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91. Jun Hasegawa : Studies on Tablets. V.[1] Static Electrification in Tablet Compression.

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In the preceding paper,[1] frictional electrification of some medicinal crystals was reported. As described previously, a static charge is observed in tablet compression and this causes some unfavorable effects such as adhesion of small particles on tablets. It is the object of the present work to determine the static electricity appearing in tablet compression and to examine factors that may affect the phenomenon.

The only report which treats this phenomenon in tablet formation has been presented by Wolf, *et al.*[2] They considered that the origin of electric charge was piezoelectricity, the amount of charge becoming larger with the increase of compression speed and if the resistance of crystal or granule used was large enough, then a larger charge would remain on the compressed tablet due to small leakage. Piezoelectricity, however, is the phenomenon that is found along a special crystal axis. The crystal axis of the tablet component may be randomized when symmetrical crystals are compressed. When an asymmetrical, i.e., flat or needle-like, crystals are compressed, it may be necessary to consider piezolecticity since the crystal axis is not randomized and actually piezoelectricity of some crystalline powders was investigated by Scheibe[3] using the fact described above. However, the same amount of charge of different sign is formed by piezoelectricity on the crystal surfaces and will disappear immediately after the removal of pressure. Therefore, it is considered that the static charge remaining on the compressed tablet is caused by frictional electrification between die wall and crystal, and not from piezoelectricity.

Instrumentation

It is necessary to record the upper-punch force, lower-punch force transmitted, speed of compression, and static charge appearing on the tablet at the same instant. The whole experimental instrumentation is shown as a block diagram in Fig. 1.

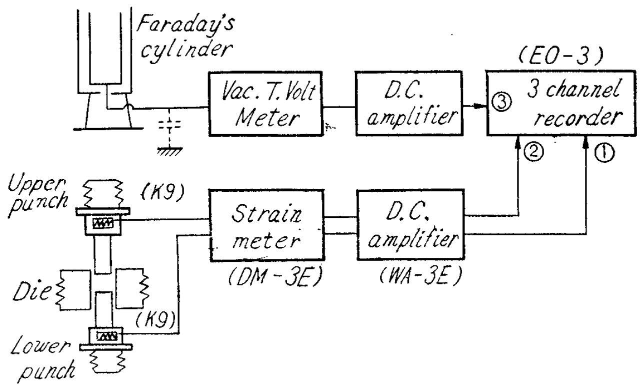


Fig. 1. Block Diagram of Experimental System

The upper- and lower-punch forces and the speed of tablet formation were determined using a dynamic wire resistance strain meter (DM-3E), 3-channel pen-writing oscillograph (ED-3), and DC amplifier (WA-3E, all of Kyowa Musen Co.). Faraday

* Hongo, Tokyo (長谷川 淳).
1) Part IV : This Bulletin, 7, 485(1959).
2) Wolf, *et al.* : J. Am. Pharm. Assoc., **36**, 409(1947).
3) A. Scheibe : "Piezoelectrizität des Quarzes," 24(1938), Theoder Steinkopff, Dresden.

cylinder, and vacuum tube voltmeter described in the previous report, and a newly designed DC amplifier were used for the determination of static electrification. Two strain gauges (K-9, Kyowa Musen Co.) were fixed on both punches as shown in Fig. 5 and one of them was used as the compensator of temperature. The compressed tablet was replaced into the Faraday cylinder using a plastic pincette and the induced voltage recorded. Static charges can be calculated from the voltage and capacity of the Faraday cylinder. The circuit diagram of DC amplifier is given in Fig. 2.

