

1

2,881,085

THIN FILM COATING FOR TABLETS AND THE LIKE

Clarence J. Endicott and Albert A. Dallavis, Waukegan,
and Henry M. N. Dickinson, Lake Bluff, Ill., assignors
to Abbott Laboratories, North Chicago, Ill., a corpora-
tion of Illinois

No Drawing. Application November 9, 1953
Serial No. 391,123

10 Claims. (Cl. 106—171)

This invention relates to tablets and other individual dosage forms which are characterized by a thin film coating of a water permeable plastic composition, and to the method of making such tablets and dosage forms. The invention also relates to a thin water permeable tablet coating film, and to a liquid composition useful for laying down the aforementioned film.

In the tablet coating art it is a well known procedure to first coat a compressed pellet or tablet with a water repellent resinous material such as zein or shellac which is used to protect the tablet from moisture later applied. Next are applied the sub-coating materials such as gelatin and acacia along with dusting of the sub-coating with powders especially designed for this purpose and known as sub-coating powders. This sub-coating procedure is required in the normal tablet coating art because a bare, compressed tablet usually has sharp edges which will not take a subsequent sugar coat evenly in the same amount as will be deposited on the surfaces of the tablet and will leave weak spots in the coating. Sub-coating is applied in order to round the corners and convert the tablet into more or less of an oval shaped object without sharp corners. Then a coating of heavy syrup with color added is usually applied over the sub-coat and numerous individual layers of this heavy syrup coating with color are applied. Usually a sub-coating powder is suspended in the heavy syrup coating composition prior to its application. Finally several coats of a heavy syrup coating with color are put on top of the previously applied coats and then a thin syrup coating is applied over the entire mass. Finally it is desirable to employ a polishing operation such as for instance, the application of a wax to the coated tablet. The result is a substantially oval shaped coated tablet having no sharp corners and characterized by pleasing appearance and taste. Tablet coating is, however, quite an expensive operation and requires from four to six days for the complete application and polishing of the tablet. The long time is required because the syrups and the sub-coats are put on from aqueous solution or suspension and between each coat it is necessary to rotate the tablets vigorously in a coating pan with air blowing over the tablets in order to evaporate the moisture and form a hard dry coat. It is recognized that coating adds considerably to the cost of a suitable tablet.

It is therefore an object of this invention to provide a tablet which is coated with a thin plastic film which is substantially water permeable and which may contain color.

It is another object of the invention to provide an inexpensive and efficient method of coating tablets which will materially shorten the tablet coating cycle.

According to the invention there is now provided a tablet coating composition which is comprised of a portion of a hard, water soluble or water dispersible wax-like substance and a portion of a film forming resinous substance. Several other ingredients may be added to the previously named ingredients in order to enhance the

2

properties of the coating obtained from the composition. Among the more important of these additional materials are coloring materials, water insoluble waxes, plasticizing agents, and possibly wetting agents and drying agents.

The hard, water soluble wax-like substances to which the invention pertains are materials of the polyethylene glycol type having a melting point of at least 50° C. Water dispersible waxes which may also be used either alone or in addition to the water soluble polyethylene glycol are glyceryl monostearate and diglycol stearate. Among the film-forming resins to which the invention pertains, the cellulose acetate phthalate resins are suitable for use. The cellulose acetate phthalate plastics are those described in United States Patents Nos. 2,093,462, 2,093,464, and 2,126,460. These are known as the polycarboxylic acid partial esters of cellulose esters of lower aliphatic monocarboxylic acids, such as, cellulose acetate phthalate, cellulose propionate phthalate and cellulose butyrate phthalate.

Among the coloring agents which may be used in the practice of this invention are any of the non-toxic dyes, lakes and pigments which have been certified for use in the food, drug and cosmetic industries. For example, we have found that dyes of the type represented by red D. and C. #37, green F. D. and S. #1, yellow D. and C. #11, red D. and C. #21, orange D. and C. #4, red D. and C. #18, and red D. and C. #39 are suitable for use as colorants in the coating composition. Among the pigments which we have found suitable are yellow hydrated iron oxide, brown hydrated iron oxide, red iron oxide, black iron oxide, titanium dioxide, and the ultramarine blues. Many lakes are found suitable in the practice of this invention and D. and C. red #3, D. and C. orange #17, D. and C. green #1, D. and C. red #1, D. and C. yellow #1 are representative of the class. A lake is a dye which has been precipitated on an insoluble metal compound. In the case of D. and C. dyes, which means those suitable for use in the drug and cosmetic industry, it is necessary to deposit the dye on a pharmaceutically acceptable carrier such as aluminum hydroxide.

