Der Einfluss eines Thiapyronderivates auf die Spaltfähigkeit des Rattenserums für Tributyrin und Acetylcholin[a]

Testsubstanz	Substrat	µl CO_2/30 min	Hemmung (%)
Kontrolle	Tributyrin	144,0	
A_1[b]	Tributyrin	100,0	30%
Kontrolle	Acetylcholin	158,0	
A_1	Acetylcholin	153,4	0%
Coffein[c]	Acetylcholin	160,0	0%

[a] Die Prüfsubstanz wurde in einer Endkonzentration von $2{,}1 \times 10^{-3}$ *M*/Ansatz zugesetzt.
[b] Die Befunde wurden auf Signifikanz im *t*-Test geprüft.
[c] Das Coffein wurde in einer Endkonzentration von 4×10^{-2} *M*/Ansatz zugesetzt.

annimmt, dass die Spaltfähigkeit des Serums für Acetylcholin und Tributyrin von einem einzigen Ferment (Pseudocholinesterase) bewirkt wird, stellten wir ergänzend Versuche mit Acetylcholin als Substrat an, in der Erwartung auch in diesem Falle eine Hemmung nachweisen zu können. Diese Vermutung konnte jedoch experimentell nicht bestätigt werden. Auf Grund der Hemmversuche gelangen wir zu der Annahme, dass sowohl das Tributyrin als auch das Acetylcholin im Rattenserum von zwei verschiedenen Esterasen hydrolysiert wird. Die Tributyrinase scheint ein mässig spezifisches Enzym zu sein, das demzufolge mit dem Begriff «Pseudocholinesterase» nicht mehr in Einklang gebracht werden kann. PILZ konnte in seinen Studien zur vermeintlichen Identität der Acetylcholin und Tributyrin spaltenden Fermente des menschlichen Serums zur gleichen Schlussfolgerung gelangen[9]. Ob dies auch für andere in der Pharmakologie gebräuchliche Tierarten zutrifft, kann noch nicht absolut entschieden werden.

Aus diesen Befunden ergibt sich zwangsläufig die Frage – die auch von mehreren Autoren älterer und jüngster Zeit gestellt und im wesentlichen negativ beantwortet wurde – ob die im Serum nachweisbare Acetylcholin spaltende Esterase mit der Acetylcholinesterase der Erythrocyten und des Nervengewebes identisch ist. Wie aus den neusten Befunden von PILZ hervorgeht, soll beim Menschen die Acetylcholinesterase und die Serumcholinesterase ein einziges Ferment bilden, das nur Acetylcholin spaltet. Bekanntlich wird die Acetylcholinesterase u. a. durch Coffein selektiv gehemmt[10]. Auf die unspezifische Cholinesterase soll dieser Stoff keinen Einfluss ausüben. In unseren Versuchen mit Rattenserum konnten wir in Gegenwart von Coffein als Hemmstoff und mit Acetylcholin als Substrat keine signifikanten Unterschiede nachweisen.

Schlussfolgerung. 1. In einem Thiapyronderivat konnte ein neuer Tributyrinase-Hemmer entdeckt werden.

2. Das untersuchte Thiapyronderivat vermag im Sinne einer Hemmung nur die Spaltfähigkeit des Rattenserums für Tributyrin zu beeinflussen, nicht aber die für Acetylcholin, was der bisherigen Auffassung über die Existenz einer einzigen sogenannten «Pseudocholinesterase» widerspricht.

3. Die im Rattenserum nachweisbare Acetylcholin spaltende Esterase kann jedoch mit der in den Erythrocyten und im Nervensystem vorhandenen spezifischen Cholinesterase nicht absolut identifiziert werden, da das erstgenannte Ferment auf Coffein nicht anspricht.

Summary. A new tributyrinase-inhibitor could be found in a thiapyronderivate (3-benzyl-4-hydroxy-5-carbaethoxy-6-methylthiapyrone[2]). The splitting of acetylcholine is neither positively nor negatively influenced by this substance. The result is that the pseudocholinesterase, found in the serum of rats, represents no uniform system of enzymes.

