Section on Historical Pharmacy

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THE TABLET INDUSTRY—ITS EVOLUTION AND PRESENT STATUS.

Continued from Page 848, June issue.

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BASES.

These are cane sugar, milk sugar, ammonium chlorid, citric acid, sodium carbonate, and sodium chlorid. When an excipient is used to increase the weight of granulation or the size of a tablet or to facilitate the solubility of an active agent, it is termed a base. Milk sugar, for example, is commonly mixed with certain triturations in sufficient quantities to produce tablets of a given size. Sodium carbonate is a commonly used base in the manufacture of calomel triturates. Milk sugar is now universally employed for the manufacture of molded tablets, not solely for its action as a base, but because of its adhesiveness and the property it possesses of producing tablet of a porous nature, a property of great service in preparing tincture triturates. Mixtures of cane and milk sugars can often be employed to advantage. Ammonium chlorid, sodium chlorid, and citric acid not only add bulk, but facilitate the solubility of corrosive sublimate.

DISINTEGRATORS.

Starch and gelatine are used for this purpose. At one time a mixture of bicarbonate and citric or tartaric acid was employed. The most commonly used disintegrator at present, however, is starch. Its value lies in the property it possesses, when dry, of absorbing moisture and expanding, thus disintegrating the tablet. Such tablets when properly made should fall into powder almost immediately on immersion in water. The amount of starch used varies from 5 to 20 per cent, depending upon the nature of the ingredients. Even after starch was quite generally employed as a disintegrating agent, much criticism on the score of "insolubility" was still forthcoming. The first observation on "insolubility" recorded after Killgore's application for a patent will be found in Arnold's remarks.[46] This observation is referred to by Dieterich.[47] It should be noted, however, that there is a possibility that the knowledge of the properties of starch as a disintegrator had not at that time found its way into Germany. In 1899, J. E. Groff,[48] twelve years after Killgore's discovery, refers to the finding of undisintegrated quinine tablets in the excrement of patients. Joseph R. Wood,[49] in 1904, refers to the uncomplimentary term "brickbats," then applied to tablets, largely on the ground of their "insolubility." Such tablets are stated

[46] Corr.=Bl. f. Schweiz. Aerzte, 1890, *20:* 94.
[47] Pharm. Ztg., 1890, *35:* 400.
[48] Am. Drug., 1899, *34:* 196.
[49] Am. Drug., 1904, *44:* 105.

to be distinctly unsafe in typhoid fever. C. S. N. Hallberg,[50] in 1901, made an investigation of the time required to disintegrate tablets in artificial gastric and intestinal juices, with unfavorable results in a number of cases. Some believe that these unsatisfactory tablets were due to inexperience, lack of care, or too much adhesive, but after twenty years' experience some non-disintegrating tablets are still encountered, and the question is being studied. For example, Lowry[51] proposed the use of starch paste, instead of starch, to cause more ready disintegration. The discussion of the paper clearly shows that all of the difficulties in regard to disintegration have not yet been solved. In 1909, H. Dichgans[52] recorded some results where tablets had not disintegrated at the end of twenty-four hours, and Seel and Freiderich,[53] in 1911, reported on tablets which would not disintegrate in water.

Some are of the opinion that the kind of starch used is of the utmost importance; others think that cornstarch is as well adapted for the purpose as potato starch. Very few observations on this point have been published, the most comprehensive being those of Blaschnek,[54] in 1909. His investigation included potato, wheat, corn, rice, and marantha starches. The results clearly show a distinct advantage for marantha and potato starches. These two, according to his observations, seem to run nearly parallel. The point made by this investigator is that the starch must be nearly anhydrous if the best results are desired. The criticism on this point by some is, that if the starch is too dry the tablet has a tendency to disintegrate spontaneously, due to the moisture absorbed from the atmosphere. Blaschnek, however, claims that this criticism is not well founded, though his observation in this direction is not borne out by many other observers. Gelatine acts like starch, but the results are generally unsatisfactory, and it is, consequently, very little used at present. The mixture of a bicarbonate and an acid when immersed in water reacts and gives off carbon dioxide, thus mechanically breaking up the tablet. This method, as far as the writer knows, is not practiced now. Powdered agar-agar and Irish moss have been advocated as disintegrators, but so far they have not been used to any extent.

ABSORBENTS.

These include milk sugar, starch, magnesium carbonate, and powdered licorice root. The purpose of these agents is to absorb moisture or medicated liquids. For example, starch is frequently mixed with extracts, not only to facilitate drying, but also to act as a disintegrator when the material is in tablet form. Milk sugar constitutes the base of most of the hypodermic tablets, is an excellent absorbent, and produces porous tablets. Tablets are medicated homeopathically by simply adding the medication in liquid form and allowing the liquid to evaporate. Magnesium carbonate and powdered licorice root are not so well adapted for absorbing moisture as starch.

LUBRICANTS.

In the compression of drugs difficulty is generally experienced because the material adheres to the punches and dies. Agents used to minimize this diffi-

[50] Merck's Rept., 1901, *10:* 211, 245.
[51] Proc. Maryland Pharm. Asso., 1905, 26, 78; Abstr. Proc. Am. Pharm. Asso., 1906, *54:* 663.
[52] Pharm. Ztg., 1909, *54:* 850.
[53] Med. Klinik, 1911, *7:* 887, 927.
[54] Pharm. Post, 1909, *42:* 169; Abstr. in Pharm. Ztg., 1909, *54:* 178.

culty are called lubricants. A few granular compounds, like sodium bromid, potassium iodid, chloral hydrate and hexamethylamin, do not need lubrication. Dunton included lubricants and certain methods of application in his patent of 1875.[55] The principles announced then still hold to a large extent. A few new lubricants have been added. Those in use at present are talcum, liquid petrolatum (white oil), theobroma oil, boric acid, starch and stearic acid.

Purified talcum is the most common and abundantly used lubricant. It is used both alone and in conjunction with "white oil." The amount varies from one to five percent, based on the weight of the granulation, but the writer has found as much as 30 percent in the finished product. The addition is usually made to the granulation and is never employed in soluble tablets. Talcum is generally added for the purpose of overcoming "picking."

Liquid petrolatum ("white oil") of suitable quality is very generally used, both alone and in conjunction with talcum. It tends to prevent "sticking." About one drachm to each pound is ample. It should be used either not at all in the manufacture of soluble tablets, or as sparingly as possible, because it has a tendency to retard solution and produce milkiness. Dunton advocated the use of paraffin dissolved in a volatile solvent, over twenty-five years ago. The distribution of "white oil," cacao butter, and petrolatum by means of a volatile solvent is not productive of the best results. Experience has shown that the solution penetrates the granules and thus deposits a large part of the lubricant where it is of little or no service; furthermore, it is expensive and not without danger. Talcum and oil are frequently used together to prevent "picking" and "sticking." In analysis the presence of these lubricants should be kept in mind.

Boric acid is the only permissible lubricant for soluble tablets. When rapid solution is required the acid must be applied in an impalpable form. The amount used should never exceed 5 percent except in cases where it is one of the medicaments itself.

Theobroma oil (cacao butter), either alone or in solution, was brought forward in Dunton's patent in 1875, before mentioned. White and Rodwell are frequently given credit for its introduction into the tablet business, but this honor clearly belongs to Dunton.

Starch is not usually classed as a lubricant, although its value and usefulness for this purpose are well recognized.

Stearic acid has been advocated and used, but is not employed to any extent at present in making medicinal tablets. It is used to some extent in compressed confectionery.

FILLERS.

The term "filler" is applied to substances like terra alba, fuller's earth, kaolin, and other inorganic bodies serving the purpose of a base. They are usually considered inert and therefore harmless, but their introduction into the system must be looked upon as decidedly undesirable. Their use in confectionery is forbidden by law, and if they are undesirable for this purpose, why should they be introduced into the stomachs of the sick? There is no excuse for the practice.

Thus, it is clearly shown that the number of ingredients employed in the manufacture of tablets is legion, and all are agreed that it is absolutely necessary for

[55] U. S. Pat. 168240, dated Sept. 28, 1875.

every manufacturer to possess a great deal of knowledge as to their quality and purity, which can be gained only by proper chemical and pharmaceutical supervision.

CHEMICAL CONTROL.

The industry involves a multiplicity of details which must be carefully observed if this form of medication is to be prepared with the uniform composition usually claimed. It is necessary to know the character, purity and composition of the initial ingredients to be used. If this information is lacking it is practically impossible to even approximate in advance of analysis the amount of an active agent or agents in the finished product. The quality of medicinal chemicals available on the market is, on the whole, very satisfactory, but it would be unwise to take for granted that all of these drugs are as represented. Again, a chemical may deteriorate by being kept for an undue length of time or under improper conditions. There may be loss of water of crystallization on account of faulty containers or storage. Greater variation is liable to occur in tablets in which plant extractives are employed. These extractives are often made under the same roof as the tablets, and the possibility of taking chances under these conditions is sometimes greater than when they are purchased outside. On the contrary the quality of a home-made product is well known to the maker, and if it is carefully supervised the chances for deficiencies are diminished. The potent agents in plant products may vary to a great extent. Time is also believed to be an important factor, but this has not been definitely determined in many cases.

