

properties is important to the formulation, production, and quality control of tablets. The quality of tablets and the rate of productivity have been found to be influenced by the size of the granule. Automation requires standardization of the granule size for reproducibility. The testing of the granule by means of the granule flow meter and the modified friabilator may prove to be useful methods for evaluating several of the physical properties of granules.

CONCLUSIONS

(a) The effect upon the granule volume by the granule size was not clearly defined. (b) The degree of granule friability was found to decrease as the size of the granule increased. As the size of the granule becomes smaller, there is a greater loss of weight due to the friability of the granule. (c) Granule flowability was found to be inversely proportional to the granule size of the granule sizes tested. As the granule size becomes smaller, the flow of the granules through an orifice was found to be greater. (d) As the granule size decreases, the weight of the die fill increases. As the depth of fill is increased, the effect of the granule size upon the die fill is increased. As the speed of the tablet machine is increased, the effect of the granule size upon the die fill is decreased. As the diameter of the die is increased (greater fill space), the effect of the granule size is decreased and there is a smaller weight of fill difference between the sizes. (e) As the granule size becomes smaller, the tablet weight variation was found to decrease. This was found to exist especially in the 8/12, 16/20, and 30/60 groups. (f) No defined or observable relationship between

the granule size and the hardness of the corresponding tablet was noted under the conditions of this test. However, difference in hardness between the groups was observed. (g) Due to the variability and limitations of accuracy of the tablet disintegration apparatus, no effect was noted in regard to granule size and disintegration time.

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Keyphrases

Granule size—effect, physical properties
 Tablets, physical properties—granule effect
 Friability—granule size
 Flowability—granule size
 Die weight fill—granule size
 Weight, tablets—granule size

Electrostatic Characteristics of Pharmaceutical Solids and Packaging Materials I

Design of Testing Equipment and Preliminary Findings

By LEON LACHMAN and SONG-LING LIN

The design and operating principles of an apparatus capable of measuring the inherent static charge on materials, as well as being able to induce a positive or negative electrostatic potential, are described. The dual polarity high voltage power supply unit of this instrument can apply up to 10,000 v. to the materials under study. The voltage accumulation or decay of the sample being evaluated in the modified Faraday cage of the apparatus can be read on the ammeter of the electrostatic voltage sensing pistol or displayed on an X-Y recorder from the sensing pistol. Measurements are reported on the relative static electrification tendencies of sodium chloride, stearic acid, sulfisomidine, and iodochlorhydroxyquin when exposed to negative and positive potentials of 6,000 v.

THE ACCUMULATION of electrical charge on solid and solid-liquid systems by the process of

static electrification is one of the earliest physical phenomena known. However, because of the complexity of the problem and mechanisms involved and an incomplete understanding of solid-state reactions, this phenomenon has only within the past 20 years received considerable

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attention. Consequently, the problem associated with electrostatics of solids is still not completely understood, and this has, for the most part, not permitted the characterization of the static electrification behavior of a given material quantitatively.

Static electrification may be defined to encompass all processes which produce segregation of positive and negative electrical charges by mechanical actions operating through contact, impact, or friction between two surfaces, or by rupture or separation of solid and liquid surfaces. It is evident from this description that common pharmaceutical processing procedures, such as mixing, micronizing, milling, sieving, compressing, spray drying and congealing, pan coating, and packaging can induce static electrification. The forces of attraction and repulsion that exist between charged surfaces can cause difficulties in the efficient operation of processing equipment, as well as fire and explosion hazards, and affect the quality of the pharmaceutical product.

For example, in the preparation of tablets there is an accumulation of electrostatic charges resulting from the blending, granulating, and compression processes. In solids blending, electrostatic charges developed on the surface of the particles is one of the principal factors for the phenomenon of unblending. This unmixing effect can cause drugs to be nonuniformly distributed in the mixture resulting in unit doses of variable drug content.

