Thyroid status of the organism against the background of induction of the liver monooxygenase system

M. T. Rasulova[1*]

[1]Fergana Medical Institute of Public Health, 2A, Yangi Turon Street, Fergana, 150100, Uzbekistan

Abstract. Zixor induction occurred only with an increase in the amount of free T3. Free T4 levels even tended to decline. At the same time, the same trend was observed in the amount of TTG. Our research shows that there is a relationship between the functional status of the liver monooxygenase system and the amount of thyroid hormones in the body. However, the question of the degree of closeness of this connection, that is, whether this connection is direct or indirect, remains open. So far, studies show that the high activity of the monooxygenase enzyme system of the endoplasmic reticulum of hepatocytes is accompanied by high levels of thyroid hormones - triiodothyronine and thyroxine

1 Introduction

In order to determine the relationship between the liver monooxygenase system and the thyroid status of the organism, we modified the activity of the monooxygenase system by induction and inhibition. The inductors of this system are inductors that differ from each other in terms of induction mechanisms - benzonal and zixorin. Benzonal (1-benzoyl-5-ethyl-5-phenylbarbituric acid) is a phenobarbital-type inducer of cytochrome R-450. Under its influence, the amount of microsomal protein in the liver, cytochrome R-450 and NADFN cytochrome R-450 reductase activity increases sharply. Indeed, the results of our study showed that when binding the liver monooxygenase system with benzonal, the duration of hexahedral sleep in experimental animals was reduced by 36.6% compared to intact animals (Table 1).

* Corresponding author: asadjon_2515@mail.ru

Table 1. Quantity and activity of its components when induced by the liver monooxygenase system using inductors.

Animal groups	Hexenal sleep duration, min.	The amount of microsomal cytochromes, nmol / mg protein		Microsomal enzyme activity, nmol / min • mg protein	
		P-450	b_5	Aniline-Hydro-Silaza	Amido-pirin-N-demethylase
Intakt	28.00±0.87	0.99±0.09	0.41±0.03	0.94±0.08	2.79±0.26
Benzonal	17.75±0.75	1,52±0.13	0.48±0.03	1.29±0.11	4.22±0.41
Changes %	- 36.6	+ 53.5	+ 17.1	+ 37.2	+ 51.3
P -n relation to intact blind sellers	< 0.001	< 0.001	> 0.05	< 0.001	< 0.001
Ziksorin	22.13±2.50	1.39±0.08	0.50±0.05	1.19±0.04	5.02±0.48
Changes %	- 21.0	+ 40.4	+ 22.0	+ 26.6	+ 79.9
P in relation to intact blind sellers	< 0.05	< 0.001	> 0.05	< 0.05	< 0.001
P elative to the benzonal group	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05

2 Methods

At the same time, the content of cytochrome R-450, the main component of the monooxygenase system, was found to be 53.5% higher than that of intact animals. Although the absolute value of cytochrome b5 increased by 17.1% compared to intact animals, this increase was found to be statistically unreliable (R> 0.05). The activity of aniline hydroxylase and amidopyrine-N-demethylase microsomes in benzonal induction was 37.2 and 51.3% higher than intact animals, respectively.

The results of morphological studies showed that changes in the liver of experimental animals with benzonal administration were observed mainly in the 3rd functional part of the liver, ie in the part where the monooxygenase system is located. Dilation of blood vessels, especially sinusoids, was observed in this section. The blood vessels are filled with blood. Kupfer macrophages in the sinusoidal wall are hypertrophied. They are embedded in the sinusoidal cavities, and their cytoplasm contains phagosomes with hematoxylin.

The dissected cavity is enlarged, in which lipocytes are hyperplasia. Liver cells are significantly enlarged in size, their cytoplasm contains many fine-grained eosinophilic inclusions, and they are pale in color (Fig. 1). Their nuclei are activated and hyperchromatic.

The results of the study indicate a serious induction of the monooxy-genesis system of the liver when benzonal is administered.

