

# Efficacy of oral iodized peanut oil is greater than that of iodized poppy seed oil among Indonesian schoolchildren<sup>1–5</sup>

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## ABSTRACT

**Background:** Oral iodized poppy seed oil is an appropriate measure for controlling iodine deficiency in areas where iodized salt is not yet available. However, a more effective and cheaper iodized oil preparation is needed.

**Objective:** The aim of this study was to compare the efficacy of iodized peanut oil with that of iodized poppy seed oil.

**Design:** Schoolchildren aged 8–10 y were supplemented with a single oral dose of iodized peanut oil (P200, P400, or P800 mg I), iodized poppy seed oil (PS400 mg I), or peanut oil (placebo). The concentration of urinary iodine (UI) was measured at 0, 4, 12, 25, and 50 wk, whereas thyroid volume and serum thyrotropin and free thyroxine concentrations were measured at 0, 25, and 50 wk.

**Results:** UI was higher in all treatment groups than in the placebo group, except at baseline. UI in the P200 group was not significantly different from that in the PS400 group at all times of measurement. In a comparison of preparations supplying 400 mg I conducted by using a mathematical model, iodine retention from the peanut oil preparation was 3 times that from the poppy seed oil, and the protection period for peanut oil was twice as long as that for the poppy seed oil ( $P < 0.001$  for both). The reduction in thyroid volume was greater in the treatment groups than in the placebo group ( $P < 0.001$ ). No significant differences in serum hormone concentrations were observed between groups before or after treatment.

**Conclusion:** Iodized peanut oil is more efficacious in controlling iodine deficiency than is iodized poppy seed oil containing the same amount of iodine. *Am J Clin Nutr* 2006;84:1208–14.

**KEY WORDS** Iodized oil, peanut oil, poppy seed oil, efficacy, iodine, deficiency, schoolchildren, Indonesia

## INTRODUCTION

Effective control of iodine deficiency is still a challenge in many developing countries (1–3). Despite the remarkable success of global salt iodization programs (4, 5), limited progress has been made in some countries or regions because of a shortage in the supply of iodized salt, a lack of political commitment and legislation, a low awareness of the importance of iodized salt, and inadequate monitoring (6–9). In some emergency situations, the distribution of iodized salt may also be complicated. Single intramuscular injections of iodized oil provide adequate iodine for 2–3 y (10, 11), but injections have serious disadvantages, including the potential to serve as a vector for communicable diseases and the expense involved (12). Oral administration of iodized oil has been advocated as an alternative, but experience with this

method is limited, and the optimal dose and the frequency of dosing remain uncertain (13, 14).

Until recently, the main raw material for iodized oil has been poppy seed oil. A study by van der Heide et al (15) indicated that iodine from iodized oil prepared from ethyl oleate was retained longer in both men and rats than that prepared from ethyl linoleate or ethyl esters of poppy seed oil fatty acids. Oils such as peanut oil, which are rich in oleic acid, also have the advantage of being a cheaper raw material than poppy seed oil. Therefore, we decided to compare the efficacy of a preparation of iodized peanut oil introduced into the Indonesian market (16) with that of the established iodized poppy seed oil preparation. While this work was underway, Ingenbleek et al (17) reported on the efficacy of iodized rapeseed oil, the composition of which is not unlike that of iodized peanut oil. Preliminary results from the study presented here were published previously (18).

## SUBJECTS AND METHODS

### Subjects

All schoolchildren ( $n = 355$ ) aged 8–10 y attending 4 primary schools in Cilacap district, Central Java Province, Indonesia, where goiter is highly prevalent ( $>30\%$ ) (19), were examined by a medical assistant from the Subdistrict Health Center. Only apparently healthy subjects were considered for entry into the study.

The ethical guidelines of the Council for International Organizations of Medical Sciences (20) were followed. It was possible to include a placebo group in this study because plans have been drawn up to introduce iodized salt in the area and because iodine deficiency in the population was not severe. The Ethical Committee for Studies on Human Subjects, Faculty of Medicine,

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**TABLE 1**

Fatty acid composition of iodized poppy seed oil and iodized peanut oil administered orally

Fatty acid	Proportion of fatty acids	
	Poppy seed oil <sup>1</sup>	Peanut oil <sup>2</sup>
	g/100 g	
Saturated		
Palmitic acid (16:0)	9.0	14.6
Stearic acid (18:0)	3.0	0.2
Unsaturated		
Oleic acid (18:1n-9)	14.0	41.1
Linoleic acid (18:2n-6)	73.0	38.9
α-Linoleic acid (18:3n-3)	0.0	1.5
Long-chain (≥20 carbons)	0.0	1.8
Other	1.0	1.9

<sup>1</sup> From reference 21.

