THE PREPARATION OF TABLETS

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Tablet history, like the tablet itself, is compressed into a comparatively small space—a mere fraction of the age-old story of pharmacy. There seems little doubt that in 1843 a patent was granted to a North Country chemist, William Brockendon, for a machine designed "for shaping Pills, Lozenges and Black Lead, by pressure in a die", and potassium bicarbonate was the first drug to be compressed into a tablet.

Most drugs in solid form can be compressed, and, in addition, the active ingredients of liquid galenicals such as tinctures and liquid extracts, may be isolated and offered in tablet form.

Tablets can be made in a wide variety of shapes and sizes, and such diverse pharmaceutical products as dental cones, pessaries and bougies can be made by compression. For the purpose of this paper, however, it is proposed to consider only the preparation and manufacture of tablets which are administered orally. The fact that they are used so widely suggests that tablet medication has certain advantages, and these may be briefly stated.

1. *Accuracy of Dosage*

This is of prime importance, and can be achieved by the use of adequate mixing plant and frequent check weighings of the tablets when they are being made. Alternatively, the granules may be assayed for active agent content before they are compressed, and the tablet weight calculated to give the theoretical dose of drug. Whatever the method used it should be possible to obtain uniformity of dosage within $\pm$ 5 per cent. of theory, a factor of particular importance where small doses of potent drugs are required.

2. *Stability*

A tablet should retain its appearance and potency for a reasonable period. Access of moisture to the drug must be prevented, a matter of particular importance for a preparation such as penicillin oral tablets where inactivation may occur without visible signs of deterioration.

3. *Economy*

Few pharmaceutical preparations lend themselves so readily to manufacture by mass production methods, thereby lowering the cost of medication.

The standards of pharmaceutical elegance that apply to older forms of dispensing should be maintained. Tablets should be symmetrical in appearance and free from imperfections. Any colour included in the formula should be uniformly distributed to avoid a mottled appearance. If the drug has a nauseous taste, or is liable to chemical change when exposed to air, it should be protected by a suitable coating. Tablets

should be compressed sufficiently hard to withstand normal hazards of packaging and transport, in order to reach the consumer in as perfect a condition as when they were made.

Whilst tablets have been widely used for many years, the principles underlying their formulation and the methods used in their manufacture were not readily available. The Seventh Addendum to the British Pharmacopœia, 1932, imposed for the first time standards for uniformity of weight, accuracy of dosage and, where necessary, limits for the time of disintegration. This led to a general examination of standards and manufacturing methods, and resulted in an all round improvement in the quality of tablets.

Firth[1] pointed out that the physical form of a drug may have a marked effect on the ease or difficulty with which it can be compressed and Fishburn[2] elaborated this with particular reference to sulphanilamide. The plant chemist may, therefore, be required to produce a drug which is not only chemically pure, but which is in the physical form which has been found to be most satisfactory for tabletting. Aspirin crystals are the best example of this, others include exsiccated ferrous sulphate, calcium lactate and dry extract of cascara.

A tablet is made by compressing a predetermined volume of granules in a die between two punches. For a few substances, usually crystalline and soluble in water, tablet making is a comparatively simple process. The crystals are dried to remove adherent moisture, sieved to uniform size, and then compressed without further admixture. Halides of the alkali metals, potassium chlorate, sodium nitrite, hexamine and urea, can all be treated in this way.

Substances in powder form do not readily pour or flow evenly, but when placed in the hopper of a compressing machine will give an irregular feed into the die, making it impossible to obtain an accurate dose of drug in each tablet. This difficulty is overcome by converting the powder into uniform, free-flowing granules, possessing the essential cohesive property which will enable them to retain a firm hard shape after compression. The manner in which this is achieved is called the granulation process, and it is the most important operation in tablet making, the quality of the granules largely controlling the difficulties encountered in tablet making.

