For the results, growth ratings of 0 or 1 were scored as inhibition. Each compound was evaluated on five tubes, with percent inhibition values being reported. This procedure indicates the percentage of tubes that did not show plaque formation after the stated incubation period. The solvent served as the control (Table III).

RESULTS AND CONCLUSION

The biological results for VII–X (Table III), when compared to chlorhexidine acetate, indicate that two biguanide residues are not required for activity. The length of the alkyl chain need only be extended to achieve the higher lipid solubility required for activity. The two most active compounds tested, IX and chlorhexidine, have log P values near 5, suggesting an optimal log P for this series. This information will enable prediction, prior to synthesis, of the expected relative activity of biguanides based on lipophilic considerations.

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Calibration of a Horizontal Pendulum-Type Tablet Breaking Strength Tester

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Abstract ☐ A rapid, simplified method of checking the calibration of a new motorized pendulum type of tablet hardness tester and the accuracy and precision of three testers were determined. Two force gauges were calibrated, and both gauges were used by two operators to determine the accuracy of the new testers. This calibration method using the force gauge was reliable for checking the accuracy. The results show the various new testers to be in calibration and to give reproducible results.

Keyphrases ☐ Tablet hardness testers—motorized pendulum type, method for checking calibration and determining accuracy and precision, three testers compared ☐ Hardness testers, tablet—motorized pendulum type, method for checking calibration and determining accuracy and precision, three testers compared ☐ Strength, tablet—testers, motorized pendulum type, method for checking calibration and determining accuracy and precision, three testers compared

Certain deficiencies in the more popular tablet hardness testers have been reported previously (1–3). A new type of tablet hardness tester[1], which operates on the principle of a pendulum being displaced by consistent loading obtained by an electric motor-driven anvil, was made available in 1970 (4). The operation and merits of this tester were reported previously (1). Among its advantages compared to the more typical pneumatic type were: (*a*) more uniform force application, (*b*) less maintenance, and (*c*) the need for fewer calibration checks.

Since that report was completed, a new tablet breaking strength tester[2] became available. Its operating principle is the same as the original but the load scale readout is horizontal rather than circular. The overall size of the new tester is larger, and there are two anvil opening settings, 15 and 35 mm, to accommodate small and large size tablets. Also, the maximum scale values have been increased to 20 kg and 28 Strong-Cobb units to allow for the breakage of harder tablets such as troches and mints. A schematic diagram is shown in Fig. 1.

At the time the new tester was marketed, the manufacturer did not offer a method for checking the calibration. A persistent problem in the use of tablet breaking strength testers has been the lack of a suitable calibration checking device. The objectives of this study were to develop a rapid method for checking the calibration of the horizontal pendulum-type instrument and to determine the accuracy and reproducibility of this new tester.

EXPERIMENTAL

Two force gauges[3] (range of 0–25 kg in 0.25-kg increments) were calibrated against a tension compression testing machine[4] using the

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[1] Heberlein.

[2] Heberlein model 2E, Dr. K. Scheuniger & Co., Zurich, Switzerland.

[3] Model U, W. C. Dillon & Co., Van Nuys, CA 92407

[4] Instron Corp., Canton, Mass.

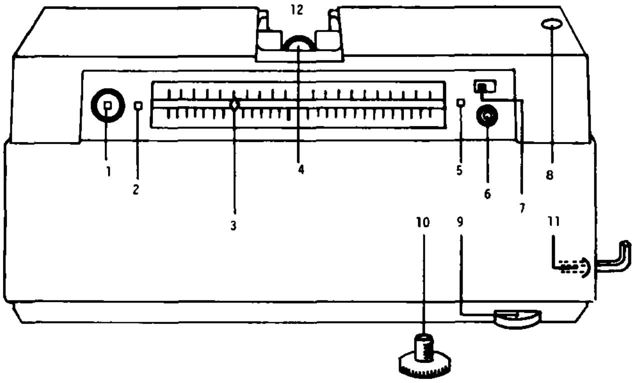

Figure 1—*Schematic diagram of new tester. Key: 1, main switch; 2, pilot lamp; 3, pointer; 4, tablet; 5, pilot lamp; 6, test button; 7, range switch (15 or 35 mm); 8, level; 9, leveling screws (front and back); 10, pendulum lock screw; 11, zero adjustment for pointer; and 12, milled portion of bridge.*