<sup>2</sup> From reference 16.

University of Indonesia, approved the study. Informed consent was obtained from the parents of each subject before the start of the study. Iodized oil was given at the end of the study to those children who were still considered iodine deficient.

**Study design**

This study was designed as a community-based, double-blind, placebo-controlled supplementation trial. A sample size of 50 per group was calculated with a power index of 2.80, α = 0.05, and β = 0.20 to obtain a significant difference of 10% in urinary iodine concentrations between groups with an expected dropout rate of 20%. Eligible children (n = 347) were randomly selected and randomly allocated to 1 of 5 groups (50 per group) to receive 1 of the following preparations: 1 mL peanut oil as placebo (P0); 0.5, 1.0, and 2.0 mL iodized peanut oil (Yodiol, 400 mg I/mL; PT Kimia Farma, Indonesia), providing 200 mg I (P200), 400 mg I (P400), and 800 mg I (P800), respectively; or 1 mL ethyl esters of iodized poppy seed oil (Lipiodol UF, 400 mg I/mL; Guerbet Laboratory, France), providing 400 mg I (PS400) (21). The placebo group was used to control whether the subjects were exposed to extraneous iodine during the study. Neither the studied subjects nor the researchers were aware which supplement (treatments or placebo) each subject received. A code was broken only at the completion of the trial. The dropout rates for all treatment and placebo groups were <5% (4% for PS400 and P200, 2% for P400, and 0% for P800 and P0). The fatty acid composition of peanut oil compared with that of poppy seed oil is shown in **Table 1**.

In a previous study by Furnee et al (22), the retention of iodine from orally administered iodized oil was found to be reduced significantly by intestinal parasitic infestation. Therefore, 1 wk before oil administration, all subjects were dosed with the broad spectrum antihelminth albendazole (400 mg per dose; SmithKline Beecham, Jakarta, Indonesia) to control *Ascaris lumbricoides* because it is known that these parasites are endemic (23).

The iodine status of the children was assessed on the basis of 4 different indicators, ie, thyroid volume, urinary iodine concentration, serum thyroid-stimulating hormone (TSH), and serum free thyroxine (FT<sub>4</sub>) at baseline and after 25 and 50 wk. Urinary iodine concentrations were also measured at 4 and 12 wk.

**Measurement of thyroid volume**

Thyroid volume was measured with ultrasound by the main researcher (JU), who had been trained in the technique. Ultrasonography was performed on each subject in the sitting position with the use of equipment with a transducer of 7.5 MHz (SDR 1480; Phillips, Eindhoven, Netherlands). The transducer was first kept horizontal at an upright angle to the neck to observe the cross section of the thyroid, measuring maximal width and maximal depth. Next, the length of each lobe was determined by longitudinal application of the transducer to the subject's neck. A coworker recorded the observations of the ultrasonography and provided a continuous flow of persons to be examined. The volume was calculated by using the following formula: volume = 0.479 × maximal depth × maximal width × length (cm<sup>3</sup>) (24). The thyroid volume was the sum of the volumes of each lobe. Results of ultrasonography from the study population were compared with normative data based on body surface area from populations with sufficient iodine intakes (25).

**Serum TSH and serum FT<sub>4</sub>**

Venous blood samples (3 mL) were drawn from an antecubital vein from nonfasting subjects between 0830 and 1200. Immediately after collection, the blood was placed on ice, protected from light, and, within 2–3 h, centrifuged (2000 × g, 10 min, room temperature) at the laboratory of the district health center to obtain serum. Serum was frozen in a series of containers at –70 °C before being transferred, packed in dry ice, to the laboratory of Endocrinology, Academic Medical Center (Amsterdam, Netherlands) for analysis.