Among the water insoluble waxes which we have found suitable are beeswax, lanolin, stearic acid, onesta wax, cocoa butter and cetyl alcohol. Onesta wax is the trade name for a high melting point hydrogenated vegetable oil fraction which resembles beeswax in consistency. For plasticizing agents we may use castor oil, mineral oil, corn oil, sesame oil and propylene glycol. If desired we may also substitute a portion of a drying oil such as soy bean oil or the like and we also may use surface active agents such as the polyoxyethylene sorbitan derivatives and the sulfated fatty alcohols of the Duponol type.

When the foregoing composition is applied to tablets in the manner which we recommend as part of our invention it is possible to provide a suitable coating for a tablet or the like with the use of a relatively few coats or applications of the coating material. A highly important advantage of this invention is that the coating composition described herein can be applied from solvent solution such as acetone, alcohol or a combination thereof and as a result the drying time between coats is reduced from approximately an hour or two in the case of water down to about 5 minutes in the case of the solvent solution. Hence, it is possible to completely coat a tablet in a matter of minutes where prior practices have required four to six days to obtain a suitable coating.

When the coating composition claimed herein is applied without coloring agent a pleasing white tablet is obtained. The white coating may be rendered opaque by the addition of a quantity of titanium dioxide for example, if desired. The invention is most highly suitable, however, to the application of colored film coat-

ings of the type described in which a small quantity of a suitable coloring agent such as the dyes, lakes and pigments previously set forth are incorporated into the solution prior to application on the tablets. In this manner a highly pleasing appearance is given to the tablets and the tablets may be regarded as "elegant" in the terms of the trade. A tablet coated according to the practice of this invention is considerably smaller in size than one coated by the initially described standard procedure and the smaller tablet is more acceptable because it can be swallowed more easily. The film of this invention very effectively coats the tablets so that no unpleasant taste can be perceived but at the same time distinctive markings punched into the tablet core will show through very clearly and be readily discernible on the surface. Since no sugar coating is required in order to give these tablets elegance the taste appeal to children may be overcome and the chance of accidental ingestion of the tablets is substantially minimized. Also the absence of sugar is a distinct advantage in those instances where it is desirable to limit caloric intake. A sweetening or flavoring agent may be added of course, if desired.

We prefer to use between about 14% and 20% weight by volume of the hard, water soluble or water dispersible wax-like substance in making up the fluid coating composition for application to tablets. Likewise, we may use between about 4% and about 7% weight by volume of the film-forming resinous substance. The waxy adjuvant is not used in a concentration greater than 5% weight by volume and the plasticizing agent is used in a concentration of from 1% to 5% weight by volume.

In the finished dry coating on the tablet we use between about 66% and about 84% by weight of the hard, waxy, water-soluble or water dispersible substance. Likewise we use between about 16% and about 34% by weight of the film-forming resinous substance. The percent by weight of additives such as colorants, plasticizers and waxy adjuvants is quite small and usually does not exceed 5% by weight in total amount.

The terms "weight by volume," "weight per volume" and "w./v." are used herein for their customary meaning as understood in the pharmaceutical industry. All three expressions mean the same thing, that is, the weight of ingredient per unit volume of suspension or solution. The expression is used for convenience in designating the amount of a solid that is to be dissolved or suspended in a liquid to give a definite ultimate volume of solution or suspension. In other words, 10% weight per volume means, for example, 10 grams of solid dissolved or suspended in a liquid and the liquid made up to a total volume of 100 ml.

The following examples are presented in order to describe the invention more fully but it should be understood that the invention is not intended in any way to be limited by the examples. In the examples reference is made to a cellulose acetate phthalate solution which is made up as follows:

10 grams cellulose acetate phthalate
3 ml. propylene glycol
1 ml. Span-80
40 ml. of alcohol
Acetone q.s. ad. to 100 ml.

The amount of cellulose acetate phthalate plastic in the solution is 10% weight by volume and in the examples when it is stated that, for instance, 300 cc. of cellulose acetate phthalate solution is used, it is to be understood that there will be 30 g. of cellulose acetate phthalate in the solution, or 10% w./v.

