Notes

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Techniques for Manufacturing Pharmacy. II.[1] Prediction of Tableting Troubles such as Capping and Sticking. (2)

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Previously,[1] a device for measurement of the state of binding between a tablet surface and punch face was proposed to see the ability of a powder material to form a "good" or "bad" tablet, in combination with determination of passive pressure of a lower punch.

The present work consisted of the following.

(a) Four factors, that is, pressure of an upper punch loaded, passive pressure of a lower punch, lower punch force to extrude a tablet, and slipping force of tablet surface, were determined during direct compression of familiar tablet additives.

(b) Material which formed a "bad" tablet (particularly with respect to capping and/or sticking) was mixed with another material to form a "good" tablet and the four factors mentioned above were determined.

(c) A mixture consisting of two components, which still formed a "bad" tablet, was mixed with another material to form a "good" tablet and the four factors were also determined.

Prediction of the ability of a given material or mixture to form a "good" or "bad" tablet was investigated in a previous work,[1] and a method for improving a given material or a mixture which forms a "bad" tablet is presented here.

Experimental

Apparatus——The compression fixture for determination of slipping force of a tablet surface and passive pressure of lower punch was the same as before.[1] To monitor the pressure of the loaded upper punch and lower punch force to extrude a tablet, the strain gauges (type S-104, Shinkoh Tsushin Co., Ltd., resistance 119.3 Ω, gauge factor 1.92) were connected in series; power supply unit (type DS 6/MTY-A, Shinkoh Communication Ind. Co., Ltd., Kanagawa), dynamic strain amplifier (type DS 6/MTY-A, Shinkoh Communication In. Co., Ltd.), and Visigraph FR-301 (San-ei Instrument Co., Ltd., Tokyo) were the same series as in measurement of the slipping force of a tablet surface and the passive pressure of lower punch.

Materials——Pharmaceutical materials used in the experiments were plain compound or mixtures which are widely used by direct tableting as tablet additives, and the formulae of these materials are shown in Table I. These materials were mixed thoroughly at need by a V-shaped mixing apparatus (Tokuju Kosakusho, Tokyo).

When four factors, that is, slipping force of a tablet surface, passive pressure of lower punch, pressure of loaded upper punch, and lower punch force to extrude a tablet, were to be determined, suitable amount of each powder material was used for making a tablet, depending on the density of a material.

Result and Discussion

Logically, knowledge of the physical properties of the material, such as moisture content, porosity, particle size, fluidity, angle of repose, *etc.*, should be helpful in understanding the relationship between tableting results and materials. To measure many of the physi-

1) Part I: S. Naito and K. Nakamichi, *Chem. Pharm. Bull.* (Tokyo), 17, 2507 (1969).
2) Location: *Yamashina Misasagi, Higashiyama-ku, Kyoto, 607,* Japan.

Table I. Formulas of Materials Compressed into Test Tablets

Material No.	Trade name or compound name	Composition	Manufacturer
1	Per-filler	mixture (a)	Fr.
2	Solider	mixture (a)	Fr.
3	CMC NS-300	Na carboxymethylcellulose	G.
4	ECG 505	Ca cellulose gluconate	G.
5	Neusilin S_1	$MgO \cdot Al_2O_3 \cdot 2SiO_2$	Fu.
6	Neusilin SG_1	$MgO \cdot Al_2O_3 \cdot 2SiO_2$	Fu.
7	Neusilin FH_2	$MgO \cdot Al_2O_3 \cdot 2SiO_2$	Fu.
8	Neulilin FL_2	$MgO \cdot Al_2O_3 \cdot 2SiO_2$	Fu.
9	Zeopan		Fu.
10	Avicel	cellulose, fine crystal	A.
11	Kyowa Suimagu	magnesium hydroxide	K.
12	calcium hydrogen phosphate, anhydride		K.
13	anhydrous calcium hydrogen phosphate, fluffy		K.
14	anhydrous calcium hydrogen phosphate, ponderous		K.
15	magnesium silicate (JP VII)		K.
16	magnesium silicate, fluffy		K.
17	magnesium silicate, ponderous		K.
18	calcium hydrogen phosphate (JP VII)		K.
19	aluminum silicate synth. (JP VII)		K.
20	aluminum silicate, super-fluffy		K.
21	aluminum silicate, fluffy		K.
22	aluminum silicate, ponderous		K.
23	anhydrous aluminum hydroxide gel (JP VII)		K.
24	anhydrous aluminum hydroxide SN		K.
25	anhydrous aluminum hydroxide S-100		K.
26	magnesium oxide (JP VII)		K.
27	magnesium oxide, ponderous		K.
28	magnesium oxide, granules		K.
29	Sanalmin A	mixture of aluminum hydroxide gel and magnesium hydroxide	K.
30	Sanalmin		K.
31	Licamit U-100	calcium hydrogen phosphate	K.
32	Neusilin SG_2, neutral, fine particles		Fu.
33	Neusilin SG_2, fine particles		Fu.
34	Neusilin S_2, super-fine particles		Fu.
35	Neusilin FL_2, neutral		Fu.
36	Neusilin FH_1		Fu.
37	Neusilin FL_1		Fu.
38	Neusilin, neutral, super-fluffy		Fu.
39	magnesium silicate SN		K.
40	aluminum silicate synth. SN		K.
41	phenovalin (JP VII)		

