The present invention relates to apparatus for punching miniature tablets, particularly tablets containing medicinal agents, of such small size that a considerable number of them can be filled into a capsule or other envelope so as to constitute the same a full dose of a medicinal agent or a predetermined fractional dose of such agent.

The general object of the present invention to provide apparatus which is capable of punching or compressing tablets from granular material which are of a uniform size no greater than \( \frac{3}{40} \) inch along any dimension, and preferably of a size within the range of \( \frac{3}{40} \) and \( \frac{3}{40} \) inch along their largest dimension, usually the diameter. Tablets of this range of sizes will be referred to herein as "miniature."

It will be understood that the term "tablets" referred to herein is intended to include also oval or more or less spherical pills in addition to the more or less flat or slightly convex tablets; and also other shapes, provided that their maximum dimension is no greater than \( \frac{3}{40} \) of an inch.

More specifically, it is an object of the invention to provide an improved apparatus for the manufacture of miniature tablets (which expression is intended to embrace tablets whose maximum dimension is no greater than \( \frac{3}{40} \) inch), such tablets being of uniform size and of uniform shape, and containing substantially the same quantity of medicinal agent, whereby uniform action of a counted number of the tablets contained in a capsule is insured.

It is known to provide unit dosage capsules containing a large number of pellets which may be coated with various substances, or with different thicknesses of a given substance, in order to insure that the pellets will become active at selected points of the alimentary tract, or will progressively or successively become active over an extended period of time, the medicinal agent being incorporated in the core of the pellet or in the coating, or in both. While this form of dosage unit and this mode of controlling the region in which the pellets are to release their medicinal agent and also the time during which the contents of a capsule are to provide the active medicinal within the alimentary tract, are attractive and promising in theory, they have not proved entirely satisfactory in practice.

The encapsulated pellets have been found to produce effects of varying and unpredictable degrees, in consequence of which the use of such pellet-containing capsules has been avoided by many physicians. Moreover, when the capsule contains pellets having coatings designed to cause release of the medicinal agent at different sections of the alimentary tract, or at different time intervals so as to produce a longer-lasting action, these desired effects are not always produced in the desired regions or at the desired times or in the desired degree, even in the case of capsules obtained from the same bottle.

Physicians have found that the encapsulated pellets are not reliable in their action and that, in particular, they cannot be certain as to the total dosage contained in a capsule having therein a large number of pellets as heretofore prepared. The pellet-containing capsule has been found to be especially unreliable where the range of a given medicinal per dosage unit is relatively small, for in such case the physician must be on guard to insure that neither an underdose nor an overdose of the medicinal is administered.

I have found that the non-uniform action of pellets containing many pellets therein is due to the fact that pellets are not and can not be manufactured on a commercial scale in uniform sizes or weights. The pellets contained in a capsule are in fact of quite different and random sizes, and where any number of the pellets are coated to more or less uniform diameters, the coatings will vary in thickness in inverse relation to the size of the particle cores. Thus, pellets which appear to be of more or less uniform size may actually consist of medicinal agent-containing cores of different sizes which are enveloped by coatings of greater thickness for the smaller particles, with the result that pellets intended to have their coatings dissolved away in the same region of the alimentary tract will, in fact, because of the longer time required to dissolve the thicker coatings, be active in different parts of the alimentary tract, or even become active at all where particles pass the region where their coatings are dissolved. In consequence, capsules containing the same volume of pellets can actually contain different amounts of the active medicinal; and in addition, the area or areas of activity of the particles in the alimentary tract will not always be the same for the individual members of any group of capsules. It is also to be noted that in the case of measured volumes of pellets, whether coated or not, the volume of the voids, and hence the weight of medicinal agent per capsule, will vary with the size of the pellets.

