# Results Of Research On The Possible Cumulative Effect Of Certain Food Additives

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### ABSTRACT

The article presents the results of our own research on the detection of the cumulative effect of the studied food additives of different classes in the comparative aspect. The results obtained allowed us to conclude that the flavor identical to natural and artificial flavor with prolonged ingestion can cause pathological processes in the liver, as well as lead to over excitation of the nervous system, followed by a sharp inhibition.

KEY WORDS: food additive, flavor, experiment, indicators, results.

### 1. INTRODUCTION

In the modern food industry, various methods of improving the quality of food products and the improvement of technological processes find application, but the use of food additives has turned out to be the most cost-effective and easily applicable. Despite the frightening evidence from research, when using food additives in most cases, such an important aspect of the problem as the toxicity of chemicals, which is usually understood as the ability of a substance to harm the body, is ignored. Most nutritional supplements have no nutritional value and, at best, are biologically inert, and at worst, turn out to be biologically active and not indifferent xenobiotics for the body. And the use of food additives, therefore, is permissible only if they, even with prolonged use, do not threaten a person's life.

Each practical proposal for the introduction of a particular food supplement made by research institutes of various branches of the food industry requires a hygienic assessment, which often even with little suspicion of the possibility of an adverse effect on the body will entail the formulation of special experimental studies. In some cases, the replacement of one chemical substance with another is caused not only by considerations of technological or economic feasibility, but also by the need that arose as a result of new scientific data indicating the undeniable harmfulness of this substance.

The main criterion for the admission of a new food additive in all cases will be harmlessness, both of the additive itself and of food products processed with certain drugs.

Food additives should not be allowed to be used in cases where the necessary effect can be achieved by technological methods that are technically and economically feasible. It should also not be allowed to introduce food additives that can mask technological defects and spoilage or reduce the value of the food product. When considering the acceptable concentrations of the additive (or the products of its interaction with food components) in the food product, the results of toxicological and other biological tests of substances proposed as a food additive, its probable total daily intake into the human body from all sources will be taken into account available recommendations regarding the level of content of the additive in the product and its acceptable daily intake in the human body with food. In principle, the lowest concentration of the additive in the product necessary to achieve the technological effect can be resolved. The starting point for determining the concentration of the nutritional supplement will be the justified so-called acceptable daily intake of food additives in the human body, established taking into account the "safety factor", that is, 100, and sometimes 500-100 times, depending on the specific research results. It should be based on the fact that the dose of the food supplement should be significantly lower than the level that can be harmless to the body.

In this regard, we had the task in an experiment on white rats to compare the degree of toxicity of the studied natural, identical to natural and artificial food additives with intragastric intake, both with a single administration and with a long-term.

In conditions of prolonged use of various types of food additives in food production, there is a danger of chronic poisoning, which inflict incomparably more serious damage to health, as their symptoms are often vague and develop slowly [1]. At the same time, food additives, in particular flavorings, are not considered dangerous and are widely used in the food industry. The problem of using flavors of various origins is further complicated by the fact that the supplement enters the body throughout life. Factors contributing to the development of chronic poisoning include the ability of a number of chemicals to cumulate, which is quite acceptable for food flavorings. however, small doses, with their more frequent repeatability, may turn out to be significantly more dangerous for the body than large, but with relatively rare, their ingestion. Therefore, nutritional supplements, as well as methods of technological processing of food products should be carefully studied in order to maximally eliminate their danger to human health.

## 2. MATERIALS AND METHODS

The purpose of the experiment was to solve the problems of detecting the cumulative effect of the studied food additives, on which their toxicity depends on the systematic long-term intake of the natural flavoring "Mint Del'Ar 11.02.235", a flavoring identical to the natural "Pomegranate 78484-343" and the artificial flavoring "Vanillin 11.05 .107 P "into the body in small doses, as well as to study their toxicodynamics and the nature of the effect on the animal organism, that is, the identification of target organs.