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Institut für Pharmakologie der Friedrich-Schiller-Universität Jena (Deutschland), 22. September 1960.

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PRO EXPERIMENTIS

An Inexpensive, very Accurate Automatic Syringe

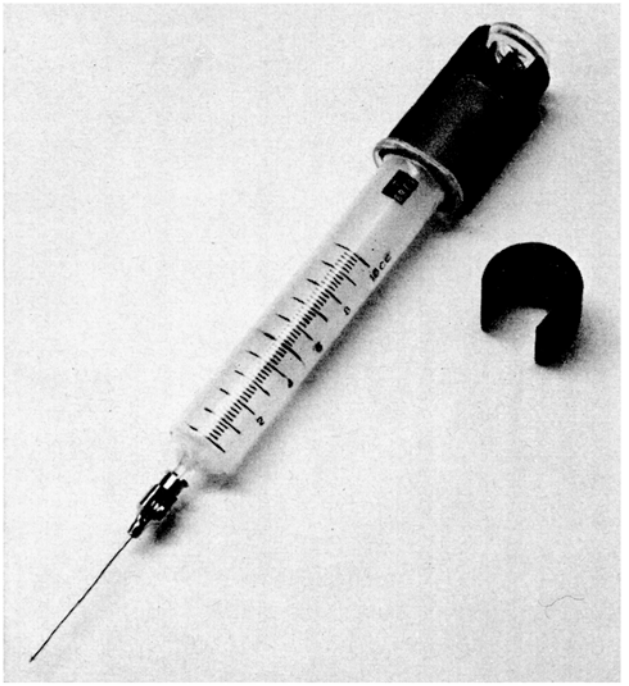
Syringes are widely used to transfer sensitive liquids such as, for example, Grignard reagents, because the small needle opening makes it unnecessary to take precautions to exclude air. It is equally obvious that a positive displacement apparatus is not affected by the viscosity or surface tension of the liquid being transferred. A single calibration of a syringe with one liquid provides for delivering identical volumes of all liquids including very viscous ones. Transferring viscous liquids with pipettes is extremely difficult and very inaccurate. It is generally not appreciated, however, that syringes can be used with *greater* convenience and accuracy than can automatic pipettes. For example, pipettes give, at best, an accuracy of $\pm$ 0.1% whereas with this simple device, accuracies range from $\pm$ 0.01 to $\pm$ 0.06%. The sampling and transferring usually require about 20 sec.

The apparatus consists of a syringe and fitting plastic collar[1] shown in the Figure. A rod is drilled 0.0001 to 0.0002 inches larger than the syringe piston, machined to length, making sure that the ends are parallel, and one side machined or sawed away in order that the collar will slip easily onto the syringe piston.

Technique. Approximately 10% excess liquid is drawn into the syringe. The collar is placed on the syringe piston and, with the needle held upward, the syringe is tapped lightly to dislodge bubbles and the piston driven against the collar with the thumb. Any liquid which has wet the needle or syringe is wiped off. The syringe is emptied by maintaining a positive pressure on the piston with the thumb, and removing the collar with a rapid transverse motion. The pressure is maintained to drive the piston home. It is preferable to avoid using lubricants other than the transferred liquid. Typical results are shown in the following Table.

Zusammenfassung. Es wird ein einfacher Apparat beschrieben, der eine normale Spritze in eine genaue automatische Pipette umändert.

[1] The plastic should machine easily, wear well, and not be affected by solvents. Bakelite or similar resins are ideal.
[2] Present address: Converse Memorial Laboratory, Harvard University, Cambridge.



Calibration of volumetric syringes

Volume (ml)	Range (ml)	Average Deviation (ml)
9.0117	0.0013	± 0.0006
3.2957	0.0014	± 0.0007
0.6116	0,001	± 0.0005

T. G. TRAYLOR[2] and R. A. CRANE

The Dow Chemical Company, Pittsburg (Calif.), April 20, 1960.