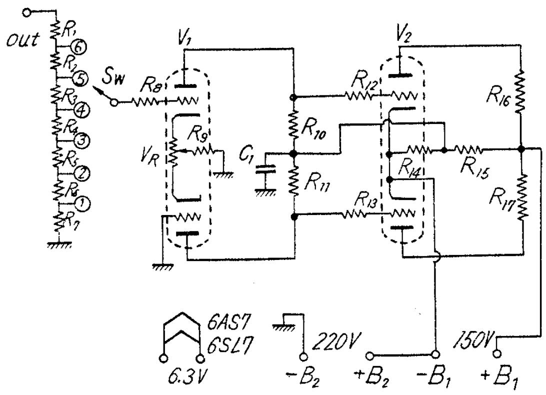


Fig. 2. Circuit Diagram of DC Amplifier

R_1	500 KΩ, 1/4 W	R_{15}	50 KΩ, 1W
R_2	200 KΩ, 1/4 W	R_{16}, R_{17}	1.7 KΩ (Recorder)
R_3	80 KΩ, 1/4 W		
R_4	50 KΩ, 1/4 W	VR	100 Ω, variable
R_5, R_6, R_7	30 KΩ, 1/4 W	C_1	1 μF, paper condencer
R_8, R_{12}, R_{13}	1 KΩ, 1/4 W		
R_9	2 KΩ, 1/2 W	Sw	Sensitivity select
R_{10}, R_{11}	100 KΩ, 1/2 W	V_1	6 SL 7
R_{14}	10 KΩ, 1 W	V_2	6 AS 7

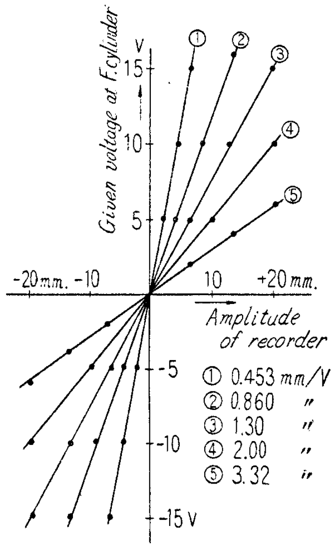


Fig. 3.

Sensitivity of Amplifier

It has good linearity and sufficient current amplitude to drive the pen recorder (1 mm./1 mA) as shown in Fig. 3, in which total characteristics of the determination system for static charge is given, the ordinate represents the given voltage in the Faraday cylinder and the abscissa is the amplitude of pen galvanometer, and the sensitivity for each position of Sw in Fig. 2 is tabulated.

The typical results of the measurements of tablet formation are shown in Fig. 4, in which 0.30 g. of Aspirin crystals (20/32 mesh) are compressed at 14° and R.H. 43%. Both punches were flat-faced and 9 mm. in diameter. A force of 2.21 tons of upper punch was applied and 1.05 tons of the force was transmitted to the lower punch. The ratio of transmission, upper/lower punch force, R, is considered as one of the characteristics of a crystal at compression, and is discussed throughout this study together with static charge. The voltage caused at the Faraday cylinder was -11.0 and the charge was calculated to be -14.9×10^{-10}C since the capacity was 135 pF. The time axis is shown at the right in Fig. 4 and the time interval given is 10 seconds.

Because the punches and die described were grounded through a resistance of 2 KΩ,

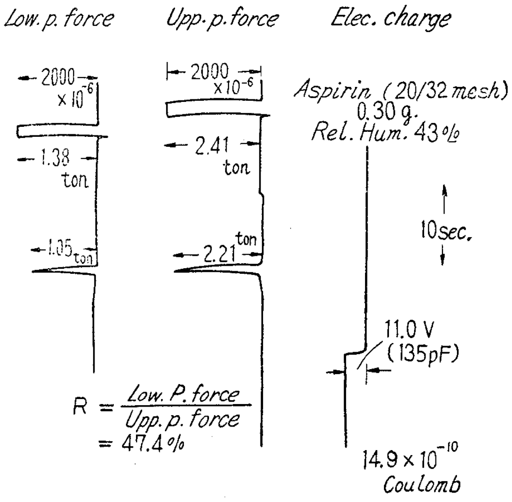
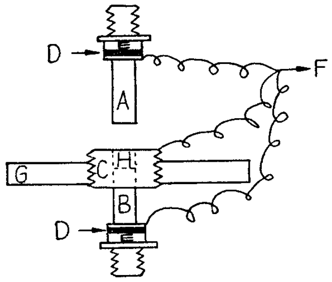