(a) A special formula which cannot be published.
Fr.: Froint Sangyo Co. Ltd. (Tokyo)
G.: Gotoku Yakuhin Kogyo Co. (Tokyo)
Fu.: Fuji Kagaku Kogyo Co. Ltd. (Toyama)
A.: Asahi Kasei Kogyo Co. Ltd. (Tokyo)
K.: Kyowa Kagaku Kogyo Co. Ltd. (Tokyo)
Phenovalin is not one of tablet additives and was used for comparison.

cal properties at constant is very difficult in practice and, therefore, the purpose of the present investigation was to find a way to improve the formula of a material which formed a "bad" tablet by considering the tableting results from four factors of tableting, such as slipping force of tablet surface, passive pressure of lower punch, pressure of upper punch loaded, and lower punch force to extrude a tablet.

"Excellent" in the results of tableting means tablets which passed the rules shown in the footnote to Table II. Not all of the "Excellent" materials could always succeed in tablet

Table II. Data of Pressure of Upper Punch Loaded, Lower Punch Force to extrude Tablet, Passive Pressure of Lower Punch and Slipping Force of Tablet Surface obtained from Tablet Additives

Material	UP	PLP	LP	SF			TW	J	Bi	S	C	R	Cr	M
				1st	2nd	3rd								
1	728±270	1025±353	92±25	11±10	7±4	7±4	0.55	G	−	−	−	−	−	
1-16			302±134				0.64	B	−	−	+	−	−	
1-23			722±311				0.60	B	+	−	+	−	−	
1-41			395±160				0.57	B	−	−	−	−	+	
1-25			1008±227				0.57	G	+	−	−	−	±	
1-28			185±134				0.72	G	−	−	−	+	−	
1-31			160±160				0.75	G	−	−	−	+	−	
1-26			235±42				0.55	E	−	−	−	±	−	
2	385±281	546±202	185±34	6±1	5±0	5±0	0.25	W	−	−	−	−	+	
2-18	416±208	168±101	1252±252	9±3	8±3	9±3	0.34	W	+	−	−	−	+	
2-18-4	1290±551	638±50	840±185	7±6	6±4	6±3	0.54	B	−	−	−	−	+	
2-18-10	1061±302	512±67	622±143	7±4	6±3	4±2	0.50	B	−	−	−	−	+	
2-18-28	832±395	689±202	697±395	10±5	6±2	5±2	0.61	B	−	−	−	−	+	
3	1134±302	521±101	260±76	5±0	5±0	5±0	0.55	B	−	−	+	−	−	
4	3890±634	2318±344	118±34	5±0	5±0	5±0	0.70	G	−	−	−	+	−	
