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Physiological Properties Of Platelets In Newborn Calves With Functional Disorders Of The Digestive System, Treated With The Sorbent "Ecos".

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ABSTRACT

In newborn calves with functional digestive disorders, an increase in platelet aggregation functions was found in vitro and in vivo. These disorders are based on deep changes in the lipid composition of platelet membranes, an increase in the level of medium molecules in plasma and blood plates, activation of lipid peroxidation in them, increased synthesis in the vascular wall of von Willebrand factor and intensification of thromboxane formation in blood plates. Activation of thromboplastin formation is the leading cause of increased blood coagulation in newborn calves with functional digestive disorders. Against the background of their use of Ecos, positive dynamics of platelet hemostasis was observed in newborn calves with functional disorders of the digestive system. These effects are due to the improvement of metabolic processes, a decrease in the toxic effect of lipid peroxidation and medium molecules in plasma and platelets and the optimization of the reception of exogenous signals by platelets. However, the use of "Ecos" was not sufficient for the complete correction of platelet hemostasis. The positive dynamics of its activity is associated with a weakening of the adhesion and aggregation of platelets in newborn calves. The insufficiently pronounced decrease in intravascular platelet activity during the correction of Ecos in newborn calves with functional disorders of the digestive system does not allow considering its use as sufficient to reduce the risk of thrombotic complications. Given the weak level of correction with the help of Ecos, platelet hemostasis in newborn calves with functional disorders of the digestive system, it is necessary to combine it with other means of correction. This will strengthen the positive effect of Ecos on the platelet functions of newborn calves, consolidate its effect and reduce the recurrence of the risk of developing vascular complications. Keywords: platelets, newborn calves, functional disorders of the digestive system, Ecos, physiology,

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INTRODUCTION

The emergence of functional disorders of the digestive system in newborn calves is often combined with endogenous intoxication [1,2], caused by random proteolysis of proteins [3,4] and activation of lipid peroxidation (POL) [5,6], leading to massive release of medium molecules into the bloodstream [7-10]. This is accompanied by disorders of platelet hemostasis [11,12], contributing to the development of intravascular thrombus formation [13,14]. At the same time, the features of platelet abnormalities in calves with functional disorders of the digestive system and the approaches to their correction have not been studied enough [15,16].

The use of sorbents is an integral component of the correction of endogenous intoxication [17]. It has been suggested that it is possible to correct the functions of platelets in newborn calves with functional disorders of the digestion using the "Ecos" sorbent - hydroaluminosilicate from Belgorod Region deposits.

The aim of the work is to identify the possibility of correction of platelet hemostasis in newborn calves with functional disorders of the digestion using the sorbent "Ecos".

MATERIALS AND METHODS

Research was conducted in strict accordance with ethical principles established by the European Convent on protection of the vertebrata used for experimental and other scientific purposes (adopted in Strasbourg March 18, 1986, and confirmed in Strasbourg June 15, 2006) and approved by the local ethic committee of Russian State Social University (Record Nº12 dated December 3, 2015).

The study included 25 newborn calves with functional digestive disorders. In patients with calves, all signs of functional digestive disorders with bright intoxication were noted. The control group consisted of 267 healthy newborn calves. The examination included determination of the activity of plasma lipid peroxidation was determined by the content of thiobarbituric acid-active products using the Agat-Med kit. Determined the antioxidant potential of the liquid part of the blood. Intra thrombotic LPO was assessed by the concentration of the basal level of malonic dialdehyde (MDA) in the reduction reaction with thiobarbituric acid. The level of middle molecules was found out in plasma and washed and resuspended platelets. The number of platelets in capillary blood in the Goryaev chamber was counted. Platelet aggregation (AP) was studied by a visual micromethod using as inducers ADP (0.5×10⁻⁴ M), collagen (dilution 1:2 of the main suspension), thrombin (0.125 units / ml), ristomycin (0.8 mg / ml), adrenaline (5×10⁻⁶ M), as well as combinations of ADP and adrenaline, ADP and collagen, adrenaline and collagen to simulate real blood flow conditions.

