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Human iodine requirements determined by the saturation kinetics model

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Abstract

Iodine plays a decisive role in metabolism and the process of early growth and development of most organs, especially of the brain. Effects of iodine deficiency include goiter, stillbirth and miscarriage, neonatal and juvenile thyroid deficiency, dwarfism, mental defects, deaf mutism, spastic weakness and paralysis. In this study, the application of a mathematical model (derived from Machaelis-Menten enzyme kinetics) to iodine measured in urine samples from a randomly selected group derived from the Egyptian village of West El-Mawhoub in the Dakhlah Oasis resulted in the conclusion that iodine excretion parameters can be used to characterize iodine utilization and accurately predict the level of salt iodination required to maintain proper physiological functions. The four parameter saturation kinetics model analysis indicated that a salt iodination level of 63 mg/kg reduced the severity of IDD, with 83% of the studied subjects having urinary excretion levels of 1.18 μmol/L. This gives a convenient mechanism for providing adequate dietary iodine with a non-invasive index for the avoidance of IDD. Commercially available salt was analyzed using standard iodiometric titration methods to determine iodination levels. Analysis revealed that only 20% of the commercially available salt complied with the manufacturer's label and revealed the presence of large individual variability between batches amounting to −95 to +150% of the claimed iodine level. Therefore, salt iodination requires careful supervision to ensure that promised iodine levels are being delivered and consumed.

Keywords: Mathematical model; Nutrient requirement; Iodine deficiency; Goiter; Nutrition intervention

1. Introduction

Iodine present in the earth has been gradually leached away from the soil surface by glaciations, snow and air and carried out by wind, rivers, and floods into the sea and oceans, where the concentration of iodide in deep sea water is about 50-60 μg/L [1]. Evaporation from the ocean into the atmosphere occurs, where it is then concentrated in rain and falls back to the earth replenishing the soil. It is estimated that every year about 400 tons of iodine escape from the oceans [2].

Iodine deficiency persists in the soil indefinitely and the iodine content of plants grown in such soils may be as low as 10 μg/kg compared to 1000 μg/kg dry weight in plants in a non-iodine-deficient soil. As a result, human and animal populations, which are totally dependent on food grown in iodine-replete soil, become iodine deficient. This accounts for severe iodine deficiency in vast populations in Asia living within systems of subsistence agriculture [1].

Iodine is a trace element present in the human body in minute amounts (15-20 mg in adults). The only confirmed function of iodine is as an essential substrate for the synthesis of thyroid hormones, tetraiodothyronine (thyroxin or T_4) and triiodothyronine (T_3) [3]. Thyroid hormones play an important role in cellular metabolism, early growth and development of most organs, especially of the brain [4,5]. Consequently, a deficit in iodine and/or in thyroid hormones occurring during this critical period of life will result not only in the slowing down of metabolic activities but also in irreversible alterations in brain development [6]. The effects of iodine deficiency include goiter, stillbirth and miscarriage, neonatal and juvenile thyroid deficiency, dwarfism, mental defects, deaf mutism, spastic weakness and paralysis [7].

The normal intake of iodine is 100-150 μg per day and the thyroid has to trap about 60 μg per day to maintain an

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adequate pool [7]. The excretion of ingested dietary iodine in the feces has been reported to be 30% [8] and is dependent on the type of food eaten.

Thyroglobulin is a protein found in the colloid of follicular cells that binds the thyroid hormones. Thyroglobulin function as an iodine store and in healthy adults [8-15 mg] is 160-300 times the minimum daily requirement to maintain an euthyroid state [9,10]. This intake is sufficient to prevent clinical manifestation of iodine deficiency disorders for at least several months even if iodine would become absent from the diet [9,10].

A fall in the level of T_4 increases thyroid stimulating hormone (TSH) output from the pituitary enhancing uptake of iodide, and increased turnover associated with hyperplasia of the cells of the thyroid follicles. The reserves of colloid containing thyroglobulin are gradually used up so that the gland has a much more cellular appearance than normal.

The size of the gland increases with the formation of a goiter, enlargement is regarded as significant in the human when the size of the lateral lobes is greater than the terminal phalanx of the thumb of the person examined. Measurements that are more precise can now be made using ultrasound [7]. Goiter becomes almost universal in a population with an iodine intake less than 10 μg per day [7].