4-2		689±109					0.40	B	−	−	+	−	−	
4-26		328±76					0.50	B	−	−	+	−	−	
4-10		1050±370					0.55	G	−	−	−	+	−	
4-30		764±227					0.55	G	+	−	−	−	−	
4-28		2503±101					0.90	E	−	−	−	±	−	*
5	1362±1092	991±227	470±328	47±30	21±6	23±8	0.50	G	−	−	−	+	−	
5-29				135±32	9±2	9±2	0.42	W	−	+	−	−	+	
5-41			840±647	166±51	14±5	13±4	0.55	W	−	+	−	−	+	
5-23			865±269				0.51	W	−	+	−	−	+	
5-25			596±84				0.45	B	+	−	−	−	+	
5-31			655±277				0.72	B	+	−	+	−	+	
5-16			630±344				0.62	G	+	−	−	−	−	
5-26			479±286				0.40	G	−	+	−	−	−	
5-28			1201±865	10±4	9±3	9±4	0.86	G	+	−	−	+	−	
5-1				17±3	14±2	12±0	0.50	E	−	−	−	+	−	
5-7				12±3	10±0	10±0	0.48	G	−	−	−	+	−	
5-17				5±0	5±0	5±0	0.56	E	−	−	−	±	−	*
5-19				8±0	5±0	5±0	0.43	E	−	−	−	+	−	
5-41-19	842±250	521±176	521±50	42±30	5±1	5±1	0.50	W	−	+	−	−	+	
5-41-17	1477±260	1109±395	260±50	72±41	6±3	6±2	0.59	W	−	+	+	−	+	
5-41-24	1269±166	848±252	764±437	106±83	10±0	10±0	0.50	W	±	+	+	−	+	
5-41-1	1050±208	630±185	454±176	139±107	8±3	8±3	0.56	B	±	+	−	−	−	
5-41-3	1248±510	580±101	252±101	10±9	5±1	5±1	0.54	G	−	−	−	+	−	
5-41-11	1726±270	1268±370	193±59	9±5	6±2	6±2	0.64	E	−	−	−	−	−	
5-41-4	1373±146	1294±151	143±17	5±1	5±0	5±0	0.60	E	−	−	−	−	−	*
5-29-1	926±114	773±25	168±59	7±2	7±1	7±1	0.44	E	−	−	−	+	−	*
5-29-11	1342±166	874±84	118±17	4±1	4±1	4±1	0.53	E	−	−	−	−	−	
6	853±478	697±470	1042±680	273±154	68±30	57±35	0.50	B	+	+	−	+	+	
6-7				8±3	7±3	7±3	0.62	G	+	−	−	−	−	
6-17				5±0	6±1	6±1	0.59	G	+	−	−	−	−	
6-28				11±1	10±2	9±1	0.64	G	+	−	−	−	−	
6-29				17±7	15±8	15±7	0.45	G	−	−	−	+	−	
6-1				5±0	5±0	5±0	0.49	E	−	−	−	−	−	
6-19				5±0	5±0	5±0	0.46	E	−	−	−	−	−	
6-41				106±58	10±0	10±0	0.55	W	−	+	−	−	+	
6-41-12	1165±510	580±59	731±294	8±6	6±3	6±3	0.69	W	+	−	+	−	+	
6-41-15	1435±322	966±244	622±143	88±54	10±8	10±8	0.60	W	−	+	−	−	+	
6-41-19	1092±437	613±92	479±193	1±0	1±0	1±0	0.58	W	−	−	−	−	+	
6-41-4	1414±83	1352±101	151±8	4±1	4±1	4±1	0.60	E	−	−	−	−	−	*

