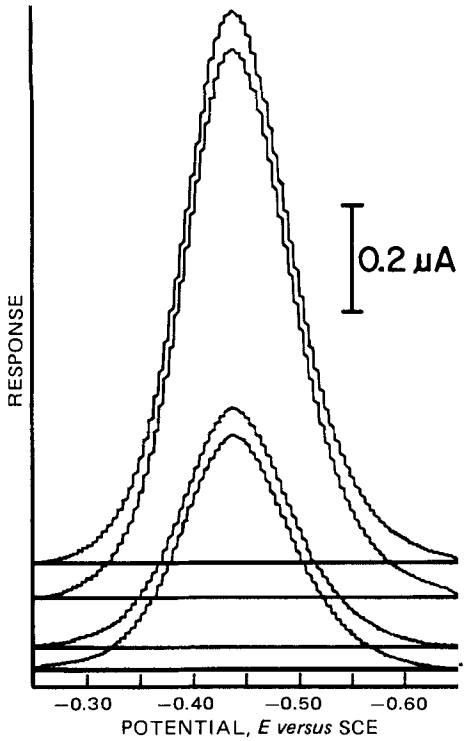

Figure 1—*Differential pulse polarographic scans of two pyrophosphate kits (8.3 × 10⁻⁴ M total tin). The top two scans are of a kit containing 70% of the tin as Sn(II) and 30% as Sn(IV). The lower two scans are of a kit containing 30% Sn(II) and 70% Sn(IV). The peaks occurred at −0.44 v. The vertical positioning of the scans is unimportant, since peak height was measured from the baseline of each peak.*

to the maxima. However, the potential shift could also be an indication of the differences between the Sn(II)–pyrophosphate and Sn(II)–polyphosphate complexes. Nothing was done to suppress the maxima because the polyphosphate variability was not so great to warrant an added step, namely the addition of a surfactant to the supporting electrolyte prior to each analysis.

Several supporting electrolytes were used, but only 1 *M* H_2SO_4 was satisfactory. Since Sn(IV) is not soluble in this electrolyte (6), it does not produce a reduction peak that could interfere with the Sn(II) peak.

Sn(II) solutions in 0.12 *M* HCl were tested by the differential pulse polarographic technique. The method was effective in quantitating Sn(II) at concentrations as low as 8×10^{-6} *M* (2 μg of stannous chloride dihydrate in 1 ml). Sn(IV) interference was not examined at these low Sn(II) concentrations.

DISCUSSION

Classical dc polarography, electrolysis on a microscale in which the magnitude of current flow is proportional to the sample concentration, is useful in tin analysis (6). Differential pulse polarography is a relatively new, highly sensitive version of this technique (7) and is a convenient and effective method for the quantitation of Sn(II) in pyrophosphate and polyphosphate radiopharmaceutical kits. One should not assume that simple Sn(II)–hydrochloric acid solutions can be used as standards, since different peak potentials and slopes can be expected for different kit types as the result of different matrixes. This Sn(II) analytical technique is currently being studied for its value in the qualitative control testing of other radiopharmaceutical products.

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GI Absorption of Niacin in Humans

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Abstract □ By using the GI tube technique, niacin was shown to be equally well absorbed from the stomach and the upper small intestine. The maximum plasma niacin concentrations occurred 10–20 and 5–10 min, respectively, after instillation. Thus, the physiological prerequisites for a physically retarded niacin preparation were established.

Keyphrases □ Absorption, GI—niacin, stomach and small intestine compared, humans □ Niacin—absorption from stomach and small intestine compared, humans □ Vitamins—niacin, absorption from stomach and small intestine compared, humans

It is generally accepted that weak organic acids or bases are absorbed primarily by penetration of the unionized form of the drug through a lipoidal barrier (1). Niacin (nicotinic acid) (pKa 4.8) should theoretically be better absorbed from the stomach than from the small intestine. However, salicylic acid (pKa 3.0) is reportedly well absorbed even at pH values where it is predominantly ionized (2).

