New Approach to Development and Manufacture of Enteric Compression Coatings

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Five commercially available polymers were evaluated for the preparation of enteric compression coatings utilizing a unique polymer incorporation method, which was part of the granulation process, and which was applicable to all of the polymers with slight modifications. The effect of polymer plasticization, the various methods of polymer incorporation, diluent ingredient properties, and physical factors of the compression coating operation were related wherever possible to the enteric disintegration properties of the manufactured tablets. The compression coating formulations developed of 4 polymers were indicated to be enteric by *in vitro* disintegration tests, but only 3 of the polymer formulations were clearly enteric according to preliminary *in vivo* tests using an X-ray technique and human volunteers.

THE CONVENTIONAL method of enteric coating in a coating pan is time consuming, empirical, difficult to reproduce, and cumbersome. For large-scale production, newer methods of enteric coating have been developed. These include film coating and compression coating. The problem of developing highly satisfactory enteric film coatings, which will be stable in the gastric environment and at the same time will be impermeable to water and prevent leaching of the drug, is difficult to resolve. In the enteric coating field, compression coating appears to have the most potential based on greater precision and reliability of fabrication, in comparison to the pan-coating operation which is the other primary enteric coating technique.

Zapapas *et al.* (1) developed an enteric coating formulation of triethanolamine, lactose, and magnesium stearate. James *et al.* (2) developed an enteric compression coating formulation with a carboxylated polymer of vinyl acetate. Swintosky obtained a U. S. patent (3) for an enteric compression coating formulation consisting of 50 to 90% of a pharmaceutically available organic acid and a pharmaceutical binder. Miller and Lindner (4) patented an enteric compression coating formulation of penicillin, a water-soluble sulfonamide, and ammoniated polyvinyl acetate phthalate.

In this study a new method of enteric granulation preparation was utilized which may be more rapid and economical than other conventional compression coating granulation manufacturing procedures. The factors of formulation, granulation manufacture, compression properties, and probable mechanisms of enteric action were studied for their effects on the enteric characteristics of the final tablet coatings.

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EXPERIMENTAL

Polymeric Materials

The polymers studied (Table I) were selected for evaluation on the basis of meeting the following criteria as completely as possible: (*a*) water insolubility or substantial insolubility at pH values of 1.2 to 5, with increasing solubility at higher pH values, (*b*) resistance to moisture and water, (*c*) solubility in common organic solvents, (*d*) stability to heat and light under extreme conditions of pharmaceutical storage, (*e*) white or light in color and free from objectionable taste or odor, (*f*) chemical and physiological inertness, and (*g*) compressibility alone or in combination with other ingredients in the formulation. Cellulose acetate hydrogen phthalate was selected as a standard based on its wide use as an enteric coating.

Granulation Preparation Procedures

Core Formulations.—Cores of 2 dissimilar inert commonly used diluents, lactose and calcium sulfate dihydrate, as well as a radiopaque core of barium sulfate (Table II) were prepared. Lactose represented an organic soluble diluent and calcium sulfate an inorganic insoluble diluent.

Twelve-mesh core granulations of lactose and calcium sulfate and 16-mesh granulations of barium sulfate were prepared by wet granulation using a Stokes oscillator[1] and drying at 45° for 12 hr. The other formula ingredients were added to the sized granulations. Amaranth was incorporated in the cores to indicate leaching of a soluble ingredient through the coat.

Coat Granulations.—The coat formulations were prepared using the basic components and composition ranges given in Table III.

The granulations were prepared by mixing the dry polymer, coat diluent, polyethylene glycol 6000; massing the mixed powder with the granulating solvent containing the plasticizer (Table IV), if any, for 15 min. in a planary mixer to produce a very wet mass; reduction of the wet mass to pieces of about 1-in. diameter; and oven drying at 45° for 12 hr. (38° for the CAP granulations). The dried pieces were coarse-sized through a Fitzpatrick comminutor[2] operated at high speed with knives forward using a punched plate screen with 0.5-in.