Fig. 4.
Typical Result of Determination



A. Upper punch
B. Lower punch
C. Die
D. Araldite type 1 (Ciba Ltd.)
E. Gauge
F. to Vacuum tube voltmeter
G. Holder of die (Polystyrol)

Fig. 5. Floated Die and Punch

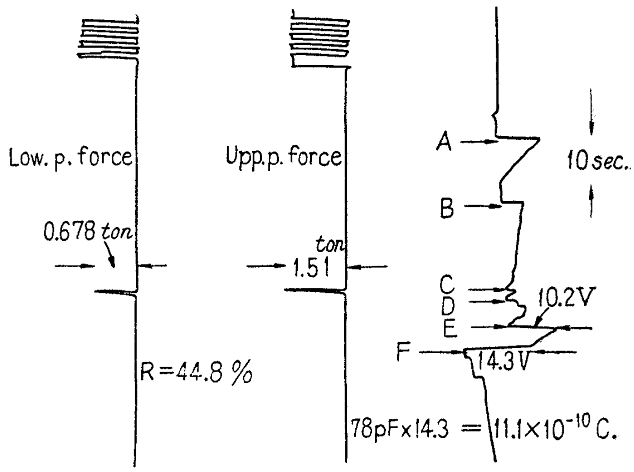


Fig. 6. Typical Result obtained with Floated Die and Punch

the electrically floated punches and die were designed to examine the effect of grounding. Each punch is separated by a layer of Araldite and the die is fixed on a polystyrol plate of 13 mm. thickness for insulation as seen in Fig. 5, at which the total resistance is over 1000 MΩ at 5 V DC by the determination of vacuum-tube resistance meter.

The typical results obtained with this system are given in Fig. 6, in which 0.30 g. of Aspirin was compressed with the upper punch force of 1.51 tons, and 0.678 ton was transferred to the lower punch, and R is 44.8%. A very complicated curve at the right side of Fig. 6 shows the static electrification appearing at each stage of tablet formation; A corresponded to the stage when the crystals were placed in the die cavity; B, the crystals scattered on the die were collected in it; C, compression was carried out by the upper punch force; D, the lower punch ejected the tablet; E, the tablet was removed by the pincette, and F, the tablet was thrown into the Faraday cylinder.

Occasional contact of paraffin paper with the die when the crystals were placed into the die cavity may be the reason why the apparent leakage of the system is different at each stage of tablet formation. Judging from the results that +10.2 V and −14.3 V were obtained at E and F, the charge appearing at C was far smaller than the one at D, the charge observed on tablet at F was nearly the same as the total charge at C, D, and E, it is then possible to arrive at the following conclusions: a) The loss of charge when replacing into the Faraday cylinder is not remarkable; b) the effect of insulation at die and punches is negligible in comparison with the results described later; and c) from the fact that opposite charges were found on tablets and die even after about 10 seconds, it is evident that the static charge is caused by frictional electrification between crystal and die wall and not due to piezoelectricity.

Marked technical difficulties in the preparation of an insulated punch, and imperfect mechanical strength of the insulating layer, obliged the author to conduct the whole experiments described below using a common set of die and punches.

The author is indebted to Prof. H. Nogami of the University of Tokyo for his guidance and encouragement throughout this study and also expresses his gratitude to Prof. Y. Suge and Dr. Z. Otaki and the Laboratory of Applied Physics of this University for their kind technical guidance and helpful suggestions.