Endemic goiter is caused by iodine deficiency as well as other multiple factors resulting in variations in the prevalence observed between areas, where iodine intake is scarcely below normal. From a public health point of view, it has been suggested that endemic goiter can be defined as a prevalence of goiter of at least grade 1B of 5% or more in pre-and adolescent individuals or of 30% or more of grade 1A among adults [11]. At this level, public health intervention seems to be called for.

The physiological requirement of iodine for humans is difficult to assess and has given rise to much controversy. Intake must be at least equal to the amount of hormonal iodine degraded at the level of the tissues and not recovered by the thyroid gland. In adults and adolescents, this amount is 50 to 150 μg iodine/day [12]. Therefore, the US National Research Council recommended a dietary allowance of iodine of 150 μg for adolescents and adults. The recommendation is 175 μg/day and 200 μg/day for pregnant and lactating women, respectively; 70-100 μg/day for children aged 1-10 years, 50 μg/day for infants aged 6-12 months and 40 μg/day for infants 6 months of age or younger.

The figure of 150 μg/day in adults is based on the following assumptions and observations, and in order to provide an extra margin of safety and to meet increased demand that may be imposed by natural goitrogens under certain condition. The daily iodine requirement for prevention of iodine deficient goiter in adults is approximately 1 μg/Kg body weight that is 50 to 100 μg/day. The figure of 100 to 150 μg/day in adults corresponds to the daily urinary excretion of iodide and to the iodine content of food in non-endemic areas. The iodine intake needed to prevent the plasma iodide level from falling below the critical limit of 1 μg/L, likely to initiate the onset of goiter, is 120 μg/day.

Several vehicles have been used for fortification with iodine including salt, bread, candy, milk, sugar, and water. Sources of salt are limited and are frequently the only commodity for which a community is not self-sufficient, thereby offering an excellent opportunity for intervention. Finally, the iodination technology is straightforward and can be adapted to many local conditions, at a low cost.

The goals of this study was to implement a salt iodination program in an iodine deficient endemic area of Egypt, and to identify, using the saturation kinetics model equation, the optimum iodine level in salt for correcting iodine deficiency disorder as characterized by urinary iodine excretion.

2. Subjects and methods

2.1. Subjects

A study was carried out to assess the iodine status among a randomly selected group derived from the Egyptian village of West El-Mawhoub in the Dakhlah Oasis (New Valley governorate). The study included 73 subjects of both sexes, ages 3-18 years. The chosen village population estimates were 6480 individuals belonging to 1114 households (1990 census). Nearly three quarters of the population depend on agriculture, while the rest are involved in non-agricultural business. The socioeconomic status of the households was scored as low. To assess the iodine status, clinical, biochemical and dietary indicators were tested on a randomly selected subpopulation of the village.

Methods included: goiter measurements; collection of morning urinary samples for iodine analysis; iodine analysis of local salt from the retail market; distribution of iodine enhanced salt samples; and a one-month follow-up to determine improved iodine status.

2.2. Goiter examination

The size of goiter was assessed according to the WHO classification shown in Table 1. This was carried out through the courtesy of Dr. Gamal A. Yamama.

2.3. Iodine analysis in urine

Urinary analysis for Iodine Deficiency Disorders is a common and acceptable method that reflects dietary iodine intake and median urinary intake tends to be representative of a population's iodine intake. Most methods of urinary analysis involve the spectrophotometric measurement of iodine in the Sandell-Kolthoff reaction [13].

At least one member of each household was requested to provide urine samples for baseline measurements and during the second home visit one month after distributing the salt preparations. Urinary baseline results were obtained for

Table 1
Classification of the goiter size according to the World Health Organization

Grade	Classification of Goiter size
O	No Goiter
IA	Thyroid lobes larger than ends of thumbs.
IB	Thyroid, enlarged, visible with head tilted back
2	Thyroid enlarged, visible with neck in normal positions
3	Thyroid greatly enlarged, visible from about 10 meters.

73 subjects, with this number reduced to 62 (85%) during the second visit. Morning urine was collected in clean dry test tubes. After labeling and capping, the tubes were placed in a deep freezer until transported to the laboratory for subsequent iodine analysis.

The analytical method for total iodine was based on the alkaline digestion method of Sandell-Kolthoff , 1937 [14] as modified by Gropple in 1988 [15].

A volume of 1 ml was pipetted from the urine samples into 10x1.5 cm test tubes and mixed with 0.5 ml KOH and 0.5 ml zinc sulfate. The samples then were dried overnight in an oven at 150°C. The ash was extracted with 6 ml of water by mechanical shaking for 30 min. After centrifugation, 2ml aliquots were diluted with 3 ml hydrochloric acid (0.33N).

