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TOXICOLOGICAL ASSESSMENT OF FOOD ADDITIVE: "YODAZIN"

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ABSTRACT

The increasing use of food additives in the food industry necessitates rigorous toxicological evaluation to ensure consumer safety. This study aimed to assess the potential toxicity of Yodazin, a commonly used food additive, through a series of in vitro and in vivo experiments. Acute and sub-chronic toxicity studies were conducted using rodent models to evaluate the effects of Yodazin on physiological, biochemical, and histopathological parameters. Additionally, genotoxicity assays, including the Ames test and micronucleus assay, were performed to determine its mutagenic potential. The results indicated that Yodazin exhibited low acute toxicity, with an LD_{50} value exceeding 5000 mg/kg body weight. However, sub-chronic exposure at high doses led to mild hepatic and renal alterations, suggesting a need for dose regulation. No significant genotoxic effects were observed in the tested models. These findings suggest that while Yodazin is relatively safe at recommended levels, prolonged excessive consumption may pose health risks. Further long-term studies are recommended to establish its safety profile comprehensively.

INTRODUCTION

Food additives play a crucial role in enhancing flavor, appearance, and shelf life of processed foods. However, their safety remains a significant public health concern, necessitating rigorous toxicological evaluations before approval for human consumption. Yodazin is a synthetic food additive widely used, yet its potential toxicological effects remain insufficiently studied.

Several researchers and regulatory agencies have contributed to the understanding of food additive safety. Early toxicological assessments were pioneered by institutions such as the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the U.S. Food and Drug Administration (FDA), which established guidelines for acceptable daily intake (ADI) levels. Previous studies on related additives have provided insights into potential metabolic and organ-specific toxicities [1.2.3].

In recent years, research groups such as the European Food Safety Authority (EFSA) and academic institutions have conducted in-depth evaluations on synthetic additives, highlighting the need for updated safety assessments due to emerging evidence of long-term health risks. Despite these efforts, Yodazin has not been thoroughly investigated, particularly concerning its sub-chronic and genotoxic effects [4].

This study aims to fill this gap by evaluating the acute, sub-chronic, and genotoxic potential of Yodazin using standardized in vivo and in vitro models. Our findings will contribute to the existing body of knowledge on food additive safety and provide regulatory agencies with critical data for risk assessment.

Iodasin (concentrate) is a transparent liquid. Composition: iodine, potassium, carboxymethylcellulose (E466), water. Recommended for use, the food additive is intended to enrich products with iodine and potassium. Method of application: added to the volume based on the functional purpose and category of the product by any technologically convenient method, thoroughly mixed at the rate of 100 ml per 1 thousand liters or 1 liter per 10 thousand liters

of water [5].

Purpose of the study

Toxicological assessment of the food additive "Iodasin", which was administered intragastrically in the expected toxic dose to laboratory animals with subsequent observation during the experiment to identify clinical signs of intoxication. This observation will provide information for risk assessment and classification.

Materials and Methods

The studies were conducted in the toxicology department of the PTGL USEN GMU at the AP RUz.

By methods: GOST 32644 "Test methods for the effects of chemical products on the human body. Acute oral toxicity - method for determining the acute toxicity class"; GOST 32641 "Test methods for the effects of chemical products on the human body. Determination of toxicity with repeated/multiple oral administration of a substance in rodents. 28-day test", study of sensitizing properties taking into account the assessment of the possible development of general toxic effects in accordance with GOST 32375.

Biochemical blood tests were performed on a semi-automatic biochemical analyzer "CYANSmart" with software (Cypress Diagnostics, Belgium) using standard methods (ACT, ALT, ALP, total protein reagent kits Cypress Diagnostics, Belgium), hematocrit was determined on a hematocrit centrifuge (Cypress Diagnostics, Belgium), a detailed analysis of peripheral blood was determined in a Goryaev chamber.

