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THERAPEUTIC AND PROPHYLACTIC EFFICIENCY OF POLYFUNCTIONAL ANTI-DISBIOTIC DRUGS UNDER CONDITIONS OF EXPERIMENTAL LIPID INTOXICATION

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Abstract

Aim: to compare the therapeutic and prophylactic efficiency (TPE) of four polyfunctional antidisbiotic drugs (PFAD) in experimental lipid intoxication.

Methods: TPE was assessed by the nature of changes in blood serum levels of biochemical markers of inflammation (elastase, MDA), bacteremia (urease), nonspecific immunity (lysozyme). The following PFAD were used: Kvertulin (quercetin + inulin + calcium citrate), Lekvin (lecithin + quercetin + inulin + calcium citrate), Lekasil (lecithin + milk thistle meal + calcium citrate) and Lysozyme-forte (lysozyme + quercetin + inulin + gelatin + calcium citrate). Lipid intoxication was carried out on rats by introducing thermal peroxide sunflower oil (TPSO) with food at a dose of 4 g/kg for 75 days. PFAD was administered from day 31 at a dose of 300 mg/kg for 45 days.

Results: there was a significant increase in the level of elastase, MDA, urease and a significant decrease in the activity of lysozyme in the blood serum of rats treated with TPSO. After the introduction of all drugs, a significant decrease in the level of elastase, MDA, urease and a significant increase in the activity of lysozyme were observed.

Conclusion: with lipid intoxication, a dysbiotic syndrome develops, manifested by bacteremia, a decrease in the level of nonspecific immunity and manifestations of systemic inflammation. Taking polyfunctional antidisbiotic drugs reduces bacteremia, enhances nonspecific immunity and prevents the development of systemic inflammation. The most effective remedy turned out to be "Lysozyme-Forte".

Key words: *lipid intoxication, dysbiosis, bacteremia, systemic inflammation, antidisbiotics, quercetin, lysozyme, prevention*

Introduction

Under the conditions of heat treatment of food fats and fat-containing products, thermoperoxidation processes take place, in which toxic compounds (peroxides, epoxides, aldehydes, ketones, trans isomers) are formed from unsaturated fatty acids [1-6].

It is established that these products cause the development of dysbiotic and inflammatory-dystrophic processes in body tissues [7-9]. For the prevention of thermoperoxide complications, it is proposed to use antioxidants and anti-inflammatory drugs [10-13].

Given that the action of toxic products of thermoperoxidation of fats on the body develops dysbiotic syndrome, the manifestations of which are bacteremia, endotoxinemia, systemic inflammation and multiple organ failure [14], we consider it appropriate to use for the prevention of dysbiotic syndrome polyfunctional antidisbiotics drugs (PFAD), which can affect the main links in the development of this pathology, namely intestinal dysbacteriosis, barrier function of the intestinal mucosa, antimicrobial function of the liver, on the condition of nonspecific immunity and inflammatory-dystrophic processes [14].

The aim of this work was to determine the therapeutic and prophylactic efficacy in thermoperoxide intoxication of a number of PFAD, which include prebiotics, antioxidants, membrane protectors and antitoxic compounds.

Methods

Thermoperoxide intoxication was reproduced in rats by introducing thermoperoxide sunflower oil (TPSO) into the feed at a dose of 4 g/kg for 75 days.

TPSO was obtained by heating sunflower oil at a temperature of +115-120 °C in the presence of $CuSO_4$ for two hours [15].

As PFAD used phytopreparations "Kvertulin", "Lekvin", "Lekasil" and "Lysozyme-forte", the characteristics of which are presented in table 1.

The experiments were performed on 42 white Wistar rats (males, 7 months, live weight 238-252 g), divided into 6 groups: 1st – control, 2nd, 3rd, 4th, 5th and 6-a was obtained with TPSO feed for 75 days at a dose of 4 g/kg. Rats of the 3rd group received per os Kvertulin, the 4th – "Lekvin", the 5th – "Lekasil" and the 6th – "Lysozyme-forte". All drugs at a dose of 300 mg/kg were administered to rats from the 31st day of the experiment for 45 days.

Euthanasia of animals was performed on the 76th day of the experiment under thiopental anesthesia (20 mg/kg) by total bleeding from the heart. Received blood serum, which determined the level of markers of inflammation [16]: the activity of the proteolytic enzyme elastase [17], the content of malonic dialdehyde (MDA) [17], the biochemical indicator of bacteremia – urease activity [17], nonspecific immunity – lysozyme activity 17] and the balance of antioxidant and prooxidant systems in the ratio of catalase activity [17] and the content of MDA (API index).