The use of different menstrua in extracting plant drugs causes great variation in the finished product. By using different solvents the yield may be doubled, in some cases, without correspondingly increased activity. In fact, the activity is frequently decreased in proportion to the increase of the extractive. The tablets in which such variable drugs are used cannot very well be uniform. The writer realizes that it is practically impossible to place every feature under chemical and pharmaceutical control, but in reality such a course is the only safe one.

SUPPLY AND STORE ROOM.

This is one of the most important units of the business, and should be in charge of a capable, well-trained and experienced man who should check up not only the quality and uniformity, but also the correct compounding of formulæ. In the case of habit-forming agents and expensive remedies he should be designated as the one responsible for their actual introduction. These drugs, particularly the former, may be surreptitiously spirited away, at least in part. Not a single ounce of material should leave this room without an order properly signed, stating the quantity and purpose for which it is to be used. Every formula should constitute an order by itself. It will serve as a useful record and tend to minimize errors. Laxness here has been found to lead to numerous difficulties, as will be shown later. The room should contain several compartments suited for the storage of the various drugs.

TRITURATING, POWDERING, AND MIXING.

Trituration is the process of reducing a substance to a fine or impalpable powder by grinding or rubbing. The substance to be triturated may be simple or mixed. If the several ingredients are triturated separately it will ultimately

be necessary to mix them, and it is believed that a powdering together of the active agents with a part at least of the excipient to be used often produces the best results. The mortar and pestle is the simplest trituratory, and the wedgewood variety is the most generally satisfactory. This trituratory was formerly used almost exclusively. Fairly satisfactory results can be obtained, provided sufficient time and energy are spent. It is, however, applicable only to small batches. Apparatus has been devised for mechanically operating the mortar and pestle. Perfect triturations by this method are, however, few. The small ball mill produces better and more satisfactory results in every way.

Ball and pebble mills. These mills consist of revolving hollow cylinders of iron, steel, porcelain, and; in some cases, the metallic mills are porcelain lined. The trituration is accomplished by balls, usually of the same material, but sometimes hard, flint pebbles are employed. At times the pebbles are eroded, so that the powdered material is correspondingly contaminated. The material, with the balls, is introduced into the cylinder, the cylinder closed and rotated until the drug is of the required degree of fineness. This form of apparatus is very satisfactory for triturating hygroscopic, irritating and poisonous drugs. Porcelain or porcelain-lined mills are most satisfactory, although somewhat more expensive. Iron mills can be used only for powdering material possessing a large amount of color. Porcelain-lined ball mills vary in capacity from a few ounces to fifty pounds. A pot mill is simply a modified form of the ball mill.

Chasers may be considered as modified forms of mortars and pestles. They consist of heavy rollers rotating on a flat surface, or in a trough. These rollers are either of stone or iron. The action is slow but positive and satisfactory. They are suitable for powdering or mixing almost anything. Even white goods can be powdered in them if care is exercised. There is always some elevation encircling the rollers, to retain the material within a certain area. The entire machinery is usually enclosed in a separate chamber to avoid contamination either from the outside or by the spread of powder through a room in the course of powdering. If it is desired to prepare a special, high-grade powder, the rollers are encircled with cylinders of various heights. The higher these cylinders the finer the powder. The principle is that the rollers, in revolving, not only powder the material but also mechanically raise the finer powder in the form of dust, which falls over the side of the cylinder where it collects and can be removed. This form of apparatus is excellently suited for the preparation of high-grade, uniformly fine, soft powders. The method is, however, one of the most expensive, and is employed only for special products.

High-speed mills. For powdering large quantities, high-speed mills are essential. Very satisfactory mills are at present available. The details of construction differ, but the principle of powdering is the same. It lies in the fact that the drug is brought into contact with the beaters at a high rate of speed, varying from 2,500 to 3,000 revolutions a minute. The powder is usually kept in contact with these beaters until it is sufficiently fine to be ejected. From this it can readily be seen that the powdering is done by impact. The material is struck with repeated powerful blows and thus shattered into powder. The fineness is controlled by the rate of speed and by mechanical devices. Various in-

gredients may be simultaneously powdered, and thus mixed, but, as a rule, the several ingredients are powdered separately.

Mass mixers. This form of apparatus is suitable for the mixing of material containing more or less moisture. For example, it is of service in mixing solid extracts with powder, and it may be possible, by this form of apparatus, to mix together a product containing considerable moisture with dry material, so that it may be granulated.

Powder mixers. Various forms are available. The essential features of all are a semi-cylindrical trough, covered with a box-shaped lid, and a metallic spiral for mixing. Sometimes a sieve is placed at the bottom of one end, to guard against the introduction of material too large to pass through the sieve introduced. When two powders of materials of different specific gravity are to be mixed, great care must be taken because of the tendency of the heavier and the lighter powder to separate into layers, thus resulting in mixtures of variable composition. If the milk sugar or other vehicle is included in the mixing operation, the mixture is ready for making molded tablets, but if intended for compression the powder requires granulation.

GRANULATION AND MIXING.

Granulation is essential to the manufacture of satisfactory compressed tablets. It consists in thoroughly mixing the powders with suitable liquids and forcing the slightly dampened mass through a sieve of proper size. The granules thus formed are dried, after which the lubricant, or additional lubricant, is added if necessary, and the granules are again sifted. Certain chemicals come in granular form, or they may be readily granulated by milling and sifting. Before granulation it is important that the powder be reduced to the greatest possible degree of fineness, and that there be perfect mixture. Blaschnek[56] claims that granulation is not necessary. With this view, however, very few agree. No method has yet been devised nor any machine constructed by means of which it is possible to satisfactorily compress fine powders without undue pressure, except in the form of molded tablets. By means of granulation a friable mass is produced, whereas, if powder be compressed, the resulting tablet is hard and difficult to disintegrate, except in the case of soluble chemicals. Even an excess of fine powder mixed with the granulation often interferes with the satisfactory compression of the tablet, and is frequently responsible for undue variation in both weight and composition.

AGENTS OF A VOLATILE OR UNSTABLE NATURE.

One of the most difficult tasks of the tablet-maker is to incorporate in tablet form medicinal agents of a volatile or unstable nature. Among these are ammonium carbonate, camphor, nitroglycerin, salol, the valerianates and essential oils. One method in vogue is to mix all of the ingredients, granulate, and dry the granulation at room temperature as rapidly as possible, thus avoiding loss. In some instances, the manufacturer mixes a larger amount of the volatile drug with the granulation than is actually called for, thus allowing for some dissipation, yet preparing a finished product containing the requisite quantity of the drug. Another method consists in dissolving the volatile drugs in alcohol or

[56] Pharm. Post, 1909, *42*: 170.

some other volatile solvent and mixing the resulting solution with the granulation just previous to compression. This, of course, also requires a certain length of time for the elimination of the solvent. In addition there is great difficulty in uniform distribution by this procedure. For example, it would be very difficult to uniformly distribute throughout the granulation camphor dissolved in alcohol. The probabilities are that a larger proportion of the camphor would be mixed with one part of the granulation than with another part. Even should the distribution in the granulation be fairly uniform, a large amount of volatilization might still occur before the material was compressed. Neither of these procedures gives satisfactory results until the finished article is chemically adjusted.

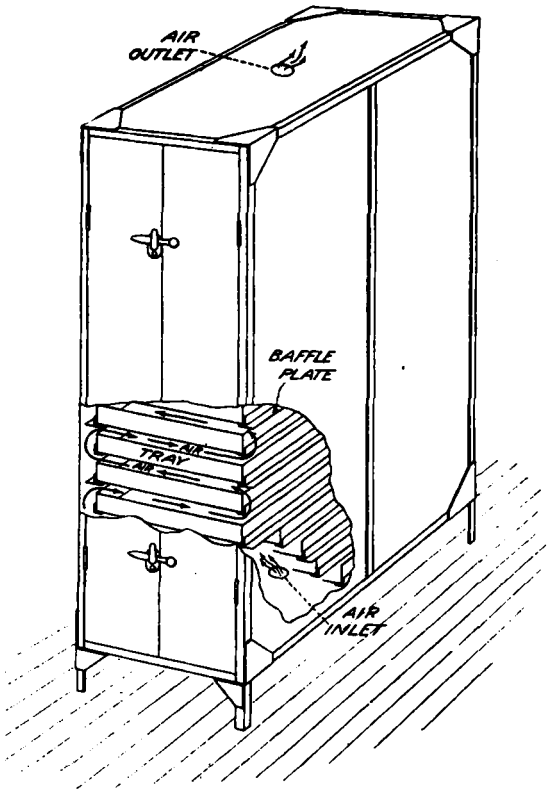

FIG. 19—Design of dryer made by Ralph R. Patch.

Another point to be considered in this connection is the fact that even after the tablets are compressed in suitable form and contain the proper amount of such active agents, there is a probability of loss by volatilization, dissociation or sublimation, resulting in a product differing in composition from the declaration appearing upon the label. In cases of this kind it is best to discontinue the manufacture of such tablets. Dealers are unable to guarantee these products for any length of time, even when the tablets are right at the outset. The claim is frequently made that this line of business is not only unsatisfactory but unprofitable, and the hope is often expressed that medical men might be induced to cease ordering goods of this character in tablet form. One manufacturer claims that even though the business is unprofitable, he manufactures such tablets on request because he desires to hold the patronage of medical men. It is argued that if one manufacturer will not fill prescriptions calling for these commodities, another manufacturer will do so, with the resulting loss of business in other lines. The medical profession should recognize these inherent difficulties and discontinue requests for such goods. If medical men persist in their requests the manufacturer himself will be compelled in self-defense to place upon the packages of such goods labels apprising the purchaser of the situation. They are unable to guarantee the goods to be strictly in accord with the prescription on account of the volatile nature of certain of the ingredients, even though the correct quantities were used at the outset.