Experimental

Preparation of Insulated Punch—A layer of Araldite (Type 1, Ciba) of 1-mm. thickness was formed between the lower part of a punch that had a screw fixing to the machine and a cylindrical block 16 mm. in diameter. The whole assembly was fixed and imbedded in plaster at 130° for 10 hr. to keep the position during hardening of the Araldite. Then the plaster was removed and the cylindrical block was finished to a punch by lathing. All punches used in this study were flat-faced and 9 mm. in diameter. The compressional pressure applied to the punch was measured in metric tons.

Plastic Pincette—Both ends of the plastic pincette were covered with metal foil and irradiated with β-ray to remove the charge.

Level of Factorials and Design of Experiment—Particle size: $P_1=20/32$, $P_2=32/42$, and $P_3=42/60$ mesh; speed of compression: $S_1=0.9 \pm 0.21$ and $S_2=2.2 \pm 0.39$ sec./tab. Single punch machine, Kimura KT-2, was operated manually at the rate as described above. Compressional force: Five levels were chosen within the the range of 1.0~2.0 tons. These factorials were combined at the level described before and the determination was carried out in a randomized block design.

Crystals used—All were the same as in the preceding report.[1] Weight of each tablets was 0.30 g. throughout this study.

Result and Discussion

The effect of particle size was examined in Expt. 1 on three kinds of crystals, Aspirin, salicylamide, and phenyl salicylate. A remarkable difference was found in the behavior of compression between these three crystals. Aspirin crystals showed a tendency to adhere to the die wall, the lower punch did not fall because of this, and the removal of the crystals from the die wall using cotton was very difficult. Such sticking was not observed with the other two crystals and this difference was considered to be due to some relationship between R and the upper-punch force.

The evident correlation between the ratio of transmission and upper punch force with Aspirin is shown in Fig. 7, in which 30 determinations of 6 groups in the combination of 3 particle sizes and 2 compression speeds were obtained, and these groups may

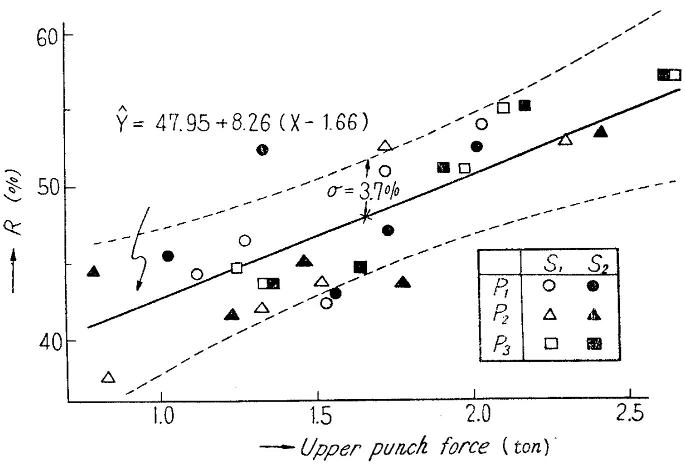


Fig. 7. Relationship between Upper-punch Force and R (Aspirin)

be evaluated by regression coefficient and mean height of regression line. The results were treated as follows :

For the test of significant difference of regression coefficient, it is necessary to calculate the sum of squares from each regression line. If there is no significant difference at each error of estimation, these errors are pooled and compared with the error from the common regression line for all determinations. If significant difference is not found, then it is considered that all regression lines had the same slope.

Observed F-value was 3.37 and not significant since it was smaller than 4.55, F-value at 5% level.

The significant difference between mean height was tested by the analysis of covariance. Main effect of particle size, compression speed, and their interaction were not significant from the result described above. Therefore, the relationship between R and upper-punch force was represented by a simple relationship shown by a regression line, the solid line in Fig. 7. For any group of particle size or compression speed, mean deviation from the regression line was 3.7%, and regression coefficient and its standard deviation were 8.26% and ±1.49% per ton. The dotted lines in Fig. 7 were calculated with these standard deviations and the area between two dotted lines represents the confidence limit of 66%.