Nor can uniformity of dosage with small pellets be insured by weighing the pellets, for considerable difficulty would be encountered in operation on a commercial scale in accurately weighing small amounts. Moreover, if the pellets are coated, and in view of the fact that uniform coatings can not be provided on irregular particles of different sizes, the same weight of coated pellets will not represent the same amounts of medicinal agent. This would be true even if the coatings were uniform; for the ratio of the weight of the coatings to that of the medicinal agent will vary with the number of pellets per unit weight. Moreover, the particles as heretofore manufactured for filling into capsules are unavoidably of very small sizes, and in the spray-coating or pan-coating of such particles, it is impossible to insure that all particles (regardless of their size and shape) will receive exactly the same thickness of coating, the irregularity in the enteric or other coating being favored by the irregularity in the sizes and shapes of the particles. It is accordingly impossible with the known pellets to insure a predetermined dose by encapsulating a counted number of pellets even if this were commercially feasible.

It is accordingly a further object of the invention to provide apparatus for punching and compressing tablets of such small size that a counted large number can be contained in a capsule to constitute a full or fractional dose of a medicament, whereby a uniform dose per capsule is obtained.

Additional objects and advantages of the invention will become apparent from the following detailed description thereof taken in connection with the accompanying drawings illustrating a preferred embodiment of the invention.

A common type of tabulating machine consists of three principal parts, namely, a bottom plunger head to which is secured one or more bottom plunger; an upper plunger head to which is secured an upper set of upper plunger; and a plate fixedly supported between the two sets of plungers. The die plate is provided with die cavities or bores within which the plungers move; such bores being provided in the die plate itself, or in individual dies which are secured within tapped openings or holes in the die plate.
During the punching operation, the lower plungers are disposed with their upper portions within the die cavities, while the upper plungers are forced into the cavities from above to compress a column of granulated material disposed within the die cavities and between the upper and lower plungers. The granulated material is rather loose in nature, and is compressed to approximately one-half or less than half of the height of the column of such material in the die cavities. In view of the comparatively large thickness of the known punched tablets, and in view of the fact that allowance had to be made for granular masses of comparatively low densities whose compressibility in consequence was greater than average, the die cavities for the known types of tablets were given a considerable height. The upper plungers had, of course, to be long enough to effect the necessary compression of the columns of granular material in the die cavities and to allow for clearance between the upper plunger and the die plate. As individual tablets as heretofore manufactured have been of a diameter of about \( \frac{1}{4} \) to \( \frac{1}{2} \) inch and even larger, their thickness was of corresponding magnitude and the die cavities were of corresponding relative height.

As described in my copending application entitled "Multiple Tablet Dosage Form," Serial No. 90,962, filed simultaneously herewith, I have found that the disadvantages and uncertainties associated with the use of the known dosage form consisting of a capsule containing a large number of pellets of many random sizes from about \( \frac{1}{2} \) inch to \( \frac{1}{3} \) inch in diameter and even smaller, and particularly the lack of constancy of medicinal agent content and of locale of release of such agent in the alimentary tract, can be overcome and a unit dosage form of constant and predetermined medicament content and behavior in the alimentary tract obtained; while retaining the flexibility of control over the time of release of the medicinal and its place and period of activity, by filling the capsule with compressed tablets of uniform size or with two or more groups of tablet wherein the tablets of each group are of uniform size.

This necessitated the use of miniature tablets of a size not heretofore encountered in commercial operations, namely, compressed tablets of a diameter of \( \frac{1}{4} \) inch or less, the lower practical limit being about \( \frac{1}{32} \) inch and, a preferred diameter size being about \( \frac{1}{36} \) inch.

However, to my knowledge, attempts to produce, on miniature th衾less or compressed tablets of uniform size and of a diameter of about \( \frac{1}{4} \) inch with known commercial tabletting apparatus wherein the diameters of the punches and cavities were appropriately reduced, proved unsuccessful, the tablets so obtained being non-uniform in size and variable in density, and being frequently in fragmented condition. Further, the punches and dies were found to have a very short life, making the entire process uneconomical.