DRYERS.

One of the cardinal principles in the successful manufacture of tablets is a thorough drying of the material. Dunton emphasized this feature many years ago. The dampened granules must be dried. Some drugs, both simple and

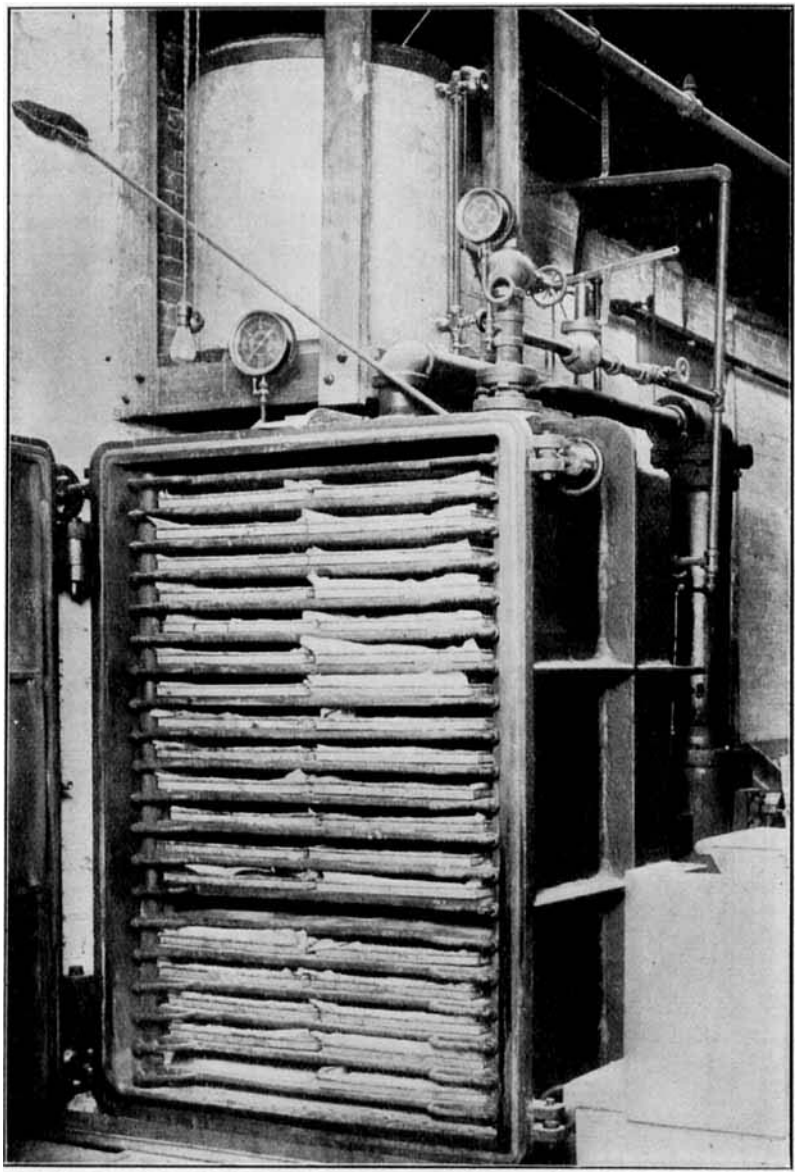

FIG. 20—Vacuum dryer.

mixed, may be sufficiently dried, under favorable conditions, in the open air, but the weather cannot be depended upon and a reliable drier must be used. It should be of the best possible construction and arranged to provide a continuous current of fresh air, at a uniform temperature, which should be under absolute control. This feature has apparently received very little attention in

the past, and is undoubtedly the cause of many shortcomings, particularly in the case of goods of a volatile or deteriorative nature. Such drugs should be dried at the lowest possible temperature. Dryers are usually heated by means of steam pipes coming from the boiler. Check valves are seldom introduced to control the heat. Observations made on some of the dryers show that the temperature varies from that of the room to 100° C., 108° C., 110° C., 115° C. and even to 120° C. The air of some of these rooms is absolutely stagnant. Ventilation and change of air are dependent almost entirely upon the opening and closing of doors, a bad practice for which there is no excuse. The dryer should be so constructed as to introduce the air at the bottom, pass it over the successive trays, and finally emit it at the top. In case the granules are dried on cloth trays, such an arrangement is unnecessary. During the past decade, drying in a vacuum has been greatly improved. In a number of factories, discarded vacuum dryers have been observed, and the management stated that they were not successful. On the other hand, other manufacturers are using vacuum dryers with great success, and hold that their use is of eminent service in the proper drying of granules for compression. The writer has seen in very successful operation one of these vacuum dryers which had displaced a battery of the old form of dryers. By means of this apparatus it is possible to conduct the drying at any ordinary temperature.

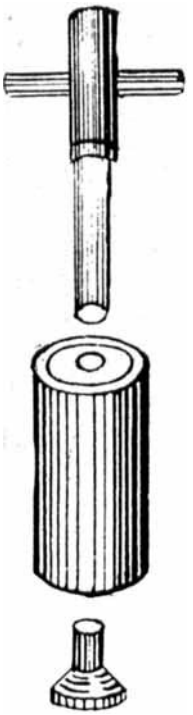

FIG. 21—Hand tablet compressor. (V. L. Kebler)

After a granulation is satisfactorily dried it is again sifted, and the lubricant, or additional lubricant, added. Flavoring agents, such as methyl salicylate, oil of peppermint, and oil of cinnamon, are also usually added at this stage, and the material is then ready for compression.

COMPRESSION OF TABLETS.

One of the prominent claims made for tablets is "uniform dosage and medication." No part of the entire process in the manufacture of tablets requires more care to produce accuracy than compression, and no feature has received greater attention. The machines now on the market are the outgrowth of many experiments to overcome the serious defects of the earlier machine. Devices of an uncertain character have given way to mechanisms of positive action. The simplest form of apparatus is the hand punch and die, useful in prescription work and in cases where only a limited number of tablets are required, but it is of little use at present. A number of hand presses are now serving the same purpose, but their usefulness also is very restricted. The automatic power machines are universally

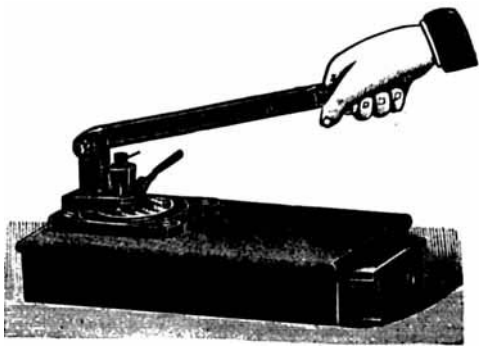

FIG. 22—Hand tablet press. (Ph. Ztg., 1902.)

employed where any number of tablets are required. Of the two types of power machines, the rotary and the vertical punch, both single and multiple, many are advocated. Some do not have a good word for the rotary; others cannot praise it too enthusiastically. The modern rotary will undoubtedly turn out the greatest number of tablets in a given time, although the output of the multiple vertical, of eighteen to twenty punches, is very large. An eighty punch vertical machine has

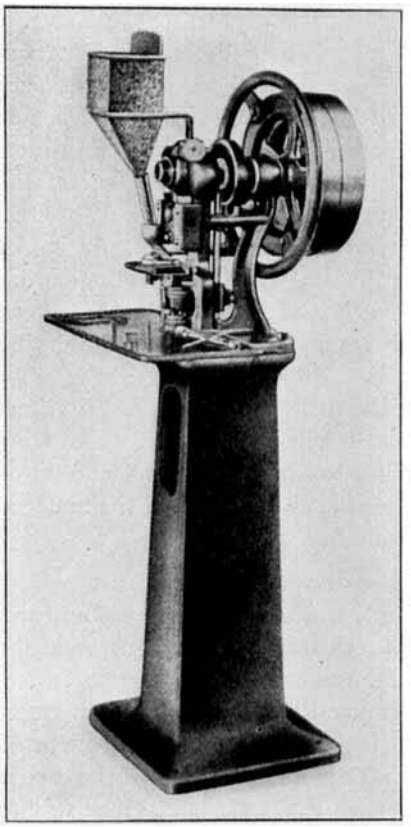

FIG. 23—Single punch vertical tablet machine (Stokes and Company).

