Citric Acid in Saliva

ISADORE ZIPKIN

Division of Physiology, National Institute of Health, Bethesda, Maryland

Positive evidence for the occurrence of citric acid in human saliva appears to be limited to a report by Pucher, Sherman, and Vickery (5), who found 0.04-1.30 mg. per cent citric acid present in 7 specimens. Previously, Kuyper (1) and Leake (2)were unable to detect citric acid in saliva. However, they both used methods which at the time were unsuited to detect less than 2.0 mg. per cent. With slight modifications the method proposed by Perlman, Lardy, and Johnson (4) has been adapted to saliva analysis using 10-cc. quantities. Some 180 saliva specimens obtained from 15 adult men have been

 TABLE 1

 Citreic Acid* in Stimulated Saliva

 \$\eta\$ (Mg./100 cc.)

Case	9 A.M.	11 A.M.	1 P.M.	3 P.M.	Average
1	0.44	1.24	1.21	1.37	1.07
2	0.73	0.55	0.85	0.51	0.66
3	0.60	0.57	0.83	0.66	0.67
• 4	0.79	0.89	0.87	0.72	0.82
5	0.56	0.60	1.04	0.75	0.74
6	0.56	0.56	0.64	0.68	0.61
7	0.86	0.70	1.37	1.02	0.99
8	1.42	1.94	1.95	1.61	1.73
9	1.74	2.14	2.40	1.86	2.04
10	1.19	1.13	1.81	1.51	1.41
11	0.98	1.00	1.42	1.25	1.16
12	0.88	0.92	1.31	1.11	1.06
13	0.67	0.55	0.81	0.52	0.64
14	1.48	1.49	1.56	1.61	1.54
15	1.00	1.40	1.13	1.31	1.21

* Expressed as the monohydrate.

analyzed, and the results (Table 1) afford considerably more evidence of the presence of citric acid in saliva than has been available heretofore. Paraffin-stimulated saliva was collected on three days at four different times, *i.e.* 9 A.M., 11 A.M., 1 P.M., and 3 P.M. The figures in the table are averages for three days according to time of day for each individual.

These results support the data of Pucher, *et al.* (5) and indicate that the average male adult's saliva may contain 0.50-2.00mg. per cent citric acid. In nearly every case; results of triplicate analyses were quite consistent. In addition, samples taken every two hours throughout the day were essentially consistent, except perhaps for the slightly higher values for the 1 P.M. specimens.

Further studies are contemplated, particularly on the relation of salivary citric acid to dental erosion and dental caries. Decalcification of dental tissues by citrate ion is suggested by the observation that calcium and citrate form a soluble, slightly ionized complex (ϑ). Also, it has been observed in previous studies from this laboratory that citrate in practically neutral drinking fluids has a pronounced destructive action on dental tissues *in vivo* (ϑ).

References

- 1. KUYPER, A. C., and MATTILL, H. A. J. biol. Chem., 1933, 103, 51.
- 2. LEAKE, C. D. Amer. J. Physiol., 1922-23, 63, 540.
- 3. McClure, F. J., and Ruzicka, S. J. J. dent. Res., 1946, 25, 1.
- PERLMAN, D., LARDY, H. A., and JOHNSON, M. J. Ind. eng. Chem. (Anal. ed.), 1944, 16, 515.
- 5. PUCHER, G. W., SHERMAN, C. C., and VICKERY, H. B. J. biol. Chem., 1936, 113, 235.
- SHEAR, M. J., KRAMER, B., and RESNIKOFF, L. J. biol. Chem., 1929, 83, 721.

Wright's Hypothesis: Its Relation to Volume Growth of Tissue Cells and Mitotic Index

JOSEPH G. HOFFMAN

Los Alamos Scientific Laboratories, Los Alamos, New Mexico

In studying the length of time spent by cells in the different stages of mitosis Wright (δ) first stated and made use of the following hypothesis: The fraction of the total time of mitosis spent by a cell in a given phase of mitosis is equal to the ratio of the number of cells found in that phase to the number of cells found in all phases of mitosis. According to this hypothesis it is possible to determine the time duration of all phases of the mitotic process if one can observe the duration of a single phase. For example, Wright estimated that telophase required 5 minutes for chicken-heart cells incubated at 37°C. From this time and the percentages of cells found in the various phases he established the time schedule for the mitotic cycle, the total duration of which turned out to be 34 minutes.

On the other hand, the mitotic index has been used as a measure of the rate of growth of cells in tissues (3, 4). This interpretation placed on the mitotic index assumes tacitly that the time required for mitosis, T, is constant. It can be shown that the mitotic index is proportional to the product of the time of mitosis, T, and the rate of cell division. For the important case of exponential growth of tissue volume such as occurs in liver regeneration (1, 4) and in transplantable mouse-tumor growth (2, 5) it can be shown that the mitotic index, m/M, is equal to $(e^{\lambda T} - 1)$ in a first approximation, where λ is the characteristic growth constant in the tissue volume growth law, $v = v_0 e^{\lambda T}$. Values of λ have been measured for regenerating liver: $\lambda = 1.33$ days⁻¹ (1), and for transplantable tumors: $\lambda = 0.37$ days⁻¹ (5). Since T is usually of the order of 40 minutes, the product λT is small, and the mitotic index is: $m/N = \lambda T$. This equation indicates the basis for Wright's hypothesis if one considers m as being the number of cells in any one of the stages of mitosis and T is the time spent