Arsenous oxide (1 ml) was added and the content of the tube vortexed, followed by warming in a water bath for 15 min at 40°C. A volume of 1 ml of ceric ammonium sulfate was then added to all tubes with 15 s time intervals between additions.

The tubes were transferred to a water bath at 40°C for 15 min. Brucin (1%) was added in 0.5ml aliquots to each tube in the water bath. The tubes were next transferred to an oven heated to 105°C for 15 min. The reduction in the color of ceric ammonium sulfate with arsenous oxide in the presence of iodine as a catalyst was measured at 430 nm.

A standard curve using potassium iodide solution containing 10-80 mg/L (10-80 p.p.m) iodine was prepared. The intensity of the developed color was measured at 430 nm. The iodine concentration in urine was calculated from the standard curve.

Quality control for iodine was maintained by including three reagent blanks to monitor contamination and estimate detection limits. Validation of the analytical techniques with each batch of samples analyzed was tested with the help of certified reference materials.

Diagnostic criteria were as follows: very severe $= <$ 0.16 μM iodine/L urine; moderate $= 0.16 - < 0.39$ μM/L; mild $= 0.39 - < 0.79$ μM/L; and normal $= > 0.79$ μM/L.

This method is similar to that proposed by PAMM (Program Against Micronutrient Malnutrition), where both are based on the Sandell-Kolthoff method that utilizes the fact that iodine catalyzes the reduction of ceric (IV) ions to cerous (III) ions by arsenic in acidic conditions. The only difference is that the alkaline ashing of samples have been replaced by digestion with ammonium persulfate, which is less explosive and safer to work with, as well as cheaper [14]. The method proposed by PAMM performs spectrophotometric readings at 420 nm, while this analyzed samples at 430 nm [13].

2.4. Distribution of salt packages

Each household received a 4 kg package of one of the salt preparations with known iodine concentration (2.5, 14, 30 or 45 mg iodine/kg salt). The head of the household was given instructions to prepare all their cooking with these salt preparations during the course of the study. Forty-four kg of commercially packed salt (manufacturer El-Nasr Malahat) were purchased. The packages were emptied, and after thorough mixing, portions were taken for iodine analysis. Accordingly, four preparations were prepared with increasing iodine concentration (2.5, 14, 30, or 45 mg/kg). Each salt preparation was packed in plastic and the bags electrically sealed. For each iodination level, a specific colored marker was fixed on the front of the package.

2.5. Iodine analysis in salt

The iodine content of salt was determined by a standard iodometric titration [16]. For determining the iodine content in salt iodinated with potassium iodate, the following method was used. Fifty grams of salt was dissolved in water and made up to 250 ml in a volumetric flask. One ml of 1 mol/L sulfuric acid and five ml of 100 g/L potassium iodide was added. The liberated iodine was titrated with 0.0025 mol/L sodium thiosulfate, using starch as external indicator near the end of the titration. The test detects the presence of iodate over the range of recommended levels of iodination (6-130 mg of potassium iodate per kg of salt).

A 5 g/L starch solution was formulated using the following procedure: 50 ml of water was boiled with 0.25 g of rice starch for 1 min to which 120 g/L of potassium iodide solution and 100g/L hydrochloric acid was added. The potassium iodide solution was made by dissolving 6 g of KI in distilled water and made up to 50 ml and the hydrochloric acid formulated by adding 10 ml of 250 g/L HCl (relative density 1.12) to 15 ml of distilled water. All three solutions were stored in brown bottles sealed with glass stoppers. The reagent is stable for 2-3 days in a temperate climate.

In the field, small amounts of salt were placed separately on a saucer to be tested and a similar amount of a locally available iodinated salt. Both portions of salt were moistened with two drops of the iodate reagent. Iodinated salt will immediately turn grayish-blue and that color remains for

several minutes before turning brown. If the salt being tested turns the same grayish-blue, it is properly iodinated. The test can be used in the field to estimate roughly the relative degree of iodination in different samples because it produces a range of grayish-blue colors over the range of recommended concentrations.

2.6. Saturation kinetics analysis

The four parameter saturation kinetics model was proposed by Mercer [17] has four parameters and is based on the two parameter enzyme kinetics equation of n kinetic order (Michaelis-Menten Equation that describes allosteric enzyme kinetics). This equation describes accurately the response to a range of nutrient intakes at all regions of the curve and is related to enzyme-related processes. This is consistent with the concept that a nutritional response is a series of enzymatic reactions [17].