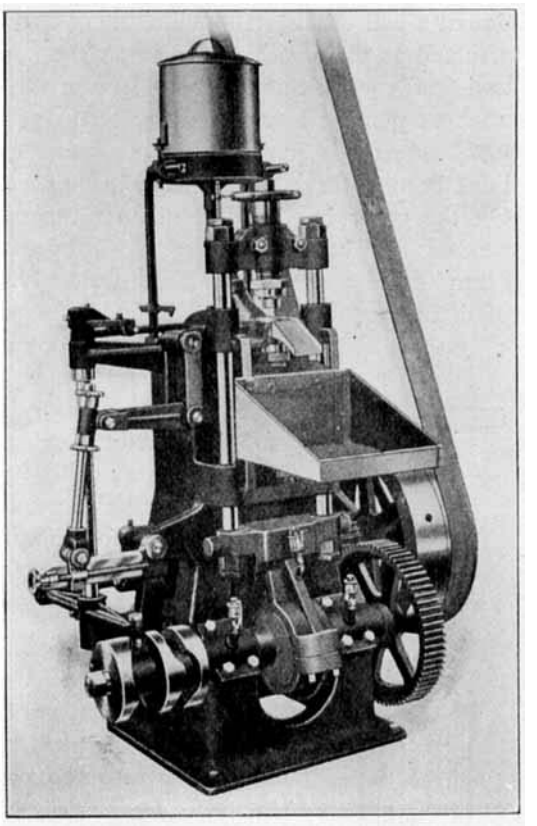

FIG. 24—Richards multiple punch vertical tablet machine.

recently been constructed. The first desideratum is a uniform tablet, and it is believed by many that the single punch machine has something in its favor in this direction, because there is less adjustment and alignment of punches and dies. The next essential is to prepare a tablet of such weight that the number actually produced from a given amount of granulation agrees very closely with the theoretical calculation. For example, if a formula calls for 500,000 tablets, the operator must determine the size necessary to produce approximately the theoretical number, including waste and loss. An experienced worker is able to do this very quickly.

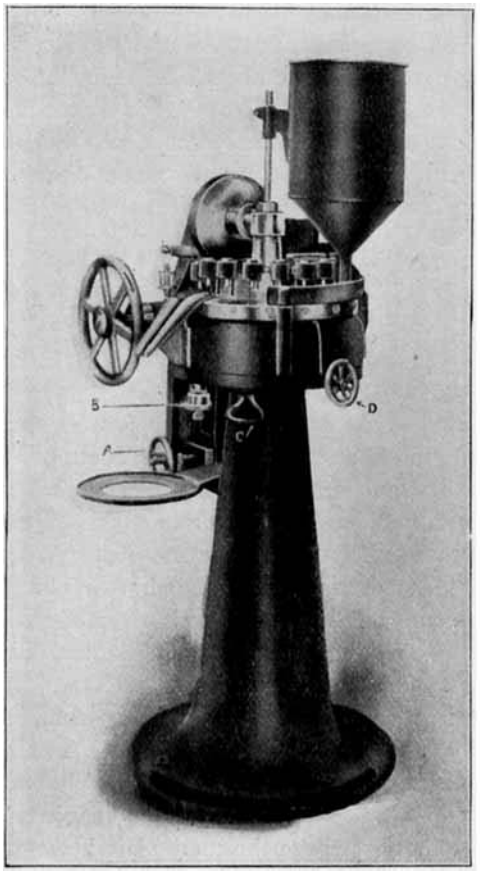

FIG. 25—No. 2 rotary tablet machine (Colton Company).

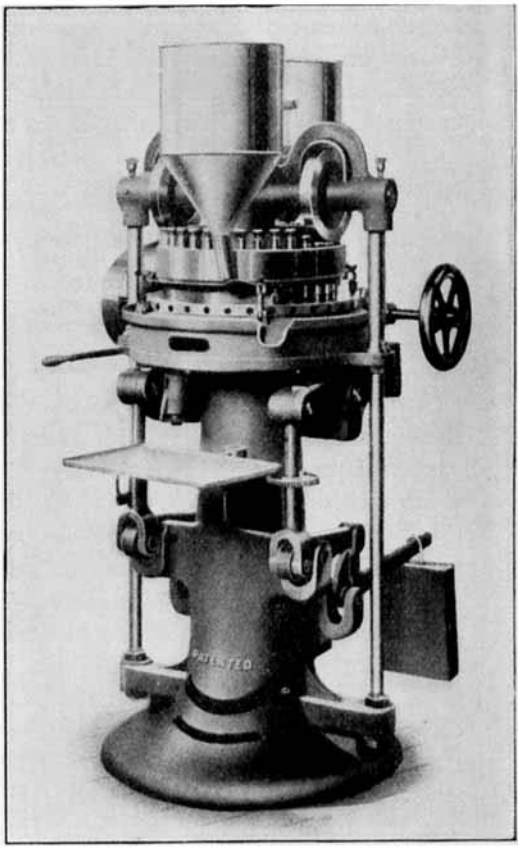

FIG. 26—Clark rotary tablet machine (Stokes Machine Company).

VARIATION IN WEIGHT OF MEDICINAL TABLETS.

A natural query at this point is, "How closely do the theoretical and practical yields agree?" On this operators are usually too enthusiastic. When the question, "How near, in practice, do you come to the calculated?" is put to them, the almost invariable reply is, "Two percent." Some admit that the variation may run as high as 3 percent, but not one has ever admitted that the variation might run as high as 5 percent, either above or below the number calculated. The writer has been shown formula after formula where the theoretical and actual yields are identical. Only a little thought will convince any one that such a feat is a rare exception. Data of this character must be taken with a grain of salt. It is very common not to take account

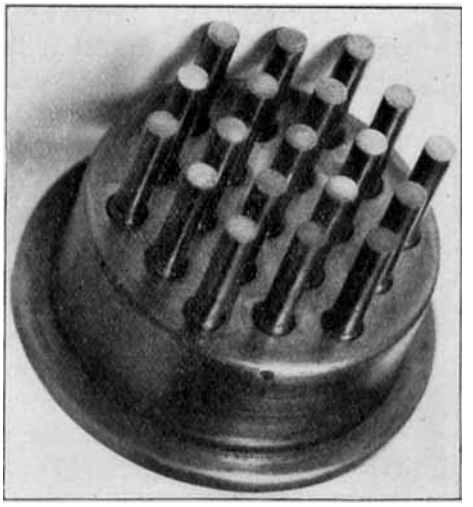

FIG. 27—Bottom punch (Fraser).

of waste and dust. To provide for these it is usually necessary to start with a larger amount of material than is required by calculation. After studying the entire question carefully and interviewing many manufacturers it is believed that a variation of 5 percent above and 5 percent below the theoretical is ample and can be readily complied with. Definite data on this point are scanty and difficult to secure. Working cards do not give them. The following are a few observations specially made by request, which represent regular runs:

Theoretical yield. *No. tablets.*	Actual yield. *No. tablets.*	Waste. *Percent.*	Gain or loss. *Percent.*
210,000	217,000	1.8	+5.10
420,000	432,000	1.3	+4.10
14,000	14,250	3.5	+5.3
29,166	28,594	1.0	—2.06

Some defects contributing to variable tablets are: (1) *Improper feeding,* due to the fact that the granulation is too fine, too coarse, too damp, or contains an excess of powder, and *excessive speed of machinery,* allowing insufficient time to uniformly fill the die or dies. (2) *Worn machinery, punches or dies.* Worn machinery may produce thick tablets one moment and thin ones the next. Worn punches and dies are the cause of "picking" (adhering to the punch), "sticking" (sticking to the die) and "whiskered" tablets, that is, tablets with elevated peripheral edges which are broken off in sifting, tending to leave ragged sides. (3) *Loosening of adjustments.* (4) *Careless weighing of the finished tablets.* The usual practice is to weigh ten tablets at intervals while a lot is being run. A common prescription balance is generally employed for the purpose. A wire gauge is also used to control the thickness of the tablets, and thus indirectly control their weight. At first it was believed that this practice was an inaccurate one, but an examination of tablets from factories where the method is in vogue showed them to be as uniform as where weighing only is practiced. It should be said, however, that where a wire gauge is used, weighing also is resorted to, but not as frequently as when weighing alone is relied upon to determine uniformity.

So far as it has been possible to determine, all tablet manufacturers and chemists believe that a total variation in weight per tablet of 10 percent, 5 percent above and 5 percent below an average, is very liberal for the larger tablets, and that if a greater variation were permitted it would encourage carelessness. That there will be some variation is conceded by all, and the variation will be greater for the smaller tablets. Manufacturers have not studied the question, at least not one of those interviewed was in a position to give any information on the point. A careful search of the literature shows that comparatively little work along this line has been done by analysts. Only one article containing data on variation in weight of individual tablets by analysts in the United States was found. Four contributions embodying information on the subject by chemists of foreign countries appear in print. The earliest was by E. J. Parry and P. A. Estcourt.[57] These investigators worked on tablets of single constituents. Their results, converted into the metric system and percentage, will be found in Table I.

[57] Pharm. J., 1894, *24:* 592-3.