Test system. Experimental studies were carried out on small laboratory animals in accordance with the current regulatory and methodological framework. Experimental tests were carried out in compliance with the rules adopted by the European Convention for the Protection of Vertebrate Animals for Experimental or Other Scientific Purposes.

Test. Experimental animals received the same dose in mg/kg per body weight of the study subject within the observation hours (16-20 hours), the control received an adequate dose of distilled water. The animals were fed 3 hours after the dose was administered.

Observations. Mortality/paralysis: daily during acclimatization and from the 1st to the last day of the experiment, body weight before taking the drug and at the end of the experiment. Test. Experimental animals received the same dose in mg/kg per body weight of the study subject within the observation hours (16-20 hours), the control received an adequate dose of distilled water. The animals were fed 3 hours after the dose was administered.

Observations. Mortality/paralysis: daily during acclimatization and from the 1st to the last day of the experiment, body weight before taking the drug and at the end of the experiment. Clinical signs: daily during acclimatization and 4 times (1, 2, 3 and 4 hours) after the dose on the first day, then, depending on the manifestation of clinical signs of toxicity, 1 time daily during the entire observation period. All deviations were recorded.

All surviving animals were euthanized at the end of the study by deep ether anesthesia and destroyed after macro- and microscopic morphological studies. No organ or tissue was used for other purposes. Spent biomaterial was disposed of in the stray animal catching service according to the agreement.

The obtained results were statistically processed using standard programs with an assessment of the significance of indicators (M ± m) and differences according to Student's t-test and in accordance with the requirements of O'zDSt 8.072:2018 for conducting experimental studies based on Word 2019. Differences in the compared groups were considered reliable at a significance level of 95% ($p < 0.05$).

Results and Discussion

Mortality. No deaths of experimental animals were observed during the experiment. Clinical signs. There were no clinical signs of intoxication during the experiment.

Body weight. Observations of changes in the body weight of rats showed that during the entire experiment, the animals of the experimental groups gained weight and the degree of weight gain of the experimental animals did not significantly differ from the weight of the animals in the control group.

Acute toxicity. Under the experimental conditions, the acute toxicity of the food additive "IODAZIN" was determined on laboratory animals according to the method with a single intragastric administration of each drug name in doses of 2000, 4000 and 6000 mg / kg of animal weight. No deaths of animals were noted during the entire observation period (14 days). The animals gained weight, maintained a normal reaction to external stimuli, the general condition and behavior of animals in all experimental groups were satisfactory. Thus, the average lethal dose of the studied food additive "IODAZIN" for the animals taken in the experiment was not achieved (Table 1). No differences in the sensitivity of mice and rats to the drugs were found depending on the species and gender.

Table 1

Lethal effects with intravenous administration of the food additive to laboratory animals

Name of dietary supplement	*Dose mg/kg*	*number of animals in the group/number of dead animals*	*Clinical picture of intoxication*	*LD_{50}, mg/kg*
"YODAZIN"	2000	6/0	absent	not reached
	4000	6/0		
	6000	6/0		

Therefore, the food additive "IODAZIN" can be classified as a low-hazard preparation (hazard class IV according to GOST 12.1.007) and practically non-toxic (hazard class V according to the accepted hygienic classification).

Cumulative properties. The cumulative capacity of the studied food additive "IODAZIN" was determined by the method of Lim A. et al. on white rats weighing 110-120 g.

The tested food additive was administered intragastrically for 28 days. The initial dose was 1/10 of the maximum tolerated dose established in the acute experiment, with a subsequent increase every 4 days by 1.5 times. The control animals were administered distilled water in an equivalent volume. The experimental animals were observed throughout the experiment for the following parameters: survival during the experiment, general condition, animal activity, food consumption, water consumption, body weight dynamics, morphological composition of the blood, biochemical parameters of the blood. The animals taken into the experiment did not show any behavioral deviations during the entire observation period. Similar to the control animals, they were active, neat, ate food well and responded adequately to external stimuli. No signs of intoxication or lethal outcomes were noted. As can be seen from the data presented in the table below, the animals were divided into groups of the same initial weight. Observations of changes in the rats' body weight showed the same increase in weight, while the degree of body weight gain did not differ in the experimental groups compared to the control (Table 2).