The ratio of the relative activities of urease and lysozyme was used to calculate the degree of dysbiosis by Levitsky [18].

The results of the research were subjected to standard statistical processing [19].

By the sum of the percent increase in the level of elastase, MDA and urease, the proinflammatory effect of TPSO (PIE) was determined [20], and by the sum of percent, the decrease in the level of these parameters under the influence of PFADZ determined their anti-inflammatory effect (AIE) [20]. Treatment-and-prophylactic efficacy (TPE) of each drug was calculated by the ratio of AIE and PIE [20].

Results

In fig. 1 presents the results of determining the level of serum biochemical markers of inflammation in the blood, namely the activity of elastase and the content of MDA. These data show that in rats treated with TPSO (group № 2), both indicators significantly increase: elastase activity by 29.2 % and MDA content by 49 %.

In rats treated with PFAD on the background of TPSO, the level of both indicators of inflammation is significantly reduced. In rats treated with Kvertulin, elastase activity decreased by 22.1 %, MDA content – by 30.8 %. In rats treated with Lekvin, elastase activity decreased by 9.7 % and MDA content by 37.1 %. In rats treated with Lekasil, elastase activity decreased by 12.5 % and MDA content by 40.6 %. In rats treated with Lysozyme-forte, elastase activity decreased by 25.2 % and MDA content by 41.3 %.

In fig. 2 presents the results of determination in the serum of rats of urease and lysozyme activity. In rats treated with TPSO (group № 2), urease activity increased by 131.4 %, while lysozyme activity decreased by 33.3%. In rats treated with Kvertulin on the background of TPSO, urease activity decreased by 66.7 %, but lysozyme activity increased by 46.4 %. In rats treated with Lekvin, urease activity decreased by 46.3 % and lysozyme activity increased by 41.1 %. In rats treated with Lekasil, urease activity decreased by 42 %, but lysozyme activity increased slightly (by 7.1 %). In rats treated with Lysozyme Forte, urease activity decreased by 75.3 %, but lysozyme activity increased by 28.6 %.

In fig. 3 shows the results of the determination of the antioxidant-prooxidant API index and the degree of dysbiosis in the blood serum. These data show that in rats treated with TPSO, the API index decreases 2.4 times, and under the influence of PFAD, on the contrary, increases 1.8 times ("Kvertulin"), 2.4 times "Lekvin"), 2 times ("Lekasil") and 2.3 times ("Lysozyme-forte").

The degree of serum dysbiosis in rats treated with TPSO increases 3.45 times. The introduction of PFAD significantly reduces the degree of dysbiosis: "Kvertulin" in 4.4 times, "Lekvin" in 2.6 times, "Lekasil" in 1.8 times and "Lysozyme-forte" in 5.2 times.

The results of calculating the amount of increases in elastase, MDA and urease (proinflammatory effect of TPSO), as well as the amount of decrease in these indicators under the influence of PFADZ are presented in table 2. According to these data was calculated therapeutic and prophylactic efficacy (TPE) of each drug.

According to this indicator, the most effective was "Lysozyme-forte", then "Kvertulin" and almost identical "Lekvin" and "Lekasil".

The data obtained by us give grounds to recommend for the prevention of pathological complications from the consumption of thermoperoxide fats to use "Lysozyme-forte", which has a permit from the Ministry of Health of Ukraine for use as a prophylactic in dental diseases.

Conclusions

1. Consumption of thermoperoxide sunflower oil causes the development of dysbiotic syndrome with manifestations of decreased levels of nonspecific immunity and antioxidant protection, increased levels of bacteremia, the degree of dysbiosis and systemic inflammation.

2. Polyfunctional antidisbiotics have anti-inflammatory and antidisbiotic effects by increasing the level of nonspecific immunity, antioxidant protection and reducing the level of bacteremia and systemic inflammation.

3. The best of the drugs was "Lysozyme-forte".

Acknowledgments

The authors declare that there are no conflicts of interest.