Material	UP	PLP	LP	SF 1st	SF 2nd	SF 3rd	TW	J	Bi	S	C	R	Cr	M
7	936±374	563±244	2100±999	167±131	14±4	14±4	0.43	B	+	−	−	−	+	
8	2517±1414	731±134	319±101	24±14	19±6	18±9	0.44	B	−	−	−	+	+	
9	551±270	269±193	890±647	169±156	86±83	69±69	0.25	B	−	+	−	+	+	
10	177±104	420±50	50±21	5±0	5±0	5±1	0.52	B	−	−	−	−	+	
10–41			260+118				0.55	B	−	−	−	−	+	
10–26			202±34				0.45	E	−	−	−	+	−	
10–28			76±34				0.63	E	−	−	−	−	−	
10–31			76±34				0.65	E	−	−	−	−	−	
10–16			185±84				0.50	E	−	−	−	+	−	
10–23			143±76				0.60	E	−	−	−	−	−	
10–25			185±50				0.50	E	−	±	−	−	−	
10–11		1655±118					0.70	E	−	−	−	−	−	*
11	2486±135	1882±118	143±34	5±0	5±0	5±0	0.82	E	−	−	−	−	−	*
11–2	780±426	244±67	353±143	6±5	4±0	4±0	0.40	W	−	−	−	+	+	
11–28		932±185					0.80	G	−	−	+	−	−	
11–26	1175±676	613±134	647±151	6±2	5±2	5±1	0.60	G	±	−	−	−	−	
11–30		412±50					0.50	G	−	−	−	−	−	
11–2–4	780±458	672±151	462±92	5±2	4±2	4±1	0.45	B	±	−	−	−	+	
11–2–28	936±541	613±134	1184±160	3±0	3±0	3±0	0.49	B	−	−	−	−	+	
11–2–10	842±426	521±101	479±84	5±2	3±1	3±1	0.41	G	±	−	−	−	−	
11–26–4	1435±114	1319±92	529±50	5±2	4±1	4±1	0.70	E	−	−	−	−	−	*
11–26–10	1695±406	1705±252	286±176	9±6	7±4	6±3	0.68	G	−	−	−	−	−	
12	1706±655	1008±193	302±168	405±151	79±60	51±31	1.00	W	+	−	−	−	+	
12–41				277±192	132±130	101±93	0.82	W	−	+	−	−	+	
12–17				13±6	12±5	9±4	0.79	B	−	−	−	−	+	
12–19				7±3	7±2	5±1	0.57	G	+	−	−	−	−	
12–28				14±3	13±2	14±2	0.98	G	−	−	−	+	−	
12–1				4±1	4±1	4±1	0.77	E	−	−	−	±	−	*
12–7				9±2	7±1	7±1	0.67	E	−	−	−	±	−	
12–29				14±2	13±1	12±1	0.55	E	−	−	−	−	−	
12–41–18	770±281	395±134	1285±420	139±121	44±44	33±32	0.55	W	+	+	−	−	+	
12–41–30	790±510	1344±168	773±378	140±98	56±34	46±30	0.50	B	−	+	−	−	−	
12–41–17	1893±125	1344±92	168±17	4±1	4±1	4±1	0.76	E	−	−	−	−	−	*
12–41–1	1539±884	1252±302	227±126	7±2	5±0	5±0	0.72	E	−	−	−	±	−	
13	1279±333	924±185	176±17	SO	245±183	167±131	0.94	B	−	+	−	−	+	
14	2007±510	1184±109	67±67	249±184	170±87	148±61	1.00	W	+	−	−	−	+	
14–2		118±34					0.27	W	−	−	−	−	+	
14–23			907±605				0.65	B	−	+	−	−	−	
14–25			1100±613				0.70	B	+	+	−	−	−	
14–30		613±218					0.64	B	+	−	−	−	−	
14–31			42±0				0.95	G	−	±	−	−	−	
14–41			773±134	10±1	10±1	9±1	0.86	G	−	+	−	−	−	
14–17				17±14	7±1	7±1	0.86	B	+	+	−	−	−	
14–19				8±4	8±4	7±3	0.59	G	−	−	−	−	+	
14–16			328±160				0.80	G	−	+	−	+	−	
14–1				10±4	8±4	8±4	0.68	G	−	−	−	+	−	
14–7				5±1	5±1	5±1	0.65	E	−	−	−	+	−	*
14–10		622±235					0.60	E	−	−	−	+	−	
14–26			302±25				0.73	E	−	−	−	+	−	*
14–28			227±176	24±6	22±9	14±6	1.07	G	−	+	−	−	−	
14–29				15±3	12±2	11±3	0.60	G	−	−	−	−	−	
15	1654±676	1067±504	806±370	253±147	62±62	54±52	0.60	W	−	+	+	−	+	
15–41				105±66	14±2	14±2	0.70	W	−	+	+	−	+	
15–28				6±0	7±1	6±0	0.70	W	−	−	+	−	+	
15–7				3±0	2±1	2±1	0.50	B	+	−	−	−	−	
15–17				1±0	1±0	1±0	0.62	B	+	−	−	−	−	
15–19				5±1	4±1	4±1	0.43	B	−	−	−	−	+	