[1] F. J. Stokes Corp., Philadelphia, Pa.
[2] W. J. Fitzpatrick Co., Chicago, Ill.

TABLE I.—POLYMERS STUDIED AS ENTERIC COMPRESSION COATING COMPONENTS

Polymer Designation	Chemical Designation	Commercial Name	Physical Form
CAP	Cellulose acetate hydrogen phthalate[a]	C-A-P	Flakes
PVM/MA 169	Poly(methyl vinyl ether/maleic anhydride)[b]	Gantrez AN-169	Powder
PVAc-C-H	Carboxylated copolymer of vinyl acetate[c]	Gelva C-3 V-30	Beads
PVAc-C-L	Same as above but lower viscosity grade[c]	Gelva C-3 V-10	Beads
PVAc	Polyvinyl acetate[d]	Vinac ASB-10	Beads

[a] Eastman Organic Chemicals, Distillation Products Industries, Rochester, N. Y. [b] General Aniline & Film Corp., N. Y. [c] Shawinigan Resins Corp., N. Y. [d] Colton Chemical Co., N. Y.

TABLE II.—CORE FORMULAS FOR *In Vitro* AND *In Vivo* TESTING

	Lactose Diluent, %	Calcium Sulfate Diluent, %	Barium Sulfate Radiopaque Core, %
Diluent	88.0	88.0	66.0
Lactose	...	...	19.0
Polyethylene glycol (40 mesh)	2.0	2.0	...
Cornstarch (dry)	10.0	10.0	15.0
Amaranth	0.5	0.5	0.3
Magnesium stearate	0.1	0.1	0.7
Granulating agent *q.s.*	12% Gelatin–4% acacia soln.	10% Starch paste	10% Starch paste

diameter openings. The coarse granules so obtained were further sized through a 12-mesh screen with a Stokes oscillator.

All compression-coated tablets were prepared with a Manesty DryCota series 500[3] compression coating machine with $^{5}/_{16}$ in. and $^{7}/_{16}$ in. s. c. punches on the core side and coat side, respectively. The cores and coated tablets had the following average specifications:

	Core	Coated Tablet
Weight	185.0 mg.	650.0 mg.
Hardness	0.5 Kg.	17–25 Kg.
Diameter	0.795 cm.	1.114 cm.
Crown thickness	0.355 cm.	0.634 cm.

RESULTS

The following factors were systematically investigated for their effect on the *in vitro* enteric disintegration, core centering, and other properties of the tablets: (*a*) the concentration of the polymer required in the coat composition, (*b*) the coat diluent materials employed, (*c*) the granulating solvent system employed, (*d*) the necessity for a plasticizer, (*e*) the addition of lubricant–intergranular enteric bonding agent and granule binder, and (*f*) the particle size and particle size distribution of the granulation.

In Vitro Enteric Properties

Each polymer (Table I) was prepared in a series of coating granulations according to the basic coat formula in the range of component concentrations shown in Table III. Based on *in vitro* enteric disintegration testing, the following results were obtained.

None of the initial CAP formulations tested, using polymer concentrations up to 30%, produced a product with enteric protection in gastric fluid. Such enteric protection was achieved when the plasticizers (Table III) were added in a compatible solvent system. Actual plasticization of the polymer in the granulations was reflected by the elastic nature of the granules. Drying the plasticized CAP granulations above 38° diminished the plasticization effect and produced brittle granules with a resultant loss of enteric properties. As with all the polymers studied, to achieve satisfactory enteric properties *in vitro*, an intergranular bonding agent (5% magnesium stearate) and a granule binder (5% PVP) were required. A 30% plasticized CAP formula (formula 1*b*, Table IV) thus prepared, produced a satisfactory enteric product by *in vitro* test. The resultant tablets were highly speckled. To produce a more elegant nonspeckled tablet, the 30% CAP granulation could be successfully combined with an insoluble granulation (formula 1*a*, Table IV) in combinations containing as little as 30% of the CAP formula. The tablets thus obtained were nonspeckled and resistant to darkening at elevated storage temperatures.