The excipients used to assist in the manufacture and to ensure the efficacy of the tablets may be required to fulfil one or more of the following functions: (1) filling; (2) absorption; (3) adhesion; (4) wetting; (5) disintegration; (6) lubrication.

1. Where small doses of potent drug are ordered, such as hyoscine hydrobromide 1/200 grain, a filler is used to provide bulk and it is customary for the weight of such tablets to be made up to approximately one grain. Substances used for this purpose include dextrose, sucrose, lactose, mannitol, dextrin, starch, kaolin, sodium citrate, sodium chloride, exsiccated sodium sulphate, calcium phosphate and chocolate base. Care is necessary in selecting a filler which is completely inert for that particular formulation[3].

2. An absorbent may be necessary if oils, tinctures or fluid extracts are contained in the formula. For aqueous or alcoholic liquids a filler such as lactose or starch will also act as an absorbent, whilst for oils, magnesium oxide and magnesium carbonate are used. Powdered liquorice root can be employed as an absorbent where its colour is not objectionable.

3. The function of the adhesive is to assist in producing granules which are free from excessive "fines". Drugs having a low bulk density and possessing little cohesive property require the use of a strong adhesive, which is generally more efficient in a solution or suspension than as a dry powder. There is a wide range of substances suitable for this purpose. Should one of the sugars be present as a filler it will also serve as an adhesive when moistened with water or dilute alcohol. Mucilage of starch (10 per cent. w/v) is most useful, but it should be freshly prepared each day. Dilute mucilage of acacia (10 per cent. w/v) can be used either alone or mixed with mucilage of starch. It must be used with caution, however, since it tends to produce hard granules which can adversely affect disintegration. Syrup 50 per cent. w/v and glucose solutions are useful, the latter often being employed to granulate substances which oxidise, such as ferrous salts. Uncoated tablets containing glucose may soften in warm climates, however, rendering the tablets unfit for use.

When preparing compressed lozenges, one aims to produce a hard tablet which will dissolve slowly in the mouth and thereby prolong local medication. This effect can be obtained by including gelatine solution (10 per cent. w/v) as the adhesive, but since its use may encourage mould growth particular care should be taken in packaging and storing the tablets. Dextrin, pectin, tragacanth and quinine mucilages have been used, and, more recently, the sodium salts of algenic acid and carboxymethylcellulose (4 per cent. w/v).

Water cannot be employed for granulating drugs which would decompose, or which are deliquescent. In such cases, organic solvents such as ethanol, methanol, *iso*propanol and acetone, are employed, but granules prepared thus are not usually so robust as those made with aqueous adhesives and they should be handled with care.

4. There are a few drugs which are water repellent and tablets made from them may not break down when administered, although an adequate amount of disintegrant is present. Guaiacol carbonate, guaiacum resin, phenacetin and phenothiazine all share this disadvantage which can be overcome by including in the formula a small proportion of non-toxic wetting agent.

5. Should the drug be sparingly soluble in water, the tablet must be made to disintegrate and this is achieved by the use of substances which readily absorb water and in so doing swell up, causing disruption of the tablet. The tablet should break up in a reasonable time, producing numerous fine particles, the combined surface area of which is greatly in excess of that of the original tablet, thereby increasing the rate at which the drug is exposed to gastric and intestinal action.

Satisfactory disintegration can be obtained by the use of 5 to 15 per cent. w/w of one of a number of starches, and amongst those commonly

used are maize, tapioca, potato, arrowroot and rice. Alginic acid (10 per cent. w/w) and sodium carboxymethylcellulose (2 per cent. w/w) are two of the more recent disintegrants now in regular use, whilst agar, gelatin, pectin and bentonite are other disintegrants worthy of mention.

The effervescence produced by the interaction of sodium bicarbonate and citric or tartaric acids is another means of obtaining quick disintegration, and magnesium peroxide, which liberates oxygen on contact with water, behaves in a similar way.