Material	UP	PLP	LP	SF 1st	SF 2nd	SF 3rd	TW	J	Bi	S	C	R	Cr	M
15–29				6±3	5±1	5±1	0.47	B	+	−	−	−	−	
15–1				4±0	4±0	4±0	0.50	G	−	−	−	−	±	
15–28–23	2683±468	1394±160	1025±664	10±4	7±1	7±1	0.69	W	+	+	+	−	+	
15–28–4	2298±208	882±185	428±109	4±1	4±1	4±1	0.70	G	±	−	−	−	−	
15–28–3	1435±166	546±277	319±34	3±1	3±1	3±1	0.60	G	±	−	−	−	−	
15–28–19	1279±135	680±160	336±76	4±0	4±0	4±0	0.59	G	+	−	−	−	−	
15–28–12	1529±177	1260±479	210±143	4±1	4±1	4±1	0.80	G	±	−	−	−	−	
15–41–19	1144±177	647±193	495±143	98±63	11±7	11±7	0.60	W	±	+	+	−	+	
15–41–22	1778±541	1260±630	470±59	6±2	5±2	5±2	0.68	B	±	−	−	−	+	
15–41–27	1102±333	714±336	378±92	59±35	5±2	5±2	0.60	B	−	−	−	−	+	
15–41–4	1622±177	1075±59	109±17	4±1	4±1	4±1	0.62	E	−	−	−	±	−	*
16	2673±1008	1428±244	470±176	265±229	130±105	101±73	0.60	B	+	+	−	−	−	
17	988±395	680±202	117±34	19±13	15±15	15±7	0.60	B	−	−	−	−	+	
18	884±416	386±118	445±160	196±66	87±28	52±18	0.75	W	−	+	−	−	+	
18–30	874±322	168±126	1402±294	45±34	19±8	18±9	0.60	W	+	+	+	−	−	
18–41				225±90	30±21	28±17	0.60	W	−	+	+	−	−	
18–7				65±59	22±11	16±2	0.55	W	−	+	−	−	−	
18–28		722±327		8±2	8±2	8±2	0.83	B	−	−	+	−	+	
18–1				8±2	7±1	7±0	0.63	B	−	−	+	−	+	
18–17				48±21	24±9	21±8	0.70	B	−	+	−	−	−	
18–29				134±82	30±27	24±13	0.50	B	−	+	−	−	−	
18–26	250±83	185±160	680±470	15±7	13±7	11±6	0.40	B	−	−	−	+	+	
18–10		756±630					0 55	G	−	+	−	−	−	
18–19				4±1	4±2	4±2	0.48	E	−	−	−	−	−	
18–7–24	770±333	748±151	328±260	10±5	8±2	7±2	0.54	G	±	±	−	−	−	
18–7–11	1082±83	1041±126	118±8	5±1	5±1	5±1	0.62	E	−	−	−	−	−	*
18–26–4	1258±666	714±294	638±126	7±4	7±5	4±1	0.72	G	±	±	−	−	−	
18–26–10	863±187	437±67	344±59	6±2	6±1	5±1	0.66	G	−	−	−	+	−	
18–28–22	1134±312	680±176	815±412	5±1	5±1	5±1	0.79	B	+	−	−	−	−	
18–28–27	624±166	370±160	176±67	7±4	7±3	7±3	0.75	G	−	−	−	−	−	
18–30–4	1664±686	1268±260	344±67	12±8	7±3	6±2	0.73	G	−	−	−	−	−	
18–30–10	1217±250	630±109	395±92	8±2	6±2	6±2	0.64	G	−	−	−	−	−	
18–41–19	728±260	537±193	958±344	5±0	5±0	5±0	0.61	W	−	−	−	−	+	
18–41–22	1383±281	983±193	470±218	7±3	5±1	5±1	0 68	W	+	−	−	−	+	
18–41–27	894±354	403±109	302±76	10±1	8±0	8±0	0.69	G	±	−	−	−	−	
18–41–4	1071±83	1025±92	168±17	5±1	5±1	5±1	0.64	E	−	−	−	−	−	*
19	1123±260	1369±202	168±84	142±127	118±107	115±106	0.47	B	−	+	−	+	−	
19–41			529±143				0.45	W	−	−	−	−	+	
19–23			672±328				0.46	B	+	−	+	−	+	
19–25			302±235				0.40	B	+	−	−	−	−	
19–16			260±218				0.48	G	+	−	−	−	−	
19–26			84±59				0.47	G	−	−	−	−	−	
19–28			496±403				0.62	G	+	−	−	−	−	
19–31			260±126				0.63	E	−	−	−	+	−	
20	1154±406	907±521	143±59	24±16	18±11	17±10	0.35	G	−	−	−	−	−	
21	1934±447	731±59	202±118	113±82	84±71	78±61	0.50	B	−	+	−	+	−	
21–41			1209±748				0.68	B	+	−	+	−	−	
21–16			664±302				0.56	B	+	−	−	−	+	
21–23			924±235				0.60	B	+	−	−	−	−	
21–25			1058±210				0.55	B	+	−	−	−	−	
21–28			706±286				0.78	G	+	−	−	−	±	
21–31			546±126				0.82	G	+	−	−	−	−	
21–26			202±59				0.50	E	−	−	−	+	−	
22	1903±572	1243±244	76±76	56±53	45±44	45±44	0.70	B	−	−	−	−	+	
23	SO	1856±571	1016±370	SO	316±297	244±124	0.50	W	+	−	−	−	+	
24	1976±863	1638±496	260±202	26±21	21±18	20±17	0.60	W	±	−	−	−	+	
25	2901±1060	1747±437	1310±395	336±162	55±29	46±21	0.50	W	+	+	+	−	−	
26	759±385	294±67	538±210	358±120	110±65	106±57	0.45	W	+	+	−	−	−	