[3] Manesty Machines Ltd., Liverpool, England (Thomas Engineering, Skokie, Ill.).

TABLE III.—BASIC COATING FORMULA AND RANGE OF CONCENTRATIONS EVALUATED

Ingredients	Concn., % w/w
Polymer (40-mesh powder)	10.0–30.0
Polyethylene glycol 6000 (40-mesh powder)[a]	1.0–1.5
Diluent (lactose or calcium sulfate dihydrate)	46.5–87.0
Plasticizer (diethyl phthalate or triacetin)	0.0–10.0
Lubricant and intergranular enteric bonding agent[b]	2.0–5.0
Granule binder[c] (powdered acacia or PVP)[d]	1.0–5.0
Organic solvent (Table IV)	*q. s.*

[a] This material was present to promote core-coat bonding. In some combinations, the material used for lubricant-intergranular enteric bonding would also promote core-coat bonding. [b] Magnesium stearate, stearic acid, polyethylene glycol 4000, and calcium stearate were evaluated. [c] A substance which serves as a strong adhesive material and holds the granules together during exposure to gastric fluid. [d] Polyvinylpyrrolidone. Plasdone K-39, General Aniline & Film Corp., New York, N. Y.

PVM/MA 169, as the anhydride, was granulated with acetone to maintain the slowly soluble anhydride form. At a level of 10% polymer, using 3% magnesium stearate intergranular bonding agent and 3% PVP granule binder, satisfactory *in vitro* enteric properties were obtained when all the fines below 60 mesh were removed from the coat granulations (Table IV).

The 2 grades of carboxylated vinyl acetate copolymers, at a 30% concentration in the coat granulation produced tablets with a disintegration time in intestinal fluid which exceeded 2 hr. At a 20% polymer concentration, when granulation fines below 60 mesh were removed, satisfactory *in vitro* enteric properties were obtained with as little as 1% magnesium stearate and 2% PVP (Table IV).

PVAc, due to its swelling properties, could not be successfully developed as an enteric coat by the granulation method described here. All formulas studied prematurely liberated the soluble dye in gastric fluid. Plasticization did not improve this property.

Of the 4 lubricant-intergranular enteric bonding agents (Table III), at the range of concentrations studied, magnesium stearate was found to be the most efficient. However, none of the intergranular bonding agents when incorporated alone resisted the action of gastric fluid. It was also necessary to employ an efficient granule binder (PVP) to prevent tablet splitting during *in vitro* disintegration testing. The compositions of the 4 final enteric compression coating formulations are summarized in Table IV. When lactose was replaced with calcium sulfate dihydrate as the coating diluent in these formulations, the coated tablets split in simulated gastric fluid in 30 min.

Isopropanol alone did not prove to be a satisfactory granulating solvent for any of the polymer systems studied. It was necessary to use an intermediate polarity mixed organic solvent system (Table IV) as a granulating agent. Also, it was found advantageous to use a warm solvent system, with the exception of the CAP granulation.

The mechanism of *in vitro* disintegration of each formulation was studied by subjecting the coated tablets to the following disintegration tests in the U.S.P. apparatus: (*a*) 3 hr. in U.S.P. XVI simulated gastric fluid, (*b*) and (*c*) 1 hr. in U.S.P. XVI simulated gastric fluid followed by immersion in U.S.P. XVI simulated intestinal fluid with and without pancreatin. The CAP formulations were also subjected to disintegration test in intestinal fluids of pH 6.9 and 7.5. The tablets were evaluated during the above tests for leaching (release of soluble dye from the core through the coat), intergranular corrosion (erosion of the coat surface particularly along the granular boundaries), coat splitting, swelling, or disintegration.

The PVM/MA 169 compression coating formulations satisfactorily resisted gastric fluid *in vitro* for up to 1 hr. with slight swelling. The tablets compression coated with PVAc-C-H and PVAc-C-L formulations resisted gastric fluid *in vitro* for 2 hr. after which they demonstrated substantial coat erosion and slow leaching of the core ingredients. Tablets compression coated with CAP were intact after 3-hr. exposure to simulated gastric fluid. Pancreatin had no effect on the disintegration of tablets coated with any of the 4 formulations.