The relationship between R and upper-punch force with salicylamide, phenyl salicylate, and Aspirin is summarized in Table I, in which $\hat{Y}$ shows an estimated value of R at upper-punch force of 1.50 tons and σ, the standard deviation of estimated value. As seen in Table I, the effect of particle size and compression speed was not found with any of the crystals and the significant regression was found only with Aspirin. The

TABLE I. Effect of Particle size on R

	R (%)			Regression		
	$\hat{Y}$(1.5)		σ	b		σ_b
Aspirin (P_1, P_2, P_3)	46.6	±	3.7	8.26	±	1.49
Salicylamide (P_1, P_2, P_3)	52.8	±	1.8	No reg.		
Phenyl salicylate (P_1, P_2, P_3)	57.2	±	1.92	No reg.		

P_1 : 20/32 mesh, P_2 : 32/42 mesh, P_3 : 42/60 mesh
R : Ratio of upper to lower punch force
$\hat{Y}$(1.5) : Estimated value of R at upper punch force of 1.50 tons, in %
σ : Standard deviation, in %
b : Regression coefficient, in % per ton
σ_b : Standard deviation of regress. coef., in % per ton

TABLE II. Effect of Particle Size on Static Electrification

		Charge		Regression	
		$\hat{Y}$(1.5)	σ	b	σ_b
Aspirin	P_1	−12.4	±1.5	−4.29	±0.57
	P_2	−10.6	±1.5	−4.29	±0.57
	P_3	−12.6	±1.5	−4.29	±0.57
	S_1	−12.4	±1.5	−4.29	±0.57
	S_2	−11.3	±1.5	−4.29	±0.57
Salicylamide	P_1	− 2.18	±0.29	−1.58	±0.16
	P_2	− 1.57	±0.29	−1.58	±0.16
	P_3	− 2.42	±0.29	−1.58	±0.16
Phenyl salicylate	P_1	− 6.89	±0.95	−3.23	±0.47
	P_2	− 7.02	±0.95	−3.23	±0.47
	P_3	−10.7	±0.95	−3.23	±0.47
	S_1	− 9.00	±0.95	−3.23	±0.47
	S_2	− 7.40	±0.95	−3.23	±0.47

$\hat{Y}$(1.5) : Estimated value at upper punch force of 1.50 tons, in 10^{-10} C
σ : Standard deviation, in 10^{-10} C
b : Regression coefficient, in 10^{-10} C per 1.00 ton
σ_b : Standard deviation of regress. coef., in 10^{-10} C per ton

reason why such relationship was not observed in the other two kinds of crystals, may be due to the fact that a remarkable affinity between crystal and die wall was found with Aspirin and a relative upper punch force was lost by friction.

The static electrification in tablet formation is given in Table II, in which a negative charge and significant correlation between charge and upper punch force were found in all cases but the coefficient of regression was specific with each crystal. The effect of particle size was significant with the three kinds of crystals.

From the comparison of estimated value at 1.50 tons, the charge decreaced with the increase in particle size of phenyl salicylate as expected, but irregular relationship was found with Aspirin or salicylamide and the electrification of the coarsest particle, P_1, was larger than P_2. The reason for this inversed correlation is considered to be that the effective surface area for friction becomes larger by crushing of the crystal particle and the effect of pressure may not be evident with phenyl salicylate since the elasticity of the crystal may be larger. The above may be supported from the fact that phenyl salicylate behaved irregularly as seen from the effect of interaction, $C \times P$, shown in Fig. 2B in the preceding report.[1]

The effect of compression speed was significant with Aspirin and phenyl salicylate but not with salicylamide. It may be considered that a small effect cannot be found with salicylamide.

The regression coefficient was negative in all cases and about 1/3 of estimated charge at 1.5 tons. It may mean that the degree of increase in charge was the same with these crystals and correlated with the increase of the effective surface area for friction. The estimated value and its confidence limit or significant difference of mean effect may be calculated from the given statistical value, number of determination, and t-value.