Serum concentrations of TSH were measured by immunoluminometric assay with a commercial kit (Brahms Diagnostica GmbH, Berlin, Germany), and FT<sub>4</sub> was measured by time-resolved fluoroimmunoassay after immunoextraction with the use of a commercial kit (Delfia, Wallac Oy, Turku, Finland). The intraassay and interassay CVs for TSH were 2.4% and 4.5%, respectively, and for FT<sub>4</sub> were 3.6% and 6.4%, respectively. Values for both TSH and FT<sub>4</sub> were within 10% of the target value of normal and elevated samples provided every 2 mo by the Dutch national external quality control scheme for hormones in serum. The reference ranges for iodine-replete subjects, as determined in our laboratory, were 0.4–4.0 mU/L for serum TSH and 10–24 pmol/L for FT<sub>4</sub>.

**Urinary iodine concentration**

A casual urine sample (5 mL) was collected between 0830 and 1200 on 2 consecutive days at baseline and 4, 12, 25, and 50 wk after treatment. The urine samples, preserved with ≈1 g thymol, were sent to the iodine laboratory of the Nutritional Research and Development Center in Bogor (Indonesia). The iodine concentration in urine was analyzed in duplicate after alkaline digestion with the use of the Sandell-Kolthoff reaction (26); average values were calculated for each child.

The model for describing urinary iodine after oral dosing of iodized oil developed by Furnée et al (13) was used. The model reflects the effects of iodine retention and elimination on urinary iodine concentration.

$$I_t = (\alpha_0 + \alpha_i)t^{-(\beta_0 + \beta_i)} \tag{1}$$

where *I<sub>t</sub>* is the urinary iodine concentration at time *t* (μmol/L), α<sub>0</sub> is iodine retention for placebo subjects (μmol/L), α<sub>*i*</sub> is iodine

**TABLE 2**

Baseline demographic characteristics and iodine status of schoolchildren aged 8–10 y living in an iodine-deficient area of Indonesia

Characteristic	Iodized poppy seed oil, 400 mg I (n = 49)	Iodized peanut oil			
		200 mg I (n = 50)	400 mg I (n = 51)	800 mg I (n = 50)	Peanut oil (n = 51)
Sex (M:F) <sup>1</sup>	19:30	26:24	23:28	29:21	20:31
Age (y) <sup>2</sup>	9.54 ± 0.77 <sup>3</sup>	9.36 ± 0.79	9.53 ± 0.78	9.39 ± 0.71	9.41 ± 0.75
Thyroid volume (mL) <sup>4</sup>	4.45 (3.72, 4.92) <sup>5</sup>	4.51 (4.00, 5.27)	4.68 (3.81, 5.35)	4.92 (4.23, 5.69)	4.33 (3.65, 5.47)
Urinary iodine concentration (μmol/L) <sup>6</sup>	0.35 (0.28, 0.71)	0.37 (0.29, 0.60)	0.34 (0.30, 0.64)	0.37 (0.23, 0.62)	0.38 (0.24, 0.64)
Serum thyroid-stimulating hormone concentration (mU/L) <sup>7</sup>	1.60 (1.10, 2.38)	1.50 (0.96, 2.20)	1.90 (1.10, 2.60)	1.80 (1.58, 2.50)	1.70 (1.20, 2.30)
Serum free thyroxine concentration (pmol/L) <sup>8</sup>	16.86 ± 2.53	16.78 ± 1.96	16.81 ± 2.07	16.98 ± 2.78	16.74 ± 2.66

<sup>1</sup> Compared by using a chi-square test (NS).<sup>2</sup> Compared by using one-way ANOVA (NS).<sup>3</sup>  $\bar{x} \pm SD$  (all such values).<sup>4</sup> Compared by using one-way ANOVA on log-transformed data (NS).<sup>5</sup> Median; 25th to 75th percentiles in parentheses (all such values).<sup>6</sup> Compared by using one-way ANOVA on log-linear-transformed data (NS).<sup>7</sup> Compared by using a Kruskal-Wallis test (NS).<sup>8</sup> Compared by using one-way ANOVA (NS).

retention for supplemented subjects ( $\mu\text{mol/L}$ ),  $t$  is the time after dosing with iodized oil (wk),  $\beta_0$  is the rate of iodine elimination for placebo subjects ( $\mu\text{mol} \cdot \text{L}^{-1} \cdot \text{wk}^{-1}$ ), and  $\beta_1$  is the rate of iodine elimination for supplemented subjects ( $\mu\text{mol} \cdot \text{L}^{-1} \cdot \text{wk}^{-1}$ ).