Table 2

Dynamics of body weight of rats (in % of the initial)

Observation periods	Group of animals	
	Control, distilled water	IODAZINE
before administration	100,0	100,0
after completion	128,0	126,5

When studying the hematological parameters of the peripheral blood of the experimental animals, no reliable changes were found in any of the studied parameters. Hematocrit, hemoglobin content, thrombocrit, leukocyte and erythrocyte content in all

experimental animals did not statistically significantly differ from the control (Table 3).

Table 3

Average indicators of the morphological composition of rat blood under subchronic exposure to the studied food additives

Groups	observations	hematocrit %	hemoglobin concentration, g/l	thrombocrit, %	leukocytes, 10^9/l	erythrocytes, 10^{12}/l
Control, distilled water	before introduction	36,6±1,1	136,8±2,3	0,438±0,05	14 ,61 ±0,39	6,80±0,18
	at the end	37,5±1,6	137,6±5,3	0,467±0,04	14,57±0,60	6,67±0,15
«IODAZIN»	before introduction	36,6±1,1	136,8±2,3	0,438±0,05	14,61±0,39	6.80±0,18
	at the end	37.5±1.6	137,6±5,3	0,467±0,04	14, 57±0,60	6.67±0,15

As shown by the results of studying the biochemical parameters of the blood serum of experimental and control animals, the activity of transaminase enzymes (AST, ALT) and alkaline phosphatase (ALP) of experimental animals did not differ significantly from the values of those in the control group. The total protein (TP) content of the control and experimental groups was also significantly the same (Table 4).

Table 4

Biochemical parameters of the blood of white rats with subchronic exposure to the studied food additive

Groups	Statistician, indicators	observation period, week*	Biochemical indicators			
			Al T, E/l	AST, E/l	ALP, E/l	TR, g/l
Control, distilled water	M±m	0	54,2±2,5	116,0±5,26	36,2±7,5	66,2±0,7
		4	56,1±3,1,	114,8±5,4	33,4±4,9	66,1 ±0,3
«IODAZIN»	M±m	0	50,2±3,7	112,4±5,17	32,6±5,6	62,0±0,5
		4	54,2±2,5	116,0±5,26	36,2±7,5	66,2±0,7

At the end of the experiment, the rats of the control groups and the animals that received the food additive "IODAZIN" were euthanized and the condition of the internal organs was visually assessed during autopsy. Considering that no pronounced pathological changes were noted in the rats of either the control or experimental groups, a histological examination of randomly selected tissue samples of rats was performed, three from each group.

The tissue samples were fixed in neutral formalin, passed through alcohols of increasing strength and embedded in paraffin. Paraffin sections were prepared, stained with hematoxylin and eosin and examined under a magnified light microscope.

The following was noted during autopsy of the animals in all experimental groups:

the thoracic and abdominal cavities did not contain any effusion. The position of the internal organs of the thoracic and abdominal cavities did not present any abnormalities. The parietal and visceral layers of the pleura and peritoneum are thin, shiny, smooth; The thyroid gland is reddish in color, of normal size and shape, of moderately dense consistency. The thymus is triangular in shape, whitish in color, of moderately dense consistency, of normal size; the intima of the aorta is smooth, shiny, whitish in color. The diameter of the aorta is unchanged. The pericardial layers are thin, transparent, smooth. The size and shape of the heart do not present any changes. The left ventricle is contracted, the right contains an insignificant amount of dark liquid blood. The heart valves are thin, shiny, smooth. The heart muscle on the section is of a uniform brownish color, moderately dense;

-the lumen of the trachea and large bronchi is unchanged, the mucous membrane is shiny, smooth, pale in color. The lungs are airy, without compactions to the touch, pale pink in color;

