TABLE 2

EFFECT ON PERCENTAGE POTENCY—PRECISE DILUTIONS VS. SIMPLE DILUTIONS

Precise dilution	Log-dose interval	Simple dilution	Log-dose interval	Percentages obtained by precise dilution			
				10%	66.67%	150%	1,000%
1:1.7783	0.25000	1: 1.78	0.25042	9.96	66.62	150.10	1,003.88
1: 3.1623	0.50000	1: 3.15	0.49831	10.08	66.76	149.80	992.20
		1: 3.2	0.50515	9.77	66.39	150.63	1,024.00
1: 5.6234	0.75000	1: 5.6	0.74896	10.06	66.73	149.82	994.45

Calculations were made by substitution in the 2-dose assay formula in which $\pm C$—i.e., log concentration relationship between standard and unknown—has been omitted. Formula then reads Percentage potency = Antilog $[2.0 \pm dP_2]$. $2.0 = \log 100$, $d = \log$ successive dose intervals, and $P_2 = \dfrac{(U_2 + U_1) - (S_2 + S_1)}{(U_2 + S_2) - (U_1 + S_1)}$

With dilution of 1 : 1.7783 log-dose interval = 0.25000. Log of 10% = 1.0; hence, by substitution, formula becomes Percentage potency = Antilog $2 + 0.25000(-4)$, whereas when 1 : 1.78 used, log-dose interval = 0.25042, and formula reads Percentage potency = Antilog $2 + 0.25042(-4)$, or Antilog 0.99832 = 9.9613%.

is 35/3, and the use of such a figure is inefficient. Although it is not very likely that the 7-dose assay would be used routinely, its P was included for the sake of completeness. It is possible that one might wish to include a larger number of dose levels on an unknown, in which case if necessary one could discard some levels at either or both ends if the limit of linearity of the dose-response curve was exceeded. Percentage potency would then be calculated on the doses of unknown remaining plus an equal number of corresponding doses of the standard.

Table 2 gives a comparison of results obtained when simple dilutions of 1:1.78, 1:3.15 or 1:3.2, and 1:5.6 replace the precise dilutions of 1:1.7783, 1:3.1623, and 1:5.6234. It should be noted that at 100% the error is zero. Since the errors at the ends of the curve are so slight in comparison with the errors inherent to the assay methods, the use of the simpler dilutions in routine tests is suggested.

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Potassium Excretion in Rats

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There is evidence that potassium is filtered through the glomeruli and reabsorbed partially by the tubules, in normal man (*1, 2*), dog (*3*), and rat (*4*). It has recently been suggested, however, that in certain circumstances potassium may also be secreted by the tubules; this was shown in anesthetized dogs during "forced osmotic diuresis" with urea (*5*), in unanesthetized dogs after administration of salyrgan or intravenous injection of a hypertonic solution of potassium chloride (*6*), and in human beings suffering from severe renal insufficiency (*7*).

When investigating the mechanism of sodium and potassium excretion in rats (*4*) a few cases in which the potassium clearances were found to be higher than that of inulin were deliberately discarded: they were (*a*) animals which in spite of the administration of 5% of their body weight of water had an abnormally low urine flow, probably as a result of accidental dehydration, and (*b*) rats in which the rate of urine flow was so high that a faulty measurement of the urine volume was assumed. It is known that under both circumstances there is a release of intracellular potassium resulting in an increase of the plasma potassium concentration. In two rats, where the urine flow amounted to .0010 and .0015 ml/100 g/min only, the ratio potassium clearance/inulin clearance was 1.1 and 1.3, respectively; similar results were found in two other animals with an extremely high rate of urine flow: .1070 and .1062 ml/100 g/min. In these cases, values for T_K (= amount of K reabsorbed expressed as percentage of that filtered [*4*]) were negative, indicating that some potassium had been secreted by the tubules and added to the glomerular filtrate.