STUDIORUM PROGESSUS

Quinine Dimorphism among 'Non-Tasters' of 6-n-Propylthiouracil

Introduction. It appears that the history of the thyroid gland has been one in which a feeding structure has been transformed into a gland of internal secretion. The thyroid hormone can be administered orally, whereas other hormones in an unaltered state are destroyed by gastric and intestinal fluids.

It is therefore of great interest from both the phylogenetical as well as the clinical point of view that thresholds for certain taste qualities are under control of thyroid hormones[1].

We started by investigating the role of saliva in the mechanism of 'taste-blindness' to phenylthiourea and similar antithyroid compounds[2]. The differential reactivity of the saliva of 'tasters' as opposed to that of 'non-tasters' led us to attempt to lower chemically the taste-threshold of 'tasters' towards the two bitter compounds 6-*n*-propylthiouracil and quinine[3].

Specifically subthreshold concentrations of l-tyrosine and or its mono- and diiodo-derivatives, in fact do lower 4–32 fold the taste-threshold of a 'taster' towards 6-*n*-propylthiouracil or quinine if administered simultaneously. Since high or low taste-thresholds towards these bitter compounds largely determine whether or not an individual belongs to a low or high food dislike category[4], we wondered about the mechanism by which quinine and 6-*n*-propylthiouracil thresholds affect an individual's likes and dislikes for food.

The existence of a quinine dimorphism has been postulated and though the genetic mechanism of this dimorphism has not yet been established, its existence is beyond doubt.

We can differentiate namely subjects with high or low taste thresholds for quinine through a simple saliva-color test (to be published) and this is irrespective of whether a subject belongs to the 'taster' or 'non-taster' mode of 6-*n*-propylthiouracil.

Materials and Method. D-Sucrose (USP, C-grade of the California Corporation for Biochemical Research), sodium chloride 'Baker Analyzed' Reagent of the J. T. Baker Chemical Company), hydrochloric acid (Certified Reagent of the Fisher Scientific Company), and quinine sulfate (U.S.P. Crystals of the Mallinckrodt Chemical Works), were used to test taste sensitivity. 6-*n*-propylthiouracil (from Nutritional Biochemicals Corporation) was chosen as a differentiator between 'tasters' and 'non-tasters'[1,2]. The compounds were dissolved in double distilled copper-free water. Serial dilutions were made, each numbered step representing a doubling concentration of the same molarity for any one compound. Taste-thresholds of 42 subjects were determined for all of the 5 taste qualities mentioned. Six additional subjects were tested only for their quinine and 6-*n*-propylthiouracil thresholds. All the 48 subjects were healthy men ($N = 37$) and women ($N = 11$), 77% of whom belonged to the 18–26 year age group.

Determination of taste-thresholds was carried out according to the HARRIS and KALMUS[5] procedure involving the final sorting out technique. In the first 2 h session the subjects were taught the taste-testing procedure by use of an instruction sheet and active participation after practical demonstration. Three ounce 'Lily' paper cups (No. 44 of the Lily Tulip Cup Corporation, New York 17, New York) were used for both the compounds and the placebo. A few days later the subjects' taste-thresholds were determined at a morning session in the following order: D-sucrose, sodium chloride, hydrochloric acid, quinine, and 6-*n*-propylthiouracil.

After the lapse of approximately a two-week interval the taste-thresholds were redetermined to check the reliability of the results. In approximately 50% of cases the thresholds were found to be identical with the value initially obtained. When variations occurred, they were in the + 0/− 1 threshold range. Stressful situations, seasonal change, the third trimester of pregnancy and thyroid administration caused greater variations in taste-threshold and subjects displaying these variations were excluded from this study[3].

Results. Figure 1 (A) depicts the distribution of taste-thresholds for 6-*n*-propylthiouracil of 48 subjects into 27

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