Optimal salt iodination was computed by applying the four-parameter saturation kinetics model (SKM) according to the following equation:

$$r = \frac{b(K.5)^n + RmaxI^n}{(K.5)^n + I^n} \quad (1)$$

Where

r = physiological response
I = dietary concentration or nutrient intake
Rmax = maximum theoretical response
K.5 = concentration or intake for 1/2 (Rmax + b)
n = apparent kinetic order
b = intercept on r axis

Observed data pairs (I, r) are fitted by standard non-linear curve fitting techniques and the four derived parameters are calculated (b, n, K.5, Rmax). These parameters can then be used to generate a theoretical response curve for varying levels of nutrient intake. Equation 2 is a mathematical derivative of equation 1 and since equation 1 is continuous in its derivatives, a slope curve can be generated using equation 2.

$$\text{slope} = \frac{nI^{n-1}(Rmax - b)(K.5)^n}{[(K.5)^n]^2} \quad (2)$$

One can then calculate a point on the nutrient-response curve associated with 95% slope reduction. The slope reduction approach was chosen since a 95% reduction in slope indicates that 95% of the potential of the nutrient for producing the response has been utilized.

Mathematical analysis was carried out using the software program Systat Version 7 (Systat, Inc, Evanston, Il 60201,).

Table 2
IDD severity among population of west El-Mawhoub assessed by clinical examination and biochemical analysis (IDD = urinary iodine excretion < 78.80 μM/L)

Grade of goiter	Number	Median of urinary iodine excretion, μM/L
0	16	0.59
IA	23	0.51
IB	24	0.46
2	10	0.28

3. Results

3.1. Urinary iodine excretion correlated with observance of goiter

The severity of IDD among the population group of West El-Mawhoub is presented in Table 2. Enlarged goiter concomitant with a decrease in the urinary iodine excretion was present in 77.5% of the population.

3.2. Effect of iodine level in salt preparations an improving iodine status

Fig. 1 and Table 3 shows that salt preparations fortified with iodine at levels of 30 and 45 mg/kg (30 and 45 ppm) were all effective in reducing the percentage incidence of IDD to roughly one third. An iodination level of 30 mg/kg resulted in 10.38 mM/L (13.18 μg/dl) of iodine being excreted in the urine after one month compared with a baseline value of 0.473 μM/L (6.0 μg/dl). A level of 45 mg/kg changed the urinary iodine excretion rate from 0.489 μM/L (6.2 μg/dl) to 11.49 mM/L (14.59 μg/dl) after one-month supplementation. Among the highest, two groups, mean urinary iodine excretions increased significantly ($P < 0.05$) compared with respective baseline data.

Median urinary excretion data among subjects with no goiter enlargement was 0.59 μM/L, while that among subjects with goiter enlargement (Grade IA + IB) was 0.51 μM/L. Subjects with Grade 2 goiter had a median urinary excretion of 0.28 μM/L (3.6 μg/dl).

3.3. Optimum level of iodine in salt preparation

The application of the saturation kinetic model (SKM) to the experimental data is illustrated in Figure 2. Urinary iodine excreted is depicted as a function of the iodine concentrations in the salt used for cooking. The fitted parameters are: b = 0.049 ± 1.28 μM/L; Rmax = 0.012 ± 6.02 μM/L; K.5 = 19.65 ± 1.85 mg/kg; and n = 2.52 ± 0.44. The parameters are interpreted in a manner analogous to enzyme kinetics. The saturation kinetic model indicated that for a maximum physiological response (Rmax), the iodine intake requirement is 63.32 mg/kg salt iodination, corresponding to 1.19×10^{-4} μM/L of excreted urinary iodine.