Physical and Mechanical Properties

Selected physical and mechanical properties of the 4 compression coating formulations having satisfactory enteric properties by *in vitro* tests, were evaluated as follows.

Particle Size Distribution.—The particle size distribution of the 4 coat formulations is given in Table V. To prevent or adequately retard intergranular corrosion in gastric media, it was found necessary to remove the fines below 60 mesh from the coat formulations *2*, *3*, and *4* (Table IV). The

TABLE IV.—FINAL ENTERIC COMPRESSION COATING FORMULATIONS

No.	Polymer and % Concn.	Diluent Lactose, %	Granulating Solvent *q.s.*	Triacetin, %	PEG 6000, %	Mag. Stearate, %	PVP, %	Disintegration Time, min.[a]
1a[b]	...	70	Gelatin–acacia soln.	...	...	30	...	72
1b[b]	CAP (30)	48.5	Ethyl acetate–isopropanol	10[c]	1.5	5	5	
2	PVM/MA (10)	84	Hot acetone (50°)	...	...	3	3	80
3	PVAc-C-H (20)	75.5	Ethyl acetate–isopropanol (1:1) 60°	...	1.5	1	2	90
4	PVAc-C-L (20)	75.5	Ethyl acetate–isopropanol (1:1) 60°	...	1.5	1	2	90

[a] Average disintegration time (in min.) in simulated intestinal fluid during U.S.P. XVI test. [b] Seventy per cent of *1a* and 30% of *1b* were mixed to give enteric compression coating formulation *1*. [c] The same concentration of diethyl phthalate was also an effective enteric plasticizer.

TABLE V.—SIEVE ANALYSIS[a] OF THE 4 COAT GRANULATIONS

Coat Formulations	On Screen, % No. 12	No. 16	No. 20	No. 40	No. 60	Through No. 60, %
CAP	...	20.57	31.20	24.11	8.51	15.60
PVM/MA 169[b]	0.23	2.03	10.78	53.91	33.02	...
PVAc-C-H[b]	...	0.43	11.84	59.20	28.53	...
PVAc-C-L[b]	...	0.39	3.91	50.78	44.92	...

[a] Determined with a Cenco-Meinzer sieve shaker at setting No. 1 for 5 min. [b] Coat formulations were freed of fines below 60 mesh.

percentage of fines removed and discarded averaged about 5% for granulations *2*, *3*, and *4*.

The selected coat formulations of each polymer, compressed over cores of calcium sulfate dihydrate and lactose, were evaluated by the following tests.

Hardness.—An average hardness of 10 coated tablets, randomly selected, was determined on a Dillon prototype direct force hardness tester.[4] In a comparison of Dillon, Monsanto, and Strong Cobb, the following relationships were found (5): 1 unit on the Dillon = 1 unit on the Monsanto, and 1.5 unit on the Dillon = 1 unit on the Strong Cobb.

Compression-coated tablet hardness was found to be a very important property affecting the enteric properties of the tablets. The approximate optimum hardness range to achieve *in vitro* enteric properties for the 4 coat formulations is summarized in Table VI. Tablets having a hardness below the optimum hardness range were subject to core composition leaching, and except for tablets coated with CAP, those which had a hardness above the optimum hardness range did not disintegrate in simulated intestinal fluid within 2 hr.

TABLE VI.—OPTIMUM HARDNESS RANGE FOR ENTERIC COMPRESSION COATED TABLETS

No.	Coat Formulation	Optimum Hardness Range, Kg. Calcium Sulfate Dihydrate and Lactose Cores[a]	Barium Sulfate Cores[a]
1	CAP	4–6	4–6
2	PVM/MA 169	24–25	15–18
3	PVAc-C-H	24–25	22–25
4	PVAc-C-L	24–25	22–25

[a] The compositions of the core tablets are given under *Experimental*.