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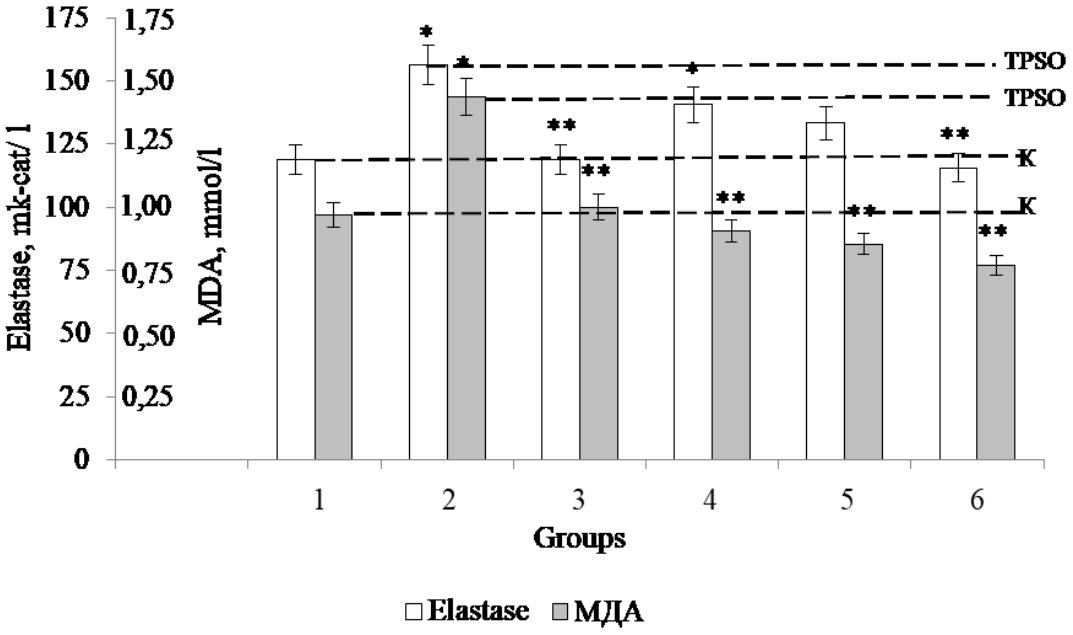
Table 1. Characteristics of multifunctional tablet forms antidisbiotic drugs

Remedy	Composition	Normative documentation
Kvertulin	Quercetin, inulin, calcium citrate	TC U 10.8-13903778-040:2012 Conclusion of the Ministry of Health № 05.03.02-06/44464 dated 17.05.2012
Lekvin	Lecithin, quercetin, inulin, calcium citrate	TC U 10.8-37420386-003:2016 Conclusion of the Ministry of Health № 05.03.02-08/8400 dated 21.03.2016
Lekasil	Lecithin, milk thistle presscake, calcium citrate	TC U 10.8-37420386-005:2017 Conclusion of the Ministry of Health № 602-123-20-2/12102 dated 25.04.2017
Lysozyme-forte	Lysozyme, quercetin, inulin, gelatin, calcium citrate	TC U 10.8-37420386-004:2016 Conclusion of the Ministry of Health № 602-123-20-2/5734 dated 22.12.2016

Table 2. Pro-inflammatory effect (PIE) TPSO, anti-inflammatory effect (AIE) and therapeutic and prophylactic efficacy (TPE) of drugs (in %)

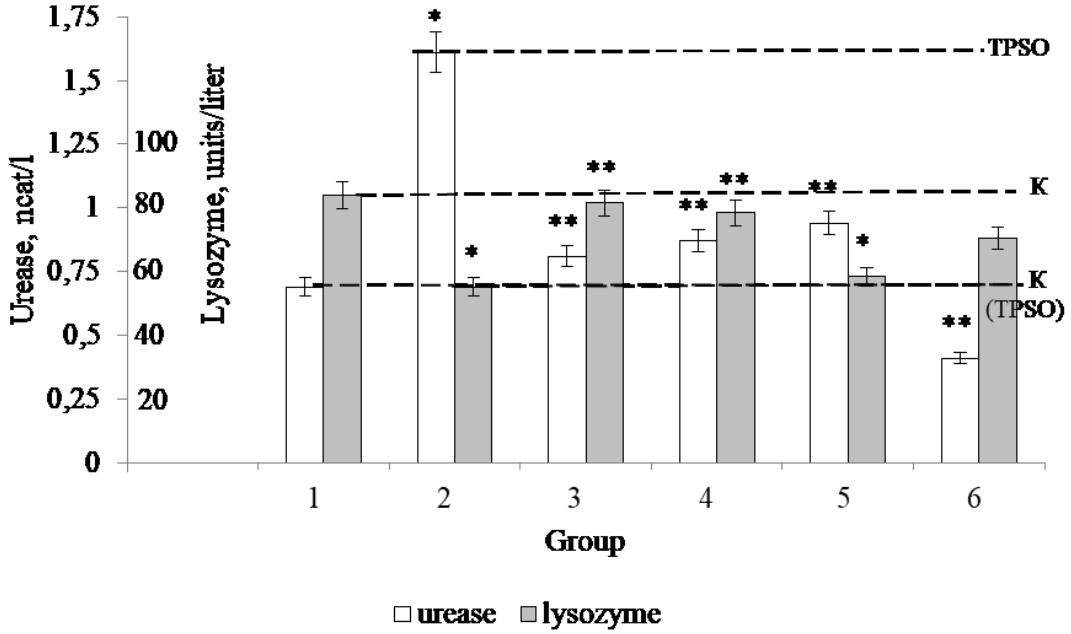
№№	Group	TPE	AIE	PIE
1	TPSO	209,6	–	–
2	«Kvertulin»	–	–119.6	57,1
3	«Lekvin»	–	–93,1	44,4
4	«Lecasil»	–	–95,1	45,4
5	«Lysozyme-forte»	–	–141,5	67,5