### Statistical methods

The Kolmogorov-Smirnov test was used to check the normality of data. Data are reported as means  $\pm$  SDs for normally distributed variables and as medians and 25th to 75th percentiles for nonnormally distributed variables. Differences between groups were examined by analysis of variance (ANOVA) or, for nonnormally distributed variables, by the Kruskal-Wallis test. If significant differences were indicated, comparisons between groups were made by using Bonferroni's multiple comparison test at a significant level of  $P < 0.05$ .

The mathematical functions, transformed into log-linear equivalents, were fitted to the 4 values of urinary iodine concentration in the 4 treatment groups. The parameters  $\alpha$ ,  $\beta$ , and  $t$  were estimated by using the maximum likelihood estimation technique (27) based on the average urinary iodine concentration measured in individuals on consecutive days. The SPSS software package (WINDOWS version 7.5.3; SPSS Inc, Chicago, IL) was used for all statistical analyses, and a  $P$  value  $< 0.05$  was considered significant.

## RESULTS

### Subject characterization

No significant differences in age, thyroid volume, urinary iodine concentration, serum TSH, and serum FT<sub>4</sub> were observed between the groups at baseline (Table 2). The children were, on average, aged  $9.45 \pm 0.76$  y and moderately iodine deficient; the median urinary iodine concentration was  $0.36 \mu\text{mol/L}$  (25th to 75th percentiles: 0.27,  $0.63 \mu\text{mol/L}$ ). The prevalence of goiter was 24% (based on thyroid volume and body surface area), and

the median thyroid volume of all children was 4.51 mL (25th to 75th percentiles: 3.96, 5.33 mL). No statistically significant differences in thyroid volume, urinary iodine concentration, serum TSH, and serum FT<sub>4</sub> concentrations were observed between boys and girls.

### Urinary iodine concentration

Urinary iodine concentrations after oral iodized oil supplementation in the different groups are shown in Table 3. At all periods of follow-up, urinary iodine concentrations were significantly higher ( $P < 0.001$ ) in all treated groups than in the placebo group, which received peanut oil. The higher the dosage of iodine in iodized peanut oil, the higher the urinary iodine concentration ( $P < 0.001$ ). The urinary iodine concentration in the group supplemented with PS400 was not significantly different from that of the P200 group and was significantly lower than that of other supplemented groups at all periods of follow up ( $P < 0.001$ ).

### The regression model of urinary iodine

The efficacy coefficients of iodine retention, iodine elimination rate, and the protection period for different groups of treatment are shown in Table 4. The iodine retention ( $P < 0.0001$ ), elimination rate ( $P < 0.01$ ) and the duration of protection ( $P < 0.001$ ) were significantly different between the 4 groups, except for the difference in duration of protection between the PS400 and P200 groups. Urinary iodine concentrations, as predicted by the regression model, after oral iodized oil supplementation for the different treatment groups are given in Figure 1. From week 4, iodine excretion declined exponentially. If a urinary iodine concentration of  $0.79 \mu\text{mol/L}$  is taken as the cutoff point below which the recommended dietary allowance is not being met, then the protection period provided by PS400 was  $\approx 42$  wk and that with P200 was 49 wk. On the basis of the mathematical model (Equation 1), the estimated durations of protection provided by P400 and P800 are 77 and 124 wk, respectively (Table 4).

**TABLE 3**

Median urinary iodine concentrations before and after 5 iodine supplementation treatments in schoolchildren aged 8–10 y living in an iodine-deficient area of Indonesia<sup>1</sup>

