TABLE II.—ANALYTICAL DATA FOR ESTERS

Compd.	C Found	C Calcd.	H Found	H Calcd.	N Found	N Calcd.	HCl Found	HCl Calcd.	
I	55.75	55.46	6.91	6.98	5.44	5.39	13.77	14.07	$C_{12}H_{17}NO_3 \cdot HCl$
	55.68		6.71		5.38		13.79		
II	58.45	58.40	7.53	7.71	4.97	4.86	12.68	12.67	$C_{14}H_{21}NO_3 \cdot HCl$
	58.55		7.47		4.81				
III	57.12	57.01	7.29	7.36	5.19	5.11	13.21	13.33	$C_{13}H_{19}NO_3 \cdot HCl$
	57.17		7.27		5.02				
IV	58.31	58.40	7.95	7.71	4.81	4.86	12.66	12.67	$C_{14}H_{21}NO_3 \cdot HCl$
	58.26		7.62		5.09				
V	59.59	59.66	7.76	8.01	4.73	4.64	11.82	12.08	$C_{15}H_{23}NO_3 \cdot HCl$
	59.73		8.01		4.58				
VI[a]	59.98	59.66	7.85	8.01	4.68	4.64	11.82	12.08	$C_{15}H_{22}NO_3 \cdot HCl$
VII	64.22	64.35	6.67	6.60	4.38	4.17	10.46	10.85	$C_{18}H_{21}NO_3 \cdot HCl$
	64.18		6.39		4.12				
VIII	65.03	65.21	6.75	6.91	3.89	4.00	10.42	10.42	$C_{19}H_{23}NO_3 \cdot HCl$
	64.88		6.64		4.04				

[a] Insufficient sample for check analysis.

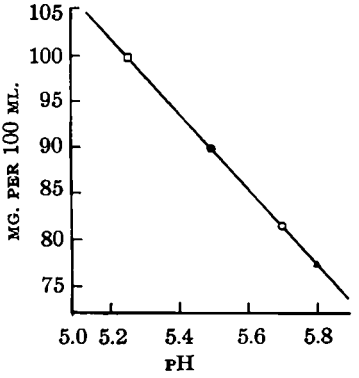

Fig. 1.—Plot of pH values *vs.* 0.03 *M* solution milligrams per 100 ml. Key: △, β-methylaminoethyl-*p*-ethoxybenzoate HCl (I); ○, β-ethylaminoethyl-*p*-ethoxybenzoate HCl (III); ●, β-*n*-butylaminoethyl-*p*-ethoxybenzoate HCl (V); and □, β-benzylaminoethyl-*p*-ethoxybenzoate HCl (VII).

ethoxy benzoic acid (5×10^{-5} *M*) in isopropyl alcohol came at 255 mμ. The alcohol of Compound VII (5×10^{-5} *M*) in isopropyl alcohol gave an absorbance reading of 0.40 at 205 mμ; the absorbance dropped rapidly before reaching 220 mμ, and at 230 mμ approached zero and remained there. The alcohol in Compound VII contained a benzyl group; since it did not change the general curve, it may be assumed that the alcohols just shift the maximum peak toward the longer wavelength. The shoulder or irregularity in the curve between

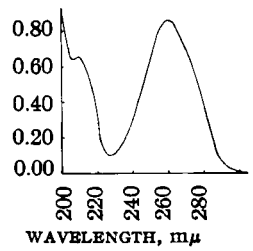

Fig. 2.—General curve which all compounds followed.

200 and 215 mμ may be due in part to the alcohol portion of ester. Six of the compounds had a molecular extension coefficient of 17,200, and Compounds V and IV had values of 17,100 and 17,800, respectively.

The surface tension results seem to follow the observations of Weiser (3) that the surface tension of water is lowered most strongly by organic compounds with a long chain of carbon atoms or with one or more benzene rings. The values obtained indicate that the substituent groups on the nitrogen influence the surface tension more than the benzoic acid group does.

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Modified U.S.P. Tablet Disintegration Apparatus

By LEONARD L. KAPLAN

IN AN EARLIER REPORT (1) a modification of the U.S.P. tablet disintegration apparatus was described which creates more uniform attrition on all sides of the test tablet surfaces and serves to obviate the need for the disks in tablet disintegration testing.