TABLE I.—*Variation in the Weight of Medicinal Tablets.*

Name of tablet.	Weight of 1 tablet.			Maximum variation.		
	Maximum.	Minimum.	Average.	Above Average.	Below Average.	Total.
	Grams.	*Grams.*	*Grams.*	*Percent.*	*Percent.*	*Percent.*
Ammonium chlorid, 3 grains	0.2093	0.1989	0.2054	1.9	3.1	5.0
do	.2048	.1698	.1886	8.6	10.0	18.6
do	.2048	.1912	.1963	4.3	2.5	6.8
Ammonium chlorid, 5 grains	.3953	.3408	.3784	4.5	9.9	14.4
do	.3110	.2981	.3046	2.1	2.1	4.2
Antipyrin, 5 grains	.2948	.2611	.2780	6.0	6.1	12.1
do	.4044	.3875	.3933	2.8	1.5	4.3
do	.3434	.3110	.3311	3.7	6.0	9.7
do	.3363	.2948	.3168	6.1	6.9	13.0
Quinin sulphate, 3 grains	.2274	.2158	.2203	3.2	2.0	5.2
Quinin sulphate, 2 grains	.4212	.3629	.3927	7.3	7.6	14.9
Quinin sulphate, 5 grains	.3655	.3434	.3564	2.5	3.6	6.1
Quinin sulphate, 2 grains	.2916	.2592	.2754	5.9	5.9	11.8
Saccharin, ½ grain	.0842	.0629	.0739	13.9	14.9	28.8
do	.0628	.0467	.0564	11.3	17.2	28.5
do	.0537	.0499	.0518	3.6	3.6	7.2
do	.0842	.0661	.0784	7.4	15.7	23.1
do	.0667	.0609	.0641	4.1	4.9	9.0
Sulphonal, 5 grains	.318	.305	.311	2.2	2.0	4.2
do	.382	.324	.361	5.8	10.2	16.0
do	.3466	.3259	.3357	3.3	2.9	6.2
do	.4490	.4011	.4192	7.1	4.3	11.4

The five different kinds of tablets examined show that 50 percent exceed a 10 percent total variation, 40.9 percent a 12 percent variation, and 22.72 percent a 15 percent variation. It will undoubtedly be claimed, and with justice, that these observations were made nearly a score of years ago, and every one will admit that there have been some material improvements during that time. In order that comparison may be readily made, the observations recorded by O. Liebreich, W. A. Puckner and A. H. Clark, G. Frerichs, and Eugen Seel and Albert Friederich are unified, summarized, put on a percentage basis and given in Table 2.

TABLE II.—*Variations in the Weight of Medicinal Tablets.*

Name of tablet.	Weight of 1 tablet.			Maximum variation.		
	Maximum.	Minimum.	Average.	Above Average.	Below Average.	Total.
	Grams.	*Grams.*	*Grams.*	*Percent.*	*Percent.*	*Percent.*
Potassium iodid[1]	0.5116	0.4754	0.4901	4.4	3.0	7.4
Arsenious acid[1]	.0521	.0496	.0504	3.4	1.6	5.0
Copper sulphate[1]	.0560	.0490	.0516	8.5	5.0	13.5
Bismuth, opium and phenol[2]	.4053	.3400	.3833	5.7	11.3	17.0
do	.4837	.4569	.4752	1.8	3.8	5.6
do	.5747	.4993	.5328	7.9	6.3	14.2
do	.5800	.5245	.5518	5.1	4.9	10.0
do	.3951	.3742	.3852	2.6	2.8	5.4
do	.4213	.3544	.3937	7.0	10.0	17.0
do	.5221	.3690	.4457	17.1	17.2	34.3
do	.3428	.2432	.3232	6.1	23.2	29.3
do	.3646	.3417	.3525	3.4	3.1	6.5
do	.3670	.3487	.3609	1.7	3.3	5.0
Pyrenol[3]	.571	.432	.529	7.9	18.3	26.2
do[3]	.577	.483	.544	6.1	11.2	17.3
do[4]	.79	.46	.58	36.2	20.7	56.9
Pyrazolphenyldimethylsalicylate[4]	.55	.48	.53	3.8	9.4	13.2
do	.6	.6	.6	0.0	0.0	0.0
do	.55	.55	.55	0.0	0.0	0.0
Salipyrin[4]	1.18	1.05	1.12	5.4	6.2	11.6

[1]Liebreich, O., Ther. Monatshefte, 1898, *12*: 476.
[2]Puckner, W. A., and Clark, A. H., J. Am. Med. Asso., 1908, *51*: 330.
[3]Frerichs, G., Apoth. Ztg., 1908, *23*: 521, 522.
[4]Seel, Eugen and Friederich, Albert, Med. Klin., 1911, *7*: 888, 927, 928.

In 1898 when tabloids (a trade name for tablets) were introduced into the German army, O. Liebreich had the examinations recorded in Table 2 made. The results are fairly satisfactory. The examination of Puckner and Clark was mainly directed to the determination of the amount of phenol present in the tablets examined. The question of variation in weight was simply incidental. The results show that 54.54 percent exceed a 10 percent variation. The same degree of variation exists on a 12 percent basis, and 45.45 percent exceed a 15 percent variation; apparently not much of an improvement in fourteen years. Someone may say, "This phenol mixture is not suitable for making tablets, and if medical men write prescriptions for such compounds to be put up in compressed form, they ought to be prepared to get almost any kind of a variable article." Volatile substances like phenol should not be compressed into tablets. In arriving at a general conclusion as to the variability in the weight of tablets, volatile-bearing articles should not be included. They are in a class by themselves.

G. Frerichs inferred from the label "0.5 gram" on packages of "pyrenol" tablets that they contained nothing but 0.5 gram of pyrenol. In fact, there is little doubt, he believes, that every physician and apothecary labors under the same impression, particularly in view of the fact that the manufacturer made this claim. With these conditions obtaining he determined to make an examination of the tablets on the market, and incidentally weighed individually about thirty-two tablets. The results show a wide variation.

The observations made by Seel and Friederich on the variability of tablets were made in connection with a study of the causes of inferiority of some medicaments in tablet form. Their data show that tablets of acetylsalicylic acid and of pyrenol vary excessively, while tablets of two other chemicals are fairly satisfactory.

It is clearly evident that sufficient observations along this line have not been made to justify any general conclusions. The range studied must be greater in every direction. Medication in tablet form varies from a single ingredient to half a dozen or more. They contain both stable and unstable drugs, and volatile agents are also improperly put up in tablet form at times. In order to obtain extended data as to variability of weight, a large number of assorted tablets taken, first from the machines in operation, second, from trade packages as found in the market, and, third, from samples submitted by manufacturers, were weighed. The goods examined represent not only many manufacturers, both large and small, but also a liberal assortment. Twenty-five tablets were weighed in each case. The results obtained are given in Table 3.

TABLE III.—*Variations in the Weight of Medicinal Tablets.*[1]

Name of tablet.	Weight of 1 tablet.			Maximum variation.		
	Maximum.	Minimum.	Average.	Above Average.	Below Average.	Total.
1.—Compressed tablets made on single punch machine:	*Grams.*	*Grams.*	*Grams.*	*Percent.*	*Percent.*	*Percent.*
Absorbent dyspeptic	0.728	0.647	0.694	4.9	6.8	11.7
Acetanilid	1.452	1.392	1.427	1.8	1.8	3.6
Acetanilid and soda comp. with quinin	.447	.420	.434	3.0	3.2	6.2
Acetanilid and quinin	.385	.330	.358	7.5	7.8	15.3
Acetphenetidin	.2065	.1765	.1874	10.2	5.8	16.0
Aloin comp. with cascara	.0708	.0619	.0654	8.2	5.4	13.6
Ammonium chlorid, 5 grains	.334	.318	.3245	2.9	3.5	6.4
do	.345	.317	.337	2.4	6.0	8.4
Antiseptic pastilles	1.080	1.054	1.068	1.1	1.3	2.4
Antiseptic, Wilson's blue	1.074	1.009	1.047	2.6	3.6	6.2
Aphrodasiac	.305	.290	.298	2.3	2.7	5.0
Aspirin	.383	.343	.363	5.5	5.5	11.0
Calomel, .1 grain	.0724	.0682	.0670	8.0	5.7	13.7
Calomel, .25 grain	.1412	.1250	.1337	5.6	6.5	12.1
Calomel and rhubarb comp	.135	.103	.126	7.1	18.2	25.3
Cascara cathartic	.0728	.0583	.0662	10.0	11.9	21.9
Celery headache	.424	.404	.415	2.2	2.6	4.8
Charcoal	.777	.710	.759	2.4	6.4	8.8
Chalk mixture	.735	.705	.727	1.1	3.0	4.1
Chlorodyne	.295	.280	.286	3.2	2.1	5.3
Cold	.280	.230	.265	5.7	13.2	18.9
Corrosive sublimate	.999	.870	.903	10.6	3.6	14.2
do	1.001	.809	.965	3.7	16.2	19.9
Cough	.158	.148	.155	1.9	4.5	6.4
Cystitis No. 2	.498	.447	.460	8.3	2.8	11.1
Digitalin	.0178	.0157	.0166	7.2	5.4	12.6
Expectorant and anodyne	.1315	.1237	.1275	3.1	3.0	6.1
Grip	.542	.512	.526	3.0	2.6	5.6
Hexamethylenamin, 5 grains	.341	.310	.331	3.0	6.3	9.3
Laxative	1.571	1.466	1.514	3.7	3.2	6.9
Migraine	.2303	.2035	.2182	5.6	6.7	12.3
Migraine improved	.430	.375	.406	5.9	7.6	13.5
Migraine No. 3	.450	.340	.387	16.3	12.2	28.5
do	.418	.352	.386	8.3	8.8	17.1
do	.398	.383	.391	1.8	2.0	3.8
Milk	1.905	1.784	1.857	2.6	3.9	6.5
Pepsin	.1684	.1486	.1588	6.0	6.4	12.4
Phenolphthalein, 2 grains	.1691	.1568	.1630	3.7	3.8	7.5
Potassium chlorate	.3403	.3230	.3331	2.1	3.0	5.1
Quinin sulphate	.1943	.1636	.1776	9.4	7.9	17.3
Quinin sulphate, 2 grains	.1712	.1546	.1636	4.6	5.5	10.1
Rheumatic No. 4	.666	.614	.646	2.1	4.9	7.0
Salol, 5 grains	.408	.392	.399	2.3	1.7	4.0
Santonin compound	.0404	.0343	.0376	7.5	8.8	16.3
Seiler	.756	.732	.744	1.6	1.6	3.2
Sodium bicarb., 5 grains	.367	.335	.357	2.8	6.1	8.9
Sodium bromid, 5 grains	.341	.317	.330	3.3	3.9	7.2
Sodium salicylate, 5 grains	.471	.448	.458	2.8	2.2	5.0
Strych. sulph., 1/60 grain	.1020	.0938	.0980	4.1	4.3	8.4
Strych. sulph., 1/30 grain	.1232	.1088	.1173	5.0	7.2	12.2
Terpine hydrate comp	.580	.500	.561	3.4	10.9	14.3
Tonic	.394	.360	.376	4.7	4.3	9.0
Worm	2.225	2.145	2.194	1.4	2.2	3.6
Zinc phenolsulphonate	.348	.327	.340	2.3	3.8	6.1
2.—Compressed tablets made on multiple punch machine:						
Acetanilid, 4 grains	.329	.282	.305	7.9	7.5	15.4
Acetanilid, 5 grains	.402	.375	.3855	4.3	2.8	7.1
do	.414	.364	.385	7.5	5.4	12.9
Acetanilid	.270	.245	.257	5.1	4.7	9.8
Acetanilid and caffein comp	.352	.311	.334	5.4	6.9	12.3
do	.958	.836	.862	11.1	3.0	14.1
Alkalin and antiseptic	1.031	.968	.996	3.5	2.8	6.3
Aloin, belladonna, strych. and ipecac	.0292	.0246	.0270	8.1	8.9	17.0
Aloin, belladonna and strychnin	.0269	.0227	.0238	13.0	4.6	17.6
Ammonium chlorid	.687	.586	.642	7.0	8.7	15.7
Ammonium salicylate and acetanilid comp.	.501	.437	.470	6.6	7.0	13.6
Antiseptic No. 1, blue	1.016	.974	.998	1.8	2.4	4.2
Antiseptic No. 1, white	.986	.926	.957	3.0	3.2	6.2
Asafoetida, 5 grains	.571	.533	.551	3.6	3.3	6.9
Bismuth sub-gallate	.432	.355	.403	7.2	12.0	19.2
Bismuth subnitrate, 2 grains	.2343	.1883	.2022	15.8	6.8	22.6
Bronchial improved	1.680	1.553	1.626	3.3	4.5	7.8
Brown mixture and ammonium chlorid	1.327	1.190	1.294	2.5	8.0	10.5
Calomel, ½ grain	.0186	.0142	.0164	13.4	13.4	26.8