6. When a tablet is made, it is necessary to introduce a lubricant to prevent adherence of powder to the punches and ensure smooth ejection of the tablet from the die. Inadequate lubrication will cause a film to be built up on the punches resulting in undesirable markings on the tablet. Powdered lubricants should be passed through a fine sieve so as to give the greatest possible covering value. It is assumed that such lubricants act by coating the surface of the granules but the granules are not in fact coated with lubricant, which is mostly located in the granular interspaces[4] and there is, therefore, some doubt as to the exact manner in which powdered lubricants function.

Purified talc (3 to 5 per cent. w/w) is widely used, but objections have been raised because of its complete insolubility and probable retention in the body. This disadvantage is overcome by magnesium or calcium stearate ($\frac{1}{2}$ to 1 per cent. w/w). Tablets thus lubricated have a fine surface polish which enhances their appearance.

Stearic acid gives a similar effect if dissolved in chloroform and added during the moist granulation process. Used thus, it is termed an "internal lubricant" since it is dispersed throughout the tablet mass and tablets containing it may be recompressed without the necessity of relubrication. The lubricating power of talc is much reduced once it has been compressed, and a further addition of lubricant is needed if the tablets should have to be re-made. The stearate group of lubricants should not be used excessively in case "waterproofing" of the tablets should occur and disintegration be seriously retarded. Hydrogenated peanut oil and light liquid paraffin are examples of other lubricants which are often used.

Dried starch has some lubricating value, and aspirin tablets can be made from aspirin crystals with 10 per cent. of dried starch which acts both as disintegrant and lubricant.

All the above-mentioned lubricants are insoluble, but it may be required to prepare tablets which dissolve completely in water to give a clear solution. The number of soluble lubricants available is smaller, and they are generally not so efficient as the insoluble. Powdered boric acid (5 to 10 per cent. w/w) is widely used, but does not readily "wet" and tends to increase the solution time of tablets containing it. Carbowax 4000, a polyethylene glycol, although wax-like in appearance is soluble in water and is effective added as a dry powder (4 per cent. w/w). Tablet makers are still looking for the perfect lubricant. It should be white or colourless, odourless, tasteless, soluble in water, pharmacologically inert and effective in low concentrations.

Having described the types of excipients and the manner in which they are used, it must now be shown how they are employed. Tablet granules may be prepared by one of three methods, the moist granulation process, the dry granulation process and the precompression process.

Each stage of the moist granulation process will be considered in some detail; a fuller account can be found in a useful book by Little and Mitchell[5].

1. *Preparation of the Ingredients in Powder Form*

Except for those crystalline substances which are compressed pure, it is usually advantageous to reduce to a fine powder all the ingredients contained in the formula. For small batches, the powders may be rubbed through a No. 80 sieve by hand. Alternatively, ball mills can be used, but these are not easily cleaned and their use is often reserved for special purposes, when, for example, exposure of the powder to the atmosphere is undesirable because of colour, taste or hygroscopicity. For larger batches, use is made of the comminuting mill, a machine which not only serves to pulverise solids to a very fine powder, but is also used to produce both wet and dry granules.

2. *Mixing of the Powdered Ingredients followed by Granulation*

Upon the efficiency of this operation will depend the accuracy of the active ingredient within the tablet. As was pointed out by Evers[6], absolutely perfect mixing of powders is unattainable, the degree of uniformity depending upon the particle size, air space and relative proportion of ingredients. The use of adequate mixing plant should ensure, however, that the distribution of medicament within the mix complies with specification requirements.

Powder mixing machines are available, and the comminuting mill will also fulfil this function. It is often convenient to mix the powders in a machine used for moist granulation and this may be of the type having a central revolving arm or blades located in the bucket of the machine, or the change-can type where the blades are lowered into the mixing bowl and then raised after use, thus making cleaning of the mixer an easy operation.