The contact, impact, and friction encountered by the surfaces of the granules as they are fed from the hopper, revolve around the turret and are compressed contribute to the overall charge development on the finished tablets. With the advent of high speed tablet presses and forced-flow powder feeding devices, frictional electrification has become aggravated. The charge on the tablet surface can cause tablets to adhere to the feed frame and "back-up" resulting in serious damage to the tableting equipment. In compression coating the charge developed on the core tablets could cause serious core dislocation problems by adhering to the transfer mechanism and not falling into the center of the bed of coating granulation in a flat position.

Although it has been generally recognized that static electrification can be a serious problem in the processing and handling of pharmaceutical solids, only a minimal number of reports appear in the literature on this subject (1-7). These reports presented limited information, and the data were given essentially in a qualitative manner.

It became evident that before more useful information could be gathered relative to the electrostatic characteristics of various pharmaceutical solids and packaging materials, a more informative method of measuring and evaluating (a) the inherent polarity and magnitude of the charge on the material, (b) the tendency of the material to take on a negative and positive potential, and (c) the decay rate of the charge from the material, must be developed. It is only by having such a reliable instrument available that it will be possible to acquire the fundamental knowledge regarding the electrostatic behavior of these materials to permit a scientific approach toward alleviating static electrification problems in pharmaceutical systems.

Such an instrument was designed and fabricated and is presently being used in these laboratories. Because of its unique capabilities, it should be of considerable utility to the pharmaceutical research scientist concerned with product and process development and packaging materials research. In this report, full details will be given relative to the design and operating characteristics of the electrostatic tester. In addition, certain preliminary findings will be presented on its use with several pharmaceutical solids.

ELECTROSTATIC TESTING INSTRUMENT

The photograph in Fig. 1 shows the electrostatic tester, X-Y recorder, and humidifying chamber. The humidifying chamber is at the right of the photograph and X-Y recorder on the left. In the center of the photograph is located the electrostatic tester that is composed of three parts: a dual polarity high voltage power supply unit, a modified Faraday cage, and an electrostatic voltage sensing pistol. A simple schematic diagram given by Fig. 2 describes the composite photograph in Fig. 1.

In order to more clearly describe the function of the various components shown in Fig. 1, the more important ones will now be described individually. The high voltage power supply component of the electrostatic tester is capable of inducing a positive or negative voltage up to 10,000 v. on the material

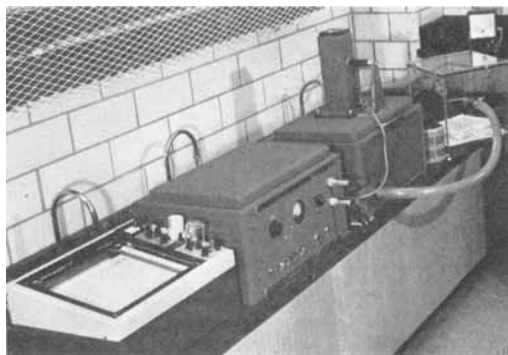


Fig. 1—Composite photograph of electrostatic tester, X-Y recorder, and humidity chambers.

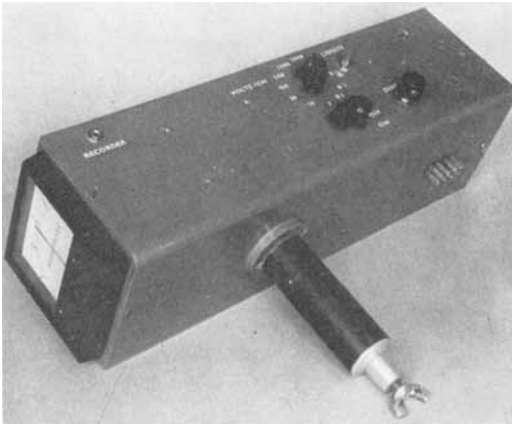


Fig. 4—Electrostatic voltage sensing probe.

the holes in the plate that fit on the Lucite posts go through these steel sections making contact with the electrodes. At the bottom of this cage is located a pan containing a saturated salt solution for humidity control, as well as humidity sensing probe. On two sides of the cabinet housing the Faraday cage, there are openings for connecting the tubing from the humidifying cabinet. The metal cabinet housing the Faraday cage is grounded.