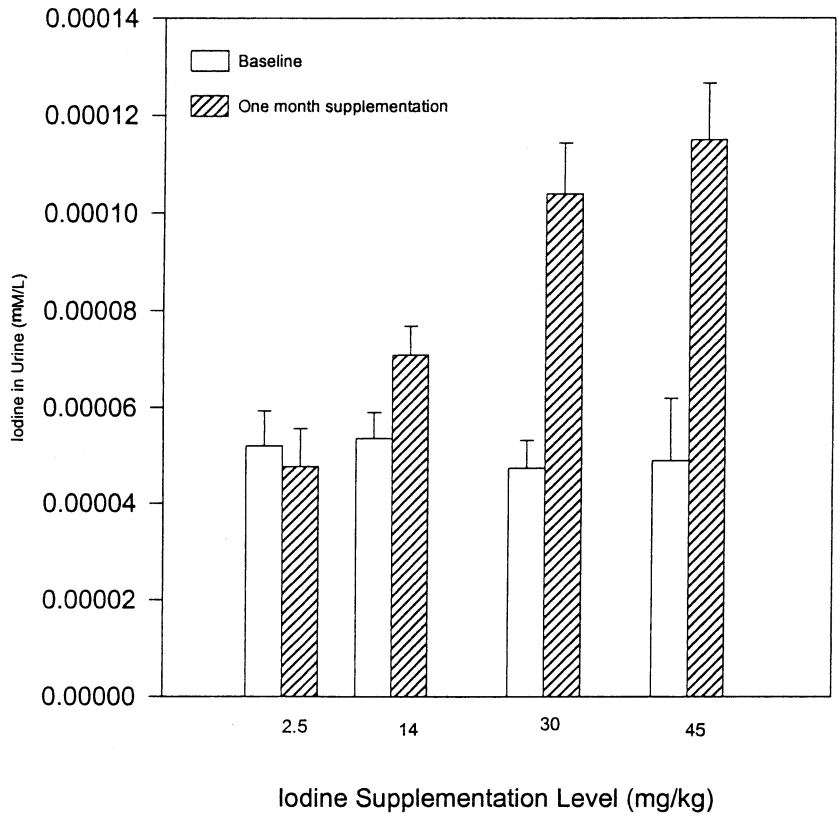

Fig. 1. Urinary excretion of iodine before and after supplementation with graded levels of iodinated salt. Values bearing the symbol * are significantly different ($P < 0.05$). Error bars represent SEMs.

3.4. Commercial salt

The commercial salt analyzed revealed that only 20% complied with the manufacturer's label as being iodinated with potassium iodate at levels of 50-80 mg/kg (50-80 ppm). Large individual variability between batches of iodinated commercial salt was found to vary from −95 to + 150% of the claimed iodine level.

4. Discussion

The 77.5% incidence of goiter enlargement among 73 subjects (mean age 17.3 years) from the New Valley region found in the present study was slightly lower than the respective percentage incidences of 82.6 and 82.1% reported earlier among males and females children respectively [18].

Table 3
Distribution of the study subjects according to patterns of severity of biochemical IDD[1] before and one month after distributing iodinated salt preparations

Iodine in salt Mg/kg	Total Number Examined	Very severe %	Moderate	Mild	Normal
2.5					
Baseline	15	7.14	28.5	42.8	21.4
After one month	9	0.0	44.4	44.4	11.1
14					
Baseline	24	8.3	33.3	41.6	16.6
After one month	21	0.0	15	35	50
30					
Baseline	18	5.6	27.8	55.6	11.0
After one month	17	0.0	11.76	11.76	76.47
45					
Baseline	16	6.25	37.5	50	6.25
After one month	14	0.0	0.0	28.6	71.47

[1] very severe = <0.16 μM iodine/L urine; moderate = 0.16 − <0.39 μM/L; mild = 0.39 − <0.79 μM/L; and normal = >0.79 μM/L.