Example I

A tablet coating solution is made up according to the following formula:

Polyethylene glycol-6000 -----g. w./v. 70.0
Cellulose acetate phthalate, 10% w./v. solution -----cc. 300
Acetone q.s. to 500 cc.

The polyethylene glycol is dissolved in a portion of warm acetone and is then added to the C.A.P. solution. The remainder of the acetone is added and the mixture is thoroughly stirred. The solution is applied to a moving bed of tablets or granules by pouring small portions onto the tablets. As the tablets rotate the material is distributed evenly over the surface thereof and in a few minutes time the solvents will have evaporated leaving a dry hard film. Thereafter a second coat is applied in the same manner and subsequent coats are applied until a film of the desired thickness is obtained. Tablets coated in this manner are pleasing in appearance and will disintegrate without delay either in water or in gastric secretions. The disintegration of the tablet may be speeded up somewhat by incorporating into the tablet one of the well-known disintegrators. In the foregoing formula the polyethylene glycol is present in about 14% and the cellulose acetate phthalate is present in an amount of about 6% weight by volume.

Example II

A solution suitable for coating tablets was prepared according to the following formula:

Polyethylene glycol-6000 -----g. w./v. 70.0
Cellulose acetate phthalate, 10% w./v. solution -----cc. 300
Yellow dye D. and C. #11 -----g. w./v. 0.5
Acetone q.s. to 500 cc.

The formula is made up the same way as in Example I except that the yellow dye is added to a portion of the acetone prior to thorough mixing of the solution. Tablets coated with 10-20 coats of this solution give a very pleasing yellow appearance and are much smaller and easier to swallow than a similar tablet which has undergone sub-coating and sugar coating in the normal tabletting procedure.

Example III

A solution suitable for use in coating tablets is prepared according to the following formula:

Polyethylene glycol-6000 -----g. w./v. 70.0
Cellulose acetate phthalate, 10% w./v. solution -----cc. 300
Castor oil -----g. w./v. 1.25
Acetone q.s. to 500 cc.

This solution is made up in the same manner as previously described and is applied to tablets in the same way. The film applies to the tablet quite evenly with a suitable distribution of film on the sides, edges and faces of the tablet. A few coats of the foregoing solution will give a film of approximately 0.005 inch in thickness and provides a suitable and pleasing film about the tablet core.

Example IV

A solution for use in coating tablets or the like is prepared according to the following formula:

Polyethylene glycol-4000 -----g. w./v. 70.0
Cellulose acetate phthalate, 10% w./v. solution -----cc. 300
Beeswax -----g. w./v. 5.0
Acetone q.s. to 500 cc.

This solution is prepared similarly to the preceding solutions except that the beeswax is dissolved in acetone by heating the acetone to a fairly high temperature. When the acetone cools, beeswax may come out in a very fine suspension but does not alter the characteristics of the film. The film obtained is quite smooth and even and deposits uniformly on the sides, edges and faces of the tablet.

5

Example V

A preferred solution suitable for application to tablets to form a thin film thereon was made up according to the following formula:

Polyethylene glycol-6000	g. w./v.	70.0
Cellulose acetate phthalate, 10%	w./v. solution	cc.
Yellow dye, D. and C. #11	g. w./v.	0.5
Castor oil	g. w./v.	1.25
Stearic acid	g. w./v.	5.0
Acetone q.s. to 500 cc.		

The polyethylene glycol and the stearic acid are added to warm acetone and when the acetone has cooled somewhat the yellow dye and castor oil are also added. The entire solution is mixed with the cellulose acetate phthalate solution and thereafter applied to tumbling tablets in customary tablet coating procedures. For instance about 10 cc. of the solution may be applied to about 2000 tablets in a rotating pan and after about 5 minutes the coat will be evenly distributed on all of the tablets and will be substantially dry. Thereafter another 10 cc. portion may be applied and the procedure repeated a number of times until a coating of suitable thickness has been established.

Example VI

A solution suitable for application to tablets and the like to form a thin film thereon is made up according to the following formula:

Polyethylene glycol-6000	g. w./v.	100.0
Cellulose acetate phthalate, 10%	w./v. solution	cc.
Red dye, D. and C. #37	mg. w./v.	100
Corn oil	g. w./v.	1.25
Cocoa butter	g. w./v.	5.0
Acetone q.s. to 500 cc.		