It is known that with repeated intake at small time intervals, any foreign substance can either accumulate in the body itself (material cumulation) or cause a summation of the effect in the form of replication of functional disorders of organs and systems (functional cumulation) [1]. Two methods for studying the cumulative properties of foreign substances are most used: the Lim method with the authors and the Kagan method, Yu.S. and Stankevich V.V. Their advantage lies in the fact that they use the most statistically determined indicator LD50 and test several doses of the substance. Given the shortcomings and advantages of these methods, for food additives it is more correct to judge the cumulative properties of small doses of xenobiotic not only by clear signs of disruption of the body, but also taking into account the degree of change in functional indicators. We conducted experimental studies according to the method of Lim et al. [3]. In order to study the toxicodynamics of food additives are required.

The criteria for assessing the toxicity of the natural flavoring "Mint Del'Ar 11.02.235", the flavoring identical to the natural "Pomegranate 78484-343" and the artificial flavoring "Vanillin 11.05.107 R" were: animal behavior, eating food, animal weight in dynamics, peripheral morphological composition blood activity of alkaline phosphatase (ALP), aspartate aminotransferase (ACT) and alanine aminotransferase (ALT), the level of total protein in blood serum.

The experiment involved white rats (females) weighing 100-140 grams, which were divided into 4 groups of 6 pieces each: the first group served as a control and received distilled water; the second group received a natural flavoring "Mint Del'Ar" at a dose of 200 mg / kg, the third group received a flavor identical to the natural "Pomegranate 78484-343" at a dose of 13 mg / kg, the fourth group received an artificial flavoring "Vanillin 05/11/107 R" in dose of 200 mg / kg. Moreover, the doses received by animals of the studied food additives were 100 times higher than the recommended technological ones.

#### 3. RESULTS AND DISCUSSION

As the results of the study showed, with intragastric administration of a natural flavoring at a dose of 200 mg / kg, identical to a natural flavoring at a dose of 130 mg / kg and artificial flavoring at a dose of 200 mg / kg, they did not affect the main integral indicators. Rats had a neat appearance, reacted normally to external stimuli, the daily intake of dry food and water in all groups of animals was normal.

The introduction of the artificial aroma "Vanillin 05/11/107 P" at 2 and 4 weeks of observation caused a statistically significant increase in animal body weight compared to the control. The body weight dynamics of animals treated with natural flavoring and identical to natural throughout the experiment did not have significant differences with the control. Throughout the entire experiment, death was not observed in any of the animal groups.

The long-term, for 4 weeks, introduction of the toxicity of the natural flavoring "Mint Del'Ar 11.02.235", a flavoring identical to the natural "Pomegranate 78484-343" and the artificial flavoring "Vanillin 11.05.107 R" in the stomach of rats in tested doses did not affect the hematological peripheral blood counts: the number of red blood cells, platelets, white blood cells, hemoglobin content (table 1).

Groups	No. Of	Research indicators			
of	the	Red blood cells	Hemoglobin,	Platelets, $\cdot 10^9$ /	White blood
animals	animal	$\cdot 10^{12} / 1$	g / 1	L	cells
					$\cdot 10^{9} / 1$
4th week	·			•	
	1	6,4	150	426	10,5
	2	7,8	172	476	9,5
	3	6,7	149	399	15,5
	4	7,8	170	450	15,3
ol,	5	7,1	159	421	9,8
ntro	6	7,1	158	465	10,1
Control, Water	M±m	7,15±0,23	159±3,8	439,5±12,8	11,78±1
oup t Mr,	1	7,4	162	390	13,1
	2	7,7	168	386	12,4
	3	8,5	188	463	11,9
II gr Mint Del`	4	9,1	195	399	8,0

Table 1. The peripheral blood counts of rats treated with the studied flavors for 4 weeks