Material	UP	PLP	LP	SF 1st	SF 2nd	SF 3rd	TW	J	Bi	S	C	R	Cr	M
26–28				94±69	27±3	23±2	0.70	B	−	+	−	−	−	
26–29				205±159	21±7	12±7	0.49	B	−	+	−	−	−	
26–1				8±1	8±2	7±2	0.59	E	−	−	−	−	−	
26–7				6±0	6±0	5±0	0.56	E	−	−	−	±	−	
26–17				7±1	7±1	7±1	0.61	E	−	−	−	±	−	
26–19				8±2	8±2	8±2	0.50	E	−	−	−	−	±	
26–41				96±70	14±3	13±2	0.60	W	−	+	−	−	+	
26–41–11	1082±312	974±235	302±84	9±5	6±1	5±2	0.67	W	+	−	+	−	+	
26–41–19	894±447	621±193	311±210	7±3	8±2	8±2	0.50	B	−	−	+	−	−	
26–41–3	1040±416	689±218	101±76	6±1	6±1	6±1	0.60	G	−	−	−	+	−	
26–41–4	1092±52	899±76	101±17	9±1	9±1	9±1	0.66	E	−	−	−	−	−	*
27	250±156	134±42	151±58	158±156	84±81	58±49	0.50	B	−	+	−	−	−	
28	3868±551	101±76	353±134	80±58	67±62	61±56	0.70	B	−	−	−	+	−	
28–14		1126±202					1.00	E	−	−	−	+	−	
29	988±624	899±420	311±134	36±31	18±10	18±10	0.45	B	−	+	+	−	−	
30	104±0	67±25	42±17	68±67	17±11	11±10	0.30	B	−	−	−	−	+	
30–25			1050±294				0.53	W	+	+	−	−	+	
30–28	1487±863	1604±386	588±50	279±69	80±60	31±24	0.66	W	+	+	−	−	+	
30–31			588±227				0.73	W	−	+	−	−	+	
30–41			1579±605				0.55	W	−	+	−	−	+	
30–16			647±269				0.60	B	−	+	−	−	−	
30–26			579±411				0.45	B	−	+	−	−	−	
30–23	1310±385	1083±319	991±151	60±57	19±8	16±7	0.54	B	+	+	−	−	−	
30–23–4	2454±125	1790±126	160±17	10±1	8±1	8±1	0.63	E	−	−	−	±	−	*
30–23–10	1581±166	1193±143	168±118	14±2	11±4	10±5	0.60	G	−	−	−	+	−	
30–28–4	1934±541	1352±294	580±185	11±1	10±1	8±1	0.75	G	±	−	−	+	−	
30–28–10	1144±676	999±134	428±59	8±3	5±1	5±1	0.71	G	±	−	−	±	−	
31	SO	2251±664	1041±353	SO	174±171	60±51	1.00	W	+	+	−	−	+	
32	894±395	403±118	529±176	14±5	13±4	11±3	0.40	B	±	+	−	−	±	
33	1071±208	445±92	252±151	134±96	20±6	18±6	0.46	B	−	+	+	−	−	
34	1269±343	840±126	235±101	181±101	28±6	29±10	0.46	B	−	+	−	−	−	
35	1861±1237	756±76	395±118	26±10	20±4	18±2	0.48	B	+	+	−	−	−	
36	2891±1549	1260±118	563±403	22±20	15±12	11±6	0.67	B	−	+	−	+	−	
37	1040±686	655±58	227±42	141±69	11±4	10±3	0.49	B	−	+	+	−	−	
38	520±489	554±101	218±42	20±15	10±2	10±3	0.33	B	−	+	+	−	−	
39	655±239	664±134	395±126	5±1	7±5	8±3	0.59	G	+	±	−	−	−	
40	1477±312	428±84	311±101	4±2	4±3	4±1	0.45	B	−	−	−	−	±	
41	1580±645	1218±487	504±109	56±52	19±14	16±10	0.60	G	±	±	−	−	−	
41–2		672±193					0.40	W	−	−	−	−	+	
41–28		991±437					0.75	W	−	+	−	−	+	
41–30		554±218					0.55	W	−	+	−	−	+	
41–26		773±269					0.65	W	−	−	−	−	+	
41–10		596±126					0.50	B	+	−	−	−	−	

