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PECULIARITIES OF THYROIDAL COLLOID HORMONAL ACTIVITY OF WHITE RATS' THYROCYTES DURING CONSUMPTION OF ORGANIC AND INORGANIC IODINE IN CONDITIONS OF POTENTIATED ALIMENTARY IODINE DEFICIENCY

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Hypothyroidism occupies the major place among all disorders of the thyroid gland. The reason for this is both extensive iodine deficiency areas and the influence of natural and artificial goitrogens. The purpose of the study was to compare the effect of organic and inorganic iodine on the hormonal activity of the thyroid glands in white nonlinear male rats, which were under the conditions of alimentary iodine deficiency, potentiated by mercazolilum. Because the intensity of thyroidal colloid amino acids iodination is equivalent to the activity of hormone production, the thyroid gland activity was determined histochemically by the method of A. DesMarais & Q.N. LaHam. It was determined that organic iodine activates the thyroid gland's hormonal activity more than inorganic iodine, while taking organic iodine the histochemical picture of the thyroid gland depended on the dose of iodine consumed and tended to normalize with its increase.

Key words: thyroid gland, follicular thyrocyte, thyroidal colloid, organic iodine, inorganic iodine, iodine deficiency.

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ОСОБЛИВОСТІ ГОРМОНАЛЬНОЇ АКТИВНОСТІ ІНТРАФОЛІКУЛЯРНОГО КОЛОЇДУ ТИРОЦИТІВ БІЛИХ ЩУРІВ ПРИ СПОЖИВАННІ ОРГАНІЧНОГО І НЕОРГАНІЧНОГО ЙОДУ В УМОВАХ ПОТЕНЦІЙОВАНОГО АЛІМЕНТАРНОГО ЙОДОДЕФІЦИТУ

Гіпотиреоз посідає основне місце серед усіх розладів діяльності щитоподібної залози. Причиною цього є як обширні йододефіцитні ареали, так і вплив природних і штучних гойтрогенів. Метою роботи було порівняльне дослідження впливу органічного і неорганічного йоду на гормональну активність щитоподібних залоз білих нелінійних щурів-самців, які перебували в умовах аліментарного дефіциту йоду, потенційованого мерказолілом. Оскільки інтенсивність йодування амінокислот інтрафолікулярного колоїду еквівалентно активності гормоноутворення, активність щитоподібної залозі визначали гістохімічно за методом A. DesMarais & Q.N. LaHam. Установлено, що органічний йод активізує гормональну активність щитоподібної залози більше, ніж неорганічний йод, при цьому при прийманні органічного йоду гістохімічна картина щитоподібних залоз була зумовлена дозою спожитого йоду і при її збільшенні мала тенденцію до нормалізування.

Ключові слова: щитоподібна залоза, фолікулярний тироцит, інтрафолікулярний колоїд, органічний йод, неорганічний йод, йододефіцит.

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Activity of the endocrine system is largely determined by the state of the thyroid gland (TG), which through its hormones plays a key role in the processes of metabolism, growth and differentiation of tissues, i.e. participates in most vital processes of endothermic organisms [12, 15]. However, thyroid pathology occupies the major place among all endocrine disorders (47.3%), with a tendency to its constant growth [2]. The most common thyroid disorder is hypothyroidism, in particular due to iodine deficiency in soil, water, local foods. In addition, the thyroid gland's status to larger extent than other endocrine glands depends on environmental conditions [14]: the share of anthropogenic and industrial hypothyroidism is constantly growing. Potentiation of alimentary iodine deficiency by xenobiotics and goitrogens significantly reduces the TG functional activity, which negatively affects the activity of the whole body.