The electrostatic voltage sensing pistol shown in Fig. 4 is detachable from the top of the cabinet housing the Faraday cage for use separately or within the cage. The meter indicator on the sensing pistol is used to standardize the sensor, as well as read out the negative or positive electrostatic voltage on the sample. A jack is located at the side of the sensor near the read out meter which is used for attaching the cable from the X-Y recorder. The recording jack will give an output of 100 mv. for full-scale deflection of the meter and has an output impedance of 100 ohms. For maximum stability, the sensing pistol should be connected to the power supply unit through the Jones plug at the side of the pistol. The pistol will, however, operate on the internal battery system for periods up to 2 hr. Rechargeable nickel-cadmium batteries are used to power the amplifier and chopper motor. The first three positions B₁, B₂, and B₃, shown on the range switch on the side of the pistol are provided for battery checking purposes. A fully charged battery

system will read full scale on the positive or negative sides of the meter for battery polarity. The reading ranges for the sensing probe are calibrated in v./cm. Calibration is achieved with the sample plate in place and inducing a positive or negative potential across the plate from the high voltage supply unit. When the pistol is positioned in the holder and cavity at the top of the metal cabinet housing the Faraday cage, its sensing element is 20 cm. from the charged plate. If the plate is then charged to 6,000 v. and with the range switch on the pistol set at 300 v./cm., the pistol is calibrated so that it reads full scale.

A detailed schematic drawing of the electrical circuitry and components of the pistol is shown in Fig. 5. The power supply to the pistol enters through the Jones plug connection to the power supply unit. The probe consists of a 1-cm. metal disk insulated to greater than 10^{14} ohms by a Teflon insulator. The disk is rigidly mounted to assure stability of measurement and the lead to the amplifier is shielded by a grounded conductor so that it does not pick up any stray electrical signals. Between the disk and the source of electrostatic potential is a rotating shutter which is in close proximity to the disk. The disk will see alternately the source of potential and the shutter, and since the shutter is true ground, it will cause the disk to be grounded. Simultaneously with the shutter being opposite the disk, a photocell is exposed to light by another blade of the same shutter. The photocell has an impedance of 10^{10} ohms dark and 10^6 ohms when exposed to a low level of light. Consequently, the disk is virtually grounded when the shutter is in front of it and has a high impedance when exposed to static charge. The photocell is exposed to low level illumination from the lamp, to give it optimum sensitivity and overcome any failure to return to high resistance during the dark period. A d.c. permanent magnet shielded motor is used to drive the chopper to prevent any electrical noise from developing which could interfere with the charge measurement. The $0.01 \mu\text{F}$ capacitor on the motor circuitry is used to eliminate any electrical noise from the motor brushes which could interfere with the charge measurement.

The output of the sensing system is a series of half wave pulses whose polarity is opposite that of the electrostatic charge. The potential is amplified

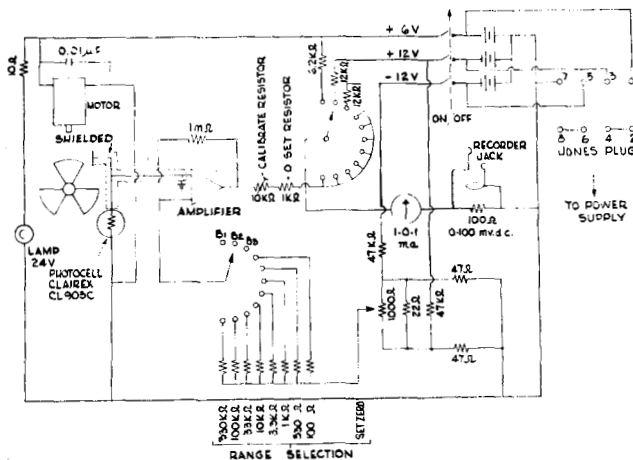


Fig. 5—Schematic drawing of the electrostatic sensing probe circuitry and auxiliary components of the probe.