Moist granulation is carried out by adding a liquid binder or moistening agent to the mixed powders. For an untried formula, liquid excipients must be added slowly in successive quantities until a damp but firm mass is obtained which can be moulded in the hand. The use of too much liquid in an endeavour to speed up granulation will give an overdamped mass which cannot be sieved until it has dried out. If one is overcautious and does not add sufficient liquid, crumbly granules are obtained which, on drying, produce an undesirably high proportion of "fines."

The damp mass is emptied into a stainless steel container and large granules produced by passing it through a coarse sieve of 4, 6 or 8 mesh. Oscillating or rotary granulators rub the mass through a sieve by means of rollers or blades; the comminuting mill is also much used for this purpose, although the principle employed is different. The hammers

are replaced by knives having a blunt cutting edge, and they are revolved inside the casing at a very much reduced speed. A particular advantage of this machine lies in its ability to handle overdamp granulations which could not normally be sieved by the more conventional type of granulator.

4. *Drying of the Granules*

It is not usually necessary or desirable to remove all traces of moisture from the granules; in fact, granules which are too dry may be as difficult to compress as those which are too moist. The greater part of the moistening agent must, however, be removed.

The modern drying oven is a large unit into which stacks of trays loaded on to trucks can be wheeled in and out. Heat may be provided by steam or electricity and the stove is designed so that warm air enters near the bottom and is directed over the trays by a system of louvers. A drying temperature of 53° to 60° C. is adequate for most drugs, but heat-sensitive substances will need longer drying at a lower temperature. The trays which hold the moist granules may consist of canvas covered wooden frames, but enamelled iron, aluminium or stainless steel trays are preferable, since they are easily washed and eliminate risk of contamination.

Whilst the method described is in common use, experimental work has been done using different sources of heat. Infra-red heat as a means of drying tablet granules has been investigated[7,8]. The heat generated within a non-conducting substance by the rapid alteration of the radio frequency field, has been used to obtain substances free from moisture, and the method has been applied experimentally to dry tablet granules[9,10]. Whilst this work is of interest, one wonders whether it has any practical significance on the manufacturing scale due to probable high operating cost.

5. *Preparation of Uniform Granules and Lubrication*

To produce tablets of accurate and uniform weight necessitates the delivery of a constant volume of granules into the die and their preparation is the next operation in tablet making. When granules are reduced in size by sieving a certain amount of powder is produced, and in fact such "fines" are necessary since by filling the interspaces of the granules, they ensure that a constant weight is delivered into the die at each filling operation. Hard granules will usually produce less "fines" than those which are not so cohesive. The weight of the tablet normally determines the approximate granule size, a small tablet weighing only one grain and of 3/16″ diameter needing finer granules than a larger tablet whose diameter may be up to ½″. A 20's mesh sieve can be used to prepare granules for small tablets and intermediate grades employed up to about 10's mesh for larger ones.

The same machines are employed to dry granulate as were used to sieve the damp mass, but finer screens are inserted. When feeding coarse, dry granules into the hopper, it should not be overloaded since frictional effects will produce more "fines" than may be desired.

The addition of powdered lubricant is the last operation before the granules are ready to be compressed, and it can be introduced manually

or by slowly tumbling in a powder mixer. Lubricants such as liquid paraffin can be sprayed on to the bulk of the granules and gently mixed throughout. Flavours and essential oils dissolved in a volatile solvent are also added at this stage.

The moist granulation process may be modified by excluding all or part of the disintegrant at the time of granulation. For a tablet which does not readily disintegrate, it may be advantageous to add half of the disintegrant during moist granulation and the remainder with the lubricant to the dry granules. This added starch disrupts the tablet into its component granules, whilst the granulated starch, still retaining the capacity to absorb water and swell up, breaks down individual granules into finely dispersed particles. It must be remembered that by adding dry starch the proportion of fine powder may be substantially increased.