Correction of alimentary iodine deficiency lies in replenishing iodine pool in the body [9]. Traditionally, inorganic iodine compounds are used for this purpose – iodides and iodates [7]. In recent years, the features of thyrotropic effects of various drugs (biologically active supplements or food products) developed on the basis of iodine of organic chemical nature have been increasingly studied [1, 4, 10]. A comparative study of organic and inorganic iodine effects on the content of iodine in the thyroid gland and ascorbic acid in the liver and adrenal glands, the weight of these organs and the body weight, which reflects certain aspects of specific thyroid function and the body status as a whole, was covered in our previous publications [8, 13]. At the same time, to expand the evidence base of the study, it is advisable to use other methods. Among the considerable variety of empirical approaches to the study of thyroid activity, the possibilities of histochemical methods, which permit to determine the hormonal activity of thyrocytes, are attracting more and more attention. In particular, in histological specimens of thyroid tissue stained by the method of A. DesMarais & Q.N. LaHam, it is possible to determine the degree of thyroidal colloid amino acids iodination.

The purpose of the study was to establish the hormonal activity features of thyroidal colloid in rats at consumption of organic and inorganic nature iodine in the conditions of the potentiated alimentary iodine deficiency.

Materials and methods. The object of study was histological specimens of the rat thyroid gland, stained by the method of A. DesMarais & Q.N. LaHam [11]. The subject of the study was hormonal activity of thyroidal colloid in the correction of alimentary iodine deficiency, potentiated by taking a thyrostatic drug, with organic and inorganic iodine.

The study was performed on 90 white nonlinear male rats with an initial body weight of 140 – 160 g, which in the spring-summer period were kept on a standard isocaloric starch-casein diet for 30 days. To create the conditions for nutritional iodine deficiency, iodine compounds were not added to the salt mixture by J. H. Jones & C. Foster. Water-soluble vitamins were consumed by rats in the form of an aqueous solution, fat-soluble vitamins and α-tocopherol – with unrefined sunflower oil; the source of dietary fiber was filter paper. All nutrients were consumed by rats according to the recommendations for animals of this species and age, access to water being free.

The state of alimentary iodine deficiency was potentiated by mercazolilum (ZAT "Health" Pharmaceutical Company, Ukraine), which was added to the food mixture in the histologically confirmed dose of 3 mg/kg body weight. Correction of iodine deficiency was performed with organic and inorganic iodine. The source of organic iodine was iodine-protein drug obtained from the Black Sea red algae *Phyllophora nervosa* (DC.) Grev. [8], the source of inorganic iodine – 0.2% solution of potassium iodide in distilled water. Both iodine-containing substances were consumed by rats in quantities that provided the following histologically determined doses of iodine: minimal (21 μg/kg body weight), moderate (50 μg/kg body weight), large (100 μg/kg body weight). Rats were divided into 9 groups of 10 animals in each. Group 1 rats consuming common vivarium feed were a universal C_1 control for animals of all other groups. Rats of group 2 were kept under the conditions of alimentary iodine deficiency; their thyroid glands were used to determine the features of the histochemical picture in hypothyroidism (C_2 control). Mercazolilum was added to the feed of groups 3 to 9. The thyroid glands of group 3 rats were used as control C_3 to determine the potential effects of mercazolilum on hormonal activity. Rats of groups 4, 5 and 6, against the background of mercazolilum intake, consumed organic iodine in the doses of 21, 50 and 100 μg/kg body weight, respectively, rats of groups 7, 8, 9 consumed similar amounts of inorganic iodine.

At the end of the experiment, the animals were decapitated under ether anesthesia. The hormonal activity of their thyroid glands was determined histochemically in histological specimens stained by the method of A. DesMarais & Q. N. LaHam. In each case, 400 follicles were processed. The specimens were examined with Bilam light optical microscope at the magnification of x320. The morphological picture was objectified with a Olympus OM-D, 5 Mpx digital camera.

Humane treatment of vertebrates used for experimental and other scientific purposes was observed at all stages of the study (Strasbourg, 1986; Kyiv, 2013). The obtained data were processed using the licensed program StatSoft Statistica v6.0 and presented as the arithmetic mean and its error (M±m); the data reliability was assessed by Student's *t*-test at the level of statistical significance $p \leq 0.05$.

Results of the study and their discussion. Indices of thyroid gland's activity were: content of follicles with hormonally active blue colloid (blue color follicles – BCF), follicles with hormonally inactive yellow colloid (yellow color follicles – YCF), follicles containing mixed fragments of blue and yellow in different ratios (blue and yellow color follicles – BYCF); follicles in which no colloid was detected (follicles without colloid – FWC), were marked as "dumb". Follicles with hormonally active thyroglobulin are stained blue, while follicles with hormonally inactive content are stained yellow. The obtained data are presented in table. 1.