The chemical structure of zixorine is 3-fluoromethyl-a-ethylbenzhydrol. Like benzonal, it increases the amount of components of the liver microsomal monooxygenase system. Under its influence, the formation of glucuronides accelerates and bile secretion increases.

In rats with zixorin induction of the liver monooxygenase system, the duration of hexenal sleep decreased by 21.0% compared to intact rats. (See Table 1).

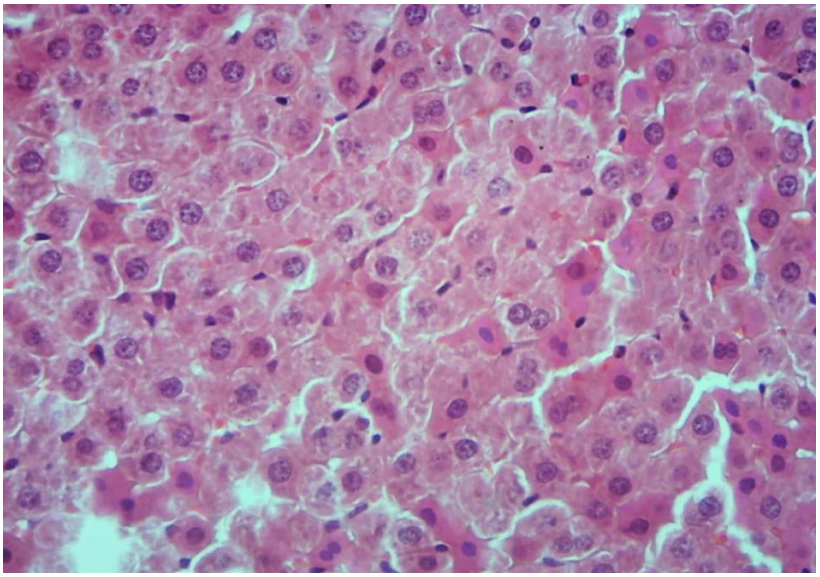

Fig. 1. Rats are benzonal of the monooxygenase system hypertrophy and hyperplasia of liver tissue in induction. Hematoxylin-eosin, ok. 10, ob. 40.

Zixorin induction also led to an increase in cytochrome R-450. It was 40.4% higher than that of the intact animals. Although cytochrome b5, like benzonal induction, increased by 22.0% relative to the control value, this increase was not statistically reliable. The aniline hydroxylase activity of microsomes in zixorin induction was 21.4% higher than the intact values, and the amidopyrine-N-demethylase activity was 79.9% higher.

The results of morphological studies showed that changes in the liver of experimental animals with the introduction of zixorine, as well as benzonal induction, were observed mainly in the 3rd functional part of the liver, ie in the part where the monooxygenase system is located. When zixorin was administered to experimental animals, dilatation of blood vessels, especially sinusoids, was observed in the 3rd functional part of the liver, as in benzonal induction. Blood stasis was observed in these blood vessels. Kupfer macrophages are also hypertrophied.

The disse space is slightly enlarged, and the lipocytes in it are also hyperplasia. Liver cells are enlarged in size, but this expansion is almost 2 times smaller than the enlargement of cells when benzonal is introduced. As with benzonal induction, small granular eosinophilic inclusions occur in the cytoplasm of hepatocytes with the introduction of zixorin. The nucleus of hepatocytes is activated and hyperchromatic.

Thus, zixorine, as well as benzonal, leads to a significant induction of the liver mono-sygnesis system.

Changes in the functional-metabolic state of the liver monooxygenase system and the amount of components in zixorin induction were similar to changes in benzo-induction, and the numerical results were not statistically significant.

Study of the thyroid status of the organism against the background of benzonal induction of the liver monooxygenase system. showed that more than (Table 2). However, the rate of increase in the amount of free T3 relative to the intact values was not statistically reliable (R> 0.05). An increase in T4 was also observed. At the same time, the total amount of T4 was 29.4% higher than that of intact, and the amount of free T4 was 74.6% higher. Although the absolute amount of TTG was 12.5% higher than the intact value, this increase was not statistically reliable.