and integrated by a differential operational amplifier whose gain is controlled by a feedback network consisting of a 1 megohm resistor and a resistor selected by the range selector switch. The output of the amplifier is indicated by a 1-0-1 millimeter in series with a 10,000-ohm preset variable resistor that is used for calibration. The output could also be taken from the recorder jack as a d.c. signal of 0-100 mv. corresponding to 0-1 ma. on the meter. Consequently, the d.c. restored signal can be read out on the meter or recorded on the X-Y recorder. The ratio of the feedback and series resistors determines the gain of the amplifier and the sensitivity of the instrument. The sensitivity can be varied over the range of 1 v./cm. to 10,000 v./cm. by switching the feedback resistor. Zero adjustment of the sensing pistol is achieved by applying a ± 12 mv. offset potential to the feedback system. The zero control consists of a 10-turn helical potentiometer of 1,000 ohm resistance.

The humidifying chamber constructed from Plexiglas employs a saturated salt solution in a tray at the bottom of the chamber for providing the particular humidity condition desired for the test. The chamber also has an in-line blower entering about 1 in. above the pan containing the saturated salt solution, whose speed is regulated by a rheostat. There are two reinforced plastic tubes 2 in. in diameter connected to the Faraday cage from the humidifying chamber for permitting the circulation of the humidified air during electrostatic tests.

EXPERIMENTAL

Material—Sodium chloride USP; stearic acid USP; iodochlorhydroxyquin¹ USP; sulfisomidine²; anhydrous ethanol.

Saturated sodium dichromate (Matheson, Coleman & Bell reagent crystal) aqueous solution to give 35% relative humidity.

Saturated sodium sulfate (Baker analyzed grade) aqueous solution to give 75% relative humidity.

Equipment—Electrostatic tester described earlier in the text; Model HR-96 X-Y recorder, Houston Instrument Corp., Houston, Tex. Hygrometer model HID 20-100 with model HS 1-6 sensor, Amlab, Inc., Rahway, N. J. Humidifying chamber for sample conditioning on Plexiglas plate prior to electrostatic measurements. Humidity cabinet for preconditioning sample plates.

Electrostatic Charge Measurement—Before performing any measurements, the unit is allowed to warm up for at least 5 min. with the 110-v. a.c. current to the power supply, sensing probe, blower in the humidity cabinet, and the recorder turned on. The Plexiglas plate which will act as the sample holder is rinsed with double distilled water, dipped into a Teflon-coated tray containing absolute ethanol, wiped gently with tissue paper saturated with absolute ethanol, and then allowed to dry under ambient conditions. The plate is conditioned at a prescribed humidity for 12 hr. before use in the Faraday cage of the electrostatic testing unit.

The electrostatic voltage sensing pistol positioned on the Faraday cage is zero calibrated by placing the palm of one hand at the sensing end of the probe and the dial reading is adjusted to zero with

the zero control knob on the probe. With the selector switch of the power supply unit set at either negative or positive ground, a piece of aluminum foil is placed over the Plexiglas plate in the Faraday cage extending from one end covering the electrode and stopping short at least 1.5 in. before the 2-in. stainless steel strip begins on the other end of the Plexiglas. This arrangement will induce a positive or negative potential on the material to be tested. The lid to the Faraday cage housing the electrostatic voltage sensing pistol is closed tightly over the cage. The humidity in the Faraday cage is now allowed to reach its desired value and 10 min. after the humidity has equilibrated to the prescribed value, 6,000 v. of positive or negative potential is applied to the aluminum foil covered Plexiglas plate. With the sensing pistol set at 300 v./cm., the dial reading on the indicator of the pistol is set to +1 ma. with the calibration knob on the sensing pistol. This corresponds to the full-scale deflection of the indicating needle on the dial. The X-Y recorder is adjusted so that the abscissa reads 6,000 v./10 cm. and the ordinate reads 12 cm./min. The applied voltage is then changed to 3,000 v. and the meter reading should be half scale (0.5 ma.) which is indicated on the recorder as 5 cm. above the origin on the abscissa. The applied voltage is then grounded and the meter should read zero (0.00 ma.) which corresponds to the origin on the axis of the abscissa on the X-Y recorder.