It was found that the thyroid glands of rats in groups 1 – 9 had organo-specific architectonics. The histochemical structure of the thyroid gland in animals of group 3 was characterized by an absolute predominance of FWC, while the number of functionally involved follicles (total BCF and BYCF) was within the range of 16% – 21%. These data differ significantly from those in groups C_1 and C_2 and indicate significant inhibition up to the absence of hormonal activity in thyrocytes, which is logical to consider a consequence of significant functional overstrain caused by consuming a thyrostatic drug against the background of iodine deficiency and impaired functional adaptation of the thyroid gland to the alimentary iodine deficiency conditions.

Table 1

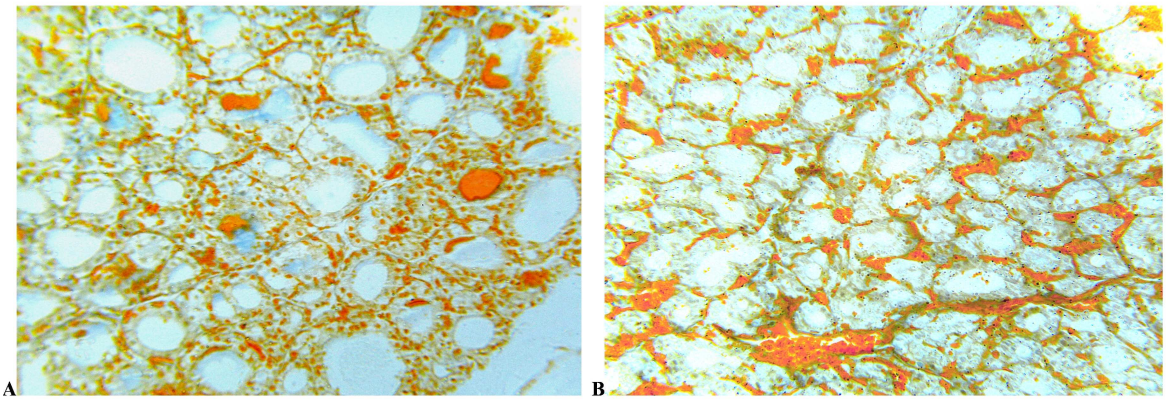
Hormonal activity of thyroidal colloid in white rats at consuming organic and inorganic iodine under the conditions of mercazolilum-potentiated alimentary iodine deficiency, M±m

Group of animals	Thyroidal colloid color			
	blue, %	yellow, %	mixed, %	without colloid, %
1 (C_1) n=10	69.75±4.67	1.50±0.30	28.75±1.02	not detected
2 (C_2) n=10	14.60±1.43 p<0.01 (1)	9.60±0.91 p<0.01 (1)	75.60±2.86 p<0.01 (1)	not detected
3 (C_3) n=10	2.22±0.68 p<0.01 (1) p<0.01 (2)	3.50±0.35 p<0.01 (1) p<0.01 (2)	15.75±1.68 p<0.01 (1) p<0.01 (2)	78.75±3.03 p<0.01 (1) p<0.01 (2)
4 n=10	7.80±0.91 p<0.01 (1) p<0.01 (2) p<0.01 (3)	29.20±2.01 p<0.01 (1) p<0.01 (2) p<0.01 (3)	44.20±1.82 p<0.01 (1) p<0.01 (2) p<0.01 (3)	19.80±2.49 p<0.01 (1) p<0.01 (2) p<0.01 (3)
5 n=10	29.25±2.81 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4)	not detected	32.25±1.14 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4)	38.50±3.33 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4)
6 n=10	35.00±3.72 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4)	5.80±0.73 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4)	19.20±2.81 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4)	39.60±4.32 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4)
7 n=10	9.67±0.98 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4)	5.33±0.72 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4)	not detected	84.33±0.72 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4)
8 n=10	9.83±1.44 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4) p<0.01 (7)	2.83±0.99 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4) p<0.01 (7)	14.67±1.77 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4) p<0.01 (7)	73.17±4.14 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (4) p<0.01 (7)
9 n=10	10.45±0.92 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (6) p<0.01 (7) p<0.01 (8)	2.91±0.31 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (6) p<0.01 (7) p<0.01 (8)	10.27±1.37 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (6) p<0.01 (7) p<0.01 (8)	76.82±2.12 p<0.01 (1) p<0.01 (2) p<0.01 (3) p<0.01 (6) p<0.01 (7) p<0.01 (8)