Friability.—The friability of the tablets was determined in a 5.5-in. diameter baffled cylinder, revolving at 50 r.p.m. (6). A loss in tablet weight of less than 1% in 20 tablets for 100 rev. was not considered significant. At their optimum hardness range, none of the tablets were friable, according to this test.

Weight Variation.—The enteric compression-coated tablets as well as the cores were found to vary less than 1% in weight.

Horizontal Expansion and Centering of Cores.—At a machine speed of 250 tablets/min. and with the same die fill and pressure settings, 1500 tablets of the 4 successful coat formulations with lactose and calcium sulfate cores were collected and observed for visible off-centering. The percentage increase in diameter and decrease in crown thickness of a sample of the sectioned exposed cores of the coated tablets were compared with uncoated cores (Table VII). In every case, the calcium sulfate cores underwent less dislocation but demonstrated a greater decrease in crown thickness than did the lactose cores. Core composition appeared to have a much greater effect on centering properties than did the polymer coat formulation.

Minimum Coat Thickness.—Cores with an average weight of 120.0 mg., average diameter of 7.93 mm., and an average crown thickness of 3.20 mm. were compression coated with varying thicknesses of the 4 different coat formulations, keeping the hardness of the coated tablets within the optimum range for each coating. The minimum coat thickness required to give adequate enteric protection by *in vitro* standards was 1.3 mm. for all formulations.

[4] W. C. Dillon and Co., Inc., Van Nuys, Calif.

TABLE VII.—INFLUENCE OF CORE COMPOSITION ON THE OFF-CENTERING OF TABLETS COMPRESSION COATED WITH CAP, PVM/MA 169, PVAc-C-H, AND PVAc-C-L

Coat Formulation	Core Comp.	Av. % Off-Centering	Decrease in Crown Thickness, %	Increase in Tablet Core Diam., %
CAP	Lactose	7.2	24.03	2.14
CAP	$CaSO_4$	5.0	31.99	2.40
PVM/MA 169	Lactose	7.5	15.37	3.15
PVM/MA 169	$CaSO_4$	6.0	31.28	1.15
PVAc-C-H	Lactose	5.18	20.11	1.50
PVAc-C-H	$CaSO_4$	2.2	25.52	1.00
PVAc-C-L	Lactose	5.0	13.41	3.39
PVAc-C-L	$CaSO_4$	2.2	31.29	2.14

Storage Stability Tests.—The final tablet formulations of each polymer with the core compositions were stored in capped bottles at 50 ± 1°, 25 ± 2°, and 2 ± 1° for a period of 8 weeks. The *in vitro* disintegration properties of none of the 4 final tablet formulations were affected by any of the above storage conditions. The tablets, enteric compression-coated with PVAc-C-H and PVAc-C-L formulations progressively increased in hardness by 5 to 10 Kg. when stored for 8 weeks at 50°. This increase in hardness did not affect the disintegration properties of the formulations.

In Vivo Evaluation[5]

The preliminary *in vivo* evaluation of the enteric compression coated tablets was based on an X-ray examination of the tablets in the gastrointestinal tract of human volunteers, using 3 to 5 volunteers for each coat formulation.

Each volunteer was given 3 tablets. The second tablet was administered 2 to 3.5 hr. after the first tablet, and the third tablet was administered 1 to 3 hr. after the second tablet. The first and third tablets were of the same size and the second was of a different size ($^3/_8$-in. and $^7/_{16}$-in. tablets with 0.25-in. and $^5/_{16}$-in. barium sulfate cores, respectively). The radiographs were taken at calculated intervals after localization of the tablets using a Fluoricon image intensifier. Figures 1 to 4 are photographic reproductions of the X-ray films as they appear on a viewer.

CAP formulations were found to be intact in the stomach of human volunteers as long as 4 hr. and 15 min., while PVAc-C-L and PVAc-C-H tablets were found intact as long as 4 hr. and 35 min. and 4 hr. and 25 min., respectively, following administration. In the intestinal tract, CAP formulations were found to disintegrate within 6 hr. and 45 min. total time following administration, while PVAc-C-L and PVAc-C-H tablets were found to disintegrate within 6 hr. and 45 min. and 7 hr. and 30 min. or less, respectively.