After completing the calibration of the electrostatic voltage sensing pistol and adjustment of the axis of the X-Y recorder, the aluminum foil is removed from the Plexiglas plate. The powder sample (150 Gm.) to be measured is spread gently on the plate to cover the same area as did the aluminum foil. The lid on the Faraday cage is secured and the humidity allowed to come up to the desired level. Ten minutes after the humidity has reached its equilibrium level, a preset voltage, which in this study was 6,000 v., is applied and the charge accumulation is recorded on the X-Y recorder. When the charge has reached its equilibrium value, the sample plate is grounded and the decay characteristics of the powder are recorded.

RESULTS AND DISCUSSION

In order to demonstrate the utility of the electrostatic tester to rate pharmaceutical powders as to their static electrification properties, a good conductor (sodium chloride), a poor conductor (stearic acid), and two powdered drugs were chosen.

Since the static electrification characteristics of solids are influenced by temperature (8-9) and humidity (10-12), the studies performed in this investigation were carried out at a temperature between 22-23° and a relative humidity of $34 \pm 1\%$. Both a positive and negative electrostatic potential of 6,000 v. were applied to the samples, and their tendencies to accept and dissipate the applied charge were displayed on an X-Y recorder. The rates of charge accumulation and decay were calculated for each of the substances evaluated.

The plots in Figs. 6-8 represent the charge and decay curves for sodium chloride, stearic acid, and sulfisomidine. Since the curve for iodochlorhydroxyquin and sulfisomidine closely resembled that shown for stearic acid in Fig. 7, it was not

¹ Vioform, Ciba.

² Elkosin, Ciba.

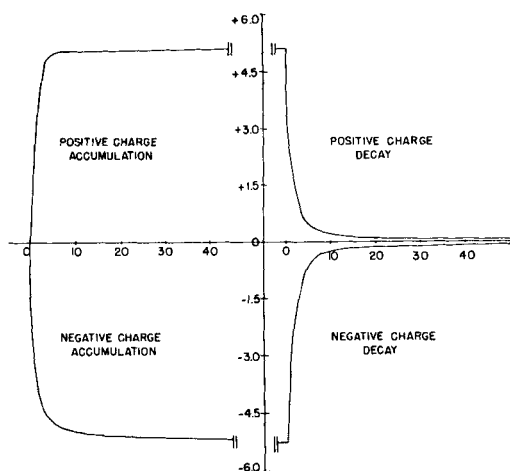


Fig. 6—Charge accumulation and decay cycles for sodium chloride at positive and negative applied potentials of 6,000 v. Abscissa is time in sec.; ordinate is voltage in Kv.

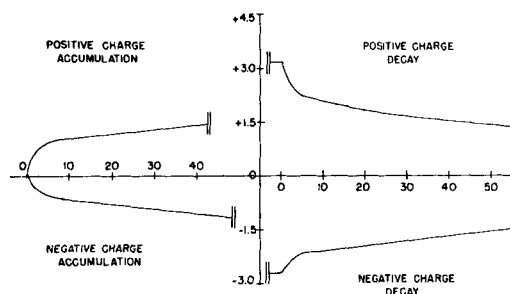


Fig. 7—Charge accumulation and decay cycles for stearic acid at positive and negative applied potentials for 6,000 v. Abscissa is time in sec.; ordinate is voltage in Kv.