Note: the numbers in parentheses indicate the group number which the comparison was made with; at p>0.05 indices were not included into the table.

Adding different amounts of organic and inorganic iodine to the diet of animals in groups 4 – 9 caused changes in the histochemical structure of the thyroid gland, the tendency and depth of which depended on the chemical nature and amount of iodine consumed.

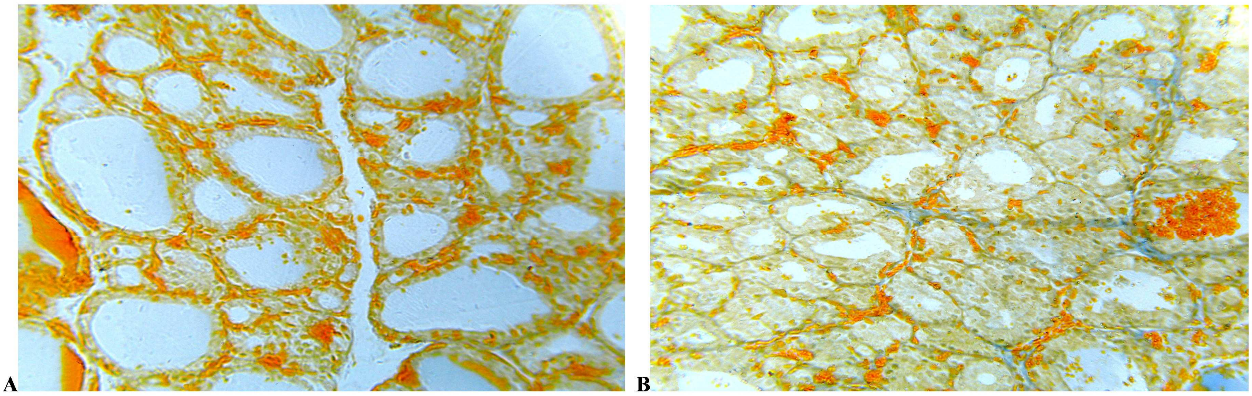
Consuming 21 μg of organic iodine by animals of group 4 was accompanied by a powerful effect on all links of hormonopoiesis in the thyroid gland (fig. 1a).



A B

Fig. 1. Thyroid glands of rats when consuming 21 μg/kg body weight of organic (a) and inorganic (b) iodine under conditions of mercazolilum-potentiated alimentary iodine deficiency. Staining by A. DesMarais & Q.N. LaHam. Magnification x320.