Intravascular platelet activity was determined visually using a phase contrast microscope. 25 calves were assigned sorbent "Ecos" - hydroalumosilicate deposits of the Belgorod region 150 mg/kg body weight for 10 days. Statistical processing of the results obtained was carried out using Student's t-test.

RESULTS

In newborn calves with functional disorders of the digestive system, an increase in lipid peroxidation was noted. Thus, the concentration of thiobarbituric acid-active products in plasma was $5.10\pm0.02~\mu\text{mol/l}$, in the control - $3.92\pm0.06~\mu\text{mol/l}$. The level of MDA in platelets increased ($1.54\pm0.004~\text{nmol/10}^9~\text{platelet}$) In the control ($0.89\pm0.02~\text{nmol/10}^9~\text{platelets}$), which indicates the activation of free-radical oxidation in them due to the weakening of intraplatelet antioxidant activity . The levels of medium molecules in plasma were average molecules $280-0.49\pm0.01~\text{conventional units}$, average molecules $254-0.32\pm0.02~\text{conventional units}$, the levels of middle molecules in platelets were equal to average molecules $280-0.061\pm0.02~\text{conventional units/10}^9~\text{platelets}$, average molecules $254-0.069\pm0.03~\text{conventional units/10}^9~\text{platelets}$.

The use of "Ecos" had a positive effect on the LPO of plasma and platelet calves. Thus, the content of thiobarbituric acid-active plasma products decreased (p<0.01). On the 10th day of correction, their concentration was $4.26\pm0.01~\mu$ mol/l. With a decrease in lipid peroxidation products in plasma, a decrease in the average molecules of 280 to 0.42 ± 0.02 conventional units is observed, while the average molecules of 254 - 0.27 ± 0.04 conventional units. With a decrease in free-radical oxidation of plasma lipids, a decrease in the basal level of MDA in platelets after the 10th day of correction was found. Against the background of Ecos, it



was possible to achieve a decrease in the basal level of MDA to $(1.32\pm0.02 \text{ nmol/}10^9 \text{ platelets})$ and the average molecules 280 - 0.057 ± 0.02 conventional units/ 10^9 platelets, the average molecules 254 - 0.063 ± 0.04 conditional units/ 10^9 platelets.

The concentration of platelets in the blood of newborn calves with functional digestive disorders before and after correction was within the normal range. In these calves, prior to the use of Ekos, acceleration of AP was found, especially under the influence of collagen (25.3 \pm 0.21 s). Slightly slower AP developed in sick calves under the influence of ADP (33.0 \pm 0.12 s) and ristomycin (26.2 \pm 0.13 s.). Thrombin (42.4 \pm 0.11 s) and adrenaline (75.6 \pm 0.16 s) antibodies occurred later, developed faster than controls (p<0.01). The time of AP development under the influence of combined use of inductors was also accelerated.

As a result of the use of "Ecos" increased the time of AP under the influence of inductors in all animals. On the 10th day of the correction, collagen was the most active inducer of antibodies $(28.0\pm0.16 \text{ s})$. ADP $(36.0\pm0.12 \text{ s})$, ristomycin $(35.0\pm0.11 \text{ s})$ were somewhat less active. Slower AP developed under the influence of thrombin and adrenaline. The time of AP was extended with a combination of inductors.

The intravascular activity of platelets in newborn calves with functional digestive disorders was characterized by its increase. Discocytes in the blood of calves with functional digestive disorders amounted to 62.0±0.20% (in the control - 82.0±0.16%). The number of disco-echinocytes in them was increased by 1.8 times. The content of spherocytes, sphero-echinocytes and bipolar forms of platelets also significantly exceeded control values. The sum of the active forms of platelets (38.0±0.3%) of the sick calves was increased 2.1 times. Small and large aggregates were contained 4.2 times and 39 times more than the control, respectively, and the number of platelets in the aggregates in animals with functional disorders of the digestive system exceeded the control 2.9 times.

