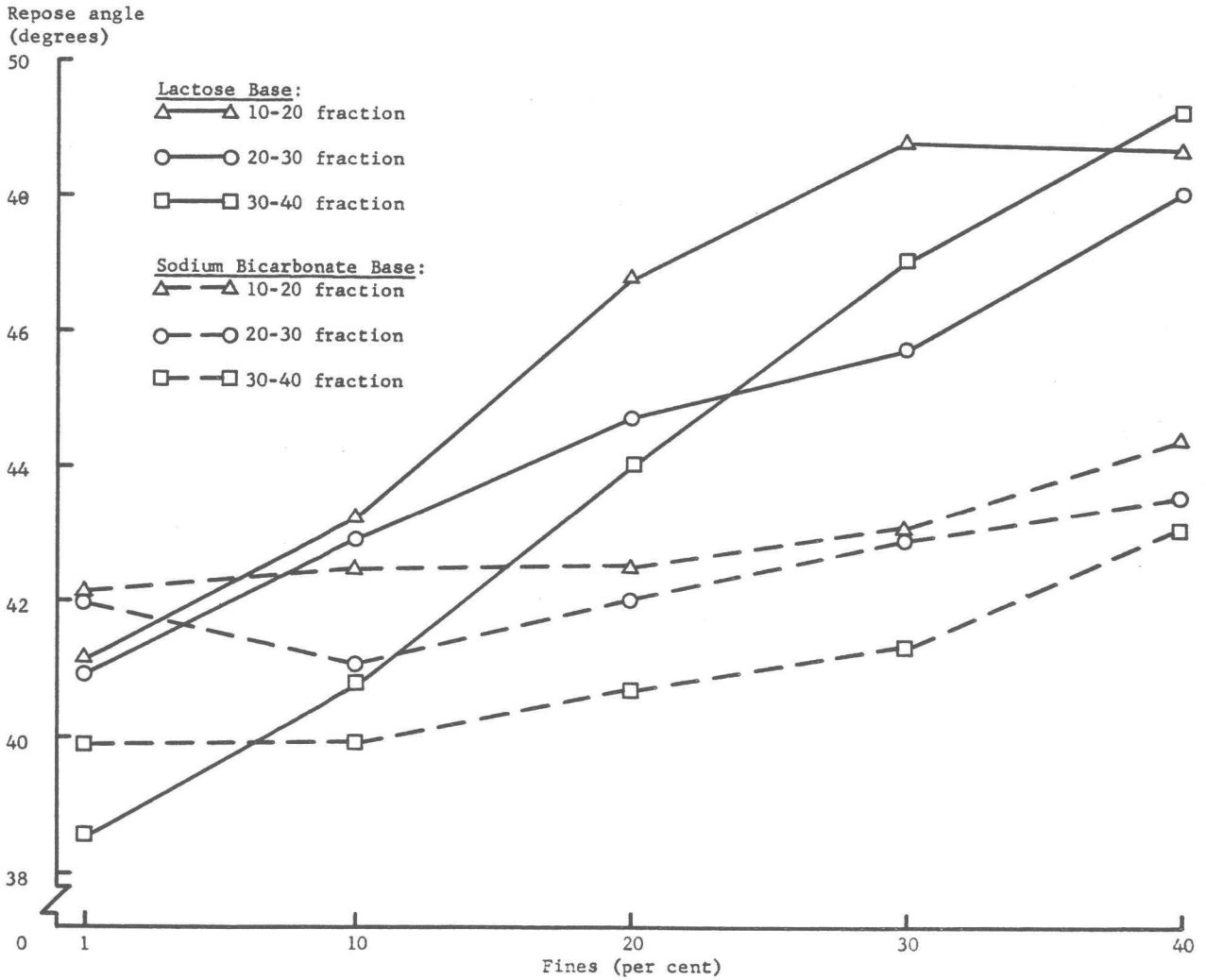

Figure IX.

Repose Angle Study

CONCLUSIONS

This study has shown that particle size, percentage of fines, surface characteristics of fines, and diameter of punch had significant effects on average weight and weight variation of compressed tablets of lactose and sodium bicarbonate.

1. The average weight of the compressed tablets increased as the granule size decreased from 10-20 to 20-30 to 30-40 fractions.

2. Average weight of compressed tablets of sodium bicarbonate base was found increasing as the percentage of fines increased. No peak for increase of average weight was found in sodium bicarbonate tablets.

3. For lactose base, average weight increased with increasing percentage of fines, reached a maximum at 30% fines, then leveled off and declined at 40% fines. This might be due to electrostatic charge of fines particles and lower density of powder.

4. In each fraction 1% fines gave least weight variation in comparison to 10%, 20%, 30% and 40% fines composition in same fraction regardless of punch size.

5. Granule size had significant effect on the weight variation for lactose base, but no significant results were obtained in sodium bicarbonate base.

6. For lactose least weight variation occurred with 30-40 fractions in all punch sizes (except 40% fines composition in 4/8 and 5/8 inch punches).

7. Weight variation of compressed tablets for all fractions and all percentage composition of fines increased numerically by increasing the punch size.

8. Fines had significant effect on weight variation in lactose as well as sodium bicarbonate base, regardless of punch size or granule size.

9. Repose angle generally decreased as granule size decreased.

10. Repose angle generally increased, as percentage of fines increased.

11. Repose angle and weight variation tended to change together, i.e. decrease in repose angle generally produced decrease in weight variations.

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