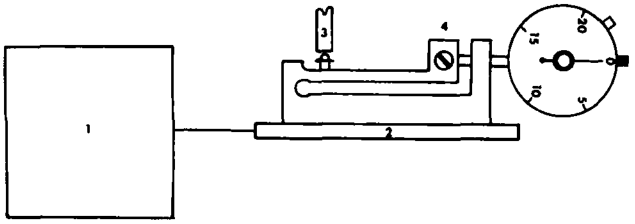

Figure 2—*Schematic view of the calibration method of the force gauge by the tension compression tester. Key: 1, tension compression tester recorder (kilograms); 2, tension compression load cell; 3, gear drive plunger (tension compression tester); and 4, calibration screw (force gauge).*

setup shown in Fig. 2. Recalibration of the force gauges, if necessary, was accomplished with an adjusting screw (Fig. 3) located on the beam just ahead of the dial and by rechecking at several load levels against the tension compression machine. With both force gauges in calibration, simultaneous load readings were obtained from the force gauge and the tension compression testing machine throughout the entire load range of the instrument.

Three pendulum-type testers were employed: Testers A and B (both new) and Tester C (in use for 12 months). To allow for the force gauge to be placed between the jaws of the tester horizontally, a 55-mm portion of the bridge was milled away at the back of the new tester (Fig. 1). The cut was made deep enough to provide a planar surface parallel to the surface supporting the tablet. The milled portion of the bridge was polished to a smooth finish to reduce the effect of drag on the force gauge.

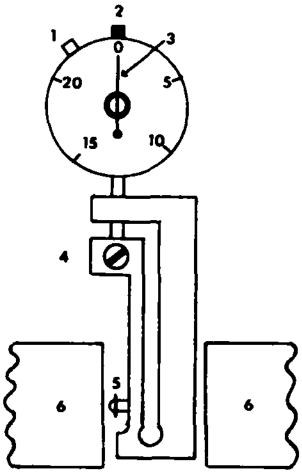

Figure 3—*Schematic view of force gauge. Key: 1, dial face zero adjustment; 2, dust cap; 3, measuring pointer; 4, calibration screw; 5, measuring point contact; and 6, tester anvils.*

Table I—Calibration of the Force Gauge Using the Tension Compression Testing Machine[a]

	Day 1	Day 2	Day 3	Day 4
Slopes				
Force gauge I	1.00	1.00	1.00	1.00
Force gauge II	0.99	0.99	1.00	1.00
Intercepts				
Force gauge I	0.079	−0.013	−0.051	−0.022
Force gauge II	0.117	−0.105	−0.054	0.032

[a] All data are based on nine readings ranging from 3 to 19 kg. The correlation coefficient for all data was >0.99.

By using the setup shown in Fig. 3, simultaneous load readings were obtained from the force gauge and the new tester at random loadings throughout the entire load range of the tester. This procedure was repeated using both force gauges and all three of the new hardness testers. Ten random readings were taken for all testers on 3 separate days by two independent operators.

RESULTS AND DISCUSSION

Both force gauges were checked against the tension compression tester to ensure the accuracy of the manufacturer's specification of ±1% of full scale. Adjustments were made, if necessary, *via* the adjusting screw on the gauge. After both force gauges were within the specified accuracy, nine sets of readings ranging from 3 to 19 kg were obtained randomly from both force gauges and tension compression tester over 4 days. The data collected were evaluated statistically to determine the day-to-day reliability of the force gauges.

A typical calibration curve for the new tester, using a force gauge as the standard, is shown in Fig. 4; complete results are given in Table I. Variation between the two force gauges and the tension compression tester from day to day was well within the ±1% accuracy claimed by the manufacturer. The gauges exhibited good linearity and reproducibility over the 4 days. The intercept values did not differ appreciably from zero, and the regression coefficients were >0.99.

After the accuracy and dependability of the force gauges were determined, they were used as the standard in testing the calibration of the new motorized pendulum-type testers. Comparisons were obtained for the three new testers against the force gauge, using kilograms as the unit of measure. Random load readings, ranging from 2 to 18 kg, were simultaneously obtained from the force gauge and the new tester, and the data collected were evaluated statistically (Tables