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The modification consists of a thin flexible insert placed inside the glass tubes of the apparatus at the lower end in contact with the bottom stainless steel wire cloth. The dimensions of this insert are external diameter 21.5 mm., internal diameter 15 mm., wall thickness 3.25 mm., and insert thickness 3.5 mm. The U.S.P. XVI specifies a basket rack assembly consisting of six open glass tubes,

TABLE I.—PRODUCTS USED IN THIS STUDY

Product	Therapeutic Class	Tablet Wt., mg.	Tablet Diam., in.	Product	Therapeutic Class	Tablet Wt., mg	Tablet Diam., in.
1	Enzyme	600	7/16 flat face	13	Antihistamine	150	5/16 reg. concave
2	Lipotropic	570	13/32 reg. concave	14	Vasodilator	730	1/2 reg. concave
3	Vitamin B_1	240	5/16 reg. concave	15	Digestant	415	3/8 reg. concave
4	Vitamin B_1	198	5/16 reg. concave	16	Multivitamin	480	7/16 square
5	Vitamin C	270	5/16 reg. concave	17	Muscle relaxant	480	7/16 reg. concave
6	Tranquillizer	205	5/16 reg. concave	18	Energizer	103	6/32 reg. concave
7	Analgesic	425	13/32 reg. concave	19	Digestant	890	1/2 reg. concave
8	Multivitamin	395	13/32 reg. concave	20	Multivitamin	450	1/2 oval
9	Enzyme	620	1/2 reg. concave	21	Vasodilator	600	13/32 reg. concave
10	Vasodilator	550	7/16 reg. concave	22	Multivitamin	850	15/32 oval
11	Diuretic	560	7/16 flat face	23	Digestant	1000	5/8 flat face
12	Antacid	777	15/32 flat face	24	Antihistamine	135	9/32 flat face
				25	Calcium pantothenate	200	5/16 reg. concave

each 7.75 cm. long, and each having an inside diameter of approximately 21.5 mm. (2). Thus, the net effect of the insert is to decrease the inside diameter of the lower end of the glass tube in contact with the wire cloth to 15.0 mm.

For any fluid of constant density passing through a stream tube, the product of the cross-sectional area and velocity is constant at all points along the stream tube (3). This is shown by

$$Q = A_1V_1 = A_2V_2 = K \qquad \text{(Eq. 1)}$$

where Q is the flow rate constant K, A is the cross-sectional area of the stream tube, and V is the velocity of the fluid in motion. This equation of continuity states that in steady flow, the mass of fluid passing all cross sections of a stream tube per unit of time remains constant. Therefore, as the cross-sectional area, A_1, of the tube is decreased by the insert to A_2, the velocity of the fluid passing through the tube at that point increases proportionately from V_1 to V_2 to maintain the constant flow rate Q. This increase in fluid velocity at the constricted point creates a turbulence as the basket rack assembly rises and falls. This turbulence causes the tablets to "bob" up and down with greater action, resulting in more uniform attrition to all of the tablet surfaces and prevents adhesion of the tablets to the bottom wire cloth.

EXPERIMENTAL

Twenty-five commercially available uncoated compressed tablet products were subjected to tablet disintegration testing by three methods: (*a*) U.S.P. XVI apparatus, (*b*) U.S.P. XVI apparatus with disks, and (*c*) U.S.P. apparatus with insert

TABLE II.—RANGE OF DISINTEGRATION RESULTS[a]

Product	Minutes — Method A[b]		Method B[c]		Method C[d]	
1	15–18	(3)	12–30	(18)	10–11	(1)
2	27–36	(9)	10–20	(10)	12–16	(4)
3	2–4	(2)	2–3	(1)	1–2	(1)
4	1–3	(2)	1/2–4	(3–1/2)	3/4–1–1/2	(3/4)
5	4–11	(7)	3–7	(4)	2–3	(1)
6	7–11	(4)	5–5–1/2	(1/2)	5–5–1/2	(1/2)
7	8–70+		3–70+		3–70+	
8	1–8	(7)	2–5	(3)	1–5	(4)
9	29–38	(9)	17–22	(5)	20–23	(3)
10	3–6	(3)	3–5	(2)	3–5	(2)
11	1/2–1	(1/2)	1/2	(0)	1/2	(0)
12	1–1–1/2	(1/2)	1–2	(1)	1/2–1	(1/2)
13	2–4	(2)	1–4	(3)	1/2–3	(2–1/2)
14	42–70+		20–47	(27)	23–29	(6)
15	70+		14–17	(3)	12–15	(3)
16	31–60	(29)	4–11	(7)	17–26	(9)
17	6–10	(4)	7–10	(3)	4–6	(2)
18	2–1/2	(0)	2–2–1/2	(1/2)	2	(0)
19	35–40	(5)	12–13	(1)	25–32	(7)
20	50–70	(20)	15–23	(8)	28–40	(12)
21	70+		10–49	(39)	48–57	(9)
22	43–63	(20)	15–22	(7)	25–32	(7)
23	70+		8–11	(3)	17–30	(13)
24	1/2–2	(1–1/2)	1/2–1	(1/2)	1/2–2	(1–1/2)
25	3–4	(1)	2	(0)	2–3	(1)

[a] Figures in parentheses represent the range spread in minutes for each product tested by each of the three methods. [b] U.S.P. apparatus. [c] U.S.P. apparatus with disks. [d] U.S.P. apparatus with insert modification.