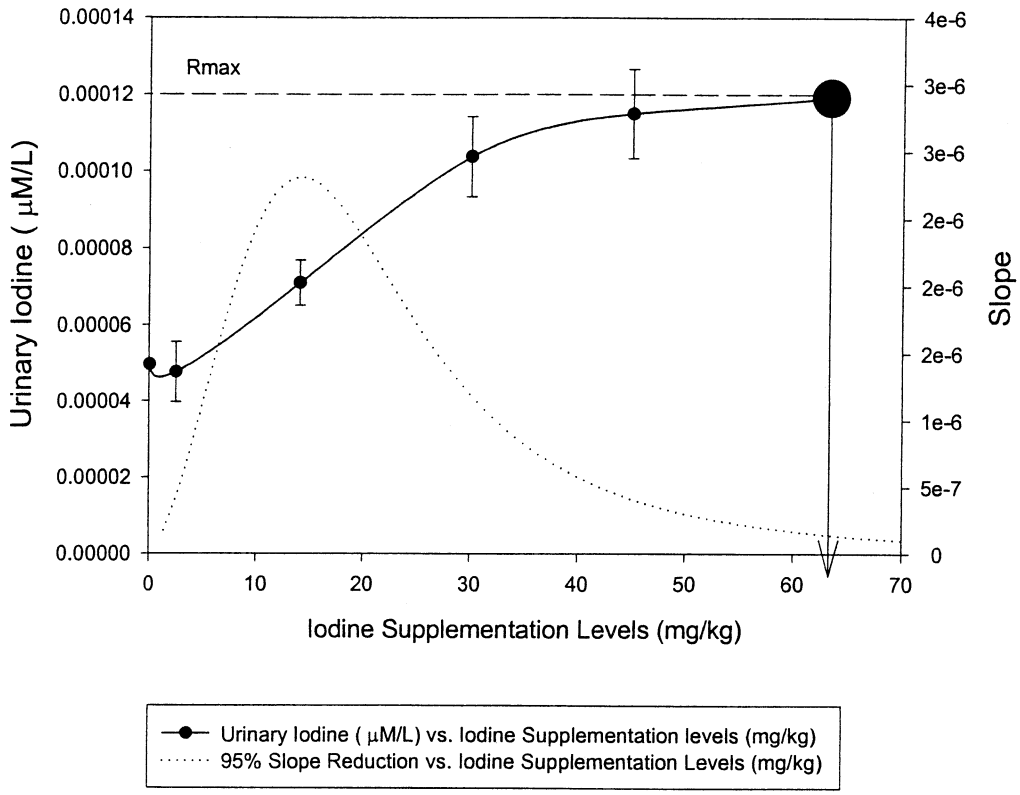

Fig. 2. Saturation kinetics response curve for urinary iodine as a function of salt supplementation level. The solid curve is the theoretical response curve predicted by the model equation. The dotted curve is the slope of the response, with standard error shown on values. The requirement is calculated for the point of 95% slope reduction. The fitted parameters are: b = 0.049 ± 1.28 μM/L; Rmax = 0.012 ± 6.02 μM/L; K.5 = 19.65 ± 1.85 mg/kg; and n = 2.52 ± 0.44.

In this study, iodine excretion parameters, determined by the application of the saturation kinetics model, can be conveniently used to characterize iodine utilization and determine a reasonable, achievable level of iodination with predictable results. Based on analysis using the saturation kinetics model, a salt iodination level of 63 mg/kg produces a urinary excretion of 1.19×10^{-4} μM/L. This gives a convenient mechanism for providing adequate dietary iodine with a non-invasive index of the avoidance of IDD. However, salt iodination requires careful supervision to ensure that promised iodine levels are being delivered and consumed.

Measurement of iodine concentrations from casual urine is now widely accepted as the best and most cost-effective way of monitoring iodine deficiency in a community [14,15,19]. Subjects with an iodide excretion below a certain cutoff point are considered to be at risk of a marginal iodine supply and therefore of goiter and other iodine deficiency disorders [1,13]. The parameters b and Rmax give the range of response, with b being the intercept on the response axis (response with no supplementation) and Rmax representing the plateau of response (maximum excretion). K.5 is the supplementation level at half-maximal response and n is the apparent kinetic order.

With these parameters, it is possible to establish any point on the theoretical curve. Since 0.79 μM/L urinary iodine excretions are considered the cutoff for IDD, it is possible to calculate that a salt iodination of 16.9 mg/kg would maintain a urinary iodine excretion of 0.79 μM/L. However, 16.9 mg/kg falls below K.5, indicating a greater physiological capacity for iodine excretion, which is known empirically to be true.

Determining a requirement is arbitrary when confronted with a nutrient, which produces a plateau of response (Rmax) as shown in Fig. 2. Standard break-point analysis puts the requirement too low. Another approach is to look at slope of response (Figure 2). Slope (response/intake) peaks at about 14 mg/kg salt iodination level. This is obviously too low for a supplementation level but represents the organisms' point of greatest response to the nutrient. In the past the point of 95% slope reduction has been selected; i.e., the intake level where the slope has been reduced by 95% and the capacity of the organism to respond been used within 5% of maximum. For urinary iodine excretion, this point is 63.32 mg/kg salt iodination, producing 1.19×10^{-4} μM/L urinary iodine. To achieve 99% capacity would require over 102 mg/kg salt iodination, producing only 1.22×10^{-4} μM/L urinary iodine, indicating the law of diminishing returns in physiological responses –a very small incremental response for a very large increase in iodination. Thus, the

modeling approach allows one to choose a desired response level and correlate an intervention program with other pertinent data. This requirement level of 63.32 mg/kg determined for the specific Rmax for this group of subjects may be specific to the population studied but should however be close in approximation to that for other groups. Variability might also be due to factors such as age, gender and physical state, and determinants of body composition that might affect iodine requirement [1].