Period <sup>2</sup>	Iodized poppy seed oil, 400 mg I (n = 49)	Iodized peanut oil			
		200 mg I (n = 50)	400 mg I (n = 51)	800 mg I (n = 50)	Placebo (n = 51)
Baseline <sup>3</sup>	0.35 (0.28, 0.71) <sup>a</sup>	0.37 (0.29, 0.61) <sup>b</sup>	0.34 (0.30, 0.64) <sup>c</sup>	0.37 (0.23, 0.62) <sup>c</sup>	0.38 (0.24, 0.64) <sup>c</sup>
4 wk	3.71 (1.82, 5.19) <sup>a</sup>	4.21 (2.33, 6.89) <sup>b</sup>	7.31 (4.07, 10.94) <sup>c</sup>	12.15 (9.19, 18.66) <sup>d</sup>	0.54 (0.30, 0.87) <sup>c</sup>
12 wk	1.91 (1.16, 4.00) <sup>a</sup>	2.39 (1.55, 3.76) <sup>b</sup>	4.38 (2.85, 7.47) <sup>c</sup>	8.84 (6.47, 11.15) <sup>d</sup>	0.66 (0.49, 0.96) <sup>c</sup>
25 wk	1.34 (0.94, 2.33) <sup>a</sup>	1.56 (1.13, 2.20) <sup>b</sup>	2.01 (1.32, 3.53) <sup>c</sup>	4.00 (2.19, 6.55) <sup>d</sup>	0.67 (0.50, 1.02) <sup>c</sup>
50 wk	0.87 (0.71, 1.11) <sup>a</sup>	0.98 (0.80, 1.44) <sup>b</sup>	1.34 (0.92, 1.92) <sup>c</sup>	1.92 (1.21, 2.69) <sup>d</sup>	0.70 (0.61, 0.83) <sup>e</sup>

<sup>1</sup> All values are medians; 25th to 75th percentiles in parentheses. Values in a row with different superscript letters are significantly different, *P* < 0.05 (Bonferroni's multiple comparisons test).

<sup>2</sup> Compared by using ANOVA on log-linear-transformed data: treatment × time, *P* < 0.001.

<sup>3</sup> Compared across groups by using one-way ANOVA on log-linear-transformed data (NS).

**Thyroid volume**

The thyroid volumes measured by ultrasound for the different treatment groups are presented in **Table 5**. No significant differences in thyroid volumes were observed between groups at baseline (*P* = 0.085), but significant differences in thyroid volumes were observed after supplementation between the placebo group and all treatment groups. After a year of supplementation, the reduction in goiter volume was significantly greater in the supplemented groups than in the placebo group at all periods of follow-up (*P* < 0.001). No significant difference in the reduction of goiter volume was observed between subjects supplemented with P200 or P400 and those supplemented with PS400.

**Serum TSH and serum FT<sub>4</sub>**

Initial median TSH values were not significantly different between the 5 groups and were within the normal range, but 2.8% of individuals had values >5 mU/L (Table 2). At 50 wk after treatment, median TSH values (mU/L) remained within the normal range: 1.60 (25th to 75th percentiles: 1.18, 2.30) in the placebo group and 1.80 (1.30, 2.70) in the iodized oil groups; none of the subjects had concentrations >5 mU/L. Mean serum FT<sub>4</sub> concentrations at baseline were in the normal range and were not significantly different between the 5 groups (Table 2). There

was a small but nonsignificant increase in serum FT<sub>4</sub> concentrations at 25 wk in all groups: 17.32 ± 3.08 pmol/L in the placebo group and 17.98 ± 3.13 pmol/L in the iodized oil groups. Serum FT<sub>4</sub> concentrations returned to baseline at 50 wk: 16.74 ± 3.05 pmol/L in the placebo group and 16.97 ± 2.51 pmol/L in the iodized oil groups.

**DISCUSSION**

This study showed that supplementation with oral iodized oil is an appropriate measure to control iodine deficiency, whereas iodized salt is not yet effective. This study also found that the fatty acid composition of the iodized oil determines the efficacy of the treatment. Four outcome indicators were used to assess the efficacy of different oral iodized oil supplementation regimens: urinary iodine concentration, thyroid volume, and serum TSH and serum FT<sub>4</sub> concentrations.