The effect of lubricant was studied in Experiment 2. 2% of talc or 0.5% of magnesium stearate was added to each crystal of 32/42 mesh through 100-mesh sieve, mixed thoroughly, and tabletted with varying compression speed and upper-punch force in a randomized block design.

Typical relationship between R and upper-punch force with salicylamide is given in Fig. 8, in which significant correlation is recognized and the increase of 8% or 14% at R

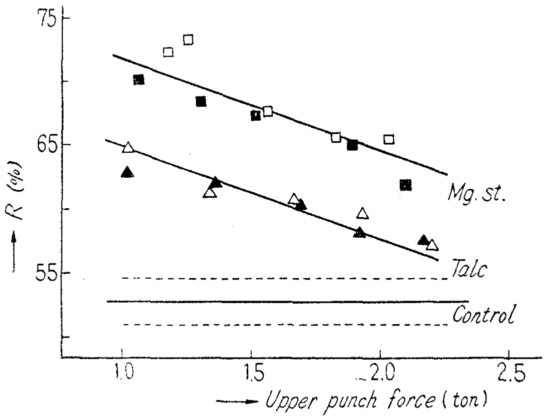


Fig. 8. Effect of Lubricant on Relationship between Upper-punch Force and R (Salicylamide)

can be observed by the addition of talc or magnesium stearate by comparing the estimated value of R. The effect of lubricant was investigated by Higuchi, *et al*[4] and they concluded that the effect was evaluated by the increase of transmission ratio. However, the increase of transmission ratio is the function of upper punch force and the effect of lubricant decreases at higher pressure range as seen in Fig. 8. The reason of such decrease may be explained by assuming that a new crystal surface is produced by the crushing and this increases friction between crystals and die wall.

4) T. Higuchi, *et al.*: J. Am. Pharm. Assoc., **45**, 51(1956).

Table III. Effect of Lubricants on R

		R (%)		Regression	
		$\hat{Y}$ (1.5)	σ	b	σ_b
Aspirin	Control	46.6	±3.7	8.26	±1.49
	Talc	45.8	±1.7	16.8	±1.53
	Mg stearate	64.8	±1,4	No reg.	
Salicylamide	Control	52.8	±1.8	No reg.	
	Talc	59.5	±1.1	−7.22	±1.97
	Mg stearate	67.3	±1.1	−7.22	±1.97
	S_1	64.1	±1.1	−7.22	±1.97
	S_2	62.7	±1.1	−7.22	±1.97
Phenyl salicylate	Control	57.2	±1.9	No reg.	
	Talc	66.2	±1.8	−3.02	±1.05
	Mg stearate.	65.0	±1.8	−8.16	±1.50

Results on other crystals are given in Table III.

An interesting correlationship was found. The regression coefficient of talc was positive and about twice that of the control, but the difference of mean height was not significant with Aspirin. This means that the poor effect of talc appears only at a higher pressure region. The effect of magnesium stearate was very marked and the estimated value of R increased 18% with Aspirin, and the regression between R and upper punch force was not observed. These circumstances explain the poor and superior character of talc and magnesium stearate as a lubricant. The same tendency was obtained with salicylamide by comparison of the estimated value at 1.5 tons, and this agreed with the investigations of Higuchi, *et al.*

The interaction between lubricant and crystal was evident as understood from the result of the estimated value at 1.5 tons and regression coefficient in each case. It may be considered that such interaction was caused by the difference of affinity between lubricant and crystal or crushing of the crystals by pressure. If the affinity between them is small enough the lubricant will move to the die wall with the replacement of air involved between the crystals at the time of compression and it may increase the reduction of friction at higher pressure regions.