	5	7,6	164	389	9,3
	6	6,2	173	355	12,0
	M±m	7,75 ±0,48	$175,5\pm 5,5$	397±18	11,1±0,6
III	1	7,6	163	392	14,0
	2	7,5	166	422	13,3
e	3	7,4	168	439	12,8
nat kg	4	6,8	173	449	9,7
gra Ig /	5	7,2	154	361	14,4
Group Pomegranat 130 mg / kg	6	6,3	171	407	13,9
VanillinGroup P, 200Pomegranate 130 mg / kg	M±m	7,13±0,4	166±3,2	412±15	13,0±0,8
lin 200	1	7,7	169	451	15,4
2	2	7,3	169	457	15,3
P, V	3	6,4	146	351	14,6
$> \vdash$	4	7,0	151	505	14,8
Group IV 05/11/107 mg/kg	5	6,8	144	400	9,7
	6	6,5	137	374	10,0
Gro 05/1 mg	M±m	6,95±0,2	152±5,3	423±25	13,3±0,95

In the diagnosis of pathological processes in the liver, the study of enzyme activity is of great importance. A change in the activity of enzymes can occur much earlier than morphological disorders of parenchyma cells of various organs occur. The study of the activity of transaminases in serum is a subtle indicator of the severity and activity of the pathological process in the liver [4]. This determines the value of the methods for studying cellular enzymes as tests of the functional state of the liver in assessing the possible adverse effects of the studied food additives (natural flavoring "Mint Del'Ar 11.02.235", a flavoring identical to the natural "Pomegranate 78484-343" and artificial flavoring "Vanillin 11.05 .107 P ").

As the results of our studies showed, the activity of alanine and aspartate transaminases in all three experimental groups of animals did not significantly change compared to the intact group (Table 2). However, it should be noted that there is a certain tendency toward an increase in the activity of these enzymes in the group exposed to the artificial flavoring Vanillin P 5880, which is quite consistent with the literature on the nature of the action of artificial food additives on the body.

The study of the total level of whey proteins, which is an informative indicator of the protein-forming function of the liver, did not reveal changes in this indicator in all experimental groups relative to the control.

When analyzing the biochemical parameters of the blood serum of rats treated with the natural flavoring "Mint Del'Ar 11.02.235", the flavoring identical to the natural "Pomegranate 78484-343" and the artificial flavoring "Vanillin 11.05.107 R" in doses of 200 mg / kg, 130 mg / kg and 200 mg / kg, respectively, there were no statistically significant changes in the level of total protein, as well as the activity of alkaline phosphatase and alanine and aspartate transaminases.

Table 2. Biochemical parameters of blood serum of rats treated with the studied flavors for 4

weeks

	N. Of t			Alkaline	General
Group	No. Of the animal	ALT E/L	AST E / L	phosphatase	protein,
	aiiiiiai	L/L	L/L	E/L	g / 1
4th week					

			ISSN 2515-8260	Volume 0	07, Issue 03, 2020
	1	72,3	121	624	71,2
	2	61,2	104	658	75,7
$C \rightarrow 1$	3	81,0	147	683	71,4
Control,	4	70,6	125	515	63,7
water	5	72,9	114	580	68,8
	6	74,6	101	520	67,7
	M±m	72,1±3,3	119±7,6	597±28	69,8±2,0
	1	64,2	118	466	65,9
	2	63,2	125	637	57,0
II group	3	64,4	112	490	75,6
Mint Del`Ar,	4	77,4	125	438	95,3
200 mg / kg	5	63,0	113	525	67,5
	6	74,1	115	411	55,2
	M±m	67,7±2,4	118±2,2	494±32*	69,4±3,9
	1	71,0	128	483	68,9
	2	76,9	135	517	61,8
Group III	3	61,6	128	579	70,1
Pomegranate,	4	76,2	118	559	81,0
130 mg / kg	5	65,8	121	523	72,1
	6	74,4	115	548	65,2
	M±m	70,9±2,5	124±3,3	535±16	69,9±1,7
	1	77,8	137	499	71,8
TV	2	90,7	145	565	50,5
IV group "Vanillin	3	58,7	117	522	64,6
05/11/107 P",	4	75,1	123	629	66,6
200 mg / kg	5	68,5	138	556	75,3
200 mg / kg	6	66,0	131	685	77,6
	M±m	72,8±4,1	132±4	576±31*	67,7±4,5