After 10 days of correction, an improvement in the indicators of intravascular platelet activity was revealed. The level of discoid forms of platelets in the blood of calves on the background of the use of "Ecos" increased to 76.5±0.4%. The content of disco-echinocytes, sphero-echinocytes and bipolar forms of platelets significantly decreased under the influence of treatment. The sum of the active forms of platelets on the background of treatment "Ecos" after its use came close to the control (23.5±0.06%). The number of small and large aggregates by the 10th day of correction was significantly different from the control. The number of platelets in the aggregates decreased, but also significantly differed from the same indicator in healthy animals (9.7±0.08%). None of the studied indicators could not get the values corresponding to those in the control.

DISCUSSION

The active POL in plasma and platelets of calves with functional disorders of the digestive system of patients indicates a decrease in the antioxidant system of the body [18-23] and causes an increase in plasma [24] and CM platelets [25]. The positive effect of "Ecos" on the state of POL and the level of medium molecules in the body of calves, obviously, is mediated by its effect on metabolism [26-30]. However, it was not possible to reach the physiological level of POL and medium molecules. The suppression of peroxidation and the increase in the antioxidant potential of the plasma against the background of a decrease in the average molecules indicate a significant detoxification effect of the sorbent "Ekos" in newborn calves with functional disorders of digestion [31].

The positive dynamics of indicators in calves against the background of the use of "Ecos" indicates a positive effect on platelet hemostasis in newborn calves with functional digestive disorders [32,33]. These effects are due to the improvement of metabolic processes, reduction of the toxic effect of POL and medium molecules in plasma and platelets and optimization of the reception of exogenous signals by platelets [34-37]. However, the use of "Ecos" is not enough for a complete correction of platelet hemostasis.

The increase in AP time under the influence of ristomycin in newborn calves that were treated with Ecos, indicates a decrease in von Willebrand factor blood levels [38–41]. At the same time, its concentration exceeded the norm, and the activity of the antioxidant system of platelets was lower than in the control. This created the prerequisites for the re-amplification of platelet aggregation activity [42-45].

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A weak decrease in the intravascular activity of platelets during the correction of "Ecos" in newborn calves with functional digestive disorders does not allow us to consider its use as sufficient to reduce the risk of thrombotic complications [46]. The decrease in intravascular platelet activity was insufficient, and therefore the risk of its enhancement and the development of thrombotic complications remained [47]. Given the weak level of correction of "Ecos" of platelet hemostasis in newborn calves with functional digestive disorders, it is necessary to combine it with another means of correction [48-50]. This will strengthen the positive effect of "Ecos" on the platelet functions of newborn calves, consolidate its effect and reduce the recurrence of the risk of developing vascular complications [51-53].

CONCLUSION

In newborn calves with functional digestive disorders on the background of the use of "Ecos", positive dynamics of platelet hemostasis activity was noted. This is due to the improvement of metabolic processes, reduction of the toxic effect of lipid peroxidation and medium molecules in plasma and platelets and optimization of the reception of exogenous signals by platelets. The decrease in intravascular platelet activity in the correction of "Ecos" in newborn calves with functional digestive disorders does not allow us to consider its use as sufficient to reduce the risk of thrombotic complications. The decrease in intravascular platelet activity was insufficient, and therefore the risk of its enhancement and the development of thrombotic complications remained. Given the weak level of correction of "Ecos" platelet hemostasis in newborn calves with functional digestive disorders, it is necessary to combine it with another means of correction. This will strengthen the positive effect of "Ecos" on the platelet functions of newborn calves, consolidate its effect and reduce the recurrence of the risk of developing vascular complications.