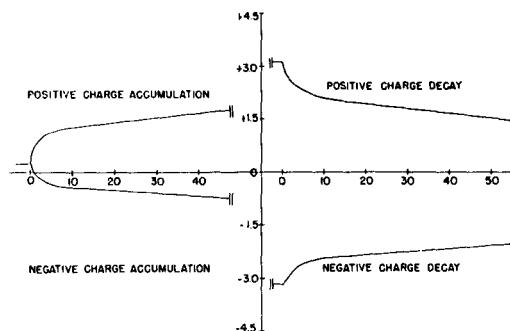


Fig. 8—Charge accumulation and decay cycles for sulfisomidine at positive and negative applied potentials for 6,000 v. Abscissa is time in sec.; ordinate is voltage in Kv.

presented. It can be seen from Fig. 6 that sodium chloride is a good conductor since the charge accumulation and decay under both positive and negative applied potential takes place readily as demonstrated by an accumulation of approximately 90% of the applied voltage within 5 sec. While in the case of stearic acid which is a poor conductor, the charge accumulation and decay is considerably slower as depicted in Fig. 7 since even after 60 sec. only about 50% of the applied potential has accumulated on the material. This is further evident

TABLE I—EQUILIBRIUM POTENTIAL ON POWDERS AT APPLIED POTENTIAL OF 6,000 V.

Materials	Polarity of Applied Potential	
	+	-
Sodium chloride	85.0%	90.0%
Stearic acid	55.0%	45.0%
Sulfisomidine	60.0%	48.0%
Iodochlorhydroxyquin	50.2%	50.3%

by the data in Table I which summarizes the percent applied potential that has been accumulated on the powder material at equilibrium (t^∞).

The data in this table were calculated in accordance with the following equation:

$$\% = \frac{\text{limiting potential at } t^\infty}{\text{applied potential}} \times 100$$

The equilibrium time, t^∞ , is taken as the time at which the voltage on the sample remained essentially at a steady state for 0.5 hr.

It is evident from the data in this table that the percent saturation at equilibrium of the applied potential was approximately twice as great for sodium chloride as for stearic acid regardless of the polarity of the applied charge. This finding is in agreement with the concept that charge flows faster in a good conductor (sodium chloride) as compared to a poor conductor (stearic acid). Equilibrium conditions of about the same magnitude are obtained for the two drugs, sulfisomidine and iodochlorhydroxyquin at both negative and positive applied potentials and are approximately equivalent to stearic acid which is a relatively poor conductor.

For sodium chloride, stearic acid, and iodochlorhydroxyquin, there exists no measurable static charge on the surface of these materials in the steady state. However, as is evident from Fig. 8, sulfisomidine differs from the other three powders in that it shows an initial inherent positive potential of approximately 240 v.

Since it was the main purpose of this initial report to describe the design and operation of the quantitative electrostatic tester, the experimental data obtained with the four powders were treated in accordance with first-order kinetics to obtain charge accumulation and decay rates. It should be understood that although the data were treated in this simple fashion and obtained relative charge accumulation and decay rates, the overall mechanism of electrification is considerably more complex, and detailed treatment of the overall process of electrification of powders will be the substance of a separate report.

The charge accumulation and decay data plotted according to first-order kinetics for positive and negative applied voltage for a poor conductor, stearic acid, are given in Fig. 9 and for the negative applied potential for a good conductor, sodium chloride, are given in Fig. 10. It can be seen that for each material and for both charge accumulation and decay at positive and negative applied voltage, there are two slopes, the first one being steeper than the second one in each case. It is felt that the initial slope is due to the inherent tendencies of the materials to be polarized by the applied electrostatic field and the second slope represents the saturation of the surface of the material with the applied potential, as well as loss of charge from the material due to radiation and conduction to the

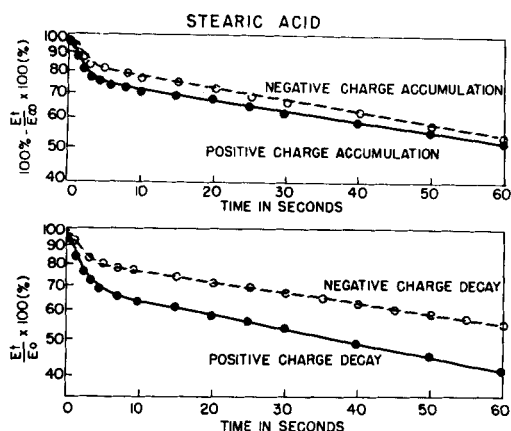


Fig. 9—First-order plot of charge accumulation and decay data for stearic acid at a positive (—) and negative (---) applied potential of 6,000 v.