Limited data are available concerning the GI absorption of niacin in humans. In a steady-state situation, about 85% of an orally administered dose (3 g/day) of niacin was recovered from the urine, and it was concluded that absorption was nearly complete (3).

In a comparative study of plain and enteric-coated niacin tablets (4), niacin was absorbed from the small intestine to only a small extent. Based on this finding, in-

Table I—Mean (Range) Plasma Niacin Concentrations (Micrograms per Milliliter) after Instillation of 200 mg of Niacin, $n = 3$

	Minutes						
	5	10	20	40	80	160	320
Stomach[a]	1.6(0.5–1.0)	2.7(1.2–4.5)	2.7(2.4–3.3)	1.4(1.0–1.6)	0.8(0.6–0.9)	0.6(0.4–1.0)	0.5(0.3–0.6)
Stomach[b]	0.4(0.3–0.5)	2.4(1.6–3.6)	3.9(2.9–4.9)	2.2(1.9–2.6)	1.0(0.9–1.1)	0.8(0.5–0.9)	0.5(0.4–0.7)
Small intestine[a]	5.3(3.5–6.5)	5.7(3.0–8.9)	4.8(2.8–6.1)	1.3(0.5–2.8)	0.6(0.4–0.9)	0.9(0.3–1.4)	0.4(0.1–0.5)

[a] Thirty minutes after ingestion of a standard meal. [b] Without ingestion of a standard meal.

vestigators suggested that the physiological prerequisites for a sustained-release niacin preparation are absent (4, 5). In general, however, absorption from enteric-coated tablets is known to be unreliable and often incomplete.

In the present study, absorption of niacin from the human stomach and the upper intestinal tract was compared by means of the GI tube technique.

EXPERIMENTAL

Three healthy, young, male volunteers with normal GI function were the test subjects. No medicine or alcohol consumption was allowed during the 24 hr preceding the tests, and only water was allowed during the 12 hr preceding the tests. In each subject, niacin absorption was studied after instillation of the drug under the following three conditions: (*a*) in the empty stomach, (*b*) in the stomach 30 min after a standard meal, and (*c*) in the small intestine 30 min after a standard meal. An interval of at least 2 weeks was allowed between two consecutive tests.

When niacin absorption from the small intestine was studied, the subjects were admitted to a hospital ward on the day before the test and the stomach tube (weighted with lead shot at the distal opening) was applied. During the night, peristalsis moved the tube into the intestinal tract. The localization of the tube was estimated by an X-ray check and by the measured distance from the nose. In all cases, the distal opening of the tube was located 1–1.5 m from the pylorus.

Niacin (200 mg) dissolved in water (25 ml) was instilled over 15–30 sec, immediately followed by two rinses with water (totaling 50 ml). Venous blood samples were drawn from the supine experimental subject before the test and at fixed time intervals after drug instillation. Blood pressure and pulse rate were registered simultaneously.

Free niacin in plasma was analyzed by the colorimetric technique of Carlson (6). Considering the high levels of niacin involved and the fact that each individual's basal values for König-positive substances before instillation of the drug were used for correction, the well-known relative unspecificity of the analytical method did not compromise the significance of the results obtained (7–9). The coefficient of variation for the analytical procedure was 5%.

RESULTS AND DISCUSSION

The highest level of niacin in plasma was found 5–10 min after instillation into the upper small intestine (Table I). During instillation into the stomach, the maximum plasma niacin concentration occurred 10–20 min after drug administration. Evidently, food did not influence niacin absorption, as evidenced by the peak plasma concentrations with and without a standard meal (Table I).

Immediately after drug instillation, an increase in pulse rate (maximum 45%) and blood pressure (maximum 20%) appeared, indicating rapid absorption. The pulse rate was normalized after 20 min. The increase in blood pressure, however, was ultimately followed by a decrease and normalized after 20–50 min.

CONCLUSION

After instillation into the small intestine of an aqueous niacin solution, the drug appears faster in the plasma and reaches higher levels than after instillation into the stomach. This finding indicates that the compound is absorbed at least as readily from the small intestine as from the stomach. Thus, the physiological basis for the development of a sustained-release niacin preparation is established.

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