

# Some Aspects of Protective Effect of Plaferon LB During Bronchial Asthma

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## **Abstract**

Modern anti-inflammatory means used for treatment of bronchial asthma are characterized by comparative efficiency and side effects. All above-mentioned makes impossible the long use of this preparation. From this point of view, Plaferon LB with its anti-oxidant, immuno-modulatory and anti-inflammatory characteristics has no side effects. This fact is approved by 18-year practice of using this preparation for treatment of different diseases. In this respect the main goal of our work was to research mechanisms of protective effect of Plaferon LB during bronchial asthma. With due regard for the results of our test, Plaferon LB facilitates the recreating process between pro- and antioxidant systems of blood and decreases the intensity of creation of peroxinitrite, establishing the conditions for decrease of heaviness of inflammatory process and improvement of health of a patient.

**Keywords:** *plaferon LB, Fe<sup>3+</sup> transferring, antioxidant system of blood*

## **Introduction**

Morphological and biochemical pathological changes that form the basis of hyper-reactivity of the respiratory tract, are developed as a result of complicated interactions between the inflammatory cells and created by them pro-inflammatory mediators. The currently available anti-inflammatory preparations used for treatment of bronchial asthma are characterized by comparative efficiency and side effects that stipulate the expediency of introducing this new remedy. From this point of view Plaferon LB with its anti-oxidant, immuno-modulatory and anti-inflammatory characteristics has no side effects. This fact is approved by 18-year practice of using this preparation for treatment of different diseases, including bronchial asthma (Kokaia, 1999).

According to the previous tests Plaferon LB stimulates adenylyl-cyclase activity and inhibits phosphodi-inositolphosphatase. Plaferon LB also inhibits the production of prostaglandin E through suppression of activity of phospholipase A<sub>2</sub> (Bakhtashvili A., 1991). D. Mikeladze and co-authors stated that Plaferon LB decreases the number of M-cholinergic, H-1-histidine, a-adrenergic receptors, inhibits protein kinase C, increases number of p-adrenergic receptors and cyclic

adenosine monophosphate in lymphocytes (D.D. Mikeladze and others, 1995, L. Kokaia, 1999).

In this view the goal of the work was to research mechanisms of effect of Plaferon LB during the bronchial asthma.

## **Materials and Methods**

The state of blood anti-oxidant and pro-oxidant systems of children with bronchial asthma (40 patients) of medium heaviness at the age from three to seven has been tested. Out of them twenty patients (1 group) were treated by Plaferon LB, the other 20 were not treated. Children in the first group were per orally treated with Plaferon LB doze 4 mg/ml as an active preparation within one week. Children in the second group were treated with 4-ml physiological solution. In the first group the children also received the remedy diluting bronchial tubes and preparation dilatating sputum.

The activity of anti- and pro-oxidant system of blood has been judged according to intensity of Electro-paramagnetic signals of its paramagnetic centers. Blood taken for test was frozen in liquid nitrogen (t=196° C), Blood electro paramagnetic spectra were measures at radio-spectrometer 1307 in Duar quartz vessel.

	N	Inact. state adren G=2.01	CP G=2.056	Fe <sup>3+</sup> TP G=4.2	Mn <sup>2+</sup> G=2.14	Fe <sup>2+</sup> G=2.2	MetHb G=6.0	FeSNO G=2.03
1. Control	20	-	15.0±1.0	30.0±0.8	-	-	-	-
2. Bronchial asthma before treatment	40	1.1±0.2	26.0±0.4 P12<0.001	20.5±1.5 P12<0.001	15.2±1.7	25.0±1.0	10.4±0.8	8.4±1.6
3. Bronchial asthma, complex treatment without Plaferon	20	1.1±0.2 P2..3>0.1	23.0±0.4 P2.3<0.01	22.0±0.5 P2.3<0.01	9.0±1.5 P2.3<0.01	22.0±1.5 P2.3>0.1	6.0±0.8 P2.3<0.01	6.8±1.5 P2..3>0.1
4. Bronchial asthma, complex treatment with Plaferon	20	0.5.0±0.1 P2.4<0.5	18.3±0.7 P2.4<0.01	25.5±0.9 P2.4<0.01	4.5±0.5 P2.4<0.001	13.0±0.8 P2.4<0.01	4.5±0.5 P2.4<0.001	3.2±1.1 P2..4<0.001

*Tab.1 Changes of paramagnetic centers of blood in children with Bronchial asthma.*

## Results and Discussion

Changes of paramagnetic centers of blood in children with bronchial asthma at the age from three to seven are given in the table. According to the Table the intensity of Electro-paramagnetic signal of oxidized hepatocuprein sharply increases during bronchial asthma and exceeds the indices typical of healthy children by 90%, and the electro paramagnetic signal Fe<sup>3+</sup> - transferrin at the bronchial asthma decreases and constitutes 70% of controlled meanings. In blood of children with bronchial asthma we registered the intensive electro paramagnetic signal, typical of inactivated state of adrenoreceptors of regular elements of blood, as well as Mn<sup>2+</sup> "inclusive complexes, Mo<sup>5+</sup> xantine oxydases, nitrosyl complexes of non-hemous iron (FeSNO, g=2,03) and met hemoglobin. As a result of the comprehensive treatment the content of hepatocuprein, Mn<sup>2+</sup> "inclusive complexes and met hemoglobin statistically decreased in patients' blood with bronchial asthma and the content of Fe<sup>3+</sup> - transferrin increases. But the electro paramagnetic signals typical of inactivated state of adrenoreceptors and FeSNO remain high.