When administered benzene, a 10-fold magnification of the microscope shows a large number of enlarged, colloid-filled follicles in the thyroid follicles of the glandular tissue (Fig. 2). This means an increase in the number of functionally active follicles.

Weak staining of the colloid in the follicular cavity also indicates an increase in thyroxine levels. Normally, the epithelium, which covers the wall of the follicles, usually consists of a single layer of uncurled cells, and in our drugs, in most cases, they have a cuboidal shape.

Table 2. Indications for thyroid status of rats induced by the monooxygenase system**.**

Grop			T_3, gen., ng/ml	T_3, free., ng/ml	T_4, free., ng/ml	T_4, free., ng/ml	TTG, мкМЕ/мl
Intakt			1.26±0.04	3.86±0.11	4.80±0.12	10.06±0.72	0.016±0.003
Benzonal			1.55±0.009	4.31±0.20	6.21±0.13	17.56±0.06	0.018±0.003
Changes %			+ 23.0	+ 11.7	+ 29.4	+ 74.6	+ 12.5
P in relation to intact blind sellers			< 0.001	> 0.05	< 0.001	< 0.001	> 0.05
Ziksorin			1.80±0.002	4.31±0.02	5.64±0.68	9.2±0.73	0.014±0.001
Changes %			+ 42.9	+ 11.7	+ 17.5	- 8.6	- 12.5
P in relation to intact blind sellers			< 0.001	< 0.05	> 0.05	> 0.05	> 0.05
P relative to the benzonal group	< 0.001	> 0.05	> 0.05	< 0.001		> 0.05	

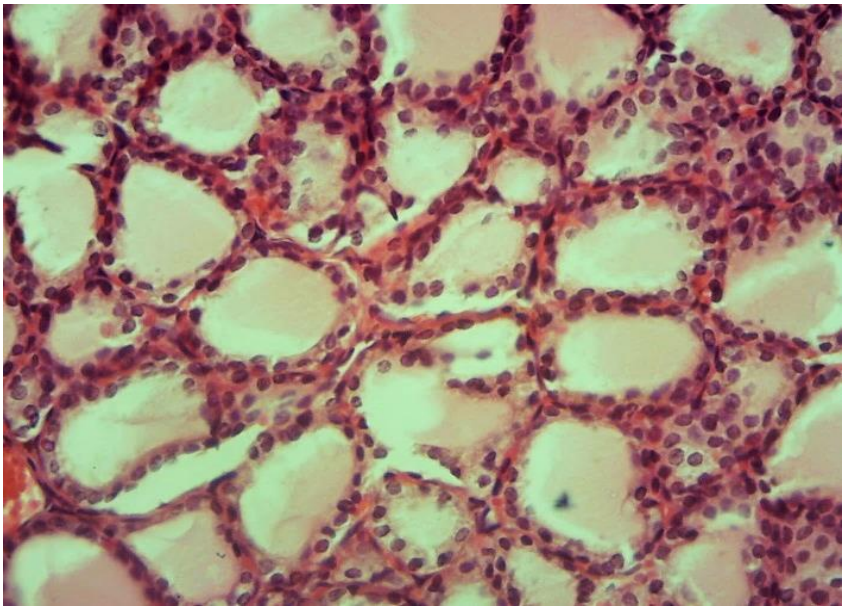

Fig. 2. Increased number of follicles in the thyroid gland of rats caused by benzonal induction of the liver monooxygenase system and weak staining of the follicular cavity. Hematoxylin-eosin, ok. 10, ob. 20.

Parafollicular, ie S-cells located in both follicular and intercellular tissue are hyperplasia (Fig. 3). The thyroid gland is a normal organ rich in blood vessels, but under the influence of benzonal, there is a sharp enlargement of blood vessels in this organ, their filling with blood and a slight swelling of the perivascular tissue.