\* - significance of differences with control (P < 0.05)

When studying the effect of the natural flavoring "Mint Del'Ar 11.02.235", a flavoring identical to the natural "Pomegranate 78484-343" and the artificial flavoring "Vanillin 05/11/107 P" on the functional state of the central nervous system of rats in an "open" field, it was found that flavoring identical to natural "Pomegranate78484-343" and artificial flavoring "Vanillin P 5880" reduced the motor activity of rats in the test "number of crossed squares" and orientational reactions in the test "mink reflex" compared with the control, which, apparently, may indicate overexcitation of the nervous system, followed by sharp inhibition. In addition, a flavor identical to natural and artificial flavor in the most tested doses enhanced the process of defecation of rats compared with the control (table 3).

Table 3. Indicators of the functional state of the central nervous system of rats treated with
the studied flavors for 4 weeks

	Groups of animals				
The studied indicators in 3 minutes	Control, Water	II group Mint Del`Ar, 200 mg / kg	Group III Pomegranate, 120 mg / kg	IV group Vanillin 05/11/107 P, 200 mg / kg	

"Mink reflex"	15,3±1,9	11,5±1,6	4,2±0,9*	6,0±2,7*
The number of crossed squares	20,6±3,4	17,5±3,1	7,2±2,3*	8,8±2,9*
Defecation	0,6±0,3	0,8±0,5	1,1±0,4	1,8±0,4*

\* - significance of differences with control (P < 0.05)

After the experiment and animal euthanasia, we determined the coefficients of mass of the internal organs, which in groups of animals received the natural flavoring "Mint Del'Ar 11.02.235", a flavor identical to the natural "Pomegranate 78484-343" and artificial flavoring "Vanillin P 5880" in the tested doses did not had significant differences with control (table 4).

A visual examination found that the internal organs of rats of groups I-IV are correctly located, cavities without effusion and adhesions. Serous membranes are smooth, shiny. The respiratory tract is free, the lungs are elastic, airy, in the context of the usual color. The heart, kidneys, liver, spleen, thymus, organs of the gastrointestinal tract, adrenal glands, pancreas, genitals - of the usual form, consistency, color and size.

	Groups of animals						
Investigated organs	Control, Water	II group Mint Del`Ar, 200 mg / kg	Group III Pomegranate, 120 mg / kg	IV group Vanillin 05/11/107 P, 200 mg / kg			
Heart	0,33±0,03	0,34±0,01	0,36±0,01	0,32±0,01			
Lungs	0,75±0,11	0,76±0,08	0,78±0,06	0,81±0,06			
Liver	5,01±0,25	4,7±0,38	4,3±0,61	4,71±0,29			
Kidney	0,81±0,05	0,81±0,04	0,82±0,04	0,79±0,03			
Spleen	0,68±0,03	0,66±0,08	0,74±0,12	0,57±0, 11			
Adrenal glands	0,027±0,002	0,029±0,002	0,030±0,002	0,029±0,003			
Testis	1,31±0,05	1,21±0,06	1,19±0,08	1,13±0,06			

Table 4. Mass ratios of the internal organs of rats treated with the studied flavors for 4 weeks

## 4. CONCLUSION

Thus, the data of experimental studies of the natural flavoring "Mint Del`Ar 11.02.235" and the flavoring identical to the natural "Pomegranate 78484-343" in the experiment do not cause changes in biochemical parameters taken into account, while the artificial flavoring "Vanillin P 5880" tends to to an increase in the activity of alanine and aspartate transaminases.

Data on the functional state of the central nervous system of rats showed that a flavor identical to the natural "Pomegranate 78484-343" and artificial flavor "Vanillin P 5880" reduced the motor activity of rats compared to the control.

The above gives reason to conclude that the flavoring identical to the natural "Pomegranate 78484-343" and artificial flavoring "Vanillin P 5880" with prolonged exposure to the body can cause pathological processes in the liver, as well as lead to over-excitation of the nervous system with subsequent sharp inhibition.

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