Plaferom LB decreases intensity of electro paramagnetic signal of oxidized hepatocuprein and exceeds the indices typical of children only by 30%. Electro paramagnetic signal Fe<sup>3+</sup> - transferrin against the background of treatment with Plaferon LB increases and reaches the controlled indices. It should be noted that treatment with Plaferon LB stipulates also the decrease of intensity of electro paramagnetic signals Mn and Mo<sup>5+</sup> inclusive complexes, MetHb, decrease of degree of inactivation of adrenergic receptors, erythrocytes and leukocytes at the surface, as well as sharp decrease of content of nitrosyl complexes of non-hemous iron in blood of children suffering from bronchial asthma.

As it is known, intensity of electro paramagnetic signals of hepatocuprein and Fe<sup>3+</sup> - transferrin reflect the antioxidant characteristics of blood. According to the obtained results growth of intensity of electro paramagnetic signals of hepatocuprein during bronchial

asthma and decrease of intensity of Fe<sup>3+</sup> - transferrin certify the decrease of antioxidant activity of blood, constituting the consequence of activation of free radical processes in organism. At the same time decrease of content of Fe<sup>3+</sup> - transferrin in blood stipulates the disorder in the provision of tissues with iron and decrease of processes of proliferation (in particular, hemo- and erythrogenesis in organism).

Intensification of processes of free radical oxidation during bronchial asthma is also approved by appearance of intensive signals of Mn<sup>2+</sup>, Mo<sup>5+</sup>-inclusive complexes, MetHb. Mn<sup>2+</sup> ions appear in blood as a result of disorder of integrity of membrane structure. In their turn, they similar to other ions of metals with variable valency represent the powerful promoters of free radical oxidation. Appearance of Mo<sup>5+</sup>-inclusive complexes in the electro paramagnetic spectrum of blood provides for the intensified creation of xantine oxydases that on the one hand certifies the development of ischemia in organism and on the other hand furthers the subsequent intensification of processes of free radical oxidation, peroxide oxidation of lipids of membrane receptors with their subsequent destruction and disorder of functions of membrane receptors, ferment complexes and cells themselves. The latter is observed in inactivation of adrenergic receptors of regular elements of blood - the result of both immediate peroxide damage of membranes of blood cells and action of ions Mn<sup>2+</sup>, separating adrenoreceptors from adenilumcylase. Besides the creation of signals of MetHb in the electro paramagnetic spectrum of blood indicates at the intensified hemolysis of erythrocytes, that is also the subsequence of activation of processes of peroxide oxidation of lipids in organism. Accumulation of MetHb under the terms of disorder in process of hemogenesis furthers the development of hypoxia in organism. (Dumbadze M., 1999).

At the same time one can't but mentioned the role of auto-antibodies towards adrenoreceptors in the mechanism of inactivation of these receptors and generally in pathogeny of bronchial asthma (Fraser C.M, et al., 1984, Homer I., et al., 1989)

Intensive electro paramagnetic signal of nitrosyl complexes of non-hemous iron, revealed by us in blood of children with bronchial asthma evidences the intensive formation of nitric oxide - the result of both activation of constitutional NO-syntasis and intensified inducible expression (Saneti G.T., et al., 1999). Intensification of synthesis of nitric oxide to some extent is the compensatory reaction of organism, stipulates dilatation of bronchial tubes and blood-vessels, decrease of adhesion and aggregation of regular blood elements (Davenpick K.L., 1994). At the same time under the terms of surplus of reactive forms of oxygen and inactivation anti-oxidant system of blood, the nitric oxide changes to cytotoxic peroxinitrite, characterized by vasopressor, procollagenase-stimulating and elastinase-stimulating effect; moreover, peroxinitrite activates cyclo-oxygenase and therefore the synthesis

of prostaglandin. So, peroxinite furthers the creation of inflammatory mediators, thus promoting the destruction of tissues and aggravation of pathological process.

With due regard for the results of our tests, Plaferon LB furthers both the restitution of activity of antioxidant system of blood - hepatocuprein -  $Fe^{3+}$  - transferrin, and decrease of intensity of creation of generators of reactive forms of oxygen - ions of  $Mn^{2+}$ , xantine oxydases, nitric oxides (See *Tab.1*). As a result of restoration of balance between the pro-and anti-oxidant systems of blood against the background of treatment with Plaferon LB the intensity of creating of peroxinitrite decreases, thus establishing the conditions for decrease of heaviness of inflammatory process and improvement of health of a patient.

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## Некоторые аспекты защитного действия плаферона ЛБ при бронхиальной астме

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### РЕЗЮМЕ

Существующие на сегодняшний день противовоспалительные препараты, используемые для лечения бронхиальной астмы, характеризуются относительной эффективностью, а также побочными действиями, что обуславливает невозможность их длительного применения. С этой точки зрения Плаферон ЛБ, обладающий антиоксидантными, иммуномодуляторными, противовоспалительными свойствами, не характеризуется побочными эффектами, о чем свидетельствует 18-летний опыт применения этого препарата при лечении различных заболеваний. В связи с этим целью работы явилось исследование механизмов защитного действия плаферона ЛБ при бронхиальной астме. Как следует из результатов наших исследований, плаферон ЛБ способствует восстановлению баланса между про- и антиоксидантной системами крови, снижается интенсивность образования пероксинитрита, и тем самым, создаются условия, способствующие уменьшению тяжести воспалительного процесса и улучшению состояния больного.

**Ключевые слова:** фармацевтический рынок, экспорт, импорт, качество лекарств