Median urinary iodine excretion obtained in the present study among subjects with no goiter enlargement was lower (Median = 0.59 μM/L) than respective median value of 14.3 mM/L (18.2 μg/dl) reported earlier [18]. Similarly, median urinary iodine excretion among subjects with goiter enlargement (Grade IA + IB) tended to be lower (0.51μM/L) than the median figures of 0.59 μM/L (7.9 μg/dl) reported earlier [18].

Median urinary iodine excretion obtained in the present study among subjects with goiter size of grade [2] was (0.28 μM/L) and agreed well with published data reported earlier 0.19-0.28 μM/L (2.4-3.6 μg/dl). The difference in the value of urinary iodine excretion could be attributed to technical difference since it had been reported that HPLC method was used for the analysis of iodine in the urine [18] whereby the standard calorimetric method recommended by ICCIDD had been adapted in the present work.

The four-parameter saturation kinetics model has several advantages: (a) being extremely robust (b) analyzing all data points even if it is hyperbolic in nature (c) makes no assumption that urinary iodine excretion by humans is constant and (d) facilitates the actual calculation of parameters from the data observed and the determination of required levels of nutrient intake to prevent deficiency. This contrasts with the model proposed by Furnee et al. [21] in which different oral preparations of iodized oil was administered to severely deficient school children and the urinary iodine excretion measured. This model assumed that iodine excretion by the body was constant and parameters were estimated after log-linear transformation of the data. The four-parameter model is more applicable than that proposed by Furnee, despite the fact that the study designs were different in both instances [22]. Combining the four-parameter model with studies of salt iodination is important as policy interventions can be implemented if necessary to address any deficiencies in the main source of iodine within a population.

Available commercial salt claimed by the manufacturer to be iodized at a level of 50-80 mg/kg (50-80 ppm) potassium iodate was analyzed in the laboratory for iodine content. The data revealed that only 20% of the analyzed salt complied with the manufacturer's label. High iodine losses from salt, amounting to 50%, have been reported due to excessive or long-term exposure to moisture, light, heat and contaminants [20]. On the average, iodine losses from salt have been reported to amount to 20% from production site to households; with another additional 20% losses taking place during cooking, before consumption [20].

Recently, the board of the International Council for the Control of Iodine Deficiency Disorders proposed guidelines towards IDD elimination - that all salt for human and animal consumption in all regions where IDD is known or suspected is iodized at the factory. The board stressed that representative salt samples obtained regularly from retail outlets or preferably from homes, have reasonable levels usually 30-100 mg/kg (30-100 ppm) iodine content sufficient to ensure an average daily intake of at least 1.18 μM (150 μg) of iodine per day. The actual requirement at the household level will vary from 20 to 50 mg/kg (20-50 ppm) depending on the quality of salt (warm moist vs. cool dry) and daily consumption of salt.

The two chemical compounds in general use are potassium iodate (KIO_3) and potassium iodide (KI). KIO_3 has 59.5% iodine, while KI contains 76.5% iodine. KI is considerably more soluble in water and less expensive than KIO_3, but it is less stable under conditions of moisture, exposure to sunlight or heat, or in the presence of impurities. For these reasons, most countries use KIO_3 for salt iodination, exception includes the U.S.A, Switzerland, Canada, and Ecuador. KIO_3 is particularly recommended for countries where the salt is less refined.

In Pakistan, 62% of the iodized salts available to the consumer at retail points were found to contain inadequate supply of iodine [17]. Ulhaq et al. emphasized therefore the importance of regular monitoring of the iodine content of salt at the plant, retail and consumer levels. Since 1922 Switzerland in a political compromise iodinated salt at a level of 3.75 mg/kg (3.75 p.p.m) to eliminate IDD. In 1962 and 1980, iodination was raised to 7.5 mg/kg and 15 mg/kg (7.5 and 15 ppm) respectively [12]. Retrospective analysis of the Swiss data showed that seven years after iodized salt was introduced the number of admission to special schools for deaf (but intellectually normal) children dropped by more than half. Body height of 19-year-old men at induction to military service showed wide regional variation [12]. Salt iodination program are therefore successful when iodine intake requirements for the populace are met. The use of the four-parameter saturation kinetics model facilitates the accuracy of determining the appropriate intake levels for iodine required to ensure the production of the maximum physiological response. This required level results in the absence of any anomalies of the thyroid gland and is sufficient to reverse the effects of low salt iodination and enable recovery from the various types of goiter as observed from this study.