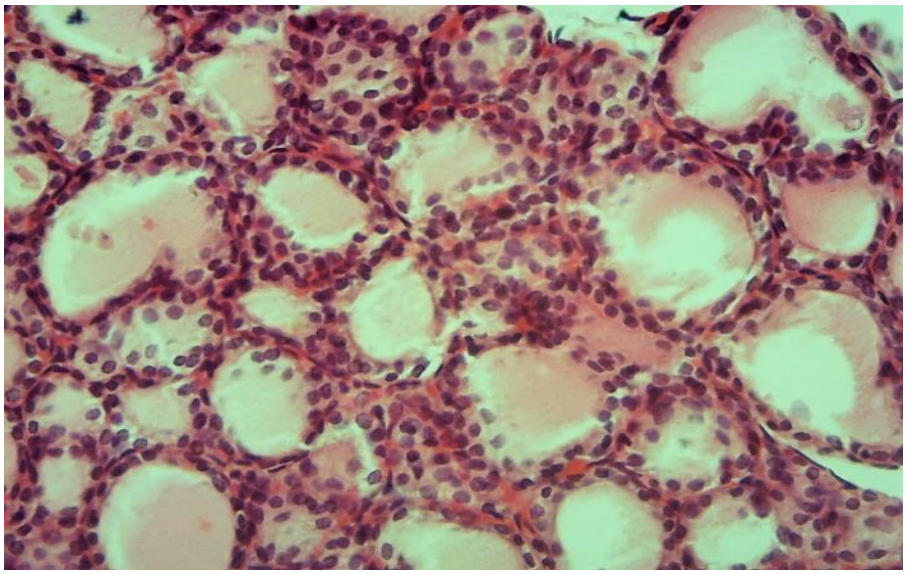

Fig. 3. Hyperplasia of parafollicular cells in the thyroid gland of rats caused by benzonal induction of the liver monooxygenase system. Hematoxylin-eosin, ok. 10, ob. 40.

Study of the thyroid status of the organism against the background of zixorin induction of the liver monooxygenase system. (see Table 2).

Although the absolute value of total T4 was 17.5% higher than the intact value, this excess was not statistically reliable. There were no statistically significant differences between the free T4 and TTG values relative to the intact values.

The difference between total T3 and free T4 in zixor induction.

The values of these materials in the benzonal induction did not differ statistically.

Thus, the results showed an increase in the levels of thyroid hormones - T3 and T4 - induced by the liver monooxygenase system with its inducers - benzonal and zixorine.

Analysis of results. In our study, "standard" inducers of microsomal oxidation, such as benzonal and zixorin, were used to induce the liver monooxygenase system. Although both of these substances belong to the phenobarbital type of inductors, they differ from each other in the "spectrum" of induction of cyto-chromium R-450 isoforms.

Benzonal cytochrome induces P-450IIB, P-450IIC and P-4501IA isoforms, while zixorine induces cytochrome R-450IA and P-450IIB isolates. When benzonal is administered to rats, cytochrome R-450 and NADFN cytochrome R-450 reductase activity are observed against the background of rapid activation of CYP2B1 and CYP2B2 transcription. Under the influence of benzonal, protein synthesis increases strongly, which is confirmed by morphological studies. For example, benzonal induction, such as phenobarbital induction, is an increase in the volume of hepatocytes mainly due to an increase in the volume of their cytoplasm and, to a lesser extent, an increase in the size of their nuclei.

In phenobarbital induction, the volume of hepatocytes, their cytoplasm and nucleus increased by 74, 77 and 42.7%, respectively, relative to the control M.V. Shown by Zakharova. However, in this study, the induction of zixorin in hepatocytes, the volume of their cytoplasm and nucleus, in contrast to phenobarbital induction, increased by only 32, 33 and 27.3%, respectively, relative to control. Therefore, based on the results of this study,

it can be concluded that zixorine, unlike phenobarbital, does not have a strong effect on the rate of protein synthesis in the cell. Unlike benzonal, protein synthesis does not increase with the introduction of zixorin. Novojeeva and hamm. (2004).