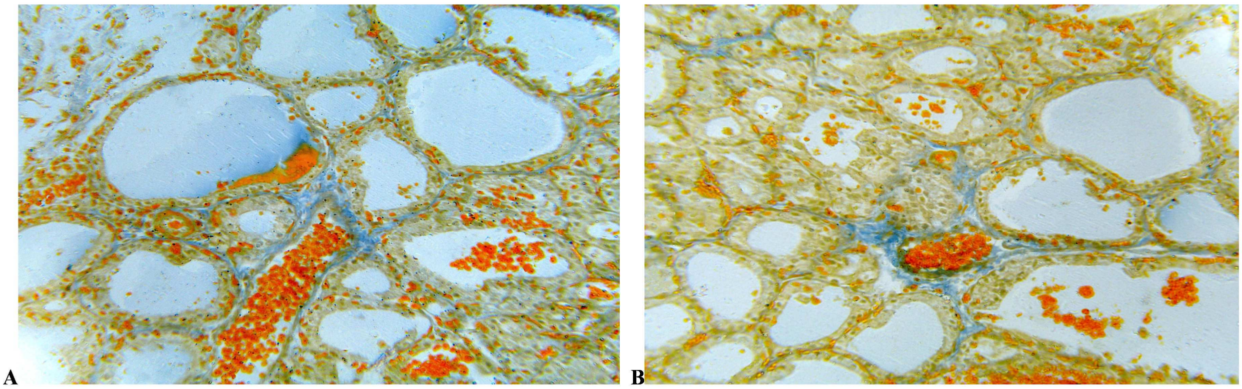
The main sign of this was a decrease in the amount of FWC (compared to C_3 p<0.01) with a simultaneous increase in the amount of BCF and YCF (p<0.05 – 0.01 compared with C_3). We consider such results to be a manifestation of the "softening" effect of organic iodine. Consuming 50 μg of organic iodine by rats of group 5 caused a reliable increase (compared to the indice in animals of group 4) in the content of BCF and BYCF against the background of increased number of follicles without colloid (in all cases p<0.01). At the same time, the structure of the thyroid gland in the discussed group was characterized by the almost complete absence of YCF (fig. 2a). Such histochemical features of the thyroid gland, we consider a sign of its further functional restructuring. In addition, in this case it is possible to speak about the existence of the "irritating dose" phenomenon, in which signs of the body's functional stress are manifested in the absence of the condition stabilization signs.



A B

Fig. 2. Thyroid glands of rats when consuming 50 μg/kg body weight of organic (a) and inorganic (b) iodine under conditions of mercazolilum-potentiated alimentary iodine deficiency. Staining by A. DesMarais & Q.N. LaHam. Magnification x320.

Consuming 100 μg of organic iodine by rats of group 6 was accompanied by an increase (compared to animals of group 5) in the amount of BCF, appearance of a small amount (5.80±0.73%) of YCF, a decrease in the content of BYCF (p<0.05 – 0.01); the FWC content was maintained at the previous level (p>0.05 compared to the index in group 5). The histochemical picture of the rat thyroid gland in this group was the most distant from that in the control C_3 with a certain tendency to approach the indices in the control C_1 (fig. 3a).



A B

Fig. 3. Thyroid glands of rats when consuming 100 μg/kg body weight of organic (a) and inorganic (b) iodine under conditions of mercazolilum-potentiated alimentary iodine deficiency. Staining by A. DesMarais & Q.N. LaHam. Magnification x320.

This redistribution of thyroidal colloid histochemical properties in thyrocytes, in our opinion, indicates the functioning of the body in terms of its adaptation to enhanced hormonopoiesis when consuming large doses of organic iodine against the background of functional imbalance.

Adding 21 μg of inorganic iodine to the diet of rats in group 7 was accompanied by a significant increase in the amount of BCF compared to the control C_3 indices (p<0.01). At the same time, the follicles with mixed content (BYCF) practically disappeared. The rest of the studied indices remained at the level of C_3 control. The histochemical picture of the thyroid gland in rats of this group is logically considered to be a consequence of the hormonopoiesis activation in follicular thyrocytes, which occurred in the conditions of the organ's insufficient functional capacity (fig. 1b). When adding 50 μg of inorganic iodine to the diet of rats in group 8, there was a significant increase in the amount of BYCF (fig. 2b); the total content of BCF and BYCF was within the range of 21% – 28%, while the number of BCF was almost at the level of the previous group 7 (p>0.05). This histochemical picture is logically considered to be a morphological evidence of the 50 μg dose of inorganic iodine insufficient efficacy to activate the specific activity of the thyroid gland undweer the conditions of consuming a thyrostatic drug against the background of iodine deficiency. Consumption of inorganic iodine by rats in group 9 at the dose of 100 μg (fig. 3b) did not cause significant changes in the studied parameters of thyrocytes hormonal activity compared to their values in animals of group 8 ($p>0.05$).