[5] The authors are indebted to Dr. P. L. Webster, Radiologist, and Mr. James Barbee, Student Health Center, Purdue University, for their help in this study.

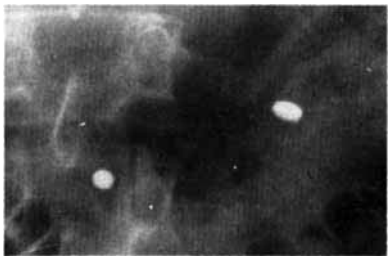

Fig. 1.—Film A_1 for cellulose acetate phthalate, illustrating second and third tablets intact in the stomach after 7 hr. and 10 min. and 3 hr. and 10 min., respectively.

Fig. 2.—Film A_4 for cellulose acetate phthalate, illustrating the third tablet disintegrating in the intestinal tract after 6 hr. and 50 min.

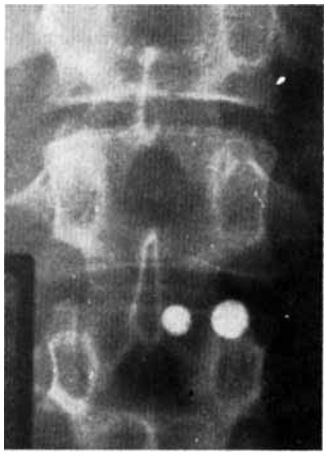

Fig. 3.—Film F_1 for PVAc-C-H formulation, illustrating second and third tablets intact in the stomach after 4 hr. and 27 min. and 3 hr. and 22 min., respectively.

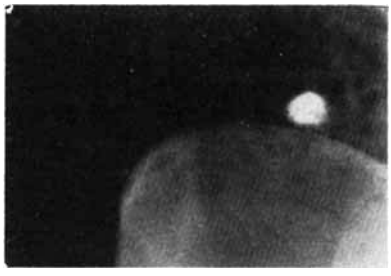

Fig. 4.—Film D_2 for PVAc-C-H formulation, illustrating the first tablet disintegrating in the intestinal tract after 6 hr. and 49 min.

In the case of tablets enteric compression-coated with PVM/MA 169, 1 tablet was found broken in the stomach after 6 hr. and 25 min. in 1 volunteer, but 4 tablets were found to be intact in the intestinal tract of other subjects where the disintegration time appeared to be 6 hr. and 35 min. or less. Thus, this formulation appears to have an enteric coating potential. The failure of 1 of the tablets in the stomach is due to the slow swelling rate of this polymer at gastric pH and the unduly long sojourn of the tablet in the stomach.

DISCUSSION

In this study, the respective polymers (Table I) were dry mixed with the coat diluent and granulated with an organic solvent system (Table IV) in which the polymer was soluble. This simple reproducible granulation–polymer incorporation method had the potential advantage, in addition to circumventing a formal coating step, of permitting the convenient uniform incorporation of higher proportions of polymers with much less solvent than would be feasible if the polymer was added in solution form.

The main objective of an enteric compression coating is to produce a strongly bonded coat layer over the core, without cracks or flaws, so that the coat will resist the penetration of gastric fluid and leaching of the core ingredients. This study indicated that this objective can be approached using the direct coat granulation method described and the following principles.

(*a*) Use of materials which weaken the interparticular bond. Shotten and Ganderton (7) refer to such materials as interparticular bonding agents. An interparticular bonding agent produces a strongly bonded tablet thereby minimizing premature intergranular corrosion and coat failure. In this application interparticular bonding agents were sought which were also enteric.

(*b*) Use of a "granule binder." This serves as a strong adhesive material and holds the granules together during exposure to gastric fluid.

(*c*) Removal of fines and fine granules. Petch (8) has reported that a coarser granule fraction gave a stronger bond.