In our study, the introduction of inducers such as benzonal and zixorine into experimental rats resulted in increased cytochrome R-450 levels, increased aniline hydroxylase and amidopyrine-N-demethylase activity of the microbes, and decreased hexenal sleep duration. showed that severe induction of the liver monooxygenase system occurs on the basis of.

When benzonal and zixorine were administered, it was observed that the response of the components of the hepatic monooxygenase system to changes in almost the same direction by the thyroid status was not uniform. For example, if there is an increase in total T3, total and free T4 in the background of the tendency to increase the amount of TTG in benzonal induction (Fig. 4), the decrease in the amount of TTG in zixor induction is observed. against the background of the trend, only an increase in the amount of total and free T3 was observed.

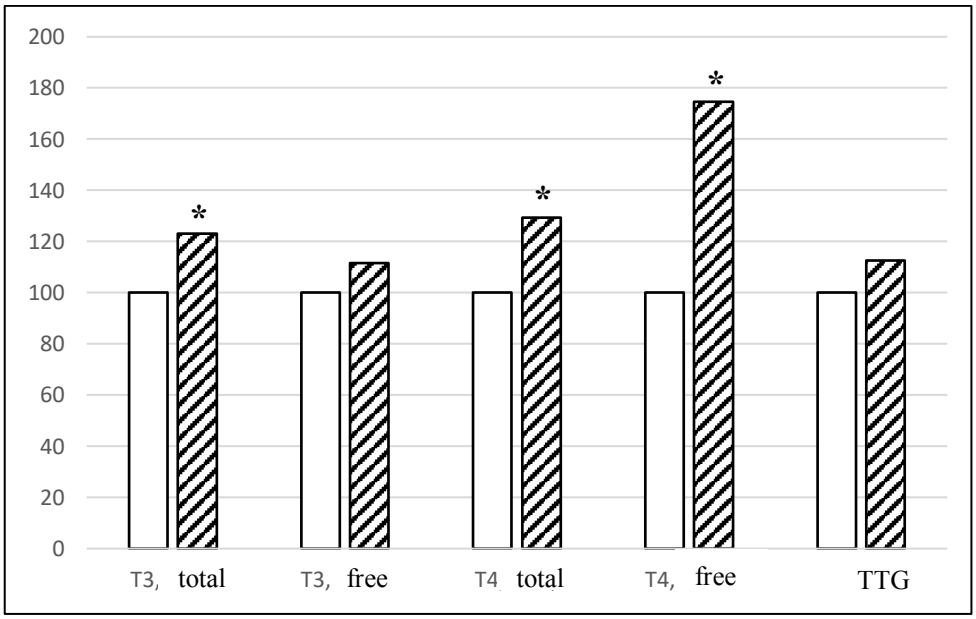

Fig. 4. Thyroid status of the organism in benzonal induction of the liver monooxygenase system. Here and in Figure 4: the amount of indicators on the ordinate axis - in%, white columns - control group, barred columns - induction, * - R <0.05 relative to the control.

The reason for such an atypical response by the thyroid system may be a difference in the induction mechanisms of the hepatic monooxygenase system, based on the different effects of the inducers used on protein synthesis. In order to visualize these changes, we analyzed the ratio of erT3 / umT3 and erT4 / umT4 in different inductions of the hepatic monooxygenase system (Fig. 5).

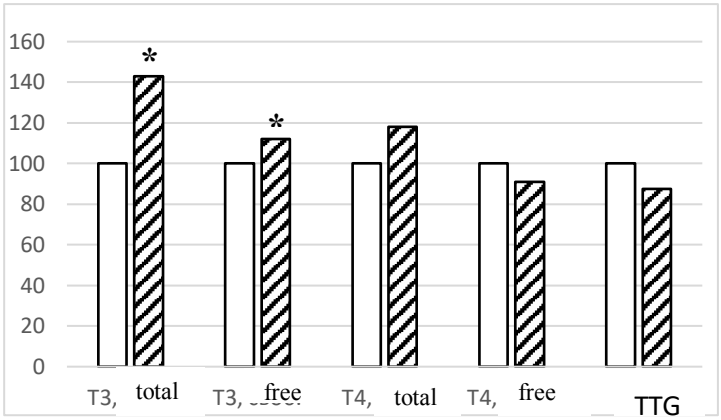

Fig. 5. Zixorin of the liver monooxygenase system thyroid status of the organism in induction.