[1]Weighings made by E. H. Grant, assistant chemist.

TABLE III.—(*Continued.*)

Name of tablet.	Weight of 1 tablet.			Maximum variation.		
	Maximum.	Minimum.	Average.	Above Average.	Below Average.	Total.
	Grams.	*Grams.*	*Grams.*	*Percent.*	*Percent.*	*Percent.*
Calomel and sodium bicarb	.2091	.1932	.2016	3.7	4.2	7.9
Calomel and soda	.253	.231	.245	3.3	5.7	9.0
Cascara comp. No. 3	.1895	.1649	.1754	8.0	5.9	13.9
Charcoal, 10 grains	.960	.918	.936	2.6	1.9	4.5
Corrective	.0986	.0909	.0939	5.0	3.2	8.2
Corrosive sublimate, citric acid, No. 2, blue	.710	.517	.624	13.8	17.1	30.9
Creosote, chocolate coated	.389	.342	.367	6.0	6.8	12.8
Cystitis No. 2	.382	.368	.375	1.8	1.8	3.6
Dover powder, 2 grains	.148	.134	.142	4.2	5.7	9.9
Dover powder, 2.5 grains	.1006	.0921	.0963	4.5	4.3	8.8
Dover powder, 3 grains	.217	.200	.209	3.8	4.3	8.1
Hexamethylenamin	.376	.292	.328	14.6	10.9	25.5
do	.337	.309	.326	3.4	5.2	8.6
Iron and mercury comp	.0912	.0858	.0886	2.9	3.7	6.6
Lime water	.350	.300	.324	8.0	7.4	15.4
Mercury with chalk	.1450	.1346	.1400	3.6	3.8	7.4
Migraine No. 1	.288	.257	.274	5.1	6.2	11.3
Migraine No. 3, 5 grains	.404	.368	.390	3.6	5.6	9.2
do	.400	.373	.390	2.6	4.4	7.0
Phenolphthalein	.2090	.1862	.1992	4.9	6.5	11.4
Potassium iodid, 5 grains	.340	.305	.320	6.2	4.7	10.9
Quinin bisulph., 2 grains	.1792	.1649	.1722	4.1	4.2	8.3
Quinin sulph., 2 grains	.1674	.1387	.1535	9.0	9.7	18.7
Quinin sulph., 2 grains, chocolate coated	.308	.262	.283	8.8	7.4	16.2
Salol, 2.5 grains	.2245	.2090	.2159	4.0	3.2	7.2
Salol, 5 grains	.413	.348	.388	6.5	10.3	16.8
Sodium bicarb., 5 grains	.352	.309	.331	6.4	6.6	13.0
Sodium bicarb., 10 grains	.666	.624	.651	2.3	4.1	6.4
Sodium bromide, 5 grains	.333	.301	.319	4.4	5.6	10.0
Sodium bromide, 10 grains	.686	.621	.650	5.5	4.5	10.0
Sodium salicyl., 5 grains	.435	.393	.419	3.8	6.2	10.0
Stomachic sedative	.351	.311	.327	7.3	4.9	12.2
Strychnin sulphate	.0376	.0300	.0346	8.7	13.3	22.0
Triple bromids No. 1	.540	.453	.488	10.6	7.2	17.8
8.—Compressed tablets made on rotary machines:						
Acetanilid comp. No. 2	.408	.371	.390	4.6	4.9	9.5
Acetanilid and soda comp	.408	.355	.378	8.0	6.0	14.0
do	.418	.387	.403	3.7	4.0	7.7
Alkaline antiseptic, nasal	1.014	.951	.972	4.3	2.2	6.5
Antidyspeptic, No. 2	.222	.204	.214	3.7	4.7	8.4
Aspirin	.442	.315	.413	7.0	23.7	30.7
Bismuth subnitrate, 5 grains	.404	.358	.381	6.0	6.0	12.0
Blaud and strych. comp	.347	.317	.328	5.8	3.3	9.1
Bronchial	1.523	1.435	1.496	1.8	4.0	5.8
Calomel	.0267	.0241	.0252	5.9	4.4	10.3
Cascara sagrada ext., 5 grains	.337	.307	.318	6.0	3.5	9.5
do	.338	.297	.316	7.0	6.0	13.0
Charcoal	1.168	1.125	1.138	2.6	1.2	3.8
Damiana comp	.335	.281	.310	8.1	9.3	17.4
Digestive aromatic	.365	.331	.344	6.1	3.8	9.9
do	.497	.363	.423	17.5	14.2	31.7
Dyspepsia	1.228	1.137	1.165	5.4	2.4	7.8
Hexamethylenamin, 5 grains	.325	.305	.314	3.5	2.9	6.4
do	.361	.325	.338	6.8	3.8	10.6
Lactated pepsin, 5 grains	.330	.310	.321	2.8	3.4	6.2
Manganese dioxid, 2 grains	.1735	.1459	.1622	6.9	10.0	16.9
Migraine	.2725	.2503	.2579	5.7	2.9	8.6
Migraine No. 2	.264	.249	.255	3.5	2.3	5.8
Papain comp	.333	.308	.319	4.4	3.4	7.8
Phenacetin, 5 grains	.427	.384	.406	5.2	5.4	10.6
Phenacetin and caffein No. 2	.360	.343	.354	1.7	3.1	4.8
Phenolphthalein	.323	.291	.306	5.5	5.0	10.5
Quinine sulphate	.1780	.1550	.1633	9.0	5.1	14.1
Quinine sulphate, 2 grains	.1598	.1411	.1511	5.8	6.6	12.4
Salol, 5 grains	.427	.400	.413	3.4	3.1	6.5
Sedative, white, sugar coated	.581	.515	.548	5.0	6.0	12.0
Soda mint, white	.295	.272	.282	4.6	3.5	8.1
Soda mint	.350	.310	.334	4.8	7.2	12.0
Sod. salicylate, 5 grains	.504	.435	.484	4.1	10.1	14.2
do	.441	.375	.406	8.6	7.6	16.2
Strontium salicylate, 5 grains	.419	.382	.397	5.5	3.8	9.3
Sulphur and cream tartar	1.290	1.230	1.256	2.7	2.0	4.7
Terpine hydrate and heroin, No. 2	.1863	.1686	.1771	5.2	4.8	10.0
Throat, mentholated	.578	.493	.534	8.2	7.7	15.9

TABLE III.—(*Continued.*)