Table IV. Effect of Lubricants on Static Electrification

		Charge		Regression	
		$\hat{Y}$ (1.5)	σ	b	σ_b
Aspirin	Control	−10.6	±1.5	−4.92	±0.57
	Talc	− 2.49	±0.40	−3.17	±0.46
	Mg stearate	− 4.86	±0.40	−1.51	±0.41
Salicylamide	Control	− 1.57	±0.29	−1.58	±0.16
	Talc	− 0.81	±0.16	−0.40	±0.10
	Mg stearate	− 0.81	±0.16	−0.40	±0.10
Phenyl salicylate	Control	− 7.02	±0.95	−3.23	±0.47
	Talc	− 7.73	±1.2	−2.08	±0.11
	Mg stearate	− 4.20	±1.2	−3.36	±0.09
	S_1	− 6.79	±0.72	−2.79	±0.44
	S_2	− 5.19	±0.72	−2.79	±0.44

The effect of lubricant on static electrification is shown in Table IV, in which a negative charge is found in all cases, but a reduction of 1/2 to 1/4 is observed by the addition of a lubricant. Significant relationship was observed between charge and upper-punch force, and it was the same as in the case of the control, decreased charge being found on tablets with increasing upper-punch force. The degree of decrease was determined specially with combination of the factorials. Such tendency may be caused by the following circumstances. The effective surface area was changed according to the upper-punch force and a complicated effect was found in the presence of a third substance, the reduction of about 1/4 being observed in some cases, but no effect was found with the combination of phenyl salicylate and talc. From these results, the static charge on tablets may not be formed by piezoelectricity, since the conductance of talc may not be enough considering its chemical structure, and effective compressional force may be increased by its addition.

The effect of compression speed was not remarkable in Expt. 2, since it was significant only with salicylamide on R and with phenyl salicylate on static electrification.

TABLE V. Effect of Surfactants on R

		R (%)		Regression	
		$\hat{Y}$ (1.5)	σ	b	σ_b
Aspirin	Control	46.6	±3.7	8.26	±1.43
	Na-L	41.4	±1.7	10.4	±0.85
	Tween 40	45.8	±1.7	10.4	±0.85
	Stearic acid	47.1	±1.7	10.4	±0.85
Salicylamide	Control	52.8	±1.8	No reg.	
	Na-L	59.8	±2.3	No reg.	
	Tween 40	54.4	±1.8	5.60	±1.23
	Stearic acid	57.1	±1.8	5.60	±1.23

TABLE VI. Effect of Surfactants on Static Electrification

			Charge		Regression	
			$\hat{Y}$ (1.5)	σ	b	σ_b
Aspirin	Control		−10.6	±1.5	−4.29	±0.57
	Na-L		− 1.78	±0.36	−2.09	±0.32
	Tween 40		− 0.40	±0.097	−0.35	±0.13
	Stearic acid	S_1	−13.5	±1.6	−6.43	±0.13
		S_2	− 6.82	±1.6	−6.43	±0.13
Salicylamide	Control		− 1.57	±0.29	−1.58	±0.16
	Na-L		− 0.177	+0.042	+0.095	±0.024
	Tween 40		+ 0.092	±0.042	+0.095	±0.024
	Stearic acid		+ 0.118	±0.042	+0.095	±0.024

The effect of surfactant was investigated in Expt. 3 and shown in Tables V and VI. The interaction between crystal and surfactant was found since these surfactants behaved as a lubricant with salicylamide when comparing the mean height of R and regression coefficient but not with Aspirin. A marked reduction of static electrification was noticed with the combination of Tween 40 and both crystals, and was about 1/20, but the opposite charge was found with salicylamide by this treatment. A great difference was found at the different compression speed with Aspirin. It is considered that the leakagein tablets increased and the charge remaining on the tablets was reduced at a lower compression speed.