Urinary iodine concentrations showed large variability and were very high in some subjects. Urinary iodine increased significantly in all treatment groups, including the placebo group, between 0 and 4 wk. The slight differences in urinary iodine concentrations in the placebo group (*P* < 0.05) could indicate that some children might have been exposed to an extraneous

**TABLE 4**

Iodine retention and elimination and the model-based duration of protection after oral administration of different iodized oil preparations to schoolchildren aged 8–10 y living in an iodine-deficient area in Indonesia<sup>1</sup>

Variable	Iodized poppy seed oil, 400 mg I (n = 49)	Iodized peanut oil		
		200 mg I (n = 50)	400 mg I (n = 51)	800 mg I (n = 50)
Iodine retention, α <sub>1</sub> (μmol/L) <sup>2</sup>	5.88 ± 1.158 <sup>a,3</sup>	8.59 ± 1.145 <sup>b</sup>	17.55 ± 1.146 <sup>c</sup>	40.41 ± 1.141 <sup>d</sup>
Iodine elimination rate, β <sub>1</sub> (μmol · L <sup>-1</sup> · wk <sup>-1</sup> ) <sup>4</sup>	0.45 ± 0.051 <sup>a</sup>	0.53 ± 0.047 <sup>b</sup>	0.64 ± 0.047 <sup>c</sup>	0.75 ± 0.046 <sup>d</sup>
Duration of protection, <i>t</i> (wk) <sup>5</sup>	42.3 (33.8, 60.0) <sup>a</sup>	49.2 (40.0, 69.2) <sup>a</sup>	76.9 (62.1, 112.7) <sup>b</sup>	123.6 (96.0, 171.7) <sup>c</sup>

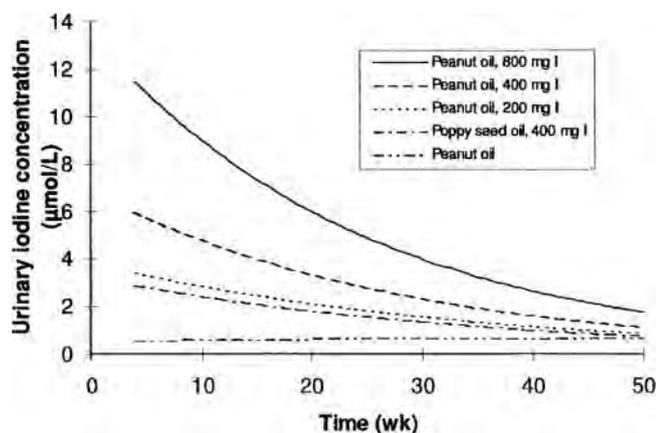
<sup>1</sup> The calculation is based on the mathematical model  $I_t = (\alpha_0 + \alpha_1)t^{-(\beta_0 + \beta_1)}$ , where  $I_t$  is the urinary iodine concentration at time  $t$  (μmol/L),  $\alpha_0$  is iodine retention for placebo subjects (μmol/L),  $\alpha_1$  is iodine retention for supplemented subjects (μmol/L),  $t$  is the time after dosing with iodized oil (week),  $\beta_0$  is the rate of iodine elimination for placebo subjects (μmol · L<sup>-1</sup> · wk<sup>-1</sup>), and  $\beta_1$  is the rate of iodine elimination for supplemented subjects (μmol · L<sup>-1</sup> · wk<sup>-1</sup>). Values in a row with different superscript letters are significantly different, *P* < 0.05 (Bonferroni's multiple comparisons test).

<sup>2</sup> Compared by using one-way ANOVA, *P* < 0.0001.

<sup>3</sup>  $\bar{x} \pm$  SEM (all such values).

<sup>4</sup> Compared by using one-way ANOVA, *P* < 0.01.

<sup>5</sup> Time after dosing when the urinary iodine concentration remained >0.79 μmol/L (100 μg/L) after correction for changes in the urinary iodine concentration in the peanut oil (placebo) group; values in parentheses are 95% CI. Compared by using one-way ANOVA, *P* < 0.001.



**FIGURE 1.** Urinary iodine concentrations in the 4 iodine supplementation groups and the placebo (peanut oil) group. Regression equation:  $I_t = \alpha_1 t^{-\beta_1}$ .

source of iodine, possibly iodized salt (19). The urinary iodine concentrations of all supplementation groups, at the different periods of follow up (4, 12, 25, and 50 wk), were significantly greater than those of the placebo group (Table 3).