Thus, the main feature of alimentary iodine deficiency potentiation with mercazolilum was the predominance of follicles without signs of colloid in the rat thyroid structure. The findings indicate not only the cessation of thyrocyte hormone synthesis in hypothyroidism, which coincides with the data [7], but also indicates a significant sensitivity of the thyroid gland to external influences in alimentary iodine deficiency. Correction of hypothyroidism morphological signs with iodine-containing drugs contributed to the activation of thyrocytes' specific activity, as evidenced by the presence of BCF and BYCF. The finding coincides with the statement [6] that the intensity of amino acids iodination in the colloid is the hormonopoiesis activity equivalent in the thyroid gland. When the thyroid function is activated by iodine-containing drugs, the amount of BCF grows. Thus, in particular, the intake of organic iodine in the minimum effective dose caused a significant (by 3.5 times) increase in the amount of BCF; the total number of follicles with hormonally active content (BCF and BYCF) was 51% compared to 17% in the control ($p<0.01$). The increase in the amount of organic iodine consumed was accompanied by an enhancement of the functional activity of thyrocytes. Thus, at the moderate dose of 50 μg, the amount of BCF increased by 3.7 times compared to rats that consumed a minimum effective dose of organic iodine – 21 μg, and the total number of follicles with hormonally active content (BCF and BYCF) increased to 61%. When consuming a large dose of organic iodine, the discussed indices grew respectively by 4.5 times, reaching 54%. At the same time, the number of BCF in the thyroid gland of rats consuming moderate and significant doses of organic iodine increased (compared to the minimum effective dose) by 94% and 100%, respectively, which, in our opinion, indicates an increase in the level of thyrocytes' functional activity with exceeding adaptive capacity of the thyroid gland and impaierment of the functional balance, which was achieved by consuming the minimum effective dose of organic iodine.

Consuming iodine of inorganic chemical nature also caused some activation of thyroid hormonopoiesis, but its manifestations differed from the manifestations of thyrocytes activation by organic iodine. Thus, in particular, when consuming the minimum effective amount of inorganic iodine, the BCF content increased more than by 4 times compared to the control C_3. However, the total amount of BCF and BYCF did not exceed 10%, and the amount of BCF remained at the level of control C_3 – 84.33±0.72% compared to 78.75±3.03% ($p> 0.05$). Taken together, the established indicates insufficient stimulation of hormonopoiesis. When consuming larger (moderate and large) doses of inorganic iodine, we found no dependence of the thyroid gland's histochemical picture on the dose: the main morphological element of the thyroid gland in rats of these groups were FWC (73% and 77% respectively) with moderate (24% and 21% respectively) number of follicles with hormonally active content (BCF and BYCF). At the same time, the number of BCF alone was even smaller – 9% and 10%. The amount of YCF when consuming all three studied doses of inorganic iodine was within the range of 6% – 2%. Summarizing the effect of inorganic iodine on the thyroid gland's hormonopoiesis, we believe that in the discussed conditions the efficacy of the studied doses was insufficient. This to some extent coincides with the information [3], in which the presence of follicles without colloid is considered a morphological sign of the thyrocytes' functional activity exhaustion. The results obtained are consistent with our data on the presence of differences in the effect of organic and inorganic iodine on the synthetic activity of follicular thyrocytes, the weight of the thyroid gland, adrenal glands and liver and the body weight [13].

Conclusions

1. Potentiation of alimentary iodine deficiency by taking mercazolilum leads to exhaustion of adaptive-compensatory capabilities of the thyroid gland, as evidenced by the predominance of follicles without colloid in its histostructure. When keeping rats on a synthetic isocaloric starch-casein diet, the dose of mercazolilum 3 mg/kg body weight is adequate to deepen the morphological signs of hypothyroidism and to prevent side effects caused by consuming a thyrostatic drug.

2. In the conditions of alimentary iodine deficiency potentiation with thyrostatic drug, consuming organic and inorganic iodine activates the hormonal function of the thyroid gland, the efficacy of which depends mainly on the chemical nature of the iodine consumed.

3. The histochemical picture of the thyroid glands in rats, which were corrected the potentiated iodine deficiency with organic iodine, was largely due to the dose of iodine consumed and tended to normalize with its increase. The efficacy of similar doses of inorganic iodine was lower.

4. The use of iodine of various (organic or inorganic) chemical nature as substrates for the production of thyroid hormones causes certain differences in hormonopoiesis, which requires in-depth study of its sophisticated mechanisms.

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