The solution was prepared in the manner previously set forth in Example V and was applied to tumbling tablets in the same way. In this example 20% w./v. of wax-like substances and 7% w./v. of cellulose acetate phthalate plastic, in solution is employed.

Example VII

A solution suitable for application to tablets and the like to form a thin film thereon was made up according to the following formula:

Polyethylene glycol-6000	g. w./v.	100.0
Cellulose acetate phthalate, 10%	w./v. solution	cc.
Green dye, D. and C. #1	g. w./v.	4.0
Mineral oil	g. w./v.	1.25
Lanolin	g. w./v.	5.0
Acetone q.s. to 500 cc.		

This solution is prepared in the same manner as set forth in the preceding examples and differs therefrom in containing 20% w./v. of the water soluble wax-like material and 4% w./v. of cellulose acetate phthalate resin, in solution.

Example VIII

A solution suitable for application to tablets and the like to form a thin film thereon was made up according to the following formula:

Polyethylene glycol-6000	g. w./v.	70.0
Cellulose acetate phthalate, 10%	w./v. solution	cc.
Orange dye, D. and C. #4	mg.	250
Orange lake, D. and C. #17	g. w./v.	4.0
Sesame oil	g. w./v.	1.25
Cetyl alcohol	g. w./v.	5.0
Acetone q.s. to 500 cc.		

The solution is made up in the same manner as set forth in the previous examples. It differs therefrom in con-

6

taining 14% w./v. of polyethylene glycol-6000 and 4% w./v. of cellulose acetate phthalate in solution. It also differs in that a portion of orange lake is substituted for a portion of dye in order to provide greater depth of color and superior covering power for the colorant in the solution.

Example IX

A solution suitable for application to tablets to form a thin film thereon was made up according to the following formula:

Polyethylene glycol-6000	g. w./v.	70.0
Cellulose acetate phthalate, 10%	w./v. solution	cc.
Yellow lake, D. and C. #1	g. w./v.	15.0
Propylene glycol	g. w./v.	1.25
Paraffin	g. w./v.	5.0
Acetone q.s. to 500 cc.		

The solution is prepared in the same manner as set forth in the previous examples and is applied to tablets in the same way. In this example 14% w./v. of polyethylene glycol-6000 is employed and 7% w./v. of cellulose acetate phthalate, in solution, is used. The lake employed in this example gives a brilliant color and has excellent covering qualities for the tablet core. Lakes are quite useful in covering up tablets which have an off color or a mottled appearance.

Example X

A solution suitable for application to tablets to form a thin film thereon was made up according to the following formula:

Polyethylene glycol-600	g. w./v.	70.0
Cellulose acetate phthalate, 10%	w./v. solution	cc.
Red lake D. and C. #3	g. w./v.	6.0
Castor oil	g. w./v.	1.25
Beeswax	g. w./v.	5.0
Acetone q.s. to 500 cc.		

The solution is made up in the same manner as set forth in the previous examples and when applied to tablets is found to provide a pleasing red color which has strong covering properties.

Example XI

The formula in Example X was duplicated substituting 3 g. of red iron oxide pigment for the lake of the previous example. In this example a dull red color is obtained when the solution is applied to the tablets and the covering power of the solution is very good.

Example XII

A solution suitable for application to tablets and the like to form a thin film thereon was made up according to the following formula:

Glyceryl monostearate	g. w./v.	70.0
Cellulose acetate phthalate, 10%	w./v. solution	cc.
Acetone q.s. to 500 cc.		

This solution is made up in a manner similar to that previously set forth and is applied to tablets in a similar fashion. If desired we may also add a colorant, a plasticizer and a wax as in the previous examples. While glyceryl monostearate is not water soluble it is water dispersible in the concentrations used herein and particularly in combination with the resinous material. Tablets coated with a film of the foregoing solution will disintegrate readily in water or in gastric secretions.

Example XIII

Example V is repeated with the substitution of a 50% acetone, 50% anhydrous ethanol solution for the acetone of Example V.

From the foregoing discussion of the invention it will

be clear that we have provided a novel and highly unusual coating for tablets. It does away with the long and involved coating and drying procedure normally used in the tablet coating art. The film is uniformly thin on the tablets and provides all of the necessary protection and elegance that can be obtained in any other tablet coating procedure. In essence, this invention makes possible the substitution of a single thin film on tablets for the previously known massive sub-coating and sugar coating thereon.