Name of tablet.	Weight of 1 tablet.			Maximum variation.		
	Maximum.	Minimum.	Average.	Above Average.	Below Average.	Total.
	Grams.	*Grams.*	*Grams.*	*Percent.*	*Percent.*	*Percent.*
4.—Triturates and hypodermics made on single punch machines:						
Bismuth and cerium oxalate	.168	.163	.165	1.8	1.2	3.0
Calomel, .1 grain	.0514	.0458	.0486	5.7	5.7	11.4
Calomel and dover powders	.107	.094	.101	5.9	6.9	12.8
Codein	.103	.097	.099	4.0	2.0	6.0
Codein sulph., .25 grain	.1019	.0970	.0994	2.5	2.4	4.9
Hepatic	.1016	.0859	.0925	9.8	7.1	16.9
Iron, arsenic and strych	.1404	.1310	.1365	2.9	4.0	6.9
Nux vomica ext., ½ grain	.0993	.0932	.0967	2.7	3.6	6.3
Rhubarb comp.,U.S.P. mass, .5 grain	.0852	.0783	.0815	4.5	3.9	8.4
Strych. sulph., 1/30 grain	.0956	.0895	.0924	3.4	3.1	6.5
Strych. sulph	.1028	.0953	.0990	3.8	3.7	7.5
5.—Compressed triturates and hypodermic tablets made on multiple punch machines:						
Acid, arsenious, 1/20 grain	.0200	.0170	.0185	8.1	8.1	16.2
Aloin, belladonna, strych. and ipecac	.0695	.0569	.0636	9.3	10.5	19.8
Aloin, belladonna, strych. and ipecac, No. 1	.0957	.0801	.0893	7.2	10.3	17.5
Calomel, .1 grain	.0882	.0715	.0750	17.6	4.7	22.3
do	.0722	.0648	.0673	7.3	3.7	11.0
Cascara sagrada, powd. ext	.0700	.0646	.0663	5.6	2.6	8.2
Morph. sulph., ¼ grain	.0892	.0780	.0828	7.7	5.8	13.5
do	.0707	.0640	.0671	5.4	4.6	10.0
Strych. sulph., 1/30 grain	.0525	.0450	.0492	6.7	8.5	15.2
6.—Triturates and hypodermic tablets made on rotary machine:						
Calomel and soda, No. 5	.2013	.1340	.1709	17.8	21.6	38.4
Cocaine hydrochlorid, ½ grain	.0127	.0098	.0116	9.5	15.5	25.0
Corrective, infant	.1881	.1390	.1535	22.6	9.4	32.0
Morphine sulphate, ¼ grain	.0177	.0151	.0164	8.0	8.0	16.0
Morphine sulphate	.0945	.0848	.0902	4.8	5.9	10.7
Rhinitis, ½ strength	.1478	.1286	.1366	8.2	5.8	14.0
Sodium salicylate, 1 grain	.1518	.1234	.1359	11.7	9.2	20.9
Strych. sulph, 1/60 grain	.0123	.0090	.0110	11.8	18.8	30.0
do	.1005	.0868	.0950	5.6	8.6	14.2
7.—Molded tablets:						
Aconitine, 1/200 grain	.0959	.0742	.0816	17.5	9.1	26.6
Aloin and podophyllin	.0896	.0753	.0839	6.8	10.3	17.1
Antiseptic, Bernay's	.1900	.1552	.1755	8.2	11.6	19.8
Arecoline hydrobromid, ½ grain	.1884	.1582	.1747	7.8	9.4	17.2
Arsenic iodid, 1/60 grain	.1155	.1002	.1093	5.7	8.3	14.0
Arsenious acid, ¼ grain	.1194	.1078	.1119	6.7	3.7	10.4
Barium chlorid, 5 grains	.341	.303	.326	4.6	7.0	11.6
Caffein, 1 grain	.1307	.1150	.1241	5.3	7.2	12.5
Calomel, 1/10 grain	.0740	.0657	.0703	5.2	6.5	11.7
Cardiac R. "V"	.378	.276	.332	13.9	16.9	30.8
Charcoal, 1 grain	.0749	.0695	.0716	4.6	2.9	7.5
Cocain hydrochlorid, ¼ grain	.0733	.0624	.0685	7.0	8.9	15.9
Cocain hydrochlorid, ½ grain	.0370	.0314	.0337	9.8	6.8	16.6
Cocain hydrochlorid, ¾ grain	.0299	.0270	.0290	3.1	6.9	10.0
Codein sulphate, 1 grain	.0792	.0716	.0763	3.8	6.1	9.9
Copper arsenite, 1/100 grain	.0751	.0679	.0718	4.6	5.4	10.0
Corrosive sublimate	.800	.665	.738	8.4	9.9	18.3
do	.216	.182	.200	8.0	9.0	17.0
do	.806	.722	.757	6.5	4.6	11.1
do	.186	.160	.172	8.1	7.0	15.1
do	.180	.152	.167	7.8	8.9	16.7
do	.211	.185	.198	6.6	6.6	13.2
do	1.123	1.000	1.082	3.8	7.6	11.4
do	1.050	.980	1.012	3.8	3.2	7.0
do	1.065	1.000	1.023	4.1	2.3	6.4
do	1.092	1.003	1.060	3.0	5.4	8.4
do	1.097	.996	1.059	3.6	5.9	9.5
do	.228	.200	.212	7.5	5.7	13.2
do	.928	.803	.897	3.4	10.4	13.8
do	.785	.602	.694	13.1	13.2	26.3
do	.183	.165	.178	2.8	7.3	10.1
Fever	.0597	.0531	.0558	7.0	4.8	11.8
Heart tonic, improved	.0762	.0654	.0725	5.1	9.8	14.9
Heroin, 1/20 grain	.0818	.0692	.0760	7.6	9.0	16.6
Heroin hydrochlorid, 1/24 grain	.0295	.0253	.0279	5.7	9.4	15.1
Ipecac pwd., ¼ grain	.0853	.0714	.0791	7.8	9.7	17.5
Mercuric iodid, yellow, 1/100 grain	.0773	.0688	.0725	6.6	5.1	11.7
Morphin and atropine	.0311	.0264	.0291	6.8	9.3	16.1
Morphin and atropine, No. 3	.1324	.0287	.0306	5.9	6.2	12.1
Morphin sulphate, ⅛ grain	.0313	.0275	.0296	5.7	7.0	12.7

TABLE III.—(*Continued.*)

Name of tablet.	Weight of 1 tablet.			Maximum variation.		
	Maximum.	Minimum.	Average.	Above Average.	Below Average.	Total.
	Grams.	*Grams.*	*Grams.*	*Percent.*	*Percent.*	*Percent.*
Morphin sulphate, ¼ grain	.0307	.0263	.0291	5.5	9.6	15.1
do	.0690	.0597	.0648	6.5	7.9	14.4
do	.0310	.0282	.0295	5.1	4.4	9.5
do	.0287	.0222	.0245	17.1	9.4	26.5
Nitroglycerin, 1/100 grain	.0334	.0298	.0313	6.7	4.8	11.5
do	.0340	.0283	.0308	10.4	8.1	18.5
Nux vomica, 1/1000 grain	.0775	.0711	.0747	3.7	4.8	8.5
Quinin & urea hydrochlorid, 3 grains	.379	.329	.357	6.2	7.8	14.0
Quinin arsenite, 1/1000 grain	.0733	.0674	.0711	3.1	5.2	8.3
Salol, 1 grain	.0842	.0680	.0747	12.7	9.0	21.7
Sanguinarin nitrate, 1/1000 grain	.0766	.0691	.0727	5.3	5.0	10.3
Strych. phosphate, 1/30 grain	.0795	.0651	.0742	7.1	12.2	19.3
Strych. sulph., 1/150 grain	.0793	.0714	.0763	3.9	6.4	10.3
Strychnin sulphate, 1/60 grain	.0325	.0297	.0311	4.5	4.5	9.0
do	.0351	.0313	.0328	7.0	4.6	11.6
Strychnin sulphate, 1/50 grain	.0331	.0297	.0310	6.8	4.2	11.0
Strychnin sulphate, 1 grain	.0853	.0667	.0768	11.1	13.1	24.2

The following summary shows the number of kinds of tablets examined, the kind of apparatus on which they were made, and the percentage of tablets having a total (above and below average) variation of more than 10, 12, 15 and 20 percent, respectively:

No. of kinds.	Variety.	Kind of apparatus.	Maximum variation of more than			
			10 percent.	12 percent.	15 percent.	20 percent.
			Percent.	*Percent.*	*Percent.*	*Percent.*
54	Compressed	Single punch	44	37	19	5.6
53	do	Multiple punch	51	43	28	9.4
38	do	Rotary	45	28	15	5.3
11	T. T.[1] & H. T.[2]	Single punch	27	18	9	0.0
9	do	Multiple punch	78	67	67	11.1
9	do	Rotary	100	89	67	55.6
57	Molded	Mold	79	56	37	10.5

The number of tablets exceeding a 10 percent variation is very high. Simple tablets do not seem to fare any better than compound ones. One type of machine yields about as good results as another for the regular compressed tablets. On the whole, the single punch appears to have a little the advantage. The rotary fares badly for the compressed tablet triturates and for the hypodermic tablets. The variation in the smaller tablets is greater than in the larger, as would naturally be expected.