The results showed a decrease in the erT3 / T3 ratio and an increase in the erT4 / T4 ratio in benzonal induction (Fig. 6, a), while a decrease in both erT3 / T3 and erT4 / T4 ratios in zixor induction (Fig.6, b).

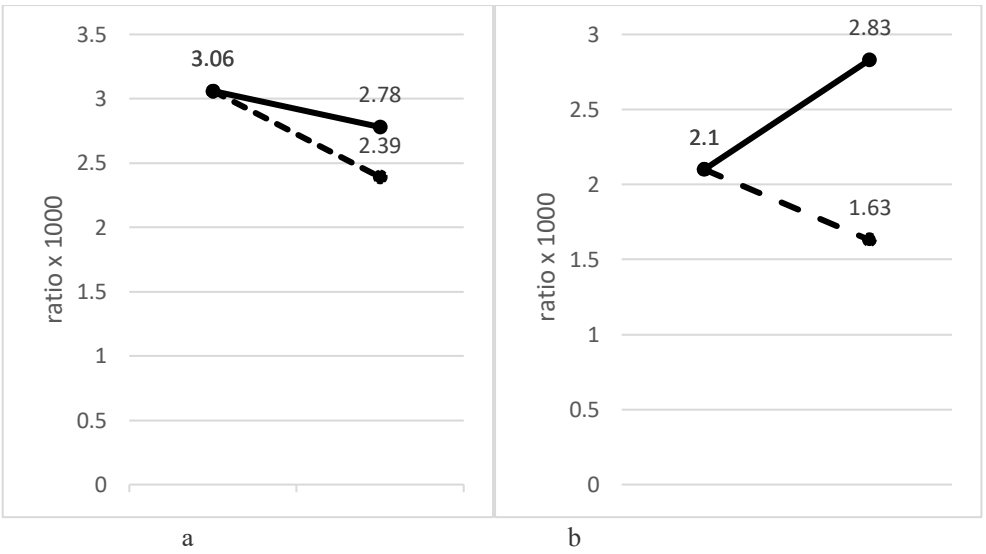

Fig. 6. The ratios of erT3 / T3 (a) and erT4 / T4 (b) in benzonal (continuous line) and zixorin (continuous line) inductions.

One possible mechanism of these changes may be the specific effect of the inductors used on protein synthesis. Benzonal induction also strongly induces protein synthesis. T3 and T4 are circulated in the blood in connection with thyroxine-binding globulin, thyroxine-binding pre-albumin and albumin.

At the same time, it is free T3 and T4 that affect all stages of metabolism, growth and development, stimulate heat production and maintain body temperature. In our study, a statistically significant increase in the amount of free T3 and free T4 in benzonal induction was observed, which led to hypertrophy of the subcellular structures of hepatocytes and increased protein synthesis. for the activation of incoming, biosynthetic processes may be the basis.

It is known that the synthesis, secretion and action of thyroid hormones are controlled by the hypothalamic-pituitary-thyroid system. Thyrotropin-releasing factor, secreted from the hypothalamus, stimulates the synthesis and secretion of thyrotropic hormones. In our study, there is a tendency to increase the amount of TTG in benzonal induction.

3 Conclusion

Zixor induction occurred only with an increase in the amount of free T3. Free T4 levels even tended to decline. At the same time, the same trend was observed in the amount of TTG.

Thus, our research shows that there is a relationship between the functional status of the liver monooxygenase system and the amount of thyroid hormones in the body. However, the question of the degree of closeness of this connection, that is, whether this connection is direct or indirect, remains open. So far, studies show that the high activity of the monooxygenase enzyme system of the endoplasmic reticulum of hepatocytes is accompanied by high levels of thyroid hormones - triiodothyronine and thyroxine [1-4].

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