Materials: a, 100%; a–b, a mixture of 50% each of a and b; a–b–c, a mixture of 35% of a and b, and 30% of c. Phenovalin (material No. 41) is not a tablet additive, and was used for the sake of comparison purpose.

UP: pressure of upper punch loaded, in kg
PLP: passive pressure of lower punch, in kg
LP: lower punch force to extrude a tablet, in kg
SF: slipping force of tablet surface, in g
TW: tablet weight, in g
J: judgement, appearence of five tablets ejected
Bi: binding tendency
S: sticking tendency
C: capping tendency
R: roughness of surface of five tablets ejected
Cr: easy to get out of shape
−: No tableting trouble was observed on surface of 5 tablets ejected.
±: Tableting trouble was observed slightly on surface of one tablet among 5 tablets ejected.
+: Tableting trouble was observed on surface of more than 2 tablets among 5 tablets ejected.
M: producibility of tablets on a large scale
* Tablet manufacturing on a large scale such as 30 kg was possible.
SO: scale out E: Excellent, all of 5 tablets have smooth surface, sharp edges and proper hardness (about 4—6 kg by Monsanto Tablet Hardness-tester). G: Good, all of 5 tablets are lacking in one of tablet natures among smooth surface, sharp edges and proper hardness. B: Bad, more than one excellent tablet or two good tablets were obtained from five tablets.
W: worst, untabletable
All data described above were mean values obtained 5 experiments repeatedly with standard errors.

manufacturing on a large scale such as 30 kg. Formula for tableting on a large scale must be considered from the results marked with an asterisk in Table II.

Material 1——Elevation of lower punch force for extruding a tablet was tried, but this did not give "excellent" tablets.

Material 4——"Excellent" tablets were obtained by increasing the passive pressure of lower punch (*cf.* material No. 4-28).