The efficacy of PS400, as indicated by urinary iodine concentrations, was not significantly different from that of P200 but was significantly lower than that of iodized peanut oil, which provided 400 mg I (P400) or 800 mg I (P800) at all periods of follow up (Table 4). On the basis of a mathematical model (13) comparing the iodized oil preparations supplying 400 mg I after adjustment for the increase of urinary iodine concentration in the placebo group, iodine retention from the iodized peanut oil preparation was 3 times that from the iodized poppy seed oil preparation. In addition, iodized peanut oil gave an estimated duration of protection against iodine deficiency that was twice that provided by iodized poppy seed oil (77 compared with 42 wk; Table 4). These findings confirmed the results from previous studies in rats and humans (15), in which it was shown that iodine was retained longer from a preparation prepared from ethyl oleate than from a preparation prepared from ethyl linoleate or from ethyl esters derived from poppy seed oil.

A study by Ingenbleek et al (17) of the efficacy of iodized rapeseed oil was published while this study was being carried out. These authors found that iodized rapeseed oil supplying 752 mg I provided a longer period of protection (30 wk) in moderately iodine-deficient adults than did iodized poppy seed oil supplying

729 mg (17 wk) when a urinary iodine concentration of 0.79  $\mu\text{mol/L}$  was taken as the cutoff point. Most of the iodine in the rapeseed oil preparation was bound to oleic acid (52.5%), whereas most of the iodine in the poppy seed oil preparation was bound to linoleic acid (72.7%). In a comparison of iodized peanut oil with iodized poppy seed oil, the proportion of iodine derived from iodized oleic acid was higher (41% compared with 14%) and from linoleic acid was lower (39% compared with 73%) in the iodized peanut oil. On the basis of the mathematical model (Equation 1), we projected that iodized peanut oil supplying 400 mg I had an estimated protection period of  $\approx 77$  wk, and iodized peanut oil supplying 800 mg I had a protection period of 124 wk in moderately iodine-deficient schoolchildren (Table 4). Apart from the type of oil used and the location, the subjects from the Chad study were older (18–40 y) and were more iodine deficient than were the children from our study.

Compared with the previous studies in schoolchildren, our results showed that oral iodized poppy seed oil supplying 400 mg I could protect schoolchildren from iodine deficiency for 42 wk (Table 4), which was about twice as long as that shown by Benmiloud et al (28) and thrice as long as that shown by Furnée et al (13), who used a cutoff point of 0.40  $\mu\text{mol/L}$  for urinary iodine. The differences in urinary iodine concentrations between these studies might be due to the severity of iodine deficiency; the median urinary iodine concentration at baseline was 0.21  $\mu\text{mol/L}$  and was 0.16  $\mu\text{mol/L}$  in the study by Benmiloud et al (28) and the study by Furnée et al (13). Other possible factors are exposure to goitrogenic substances, nutritional status, the indicators used, and the cutoff points used.

We also showed that high doses of iodine (ie, 400 and 800 mg) correct iodine deficiency without side effects, as was found in the study by Elnagar et al in Sudan (29). They found that doses of 400 and 800 mg I induced some adverse reactions, such as iodine-induced inhibition of hormone synthesis (Wolff-Chaikoff effect), and were slightly less effective than was a dose of 200 mg I.

Thyroid volumes were significantly lower in the groups supplemented with iodized oil than in the placebo group. Median thyroid volume decreased significantly in all groups, and the reduction in thyroid volume was significantly greater in all treatment groups than in the placebo group. The reduction in thyroid volume in the placebo group might have been due to salt iodization programs in the area during the study (19). The reduction in thyroid volume was positively correlated with the change in

**TABLE 5**

Goiter volume at baseline and after iodine supplementation in different treatment groups of schoolchildren living in an iodine-deficient area of Indonesia<sup>1</sup>