This failure of known machines to produce uniform tablets of a diameter less than \( \frac{1}{36} \) inch was most surprising in the light of the fact that the machines could be made to produce without difficulty medicinal tablets of larger dimensions which differed among themselves in diameter much more greatly than do the miniature tablets of my invention from the smallest type of medicinal tablet that has heretofore been successfully produced commercially. Thus, as is known, tabletting machines can produce and from such tablets producing \( \frac{1}{2} \) inch tablets simply by replacement of the punches and dies with parts of correspondingly reduced diameters.

I have found that a controlling factor in the failure of known machines to produce successfully miniature tablets with uniform diameters and plunger reduced in diameter to \( \frac{1}{36} \) inch or less, is that new phenomena make their appearance which determine the operability and durability of the machine.

I have discovered that at the reduced diameters, the punches projecting from the plungers or guides become subject to vibration and whiplash, and also to elastic distortion, which prevent the punching of tablets of uniform size and tend to cause fracture of the pressed tablets and ultimately lead to damage to the punch, punch guides, and die cavity portions.

It appears that with die cavity and punch diameters of \( \frac{1}{36} \) inch or less, the necessary clearance between the punches and the walls of the cavities becomes much more significant in relation to these small diameters than it does at the higher diameters, so far as the rigidity of the punches is concerned. Also, as the reduced diameters, the flexibility of the punches increases considerably, and this factor, combined with the proportionately larger clearances, operates to create whiplash and vibrations which act destructively on the tablets.

In accordance with the present invention, such vibration and whiplash are prevented by limiting the length of each punch to a more or less fixed maximum size in relation to the diameter of the die cavity. I have found that when the diameter of the cavity in the die is of the order of about \( \frac{1}{36} \) inch to \( \frac{1}{36} \) inch, the maximum total length of each pair of punches should be no more than about five times the diameter of the die cavity. Thus, in the case of a die having a cavity which is \( \frac{1}{36} \) inch in diameter, the length of the lower punch may be \( \frac{1}{4} \) inch and of the upper punch \( \frac{1}{36} \) inch, the thickness of the tablet being about \( \frac{1}{36} \) inch, the length of travel of the upper punch within the die cavity being likewise about \( \frac{1}{36} \) inch. By the use of short stubby punches of these dimensions, vibration and whiplash are eliminated, even when the press is operated at high frequency.

Referring now more particularly to the accompanying drawing, there is illustrated on an enlarged scale a portion of a known type of tabletting machine in which the present invention is incorporated. Only so much of the tabletting machine is illustrated as is necessary for an understanding of the present invention.

There is shown at 10 a die plate of annular form which is bored to receive a circular series of dies 11a, each of which is provided with four cavities, as shown at 11. Above the die plate 10 is arranged the punching mechanism which is shown generally at 12 and consists of a circular series of punches or guides 13, one of which is arranged directly above each of the dies 11a. The plungers 13 reciprocate vertically in a turret 14. Only the bottom portion of one of the plungers 13 is shown in the drawing and from the bottom face of the punch 15, one disposed directly above each of the die cavities 11. The plungers 13 are guided within the turret 14 and prevented from angular or rotational movement within the turret by means of guide grooves 12a.

Beneath the die plate 10 is arranged a series of bottom plungers, shown generally at 16, which are likewise guided within an annular turret or equivalent structure (not shown). Each bottom plunger 17 is provided with four punches 19 in registry with the die cavities 11 and upper punches 15. It will be understood that the turret 14 with its plungers 13, the die plate 10 and the turret or other mechanism supporting the bottom plungers 17 rotate in unison about a common vertical axis.