Of the total number of tablets, 57 percent exceed a maximum total variation of 10 percent, 44 percent a maximum of 12 percent, 28 percent a maximum of 15 percent, and 9.1 percent a maximum of 20 percent. There is little excuse for tablets exceeding a total 20 percent limit. A 10 percent variation was generally believed to be ample, but the figures do not accord with this limitation. A 12 percent variation would not relieve the situation materially, while a 15 percent variation still leaves 28 percent exceeding this limit. The large manufacturers' goods vary in weight as much as those of the small ones. It is believed that a 15 percent variation, 7½ percent above and 7½ percent below the average weight,

[1] T. T.=Tablet triturates.
[2] H. T.=Hypodermic tablets.

is very liberal and possibly excessive; yet, with this latitude, an unduly large number are found wanting. It would seem that greater care must be exercised in the manufacture of this form of medication if its time-honored claim for uniformity of weight and dosage is to be maintained.

A review of the figures in the tables shows that in a large proportion of cases the variation is about as much above as below the average. If, therefore, a number of tablets are taken for analysis, as is commonly the case, it should be found that they average the proper amount of medicament. Consequently if a patient is given a number of tablets daily he will receive the intended per diem dose. This is not ideal or scientific medication. Before accepting the conclusion even on this basis, however, let us examine the premises. It is estimated that the average tablet contains the declared amount of medication. Fortunately, the correctness of this assumption can be established by a chemical analysis in a large number of cases.

CHEMICAL ANALYSIS.

Available information on the chemical analysis of tablets is meagre. Comparatively few analyses are recorded in the literature. All chemists conversant with this industry, however, hold that a 10 percent variation above or below the amount claimed to be present is ample for the vast majority of tablets and that only in exceptional cases should this variation reach 15 percent. Tablets containing volatile agents are not considered in this general conclusion.

The earliest chemical analysis of tablets with results recorded was made by Parry and Estcourt, in 1894. Four years later O. Liebreich had some analyses made of tablets. The results obtained by these workers are shown in Table 4.

TABLE IV.—*Results of the Analyses of Tablets by Parry and Estcourt.*

Product.	Amount declared.	Amount found.	Variation.
	Grains.	*Grains.*	*Percent.*
Ammonium chlorid[8]	3.	3.08	+2.7
do	3.	2.66	—11.3
do	3.	3.03	+1.0
do	5.	5.79	+16.8
do	5.	4.70	—6.
Antipyrin	5.	4.29	—14.2
do	5.	4.86	—2.8
do	5.	4.31	—13.8
do	5,	3.80	—24.
Quinin sulphate	3.	3.06	+2.
do	2.	2.02	+1.
do	5.	4.41	—11.8
do	2.	2.06	+3.
Saccharin	.5	.66	+32.
do	.5	.54	+8.
do	.5	.51	+2.
do	.5	.61	+22.
do	.5	.44	—12.
Sulphonal	5.	4.80	—4.
do	5.	4.95	—1.
do	5.	4.74	—5.2
do	5.	5.30	+6.

[8]Parry, E. J., and Estcourt, P. A., Pharm. J., 1894, *24*: 592-3.

TABLE V.—*Results of the Analyses of Tablets by Liebreich.*[4]

Product.	Amount declared.	Amount found.	Variation.
	Grams.	*Grams.*	*Percent.*
Potassium iodid	0.5	0.4864	—2.7
do	.5	.4789	—4.2
do	.5	.4843	—3.1
do	.5	.4751	—5.0
do	.5	.5070	+1.4
do	.5	.4789	—4.2
do	.5	.5113	+2.3
do	.5	.4934	—1.3
do	.5	.4966	—0.7
do	.5	.4924	—1.5
do	.5	.4836	—3.3
do	.5	.4859	—2.8
Arsenious acid	.005	.004976	—.5
do	.005	.004917	—1.6
do	.005	.004917	—1.6
do	.005	.004976	—0.5
do	.005	.005046	+0.9
do	.005	.005174	+3.5
Copper sulphate	.05	.0560	+12.
do	.05	.0504	+0.8
do	.05	.0490	—2.0
do	.05	.0521	+4.2
do	.05	.0501	+0.2
do	.05	.0519	+3.8
Morphin hydrochlorid	.01	.00998	—0.2
do	.01	.00988	—1.2
do	.01	.00975	—2.5
do	.01	.00961	—3.9
do	.01	.00948	—5.2
do	.003	.00303	+1.0
do	.003	.00290	—3.3
do	.003	.00291	—3.0
do	.003	.00290	—3.3
do	.003	.00289	—3.7
Strychnin nitrate	.001	.00093	—7.0
do	.001	.00099	—1.0
do	.001	.00095	—5.0
do	.001	.00094	—6.0
do	.001	.00095	—5.0
Mercuric chlorid	.01	.0099	—1.0
do	.01	.0099	—1.0
do	.01	.0098	—2.0
do	.01	.0099	—1.0
do	.01	.0097	—3.0
do	.01	.0102	+2.0
do	.01	.0099	—1.0
do	.01	.0100	0.0
do	.01	.0098	—2.0
do	.01	.00996	—0.4
do	.01	.0098	—2.0

[4]Liebreich, O., Ther. Monatshefte, 1898, *12*: 476-7.

A summary on a percentage basis of these results shows the following:

	Variation greater than 10 Percent	12 Percent	15 Percent	20 Percent
	Percent	*Percent*	*Percent*	*Percent*
Parry and Estcourt	41.	27.	4.5	4.5
Liebreich	0.0	0.0	0.0	0.0

These results clearly indicate that the tablets examined by Parry and Estcourt vary unduly in many respects. The fact that these observations were made nearly twenty years ago should be taken into consideration. The analytical data obtained by Liebreich show that the tablets examined by him were very satisfactory. In not a single instance was there a variation of as much as 10 percent from the amount declared. This is an excellent showing, particularly in view of the fact that the tablets were made and analyzed fifteen years ago. All will concede that improvements in machinery and in manipulation, as well as along other lines, have been made since then.

TABLE VI.—*Results of the Analyses of Tablets by Pouchet.*[6]

Product.	Amount declared.	Amount found.	Variation.
	Grams.	*Grams.*	*Percent.*
Aconitine	0.00025	0.00031	+24.
Quinine hydrobromid	.030	.0292	—2.7
Sodium and caffein salicylate:			
Caffein	.0164	.014	—14.6

Although the results recorded by this observer are meager, they are included in order to make the data on this subject as complete as possible.

In 1899 J. E. Groff published an article entitled, "Examination of Tablet Triturates as Found in the Markets."[1] This worker examined tablets of calomel, mercuric iodid, morphin, and corrosive sublimate, as well as samples, of 1/60 grain strychnin sulphate. The strychnin sulphate, mercuric iodid, and corrosive sublimate tablets were found to be as represented, as were also the 1/10, 1/8, 1/4 and 1/2 grain morphin sulphate tablets. In one case doubt is expressed as to 1/8 grain morphin sulphate tablets. All of the calomel tablets contained either an excess or an insufficient amount of the drug. A careful reading of this article gives the impression that the methods used in making the determination and the form in which the results are expressed are unsatisfactory and vague.

The next systematic work was done nearly ten years later, when G. Frerichs[2] examined a number of pyrenol tablets. The results recorded by him show that the tablets he examined were, to say the least, of a very unsatisfactory character. In every instance the amount of chemical found was much less than the amount

[6]Pouchet, Gabriel, Ann. de Pharm. Louvain, 1898; *4*: 375; Abstr. Apoth. Ztg., 1899; *14*: 179.
[1]Amer. Drug., 1899, *34*: 196.
[2]Frerichs, G., Apoth. Ztg., 1908, *23*: 521-2.

declared. Nearly 88 percent exceeded a maximum 20 percent variation, as the following results will clearly show:

TABLE VII.—*Results of the Analyses of Tablets by Frerichs.*[3]

Product.	Amount declared.	Amount found.	Variation.
	Grams.	*Grams.*	*Percent.*
Pyrenol	0.5	0.319	—36.2
do	.5	.348	—30.4
do	.5	.337	—32.6
do	.5	.296	—40.8
do	.5	.308	—38.4
do	.5	.440	—12.0
do	.5	.408	—18.4
do	.5	.294	—41.2
do	.5	.322	—35.6
do	.5	.385	—23.0
do	.5	.382	—23.6
do	.5	.363	—27.4
do	.5	.223	—55.4
do	.5	.385	—23.0
do	.5	.383	—23.4
do	.5	.376	—24.8
do	.5	.308	—38.4
do	.5	.296	—40.8
do	.5	.445	—11.0
do	.5	.294	—41.2
do	.5	.348	—30.4
do	.5	.342	—31.6
do	.5	.292	—41.6
do	.5	.367	—26.6
do	.5	.327	—34.6
do	.5	.326	—34.8
do	.5	.338	—32.4
do	.5	.375	—25.0
do	.5	.314	—37.2
do	.5	.445	—11.0
do	.5	.341	—31.8
do	.5	.379	—24.2

P. Bruère, in his book published in 1908,[4] gives some data dealing with the composition of tablets, but they are not of such a character as to serve any material purpose in the present investigations.

(To be continued)

OUR FLAG.

"Its stripes of red, eternal-dyed with heartstreams of all lands;
Its white, the snow-capped hills which round our free land bands;
Its blue, the ocean-waves that beat 'round Freedom's circled shore;
Its stars, the print of angel's feet, that shine forever more."

—*Riley.*

[3] Frerichs, G., Apoth. Ztg., 1908, *23:* 521-2.

[4] Sur l'utilisation en pharmacie et en chimie analytique des comprimés de substances médicamenteuses et chimiques, Paris, 1908.