Others may practice the invention in any of the numerous ways which will be suggested to one skilled in the art upon a reading of this specification. It is intended that all such practice of the invention be included hereunder provided it falls within the scope of the appended claims.

We claim:

1. A fluid composition adapted for application to tablets and the like which consists essentially of about 14% to 20% w./v. of a polyethylene glycol having a melting point of about 50° C., and about 4% to about 7% w./v. of cellulose acetate phthalate, and a non-aqueous solvent for said glycol and said cellulose acetate phthalate.

2. A coated solid medicament having as the coating material a film of a physiologically acceptable composition consisting essentially of the water permeable combination of a water soluble wax and a polycarboxylic acid partial ester of a cellulose ester of a lower aliphatic monocarboxylic acid.

3. A coated solid medicament having as the coating material a film of a physiologically acceptable composition consisting essentially of the water permeable combination of about 14 to 20 parts by weight of a water soluble wax and about 4 to 7 parts by weight of a polycarboxylic acid partial ester of a cellulose ester of a lower aliphatic monocarboxylic acid.

4. A coated tablet having as the coating material a thin film of a physiologically acceptable composition consisting essentially of the water permeable combination of about 14 to 20 parts by weight of a normally solid polyethylene glycol and about 4 to 7 parts by weight of a polycarboxylic acid partial ester of a cellulose ester of a lower aliphatic monocarboxylic acid.

5. A coated tablet having as the coating material a thin film of a physiologically acceptable composition consisting essentially of the water permeable combination of about 14 to 20 parts by weight of a normally solid polyethylene glycol and about 4 to 7 parts by weight of cellulose acetate phthalate.

6. The method of coating tablets and the like which comprises applying to said tablets a film coating of a physiologically acceptable coating composition consisting essentially of the water permeable combination of a water soluble wax and a polycarboxylic acid partial ester of a cellulose ester of a lower aliphatic monocarboxylic acid.

7. The method of coating a solid medicament which

comprises applying to said medicament a film coating of a physiologically acceptable coating composition consisting essentially of the water permeable combination of about 14 to 20 parts by weight of a water soluble wax and about 4 to 7 parts by weight of a polycarboxylic acid partial ester of a cellulose ester of a lower aliphatic monocarboxylic acid.

8. The method of coating tablets and the like which comprises applying to said tablets a film coating of a physiologically acceptable coating composition consisting essentially of the water permeable combination of about 14 to 20 parts by weight of a normally solid polyethylene glycol and about 4 to 7 parts by weight of a polycarboxylic acid partial ester of a cellulose ester of a lower aliphatic monocarboxylic acid.

9. The method of coating tablets and the like which comprises applying to said tablets a film coating of a physiologically acceptable coating composition consisting essentially of the water permeable combination of about 14 to 20 parts by weight of a normally solid polyethylene glycol and about 4 to 7 parts by weight of cellulose acetate phthalate.

10. A fluid composition adapted for application to tablets and the like as a film coating thereon which consists essentially of about 14% to 20% w./v. of a water soluble wax and about 4% to 7% w./v. of a polycarboxylic acid partial ester of a cellulose ester of a lower aliphatic monocarboxylic acid, and a non-aqueous solvent for said wax and said ester.

References Cited in the file of this patent

UNITED STATES PATENTS

587,097	Kennedy	July 27, 1897
1,997,106	Comwell	Apr. 9, 1935
2,059,981	Bradley	Nov. 3, 1936
2,100,377	Brubaker	Nov. 30, 1937
2,105,364	Nowak	Jan. 11, 1938
2,191,530	Hucks	Feb. 27, 1940
2,342,478	Metz	Feb. 27, 1944
2,389,708	Zolad	Nov. 27, 1945
2,409,986	Salo	Oct. 26, 1946
2,446,584	Gold	Aug. 10, 1948
2,602,756	Hucks	July 8, 1952
2,753,288	Visscher	July 3, 1956

FOREIGN PATENTS

377,162	Great Britain	Jan. 21, 1931
493,934	Great Britain	Jan. 14, 1937

OTHER REFERENCES

- Ellis: "Chemistry of Synthetic Resins" (1935), vol. 1, page 13. (Copy in Div. 50.)
 "Cellulose Acetate Plastics," Stannett (1950), page 43.
 Ott et al.: High Polymers, vol. V, part III, page 1462.
 Bauer: Journal of Amer. Phar. Assoc., Sc. Ed., pages 124-128 (see page 127), March 1948.