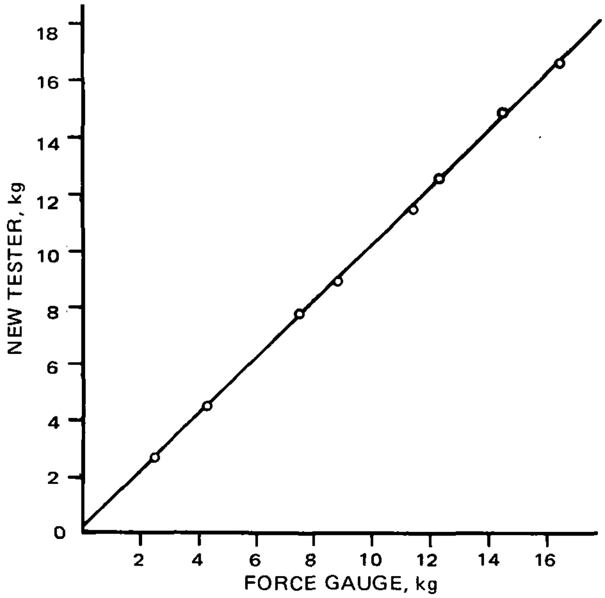

Figure 4—*Typical calibration curve for the new tester using the force gauge.*

Table II—Comparison of Force Gauge I[a] to Three New Testers[b] over 3 Days[c]

	Slope						Intercept					
	Operator 1			Operator 2			Operator 1			Operator 2		
Tester	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
A	1.03	1.02	1.01	1.01	1.02	1.02	0.061	0.068	0.118	0.103	−0.053	−0.043
B	1.00	0.994	0.988	0.995	0.992	0.990	−0.203	−0.185	−0.159	−0.171	−0.107	−0.091
C	1.00	1.00	1.00	0.999	0.993	0.998	−0.185	−0.168	−0.219	0.002	−0.035	0.017

[a] Dillon force gauge I was used. [b] Heberlein 2E tablet hardness tester. [c] Correlation coefficient for all data was >0.99.

Table III—Comparison of Force Gauge II[a] to Three New Testers[b] over 3 Days[c]

	Slope						Intercept					
	Operator 1			Operator 2			Operator 1			Operator 2		
Tester	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
A	1.05	1.03	1.02	1.04	1.01	1.03	0.087	0.059	0.040	−0.136	−0.017	−0.255
B	1.01	0.992	1.02	1.00	1.00	1.01	−0.031	0.003	−0.191	−0.157	−0.132	−0.143
C	1.01	0.995	1.01	1.01	0.985	0.980	−0.051	−0.142	−0.172	0.049	0.142	0.067

[a] Dillon force gauge II was used. [b] Heberlein 2E tablet hardness tester. [c] Correlation coefficient for all data was >0.99.

II and III). Tables II and III compare the two force gauges with the three new testers, using the kilogram scale, by two independent operators over 3 days. The slopes for all testers on all days were nearly one, and the intercepts did not differ appreciably from zero. The pendulum-type testers showed good day-to-day reproducibility, and there appeared to be no significant operator variability.

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Antimicrobial Agents: Synthesis and Antimicrobial Activity of New Aryloxyalkyl Esters of *p*-Hydroxybenzoic Acid

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G. S. REDDI [‡], and **G. S. THAPAR** [‡]

Abstract □ Several new aryloxyalkyl esters of *p*-hydroxybenzoic acid were synthesized and screened for *in vitro* antimicrobial activity. Although a few compounds showed low antifungal activity, many possessed appreciable *in vitro* antibacterial activity. However, none of these compounds was active against *Mycobacterium tuberculosis* ($H_{37}Rv$).

Keyphrases □ *p*-Hydroxybenzoic acid—aryloxyalkyl esters synthesized and screened for antibacterial and antifungal activity *in vitro* □ Parabens—synthesized and screened for antibacterial and antifungal activity *in vitro* □ Antibacterial activity—aryloxyalkyl esters of *p*-hydroxybenzoic acid screened □ Antifungal activity—aryloxyalkyl esters of *p*-hydroxybenzoic acid screened

p-Hydroxybenzoic acid esters (parabens) are known to possess antibacterial and antifungal activities and have been used extensively as preservatives (1–3). Aryloxyalkanols such as *p*-chlorophenoxyethanol (*p*-chlorophenoxetol) and 1-phenoxypropan-2-ol (propylene phenoxetol) possess marked *in vitro* antifungal activity (4).

A literature survey showed that only two aryloxyalkyl esters of *p*-hydroxybenzoic acid, namely, 2-phenoxy- and 2-(*o*-chlorophenoxy)ethyl esters, have been synthesized (5). These two esters were used as plasticizers in making films, and no pharmacological activity was reported. Therefore, the continued search for antimicrobial agents (6) prompted the synthesis of compounds that would combine the characteristic features of the forementioned esters as well as aryloxyalkanols with a view to examining antimicrobial activity. These compounds also could possibly act as *p*-hydroxybenzoic acid