One of the critical factors in this study, in addition to the selection of the polymeric material, was the role played by the nonpolymeric coating diluent in determining the enteric characteristics of the coat. To visualize gastric fluid permeability into the compression coatings, tablets were sectioned following

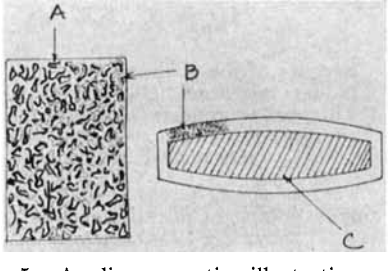

Fig. 5.—A diagrammatic illustration of the probable structure of the successful enteric compression coating layer. Key: A, matrix of partially coated granules; B, bed of intergranular enteric bonding agent—granule binder mixture; C, core.

varying periods of disintegration testing, and microscopically examined for soluble dye migration through the coat layer. Calcium sulfate dihydrate, due to its water absorbant character, drew test fluid into the coating resulting in coat failure. Lactose, though completely soluble, did not have the water-sorptive character of calcium sulfate, and was a satisfactory coat diluent in this study. Microscopic examinations of tablet cross sections also indicated that enteric compression coatings were produced when the matrix of partially coated granules is bound by the intergranular enteric bonding agent forming an impervious coat as illustrated in Fig. 5.

The greater off-centering found with the lactose cores in all of the compression-coated tablets, regardless of coat formulation (Table VII), is probably related to the greater expansion of the lactose cores during recovery which accentuates the core dislocation (9). Experiments by Kaplan and Wolff (10) have shown that calcium sulfate dihydrate is more compressible than lactose under the same conditions.

Of the 4 carboxyl-containing polymers evaluated in this study, 3 were subject to slow swelling or coat erosion in gastric fluid *in vitro*. The principle of enteric disintegration of PVM/MA 169, PVAc-C-H, and PVAc-C-L formulations appeared to be slow solubility at lower simulated gastric pH values and faster rates of solubility at higher simulated intestinal pH values. Bauer and Masucci (11) found that the disintegration of CAP coatings in intestinal contents of pH 6.9 is the result of the hydrolytic action of intestinal esterases. In this experiment pancreatin was found to have no influence on the disintegration of tablets compression coated with CAP in intestinal fluids of pH 6.9 and 7.5. This probably is due to the modification of the enteric properties of the polymer by the plasticizer, triacetin.

PVM/MA 169, which most quickly swelled *in vitro* was observed to fail in 1 subject *in vivo* as an enteric coating. A partially esterified derivative of the polymer (12, 13) with a slower dissolution rate would probably produce a more satisfactory enteric coating.

CONCLUSIONS

A method has been developed for the incorporation of slowly soluble polymer materials in a diluent by simple mixing and standard granulation procedures to produce enteric compression coatings. The granulations thus produced with each of 4 polymer materials when mixed with an intergranular enteric bonding agent, magnesium stearate, and an effective granule binder, polyvinylpyrrolidone, and compression coated at an optimum hardness range was found to be enteric by *in vitro* disintegration tests. The formulation factors, physical and tablet properties of the formulations, were investigated for their effect on *in vitro* enteric properties. *In vivo* evaluation using an X-ray technique and human volunteers indicated that 3 of the polymer systems studied were enteric and that the reported simplified method of polymer incorporation to produce enteric compression coatings is feasible.

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Evaluation of Amylose as a Dry Binder for Direct Compression

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Because of the economies of direct compression, there exists a need for good dry binders which will effect compression of drugs at relatively low filler-to-drug ratios. This paper reports an evaluation of amylose for this purpose. The results on compression effects, physical properties, stability, and drug availability show that this material has the characteristics desired of the ideal binder.

THE DEVELOPMENT of forced-feed mechanisms for tableting presses and relatively free flowing tablet excipients has stimulated interest in commercial tableting by direct compression (1). The objective of direct compression is to produce pharmaceutically elegant tablets with a minimum of processing time and cost. Since many drugs cannot be compressed directly, 1 or more agents must be added to impart suitable compression properties. Unfortunately, many of these addi-

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