There is an obvious need to maintain appropriate quality control in the production commercial iodized salt to ensure that required iodination levels are met as indicated by the data. Salt iodination is therefore an effective vehicle of delivery and can ensure that intake requirement levels are met preventing or alleviating goiter within a populace.

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References

[1] AOAC. Official Methods of Analysis 15, Washington D.C., pp. 334, 335 and 870, 1990.
[2] High Institute of Public Health, Report on assessment of the prevalence of iodine deficiency disorders in the New Valley governorate, Egypt, 1993.
[3] Hetzel BS, The story of iodine deficiency an international challenge in nutrition, Oxford University press, Oxford, 1989, pp.1-87.
[4] Koutras DA. The ecology of iodine, in: Stanbury JB, Hetzel BS (Eds.), Endemic Goiter and Endemic Cretinism, 1989. p. 206.
[5] Taurog A. Hormone synthesis and thyroid iodine metabolism. in: Braverman LE, Utiger RD, editors. The Thyroid: A Fundamental and Clinical Text. Philadelphia, PA: JB Lippincott Publishing, 1991. p. 51–97.
[6] Davis PJ. Cellular action of thyroid hormones. in: Braverman LE, Utiger RD, editors. The Thyroid: A Fundamental and Clinical Text. Philadelphia, PA: JB Lippincott Publishing, 1991. p. 190–203.
[7] Fisher DA, Thyroid hormone effects on growth and development, in: Delange Fisher, Malvaux (Eds.), Pediatrics Thyroidology, Basel S. Karger Publishing, 1985. p. 75-89.
[8] Follis RH. Patterns of urinary iodine excretion in goitrous and non-goitrous area. Anal J Clin Nutr 1964;14:253–68.
[9] Dunn JT, Crutchfield HE, Gutekunst E, Dunn AD. Two simple methods for measuring iodine in urine. Thyroid 1993;3:119–23.
[10] Stanbury JB. Iodine. in: Shils ME, Young VR, editors. Modern Nutrition in Health and Disease. Philadelphia, PA: Lea and Febiger Publishing, 1998. p. 252–262.
[11] Ulhaq M, Ahmad I, Salarzai S, Khan SM. Iodized salt in Peshawar, Pakistan: its iodine content price, and use by the people. IDD Newsletter 1996;12:1-12.
[12] Bürgi H, Klinik M. How Switzerland eliminated IDD with Iodized salt. IDD Newsletter 1991;7:1–15.
[13] Sullivan KM, May S, Maberly G. Urinary Iodine Assessment, A Manual on Survey and Laboratory Methods, PAMM, Unicef 15, 2nd ed. 2000.
[14] Sandell EB, Kolthoff IM, Micro determination of iodine by a catalytic method, Mikro Chim Acta, 1937:1-9.
[15] Groppel B. Jodversorgun und Jod status des wiederkaures (Rind, Schaf ,Ziege) hablitations schrift Universitat Leipzig, 1988.
[16] Delang F. Physiopathology of iodine nutrition. in: Chandra RK, editor. Trace Element in Nutrition of Children, Nestle Nutrition Workshop Series 8. NewYork: Raven Press Publishing, 1985. p. 291–9.
[17] Mercer LP. Mathematical model in nutrition, Nutrition Reports International 21 No.2, 1980, 189-198.
[18] Gaitan E. Environmental Goitrogens in Colombia. in: Dunn JT, Modeiros-Neto GA, editors. Endemic Goiter and Cretinism: Continuing Threats to World Health. Washington, DC: Pan America Health Organization, 1974. p. 292.
[19] UNICEF, WHO ICCIDD, Recommended iodine level in salt and guide lines for monitoring their adequacy and effectiveness. WHO, 1996.
[20] Chopra IJ. Nature, Sources, and relative biological significance of circulating thyroid hormones. in: Braverman LE, Utiger RD, editors. A Fundamental and Clinical Text. Philadelphia, PA: JB Lippincott Publishing, 1991. p. 190–203.
[21] Furnee CA, Pfann GA, West CE, van der Haar F, van der Heide D, Haustvast J. New model for describing urinary iodine excretion: its use for comparing different oral preparations of iodized oil. American Journal of Clinical Nutrition 1995;61:1257–62.
[22] Preston Mercer L, May HE, Dodds SJ. Mathematical modeling and the determination of nutritional requirements: sigmoidal and inhibited nutrient-response curves. J Nutr 1989;119:1464–71.