(B) The dry granulation process is one not widely used since it is limited to those substances already mentioned which can be compressed pure, or to drugs which require only the addition of disintegrant and lubricant before they are ready for compression.

(C) Granulation by precompression is being increasingly used, and the process has certain advantages over moist granulation. It consists in compressing the mixed powders into large but imperfect tablets or "slugs". These are sieved to produce small uniform granules which may then be recompressed into tablets of the correct weight and size. Robust rotary machines have been developed to make the "slugs" incorporating special feeding devices to ensure uniform filling of the die with powder. This point is important since a variable feed will produce friable "slugs" which readily break down to powder when sieved, instead of producing the hard granules necessary for tabletting. It will be seen that elimination of the drying process not only excludes the need for drying equipment but makes the process of precompression a continuous one, a matter of considerable economic importance. It is also suited for making tablets of incompatible ingredients which would react if moistened, for substances sensitive to heat and for making effervescent tablets.

Since no liquid binder is used, the formula must contain excipients with cohesive properties, otherwise a friable "slug" is obtained which will not readily compress, and repeated recompression may be necessary before satisfactory tablets are produced. The omission of a moistening agent tends to produce a greater proportion of "fines" than is obtained by the moist granulation process, and this may cause "capping" troubles. The process of precompression has been fully described by Peck[11].

The tablet maker from time to time encounters compressing difficulties of which the commonest is that of lamination or capping. It results in the top of the tablet becoming detached and even when this is not immediately apparent, the "cap" can be removed with the thumb nail or it will fall off when a few tablets are shaken in a bottle.

This phenomenon may be due to a number of causes and the compressor must decide whether the trouble lies in faulty granules, imperfect tools, or incorrect speed of compression. Capping is commonly experienced in granules containing a high proportion of "fines". At the

time of compression, air within the granules normally escapes via the narrow clearance between the top punch within the die. Should the interspaces be filled with fine powder, the compressed air cannot escape and much may be retained within the tablet. When the pressure exerted by the top punch is removed, the trapped air expands to attain an equilibrium and escapes from the tablet at its weakest point, which is the periphery, the cap becoming detached at once or when the tablets are handled.

The trouble may be remedied by sieving out some of the "fines" but obstinate cases require regranulation before satisfactory tablets are produced. If the speed of compression is too rapid, a stamp rather than a squeeze occurs, the entrapped air cannot escape before it is compressed and capping occurs. The remedy lies in slowing down the speed of compression and capping due to this cause is usually less frequent on a rotary machine where both top and bottom punches move to compress the granule between them, as compared with a single punch machine where the lower punch is stationary at the moment of compression. The use of excessive pressure will cause capping, as will an insufficiency of lubricant in the formula. Granules which have been overdried sometimes cause this trouble, easily rectified by slight moistening. Certain crystalline forms appear to be responsible for persistent capping, and where this is anticipated, the drug should be finely powdered before granulation.

A die which is in continuous use will begin to show a "ring" at the point of compression, causing a slight distortion in the tablet when it is made and frequently leading to capping when the tablet is ejected from the die. Certain vegetable drugs such as powdered digitalis leaf have an extremely abrasive effect on punches and dies, whose working life is much reduced. The introduction of dies made of tungsten carbide has overcome this hazard to a considerable extent, even the most abrasive substances having little effect on its mirror polish.

"Picking" and "sticking" are problems occurring less frequently, and are more readily corrected. A particle of granule or film of powder adhering to the punch face, gradually builds up until the upper and lower surfaces of the tablet are disfigured. This trouble may be caused by:— (*a*) a punch surface which has been marked or scratched; (*b*) the use of imperfectly polished punches; (*c*) lack of lubricant; (*d*) granules which are too damp. Attention to these points will usually correct any further difficulty.

"Binding" in the die is either caused by shortage of lubricant or by the use of damp granules. Ejection of a tablet is usually accompanied by a "grunting" noise from the machine, a danger signal that must be heeded.