TABLE III.—STATISTICAL ANALYSIS

Product	Test Method	Arithmetic Mean, min.	S.D.	Coefficient of Variation, %
1	A[a]	16.7	1.2	7.3
	B[b]	19.3	6.6	34.2
	C[c]	10.8	0.4	3.9
2	A	30.7	3.5	11.5
	B	12.6	3.6	28.6
	C	13.6	2.4	17.2
5	A	5.9	2.3	38.1
	B	4.3	1.1	25.1
	C	2.6	0.6	21.2
6	A	8.4	0.9	10.2
	B	5.1	0.4	7.8
	C	5.3	0.3	4.9
9	A	32.8	3.0	9.3
	B	20.3	1.5	7.3
	C	21.9	0.4	1.8
16	A	39.0	14.8	37.8
	B	6.4	3.5	54.4
	C	20.2	2.9	14.1
17	A	7.4	1.0	13.2
	B	7.9	1.2	15.4
	C	4.9	0.6	11.6
19	A	37.3	0.6	1.6
	B	12.2	0.8	6.5
	C	28.3	1.3	4.5
20	A	63.4	4.5	7.2
	B	18.1	2.6	14.2
	C	34.0	3.5	10.4
22	A	55.5	7.8	14.1
	B	18.6	2.2	12.0
	C	28.8	1.2	4.2

[a] U.S.P. XVI apparatus. [b] U.S.P. XVI apparatus with disks. [c] U.S.P. XVI apparatus with insert modification.

modification. Water maintained at 37° was used as the disintegrating medium as specified in the U.S.P. XVI monograph for uncoated tablets. Eighteen tablets of each product were tested using each method. The products used in this study and their therapeutic class, tablet weight, and tablet diameter are listed in Table I.

The results of these disintegration studies in terms of range for the 18 tablets tested for each product are reported in Table II. Observations were terminated at the 70-minute period for the purpose of this study. The figure in the parenthesis represents the range spread in minutes for each product tested by each of the three methods.

ANALYSIS OF RESULTS

Those products in which the mean average disintegration times were less than 5 minutes for all three methods and those products in which the disintegration time end points exceeded 70 minutes are omitted from the statistical analysis of this report. From a practical standpoint, the disintegration times in fractions of minutes recorded for the quickly disintegrating products could not be precisely noted, and therefore would not be valid in the statistical analysis. For purposes of laboratory expediency, the longer disintegrating tablet studies were terminated at 70 minutes and therefore also are not included in this analysis. This left ten products, identified in Table I as products 1, 2, 5, 6, 9, 16, 17, 19, 20, and 22 for the statistical analysis.

The arithmetic mean, standard deviation, and coefficient of variation for the ten products tested by each of the three disintegration methods are reported in Table III. The consistently lower standard deviation and coefficient of variation obtained with the insert modified apparatus (*Method C*) compared to the U.S.P. apparatus (*Method A*) and the U.S.P. apparatus with disks (*Method B*) indicates the degree of variance in the disintegration results caused by the apparatus. The coefficient of variation as a determinant of the relationship between the arithmetic mean and the standard deviation permits comparison of the relative variability introduced by each of the three disintegration methods. The chi-square test determining the goodness of fit of the actual data to the hypothesized distribution was applied to the coefficients of variation and standard deviations of the ten products ranked for each of the three test methods.[1] With four degrees of freedom, the tabled 1% value of chi-square is 13.277. For the coefficient of variation data, chi-square is 13.2, with a probability value of $p \backsimeq .01$. For the standard deviation data, chi-square is 17.4, for which p is less than 0.01. Hence, the hypothesis of a uniform distribution is rejected, the acceptable alternative is that the insert modification provides a disintegration method with significantly less apparatus induced variance than the present U.S.P. apparatus, with and without disks.

CONCLUSIONS

Disintegration studies conducted on 25 commercially available uncoated, compressed tablet products indicate a wide range in results for each product.

Comparative determinations of the apparatus induced variance of the three disintegration methods indicate that the U.S.P. XVI apparatus, with or without disks, introduces a significantly greater degree of variance than the insert modified apparatus.

Based upon the results of this study, the insert modified apparatus warrants consideration as an improved laboratory control method for the *in vitro* testing of tablet disintegrations.

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[1] A formula for chi-square algebraically simplified for this study is

$$\chi^2 = \frac{n}{N}(\Sigma f^2 - N^2)$$

where n is the number of methods ranked, N is the number of products tested, and f is the frequency of results per ranking column.