These findings suggested to Heller (*8*) an interesting interpretation of some previous results (*9*): Heller had found that after 24 hr of dehydration the amount of potassium excreted in the urine was increased by 35% in adult rats, but decreased by 54% in newborn animals. As no evidence of a significant decrease in the glomerular filtration rate could be shown in these adult dehydrated animals, it would seem likely, from the above results, that the enhanced potassium excretion was the result of a tubular secretion of that ion. Such secretion, however, did not seem to occur in newborn rats, in which the depression of glomerular filtration seems to be the principal factor regulating the renal excretion of potassium (*2*).

This discrepancy between the tubular function of adult and newborn rats is in line with results of two independent series of investigations carried out recently in this department. It could be shown that the urine flow of newborn rats remains unaffected after the administration of either diuretics (Dicker, unpublished) or vasopressin (Heller, unpublished). The lack of sensitivity of the tubules of newborn rats to pharmacological and physiological stimuli (*10*) is thus

in sharp contrast to the highly developed adaptability of tubules of adult animals.

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Silver Nitrate as a Test for Ortho and Para Dihydric Phenols

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On attempting to prepare salts of the two plant pigments, osajin and pomiferin (*1*), it was observed that the latter reacted with neutral silver nitrate in alcoholic solution to deposit a silver mirror and yielded a gold-colored solution, whereas the former under the same conditions gave no reaction. Further investigation of this behavior demonstrated that in general those aromatic compounds containing two or more phenolic hydroxyl groups, which were ortho or para to each other, readily reacted with neutral silver nitrate, whereas those having a single phenolic hydroxyl group, or two or more hydroxyl groups meta to each other on an aryl nucleus did not react. Substances which formed insoluble silver salts in the alcoholic solution did not give a positive test even though they possessed the requisite structural features.

The test solution of silver nitrate was made up by dissolving 1.0 g of silver nitrate (analytical grade) in 8.0 ml of distilled water. The test was carried out by dissolving 5–10 mg of the compound in 5.0 ml of 95% ethanol in a clean test tube. Three drops of the silver nitrate test reagent was added, and the solution was shaken for 15 min. It was then observed for the presence of a silver mirror and coloration. If a negative or very faint test was apparent after 10 min of shaking the test tube was warmed on a water bath at 60° for 1 min.

The results for the various compounds tested are listed in Table 1. Rutin did not give a positive test even after it was warmed on the water bath. Also, quercetin did not give a positive test but appeared to form an insoluble precipitate. Both these substances possess 2 phenolic hydroxyl groups located ortho to one another on an aryl nucleus and the results are in agreement with those previously reported by Schunck (*2*) and Weiss (*3*).

TABLE 1

COMPOUNDS TESTED WITH NEUTRAL SILVER NITRATE

Compound	Results
Osajin	No reaction, even on warming
Pomiferin*	Silver mirror; gold-colored solution; no warming necessary
Iso-osajin*	No reaction, even on warming
Isopomiferin*	Silver mirror; gold-colored solution; warming necessary
Iso-osajin monomethyl ether*	No reaction, even on warming
Isopomiferin dimethyl ether*	" " " " "
Dihydro iso-osajin*	" " " " "
Dihydro isopomiferin*	Silver mirror; gold-colored solution; no warming necessary
3′,4′,7,8-Tetrahydroxy flavanone*	Silver mirror; gold-colored solution; no warming necessary
Narigin*	No reaction, even on warming
Eriodictyol*	Silver mirror; gold-colored solution; no warming necessary
Homoeriodictyol*	No reaction, even on warming
Rutin†	No mirror formed; solution a salmon color after warming
Quercetin*	No mirror formed; precipitate observed; no further change on warming
Phenol	No reaction, even on warming
Catechol	Silver mirror; red solution; no warming necessary
Hydroquinone	Silver mirror; gold-colored solution; no warming necessary
Phloroglucinol	No reaction, even on warming
Tetrabromocatechol	Silver mirror; gold-colored solution; no heating necessary
Pyrogallol	Silver mirror; red-colored solution; no heating necessary
o-Hydroxyphenyl benzyl ketone	No reaction, even on warming
2,4-Dibenzyloxy-1,3-dimethoxy benzene	No heating, even on warming

* The author is indebted to M. L. Wolfrom for samples of these compounds.

† The author is indebted to S. B. Penick and Co., New York, for a sample of this compound.

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