Materials 5, 6, 15, 18, and 26 ——Lower punch force for extruding a tablet and slipping force of tablet surface are very large. Upper punch force loaded and passive pressure of lower punch show very small values. Four factors are accompanied by relatively large standard errors.

Material 10——"Excellent" tablets were obtained by the addition of material 11 which increases passive pressure of lower punch (*cf.* material No. 10–11).

Material 12——"Excellent" tablets could be obtained through an improvement of slipping forces (*cf.* material No. 12-1 and 12-41-17).

Materaial 14——Improvement in lower punch force for extruding tablets or slipping force of tablet surface was helpful in obtaining "excellent" tablets (*cf.* material No. 14-26 or No. 14-7 and 14-29).

In other words, material No. 26 is a very good additive for improving lower punch force for extruding a tablet (*cf.* material No. 1-26, 10-26, 11-26 and 14-26). Also, materials No. 7, 17, and 19 are useful in improving the slipping force (*cf.* material No. 5-7, 6-7, 12-7, 14-7, 26-7, 5-17, 6-17, 26-17, 5-19, 6-19, 18-19, and 26-19).

Binding

1. When main tableting troubles come from binding, lower punch force for extruding a tablet shows large values such as more than 800 kg.
2. When binding accompanied by capping and/or sticking occurred, lower punch force for extruding a tablet showed low values.

Sticking

1. When main tableting troubles depended on sticking, differences among 1st, 2nd, and 3rd observations of slipping force of tablet surface, and standard errors are relatively large.
2. When lower punch force for extruding a tablet shows large values, such as more than 800 kg, tableting troubles are accompanied by binding.
3. When slipping force of tablet surface gives a small value with sticking, another tableting trouble must be responsible in stead of sticking.
4. When slipping force of tablet surface, differences of 1st, 2nd, and 3rd observations of slipping force, and lower punch force for extruding a tablet are relatively large, nevertheless apparent tableting trouble looks like only sticking, the real tableting trouble must be the die friction with materials.

Capping

1. When capping is the main tableting trouble, difference between upper punch force loaded and passive pressure of lower punch must be large and lower punch force for extruding a tablet shows a small value.
2. When lower punch force for extruding a tablet gives a large value, capping must be accompanied by sticking and/or binding.

Others

When a tablet is very easy to get out of shape, four factors show indefinite tendency because tableting troubles come from so many factors.

In conclusion, "excellent" tablets that can be produced on a large scale show the following properties.

1. Difference between upper punch force loaded and passive pressure of lower punch must be small.

2. Difference in mean values among 1st, 2nd, and 3rd observations of slipping force of tablet surface, and standard error are extremely small.

3. When tablet surface shows roughness in "excellent" tablets, it must be true that material itself has no smoothness.

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Reduction of Selenocystamine by Thiols

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The role of the selenium compounds in the biological system has been discussed from various points of view,[2] and the reaction of selenium compounds with sulfur compounds has been considered as one of the important points to discuss the biological significance of the selenium compounds. In this connection, Dickson and Tappel[3] have shown that cysteine and glutathione are able to reduce selenocystine to selenocysteine, and Walter, *et al.*[4] have investigated the reductive scission of selenium-selenium bond of selenocystine by thiols and selenols by ion-exchange chromatography. Recently, the ability of selenium-containing amino acids to provide protection against radiation has been demonstrated in model chemical systems by Shimazu and Tappel,[5] and further Breccia, *et al.*[6] have reported that the radiation protection afforded by selenocystine, selenomethionine, colloidal selenium, selenoxanthene, selenoxathone, selenochromone and selenourea[7] at sublethal dose in rat is similar to, or sometimes even superior to that given by cysteine despite their low LD_{50} values. However, it was briefly reported the selenocysteamine[8] and selenocystamine[9] which are selenium-containing analogues of well known radioprotective agents, cysteamine and cystaamine, may not be regarded as favourable radiation protectors because of the considerable low LD_{50} values without further investigation of their protective effects. Information on the radiation protective activity of selenocysteamine and selenocystamine has not been reported so far.

On the basis of the increased interests in the biological significance of selenium compounds,[2] we have conducted the physico-chemical study on the property of selenocysteamine

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