TABLE VII. Static Electrification at Tablet Compression (Upp. p. force 1.54±0.16 ton)

	Particle size [a]	R (%)	Ejection force	Charge, 10^{-10} C	
				$\bar{x}$	σ
NaCl	(3)	55.3	0.11 ton	− 0.37	± 0.15
KCl	(3)	60.8	0.12	− 0.47	± 0.13
$KClO_4$	(2)	43.4	0.08	− 0.46	± 0.20
H_3BO_3	(3)	52.9	0.10	+ 0.65	± 0.46
Urea	(3)	66.4	0.03	− 0.47	± 0.11
Hexamine	(2)	48.2	0.28	+ 4.90	± 0.62
Sulfathiazole	(1)	33.5	0.55	[b]	
Sulfadiazine	(2)	22.6	0.53	[b]	
Phenacetine	(1)	70.1	0.04	− 7.24	± 1.37
Ethyl *p*-aminobenzoate	(3)	66.1	0.04	+22.0	± 3.91
Aminopyrine	(2)	64.5	0.15	+29.4	± 2.43

a) (1) 20/32 mesh, (2) 32/42 mesh, (3) 42/60 mesh
b) Impossible to compress into a tablet due to sticking

The static electrification was examined in Expt. 4, in which some organic and inorganic crystalline medicines were compressed to a tablet at the upper-punch force of 1.5 tons. The result is given as a mean value, standard deviation of 5 runs at R, ejection force, and the static charge as seen in Table VII.

Comparing these results with the data obtained in the chute experiment (Table III on p. 489) the static electrification appearing in tablet formation was not remarkable with inorganic or water-soluble organic medicinals and the charge obtained by unit weight was smaller than the previous results.[1] However, the result was nearly the same as the one obtained with the chute experiment with water-insoluble organic crystals. Therefore, it is estimated that the leakage of the crystal may have an effect on the static charge in tablet compression, since longer time is necessary to transfer the tablet to the Faraday cylinder. It was impossible to form a tablet with sulfathiazole or sulfadiazine due to the marked tendency of sticking as estimated from the ejection force.

As described before, these studies were carried out to find an outline of static electrification in tablet compression and it was not the purpose to evidence the mechanism of the phenomenon. It may be said that the static electrification is not caused by a simple mechanism but is very complicated. When a third substance, like a lubricant or surfactant, is added, the interactions may appear and become more complex, and it may cause the change of amount or the sign of charge.

It may be concluded that whenever the crystalline substances, organic or inorganic, are compressed into a tablet, some amount of static charge may appear on it by frictional electrification and it will be reduced by the addition of a nonionic surfactant.

Summary

Static electrification in tablet formation and the behavior of crystals to compression were investigated on four inorganic and 10 organic crystalline medicines, from the records of upper- and lower-punch forces and static charge using a wire resistance strain gauge and specially designed vacuum tube voltmeter. Same amounts but of opposite signs of charges were found between the tablet and the insulated punches or die. The amount of static charge was not markedly different from the one obtained when punches and die were grounded and it remained on the tablet after compression. Therefore, it was evident that the static charge was formed by the friction between the crystal and die wall and not due to piezoelectricity. The following conclusions were drawn from the results obtained.

1) The increase of static charge was recognized with the increase of upper-punch force and the same tendency was found when finer crystalline particles were compressed. It may be explained from the increase of frictional surface area of different particle size or by the crushing of crystals.

2) Static electrification was reduced to 1/2 to 1/4 by the addition of lubricants. It may be caused by the reduction of friction and the presence of a third substance since frictional electrification is specially determined by the given combination of substances.

3) Increased ratio of transmittance of force from upper punch to lower punch by the addition of lubricant decreased with the increase of upper-punch force and the degree of decrease affected by the crushing of crystal, and the affinity between crystal and lubricant.

4) Static charge was reduced to 1/20 by the treatment of crystal with a nonionic surfactant.

5) The amount of static charge found on unit weight of crystals in tablet formation was nearly the same as that appearing on the crystal in the chute experiments reported previously.

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