

3-1988

Potency of Current Levothyroxine Preparations Evaluated by High-Performance Liquid Chromatography

Sheldon S. Stoffer

Walter E. Szpunar

Follow this and additional works at: <https://scholarlycommons.henryford.com/hfhmedjournal>



Part of the [Life Sciences Commons](#), [Medical Specialties Commons](#), and the [Public Health Commons](#)

Recommended Citation

Stoffer, Sheldon S. and Szpunar, Walter E. (1988) "Potency of Current Levothyroxine Preparations Evaluated by High-Performance Liquid Chromatography," *Henry Ford Hospital Medical Journal* : Vol. 36 : No. 1 , 64-65.

Available at: <https://scholarlycommons.henryford.com/hfhmedjournal/vol36/iss1/17>

This Article is brought to you for free and open access by Henry Ford Health System Scholarly Commons. It has been accepted for inclusion in Henry Ford Hospital Medical Journal by an authorized editor of Henry Ford Health System Scholarly Commons.

Potency of Current Levothyroxine Preparations Evaluated by High-Performance Liquid Chromatography

Sheldon S. Stoffer, MD,* and Walter E. Szpunar, PhD†

Ten different levothyroxine products manufactured by six companies were analyzed by high-performance liquid chromatography. Although nine products met the United States Pharmacopeia requirements, one product was found to have only 47% of expected potency. Until these products become more uniform, we would not recommend interchangeability of levothyroxine preparations. (Henry Ford Hosp Med J 1988;36:64-5)

In 1980 we demonstrated that the mean thyroxine content can be different in generic tablets when compared to that of brand name products. In addition, we demonstrated that a brand name product (Synthroid®) had only 78% of expected potency (1). Since then, the United States Pharmacopeia (USP) requirements have been modified so that manufacturers must evaluate levothyroxine content by high-performance liquid chromatography (HPLC) (2). In 1984 we reported that Synthroid® had been reformulated and had 100% of expected potency (3). We reassessed the content of a number of manufacturers' products using HPLC to determine if these products are currently more uniform.

Materials and Methods

Ten different levothyroxine products manufactured by six companies were analyzed by HPLC (Applied Analytical Laboratories, Wilmington, NC) (2). Local drugstores were contacted until ten different levothyroxine products were obtained. Between 17 and 21 tablets of each product were analyzed. The tablets were split into two groups, and each group was batch-analyzed separately. The analysis for each product was completed in one day, and all products were analyzed over a three-day period. Analysis of each extraction was duplicated. Since two batch extractions were done on each product, each group of tablets was assayed four times. The only exception was product 10, which was submitted twice and treated as two separate products. Therefore, product 10 was analyzed eight times. All tablets were 0.1 mg strength and were purchased in the fall of 1986. The assays were performed in June 1987.

Results

The results of our analyses are shown in the Table. Nine products fell within the USP requirement of $\pm 10\%$, but product 10 had only 47% of expected potency.

Table
Thyroxine Content of 100 μg Tablets*

Product	Manufacturer	% of Expected Content†	Expiration Date (month/year)
1	A	95	2/88
2	B	94	1/88
3	C	95	3/88
4	C	96	5/88
5	C	102	12/87
6	D	91	10/88
7	C	98	4/88
8	E	96	1/89
9	F	100	10/87
10	C	47 { 48‡ 45	7/87

*These levothyroxine products were distributed under ten different labels.

†Coefficient of variation < 1.8%.

‡Two separate submissions: coefficient of variation = 3.6% for combined analysis.

Discussion

A recent study by Dong et al (4) showed frequent non-equivalence of levothyroxine products by tablet HPLC analysis. However, these levothyroxine products were purchased in 1981, before the introduction of the HPLC requirement for manufacturers. We suspect that the new USP HPLC requirement has improved the uniformity of levothyroxine products. However, Fish et al (5) recently reported that one generic product had only 34% of expected potency. Our data show that yet another company had at least one lot (product 10) with less than expected potency

Submitted for publication: November 25, 1987.

Accepted for publication: March 31, 1988.

Formerly Department of Internal Medicine, Henry Ford Hospital. Currently Oakland Internists, Southfield.

†Associated Endocrinologists, Southfield.

Address correspondence to Dr. Stoffer, Oakland Internists, 23077 Greenfield, Suite 205, Southfield, MI 48075.

(47%). We admit that our study is limited. To better estimate the magnitude of the problem, a larger study evaluating different lots, different time periods, and different tablet strengths is needed. We hope this paper will stimulate investigators at research centers where such a study may be feasible.

The Food and Drug Administration currently does not recommend interchangeability of levothyroxine products (6). Nevertheless, generic levothyroxine products are available and are being interchanged for each other and for the brand name products, at least in Michigan. The FDA's advice is not binding on the United States, and each state may allow interchangeability for the products that the FDA considers not interchangeable (6). We are concerned that levothyroxine products still show significant variability by HPLC (in vitro) testing. The USP has no requirement for bioavailability (in vivo) studies for levothyroxine products (7). Until levothyroxine products become more uniform, we agree with the FDA's position that these products not be interchanged. We hope that levothyroxine products will continue to be improved in the future.

References

1. Stoffer SS, Szpunar WE. Potency of brand name and generic levothyroxine products. *JAMA* 1980;244:1704-5.
2. Garnick RI, Burt GF, Borger FR, et al. In: Hormone drugs. Proceedings of the FDA USP workshop on drug and reference standards for insulins, somatropins, and thyroid-axis hormones. Rockville, IL: USP Convention, Inc, 1982:504-16.
3. Stoffer SS, Szpunar WE. Potency of levothyroxine products. *JAMA* 1984;251:635-6.
4. Dong BJ, Young VR, Rapoport B. The nonequivalence of levothyroxine products. *Drug Intell Clin Pharm* 1986;20:27.
5. Fish LH, Schwartz HL, Cavanaugh J, Steffes MW, Bantle JP, Oppenheimer JH. Replacement dose, metabolism, and bioavailability of levothyroxine in the treatment of hypothyroidism: Role of triiodothyronine in pituitary feedback in humans. *N Engl J Med* 1987;316:764-70.
6. Proceedings of the Food and Drug Administration, Bioequivalence Hearing (September 29, 30, October 1). Washington, DC: J.W. Marriott, 1986:716.
7. Greenstadt MA, Spencer CA, Lum SMC, Kaptein EM, Nicoloff JT. Non-isotopic method for determination of oral thyroxine absorption. In: Hormone drugs. Proceedings of the FDA USP workshop on drug and reference standards for insulins, somatropins, and thyroid-axis hormones. Rockville, IL: USP Convention, Inc, 1982:534-9.