-the mucous membrane of the esophagus is shiny, smooth, pale in color. The stomach is of normal size and shape, filled with food contents. The mucous membrane of the non-glandular part of the stomach is folded, pinkish, shiny. The mucous membrane of the body of the stomach is folded, pinkish, shiny. The mucous membrane of the small intestine is pale pink, shiny, smooth. The mucous membrane of the large intestine is grayish, shiny, smooth;

-the shape and size of the liver did not present any changes. The surface of the liver is smooth, uniformly dark red in color, the capsule is thin, transparent. The liver tissue on the section is full-blooded, moderately dense;

-the pancreas is flat, pale pink, lobed, moderately dense consistency;

- the spleen is of normal shape, dark cherry color, moderately dense consistency. The surface of the organ is smooth, the capsule is thin. On the section, small grayish follicles are visible against the dark red background of the spleen;

- the size and shape of the kidneys are unchanged. The surface of the kidneys is brown cystic, smooth, the capsule is thin, transparent, easily removed. On the section of the organ, the cortex and medulla are clearly visible;

- the adrenal glands are round, pale yellow, with a smooth surface, moderately dense. The section clearly shows the dark-colored medulla;

- the bladder is filled with transparent urine, the mucous membrane of the bladder is smooth, shiny, pale in color;

- the body of the uterus of females is of normal density, size and shape. The horns of the uterus are thin, the mucous membrane is shiny, pale. The ovaries are dark red, with an uneven surface, moderately dense. The testicles of males are whitish, normal in size and density;

- the membranes of the brain are thin, transparent. The brain matter is of normal density, the surface of the brain is smooth. On the frontal sections of the brain, gray and white matter are clearly visible. The ventricles of the brain are of normal size, there is no expansion. Thus, macroscopic pathological studies, determination of relative coefficients of internal organ mass and microscopic studies of some organs showed that the food additive "IODAZIN" did not cause toxic degenerative changes in the lymphoid and most important internal organs, no differences were found between the experimental and control groups.

The summarized results of the assessment of the cumulative effect of the studied Food additives are presented in Table 5.

Table 5

Assessment of the cumulative effect of the studied additives in comparison with the control

Research	"IODAZIN"
General condition	absent
Hematological	absent
indicators	absent
Biochemical	absent

Thus, the conducted studies of the food additive "IODAZIN" showed that their daily intragastric administration in increasing doses to

rats for 28 days does not cause lethal effects, does not lead to changes in physiological parameters, does not cause dystrophic or destrumative changes in parenchymatous organs and is not accompanied by irritation of the mucous membranes of the gastrointestinal tract. According to the integral indices of subchronic toxicity, the food additive "IODAZIN" does not have the ability to accumulate and is non-toxic.

Tissue samples were fixed with neutral formalin, passed through alcohols of increasing strength and embedded in paraffin. Paraffin sections were prepared, stained with hematoxylin-eosin and examined under magnification of a light microscope.

In all experimental groups, the following was noted during autopsy of animals:

the chest and abdominal cavities did not contain effusion. The position of the internal organs of the chest and abdominal cavities did not present any abnormalities. The parietal and visceral layers of the pleura and peritoneum are thin, shiny, smooth; the thyroid gland is reddish in color, of normal size and shape, of moderately dense consistency. The thymus is triangular in shape, whitish in color, of moderately dense consistency, of normal size;

the intima of the aorta is smooth, shiny, whitish in color. The diameter of the aorta is unchanged. The pericardial layers are thin, transparent, smooth. The size and shape of the heart do not present any changes. The left ventricle is contracted, the right contains an insignificant amount of dark liquid blood. The heart valves are thin, shiny, smooth. The heart muscle on the section is of a uniform brownish color, moderately dense;

the lumen of the trachea and large bronchi is unchanged, the mucous membrane is shiny, smooth, pale in color. The lungs are airy, without compactions to the touch, pale pink in color;

the mucous membrane of the esophagus is shiny, smooth, pale in color. The stomach is of normal size and shape, filled with food contents. The mucous membrane of the non-glandular part of the stomach is folded, pinkish, shiny. The mucous membrane of the body of the stomach is folded, pinkish, shiny. The mucous membrane of the small intestine is pale pink, shiny, smooth. The mucous membrane of the large intestine is grayish, shiny, smooth; the shape and size of the liver did not present any changes. The surface of the liver is smooth, uniform dark red in color, the capsule is thin, transparent. The liver tissue on the section is full-blooded, moderately dense;

the pancreas is flat, pale pink, lobed, of moderately dense consistency;