When commencing to compress a batch of granules, a few trial tablets are first made, turning the machine by hand, so that any error in setting up the machine can be adjusted before it operates at speed. Until the correct weight of granules in the die is obtained, all tablets made should be rejected. The pressure is varied until a firm tablet is obtained and the sample should then be shaken in a bottle and examined for capping and the disintegration time must be checked against specification.

The tablets should be examined for friability by determining the amount of powder produced when a known weight of tablets is shaken in a bottle under controlled conditions. The quality control of tablets has been comprehensively described by Nutter Smith[12].

Circumstances may require a tablet to be coated with a protective layer; this often consists of sugar, but it may be a pearl, silver, balsam or gelatin coating. Apart from the aspect of sales appeal, coating may be necessary for the following reasons:— 1. The tablet may have an unpleasant taste. 2. It may contain a drug which is unstable or which will deteriorate on exposure to air. 3. It may consist of drugs of different colour which would appear mottled and unsightly when compressed. 4. The active ingredients may be decomposed by gastric juice and therefore need to be protected with an enteric coat.

The following operations are employed:—

1. The application of a protective subcoat on to the tablet.
2. The gradual building up of the coating by adding concentrated syrup, removing the moisture by drying, and re-applying more syrup until a coat of the required thickness is obtained.
3. Polishing the finished tablet.

Tablets which are to be coated should be firmly compressed on deep concave punches, the compression thus obtained having a comparatively thin edge.

The subcoating consists of a thin shell of dammar resin or shellac, applied as an alcoholic solution, but it must not be used to excess otherwise the tablet will not disintegrate. Alternatively, the subcoat may consist of a mixture of gelatin, sucrose and acacia. The tablets are moistened with a small volume of liquid and allowed to roll in the pan until slightly "tacky." A dusting powder is next added until the moist tablets are covered, warm air is introduced into the pan and the tablets allowed to roll until the subcoating is dry. The process is repeated four or five times, taking care to dry after each wetting before adding more dusting powder. At this stage the edges should be filled in and the tablet sealed off from the effect of adding syrup.

Dusting powder can be made to various formulæ, a satisfactory one consisting of a mixture of precipitated chalk, icing sugar, powdered gum acacia and starch.

The coat is now built up by adding successive quantities of warm syrup in which starch grains are suspended, until just before reaching the final weight when starch syrup is replaced by a plain syrup which gives the desired smooth finish. The total amount of coating added usually equals the weight of the uncoated tablet. For coloured work, an edible dye or pigment is added to the syrup at the later stages of coating.

Before the final process of polishing can be commenced, the tablets must be quite dry, otherwise a dull finish will result. Polishing is carried out by rolling the tablets in a pan lined with a carnauba-beeswax mixture. An alternative method is to use a revolving canvas drum supported on a metal framework, into which a few drops of wax solution are added from time to time. It is convenient to have separate polishing pans for white

and coloured work, but the inside of the pan can be cleaned with a cotton wool pad moistened with chloroform.

When a formula contains ingredients which are incompatible, the uncoated tablets may be made to contain one ingredient whilst the other may be dissolved or suspended in the coating syrup and applied in the coating process[13]. More detailed information on tablet coating is available in a work by Clarkson[14], whilst a full summarisation of coatings and standards was carried out by Stephenson and Smith[15].

A method has recently been described by Whitehouse[16] by which a tablet can now have a layer of sugar compressed around it. The idea is not new, previous attempts having failed on mechanical grounds. Machines have now been developed, however, in which a tablet is compressed on one rotary machine, picked up by a travelling arm and accurately centred in a die of a second rotary machine, the die already containing a charge of lubricated sugar granules, a further amount of which is fed in to cover the tablet and the whole compressed, producing a core surrounded by an even coat of sugar. Whilst this coating differs somewhat from that obtained by the older method, it does in fact do all that is required, and the complete mechanisation and speed of the process has sound economic advantages.