In the operation of the machine, the bottom punches 19 normally extend into the cavities 11 for part of their length, the distance being governed by the thickness of the tablet to be delivered by the machine. In the course of rotation of the turret containing a hopper (not shown) containing the granular material which is introduced into the cavities 11. As the assembly continues to rotate, the upper portions of the plungers 13 are depressed, as by means of a cam plate, and the punches 15 are forced into the cavities 11, thereby compressing the granular material into the molded tablet. As the turrets and the die plate 10 continue to rotate, the bottom punches are raised until the upper faces of the punches 19 extend slightly above the surface of the plate 10 to eject the molded tablets. The tablets are swept off the die plate at an
appropriate point in the travel of the plate and collected in a suitable container. In accordance with the present invention, the distances which the punches 15 and 19 project beyond the opposing faces of the upper and lower plungers are limited by the diameter (or maximum transverse dimension) of such parts. I have found that in order to insure stable and safe operation of the machine, the total length of each pair of upper and lower punches should not exceed five times their diameter (or maximum transverse dimension), the lower limit of such total length being about three times the diameter. The length of the lower punches 19 must be equal to the length of the cavities 11 plus the short distance which the punches 19 must project above the top surface of the plate 10 to effect ejection of the molded tablets, plus the clearance between the upper face of the plungers 17 and the bottom face of the plate 10 at the end of the upward stroke of the bottom plungers. The length of the upper plungers 15, on the other hand, should be determined principally by the degree to which the granular material in the cavities 11 is to be compressed, due allowance being made for the clearance between the bottom face of the plungers 13 and the upper face of the plate 10 at the end of the stroke of the upper plungers. In short, any substantial additional length of the plungers 15 over that required to effect the necessary compression in the cavities 11 (the bottom punches 19 being assumed to be stationary during the compression stroke) is to be avoided.

Thus, if it is assumed that the clearance between the upper and lower plungers and the respective faces of the die plate 10 at the end of the maximum stroke of the plungers is about \( \frac{1}{64} \) inch, and if the extent of travel of the upper punches within the cavities 11 is equal approximately to the final thickness of the tablets (i.e., the compression ratio is about 2:1), then for a tablet of about \( \frac{3}{16} \) inch diameter and \( \frac{3}{32} \) inch thickness, the length of the upper punches should be \( \frac{1}{4} \) inch (\( \frac{1}{64} \) inch travel within the cavities plus \( \frac{1}{8} \) inch clearance). If at the end of their ejection stroke, the lower punches extend about \( \frac{1}{4} \) inch above the upper face of the die plate, then the total minimum length of the lower punches will be the length of the cavities plus such extension and clearance, or about \( \frac{1}{8} \) inch. However, while the lower punches may safely be somewhat larger than this minimum length, the length of the upper punches should be no greater than their maximum dimension transverse to their longitudinal axes.

I claim:

1. A tablet punching press having an upper and a lower plunger and a die plate arranged between said plungers and provided with tablet molding cavities, said plungers each having a plurality of punches, the upper punches being in registry with cooperating lower punches and each pair of upper and lower punches being in registry with a die cavity, the punches and cavities having a transverse dimension not substantially greater than \( \frac{3}{64} \) inch, and the punches projecting from their respective plungers for such a limited distance, the total length of each pair of cooperating upper and lower punches being no greater than five times their transverse dimension, that at the operating speeds of the press, the punches are not set into vibration.

2. A tablet punching press having an upper and a lower plunger each having a plurality of punches projecting therefrom, and a die plate arranged between the plungers and provided with molding cavities each registering with a pair of upper and lower punches, the dimension of the cavities transverse to their longitudinal axes being not substantially greater than \( \frac{3}{64} \) inch and the total length of each pair of cooperating upper and lower punches being about five times said transverse dimension.

3. A press as defined in claim 2, wherein the punches and cavities are of circular cross-section and have a diameter of about \( \frac{3}{64} \) inch.

4. A press as defined in claim 2, wherein the punches and cavities are of circular cross-section and of a diameter of about \( \frac{3}{64} \) inch, the length of the upper punches being not substantially greater than \( \frac{3}{64} \) inch.

5. A press as defined in claim 2, wherein the punches and cavities are of circular cross-section, and wherein the upper punches are of a diameter of \( \frac{3}{64} \) to \( \frac{3}{32} \) inch, the length of such punches being not substantially greater than their diameter.

6. A press as defined in claim 2, wherein the length of the upper punches is not substantially greater than their transverse dimension.

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