Period <sup>2</sup>	Iodized poppy seed oil,	Iodized peanut oil			Peanut oil (n = 51)
	400 mg I (n = 49)	200 mg I (n = 50)	400 mg I (n = 51)	800 mg I (n = 50)	
Baseline (mL) <sup>3,4</sup>	4.45 <sup>a</sup> (3.72, 4.92)	4.51 <sup>a</sup> (4.00, 5.27)	4.68 <sup>a</sup> (3.81, 5.35)	4.92 <sup>a</sup> (4.23, 5.69)	4.33 <sup>a</sup> (3.65, 5.47)
25 wk (mL) <sup>4</sup>	3.22 <sup>a</sup> (2.96, 3.68)	3.64 <sup>b</sup> (3.05, 4.29)	3.53 <sup>b</sup> (2.99, 4.26)	3.88 <sup>b</sup> (3.21, 4.61)	4.08 <sup>c</sup> (3.44, 5.26)
50 wk (mL) <sup>4</sup>	3.11 <sup>a</sup> (2.73, 3.31)	3.31 <sup>b</sup> (2.91, 3.68)	3.25 <sup>b</sup> (2.81, 3.63)	3.21 <sup>b</sup> (2.86, 3.48)	4.10 <sup>c</sup> (3.70, 5.35)
Reduction (%) <sup>5</sup>	28.6 ± 11.9 <sup>d</sup>	23.1 ± 15.7 <sup>d</sup>	26.6 ± 17.8 <sup>d</sup>	33.5 ± 14.3 <sup>e</sup>	3.0 ± 3.5 <sup>f</sup>

<sup>1</sup> Values in a row with different superscript letters are significantly different,  $P < 0.05$  (Bonferroni's multiple comparisons test).

<sup>2</sup> Compared by using ANOVA on log-transformed data: treatment  $\times$  time,  $P < 0.001$ .

<sup>3</sup> Compared across groups by using one-way ANOVA on log-transformed data (NS).

<sup>4</sup> All values are medians; 25th to 75th percentiles in parentheses.

<sup>5</sup> All values are  $\bar{x} \pm \text{SD}$ . Reduction in thyroid volume at 50 wk compared with baseline. Compared by using one-way ANOVA,  $P < 0.01$ .

urinary iodine concentrations in all groups ( $r = 0.22$ ). The thyroid volumes of previously iodine-deficient children decreased to normal values in the groups who received either iodized poppy seed oil or iodized peanut oil, which indicated that the treatment of iodine-deficient subjects with oral iodized oil effectively reduced goiter size, even when the goiter was small.

The efficacy of treatment indicated by the normalization of urinary iodine concentrations and thyroid volumes was not supported by changes in serum concentrations of TSH and FT<sub>4</sub>. Our results contrast with those reported by Elnagar et al (29), Tonglet et al (30), and Zimmermann et al (31). They found that the efficacy of oral iodized oil supplementation was evidenced by normalization of serum T<sub>4</sub> and TSH concentrations, reduction of goiter size measured by palpation, or by an increase in urinary iodine concentration. Our data showed that median TSH concentrations were in the normal range before iodine treatment, and only 2.8% of the subjects had concentrations higher than the upper normal limit. The responses of serum TSH were not correlated with the dose or type of iodized oil. The mean concentration of serum FT<sub>4</sub> before iodine treatment was in the normal range and increased slightly after iodine treatments; concentrations were not significantly different between the placebo and treatment groups. Our results concur with those of Gutekunst et al (32), Delange et al (33), and Ozkan et al (34), who observed no relation between serum TSH concentrations and thyroid volume. Bourdoux (35) reported that the circulating concentrations of thyroid hormones and TSH in mildly iodine-deficient populations are not different from those in iodine-replete populations, whereas, in moderately iodine-deficient populations, in whom the prevalence of goiter ranged from 20% to 50%, it was observed that concentrations of circulating triiodothyronine and T<sub>4</sub> were still in the normal range (35). The finding that the urinary iodine concentrations and thyroid volumes of iodine-deficient children became normal after supplementation, although serum TSH and serum FT<sub>4</sub> did not show the same response to treatment, suggests that serum TSH and FT<sub>4</sub> might be less reliable indicators for assessing and monitoring the treatment of moderately iodine-deficient schoolchildren than are urinary iodine concentration and thyroid volume (36).

We conclude that iodine retention after a single oral dose of iodized peanut oil was 3 times that after a single oral dose of iodized poppy seed oil, which resulted in double the period of protection in iodine-deficient schoolchildren. Thus, iodized oil prepared from oleic acid-rich oils, such as peanut oil and rapeseed oil, are preferred to preparations based on poppy seed oil in programs to control iodine deficiency. 

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All of the authors contributed to the study design. JU performed the fieldwork, collected the data, and wrote the manuscript. JU, WS, CEW, and RG performed the statistical analysis. WS, CEW, RG, and JGAJH edited the manuscript. None of the authors had a financial or personal conflict of interest in regard to this study.

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