Figure 1. The effect of phytopreparations on the level of markers of inflammation in the serum of rats treated with TPSO



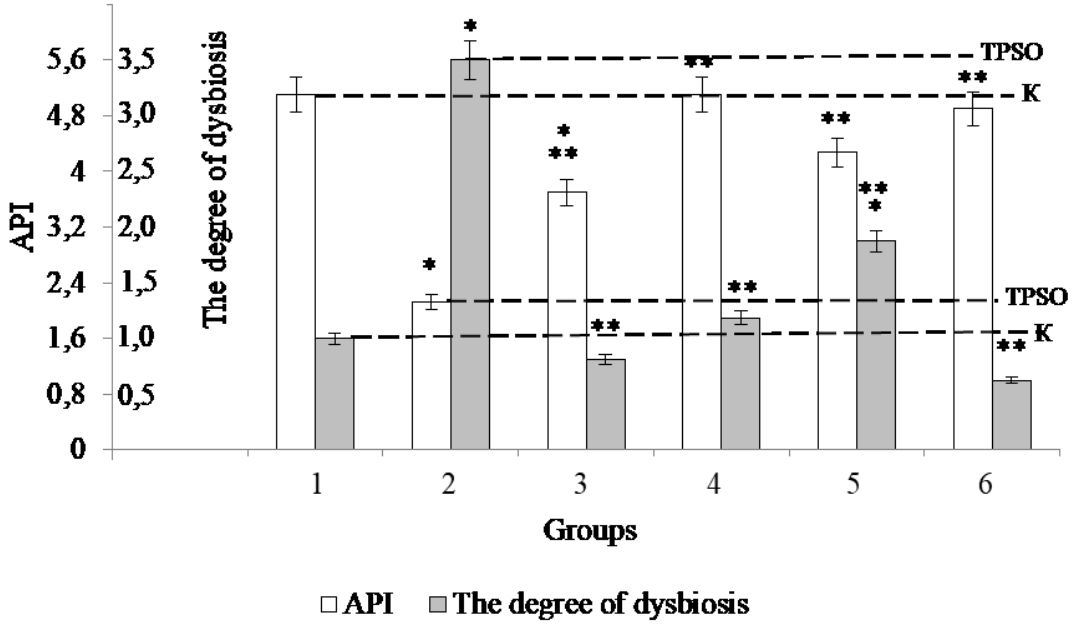
1 – control, 2 – TPSO, 3 – TPSO + "Kvertulin", 4 – TPSO + "Lekvin", 5 – TPSO + "Lekasil", 6 – TPSO + "Lysozyme-forte"

Figure 2. The effect of phytopreparations on the activity of urease and lysozyme in the serum of rats treated with TPSO



1 – control, 2 – TPSO, 3 – TPSO + "Kvertulin", 4 – TPSO + "Lekvin", 5 – TPSO + "Lekasil", 6 – TPSO + "Lysozyme-forte"

Figure 3. The effect of phytopreparations on the activity of the API index and the degree of dysbiosis in the serum of rats treated with TPSO



1 – control, 2 – TPSO, 3 – TPSO + "Kvertulin", 4 – TPSO + "Lekvin", 5 – TPSO + "Lekasil", 6 – TPSO + "Lysozyme-forte"