This brief survey of tablet coating would be incomplete without mention of enteric coating. It is sometimes necessary to administer a tablet which must pass unchanged through the stomach, but disintegrate in the duodenum. Drugs such as emetine salts, stilbœstrol and ammonium chloride, produce nausea and the tablet may be rejected by the patient before it can be utilised. Glandular products which decompose in gastric juice may need protection, likewise anthelmintic drugs which are required in a local concentration to be effective, will not be diluted by gastric juice if they are enteric coated.

The problem of applying such a coating is complicated by the fact that the rate at which a tablet may pass through the stomach is a variable factor. Individuals differ both in their gastric secretions and the rate at which food is digested. The efficacy of an enteric coating may depend upon the following factors:—

1. *The difference in* p*H between the stomach and the duodenum.* Amongst the substances which have been used for enteric coating are shellac, dammar, mastic and sandrac, all containing insoluble resin acids which would be converted into soluble salts in the intestinal tract, resulting in a weakening and disruption of the protective coat. It has been shown, however, that the duodenal contents have a mildly acid reaction[17], and other factors may be responsible for the effectiveness of these substances.

2. *The action of lipase enzymes upon the saponification of esters.* This action is employed in the use of *n*-butyl stearate for enteric coating, since it is readily hydrolysed into stearic acid and *n*-butanol[18].

Substances such as stearic acid and cetyl alcohol, either alone or mixed with one of the above-mentioned resins, have been used with success, cetyl alcohol and mastic having been reported to be 98 per cent. efficient[19].

Other substances used in the past are keratin and salol—the former is of little value, but salol is useful for the extemporaneous enteric coating of pills and tablets.

Cellulose acetate phthalate has given very satisfactory results[20] employed as a 5 to 15 per cent. solution in ethyl acetate and ethanol. Because of the volatile nature of the solvents, successive coatings can be quickly applied. Bauer and Massucci[21] state that this enteric envelope is broken down by the hydrolytic effect of the intestinal esterases in pancreatin and not by alkalinity in any part of the duodenum. Whatever the substance used for enteric coating, it must be non-toxic and inert. It is applied at the subcoating stage if the final tablet is to be sugar coated.

The efficacy of these coatings has been studied both *in vitro* and *in vivo*, the former method being most commonly used. The tablet under test is immersed in artificial gastric juice at body temperature and occasionally agitated. Opinions differ on the time considered necessary for the tablets to withstand this treatment without breaking down, periods varying from 3 to 6 hours having been proposed, but 4 to 5 hours seems a reasonable average. The tablet is then removed from the acid digestive fluid and placed in alkaline pancreatin solution, where it should break down within one hour. The artificial fluids used by Abbott and Allport[20] have been found satisfactory for this purpose.

Whilst laboratory digestion tests give an approximate valuation of the efficacy of the enteric coating, a more accurate picture is obtained from *in vivo* tests, although results obtained from one person would not necessarily be closely reproduced in another, for reasons already given. The test consists in swallowing a tablet of barium sulphate coated with the enteric substance to be examined. Its progress through the digestive system and alimentary tract is followed by radiographs taken at intervals, successive pictures showing the exact location of the coated tablet within the body[22]. The authors of the original work consider that an effective enteric coat should be stable for 6 hours, after which it should disintegrate rapidly in whatever part of the digestive tract that it may be found. Since such coatings are now used increasingly, it is probable that standards will be laid down to determine their efficiency.

In this brief survey, the principles and methods used in making oral tablets have been examined. It has been shown that satisfactory tablets can only be produced after careful thought has been given to the manner in which the various excipients are combined in the formula. Whilst for reasons of economy, tablet production is a highly specialised branch of manufacturing pharmacy, it must always be remembered that tablets are a form of dispensing and should comply with the highest standards of accuracy and elegance.

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