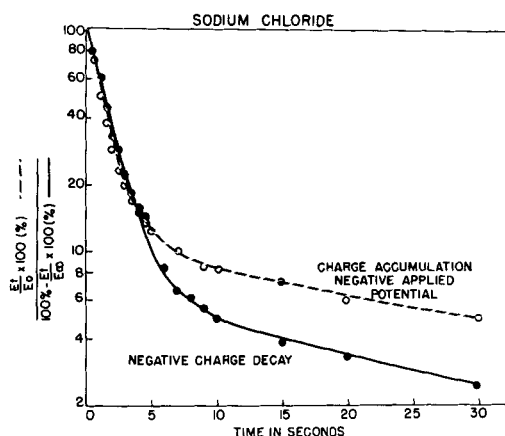


Fig. 10—First-order plot of charge accumulation and decay data for sodium chloride at an applied negative potential of 6,000 v.

TABLE II—ACCUMULATION AND DECAY OF NEGATIVE AND POSITIVE ELECTRIFICATION AT APPLIED POTENTIAL OF 6,000 V.

Materials	Charge	Accumulation Rate		Decay Rate	
		k_1	k_2	k_1	k_2
Sodium chloride	+	8.04×10^{-1}	1.77×10^{-1}	5.52×10^{-1}	1.62×10^{-1}
	-	5.36×10^{-1}	2.70×10^{-2}	4.90×10^{-1}	3.30×10^{-2}
Stearic acid	+	8.92×10^{-2}	5.90×10^{-3}	1.06×10^{-1}	8.35×10^{-3}
	-	7.90×10^{-2}	6.37×10^{-3}	5.36×10^{-2}	6.96×10^{-3}
Sulfisomidine	+	1.12×10^{-1}	8.01×10^{-3}	8.72×10^{-2}	9.96×10^{-3}
	-	7.59×10^{-2}	3.07×10^{-3}	7.67×10^{-2}	3.58×10^{-3}
Iodochlorhydroxyquin	+	1.12×10^{-1}	4.68×10^{-3}	5.82×10^{-2}	5.41×10^{-3}
	-	5.29×10^{-2}	3.60×10^{-3}	7.60×10^{-2}	9.62×10^{-3}

surrounding air. The rate constants for these plots are summarized in Table II. It is evident from these data that for the four powders the initial rate for either charge accumulation or decay is greater than the second rate. The rate of charge accumulation or decay is generally greater for the positive voltage than for the negative voltage.

These preliminary findings indicate that it is possible to rate the static electrification tendencies of powdered materials by the use of the electrostatic tester and treatment of the data in accordance with first-order kinetic principles. In subsequent publications of this series, the relationship between static and dynamic charge development of solids will be explored.

SUMMARY AND CONCLUSIONS

The design and operational characteristics of an electrostatic tester were presented. This equipment consists of (a) a power supply unit capable of inducing up to $\pm 10,000$ v. on materials to determine the tendencies of these materials to acquire and leak off electrostatic charges, (b) a modified Faraday cage to induce the applied electrostatic potential on the material, and (c) an electrostatic voltage sensing pistol capable of reading out the voltage on the sample or displaying the voltage on an X-Y recorder. The utility of this equipment to rate pharmaceutical powdered materials as to their

tendencies of acquiring static electrification has been demonstrated.

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Keyphrases

Pharmaceutical solids—electrostatic characteristics
 Electrostatic tester—design, operation
 Schematic diagram—electrostatic tester
 Static electrification—positive, negative, applied