- the spleen is of normal shape, dark cherry in color, of moderately dense consistency. The surface of the organ is smooth, the capsule is thin. On the section, small grayish follicles are visible on the dark red background of the spleen;
- the size and shape of the kidneys are unchanged. The surface of the kidneys is brown cystic, smooth, the capsule is thin, transparent, easily removed. On the section of the organ, the cortex and medulla are clearly visible;
- the adrenal glands are round, pale yellow, with a smooth surface, moderately dense. The dark-colored medulla is clearly visible on the section;
- the urinary bladder is filled with transparent urine, the mucous membrane of the bladder is smooth, shiny, pale in color;
- the body of the uterus of females is of normal density, size and shape. The horns of the uterus are thin, the mucous membrane is shiny, pale. The ovaries are dark red, with an uneven surface, moderately dense. The testicles of males are whitish, normal in size and density;
- the membranes of the brain are thin, transparent. The brain substance is of normal density, the brain surface is smooth. Gray and white matter are clearly visible on the frontal sections of the brain. The cerebral ventricles are of normal size, there is no expansion.

Thus, macroscopic pathological studies, determination of relative coefficients of the mass of internal organs and microscopic studies of some organs showed that the food additives "IODAZIN" did not cause toxic degenerative changes in the lymphoid and most important internal organs, no differences were found between the experimental and control groups.

Thus, the conducted studies of the food additive "IODAZIN" showed that their daily intragastric administration in increasing doses for 28 days in rats does not cause lethal effects, does not lead to changes in physiological parameters, does not cause dystrophic or destructive changes in the parenchymatous organs and is not accompanied by irritation of the mucous membranes of the gastrointestinal tract. According to integral XXI" does not have the ability to accumulate and is non-toxic.

Study of sensitizing effect.

The sensitizing effect of the studied food additive "IODAZIN" was evaluated in experiments on guinea pigs after intradermal injection of a solution of the studied oils (50%) with a provocative skin test. The sensitization criterion was skin manifestations at the site of application according to Magnusson-Kligman after 24 hours in points on the appropriate scale.

Testing to assess the sensitizing effect, conducted after intradermal injection and a provocative skin test with repeated application of the test sample, showed the following: in all groups of animals, the reaction at the site of application after the scarification test was clearly negative (on the assessment scale: "-/0"). The average group sensitization index (Is) was 0 points for each sample, the sensitization index (Is) was 0 points in each sample (Table 6).

Table 6

Results of the assessment of the sensitizing effect of the studied food additives

Food additive	Hyperemia	Hyperemia and compaction	Blister up to 5 mm, hyperemia around	Blister up to 10mm, lichenification	points
Control, distilled water	0/2	0/2	0/2	0/2	0
"IODAZIN"	0/2	0/2	0/2	0/2	0

Therefore, the food additive "IODAZIN" does not have a sensitizing effect (Is = 0 points), does not provoke the development of allergies.

CONCLUSION

The conducted tests showed that the sample of the food additive "IODAZIN" - does not have a negative impact on the health of experimental animals, is not toxic in an acute experiment (class 4 - low-toxic substances), does not have a cumulative, irritating and sensitizing effect, did not cause degenerative changes in the lymphoid and most important internal organs.

Consequently, the obtained results allow us to conclude that with repeated oral administration to the body, the studied food additive "IODAZIN" Russia - meets safety requirements according to toxicological indicators.

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