REFERENCES

- [1] Medvedev IN. (2018) Spontaneous Aggregation Of Erythrocytes In Patients With Arterial Hypertension With Impaired Glucose Tolerance. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 2275-2280.
- [2] Apanasyuk LA, Soldatov AA. (2017) Socio-Psychological Conditions for Optimizing Intercultural Interaction in the Educational Space of the University. Scientific Notes of Russian State Social University. 16(5-144): 143-150. doi: 10.17922/2071-5323-2017-16-5-143-150.
- [3] Maloletko AN, Yudina TN.(2017) (Un)Making Europe: Capitalism, Solidarities, Subjectivities. Contemporary problems of social work. 3 (3-11): 4-5.
- [4] Pozdnyakova ML, Soldatov AA. (2017) The Essential and Forms of the Approaches to Control the Documents Execution. Contemporary problems of social work. 3 (1-9): 39-46. doi: 10.17922/2412-5466-2017-3-1-39-46.
- [5] Oshurkova Jul, Medvedev IN, Fomina LL. (2018) Physiological Indices of Platelet-Coagulation Hemostasis in Purebred Ireshire Cows in The Course of Lactation. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(2): 419-426.
- [6] Oshurkova Jul, Medvedev IN, Fomina LL. (2018) Physiological features of platelet aggregation in calves of Ayrshire breed during the phase of plant nutrition. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(2): 1008-1013.
- [7] Skorjatina IA. (2018) Therapeutic Possibilities Of Rosuvastatin In The Medical Complex In Relation To Disaggregation Vascular Control Over Erythrocytes In Persons With Arterial Hypertension And Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(2): 977-983.
- [8] Bikbulatova AA, Pochinok NB, Matraeva LV, Erokhin SG, Makeeva DR, Karplyuk AV.(2018) Formation Of International Practice Of Holding Competitions Of Professional Skills Among Professionals With Disabilities. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 296-302.
- [9] Makhova AV. (2018) Physiology Of The Hypothalamus In The Human Body. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 478-484.
- [10] Makhov AS. (2018) The Importance Of The Needs Arising In People When Organizing Classes Rink Bandy (Mini Hockey). Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 96-101.
- [11] Makhov AS. (2018) The Basic Needs Of Hearing Impaired People In Organizing Football Training. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 121-126.
- [12] Makhov AS. (2018) Perspectives Of Rink-Bendi Development Among People With Hearing Impairment In Russia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 139-146.



- [13] Makhov AS. (2018) Specificity Of Requirements Of Russian And Foreign Hockey Players With Hearing Impairment To The Process Of Training And Competition. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 157-163.
- [14] Makhov AS. (2018) Motivational Field Of Disabled People With Musculoskeletal Injury To Participation In Training On Russian Press. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 211-217.
- [15] Bespalov DV, Medvedev IN, Mal GS, Polyakova OV. (2018) Physiological Capabilities Of The Vascular Endothelium With The Developing Arterial Hypertension In People Of Different Ages Who Had Long Had Low Physical Activity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(2): 972-976.
- [16] Bespalov DV, Medvedev IN, Mal GS, Makurina ON. (2018) Functional activity of the vascular endothelium in patients with initial signs of atherosclerosis against the background of regularly dose-related exercise stress. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(2): 1020-1024.
- [17] Bikbulatova AA, Andreeva EG, Medvedev IN. (2018) Hematological Features Of Patients With Osteochondrosis Of The Spine. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2018; 9(3): 1089-1095.
- [18] Medvedev IN. (2018) Aggregation Of Thrombocytes In Patients With Arterial Hypertension And Impaired Glucose Tolerance. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 1604-1609.
- [19] Medvedev IN. (2018) Severity Of Neutrophil Aggregation In Patients With Arterial Hypertension With Impaired Glucose Tolerance. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5):1647-1651.
- [20] Medvedev IN. (2018) Aggregation Of Erythrocytes In Patients With Abdominal Obesity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 1676-1681.
- [21] Medvedev IN. (2018) Platelet Aggregation Activity In Patients With Abdominal Obesity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5):1738-1743.
- [22] Medvedev IN. (2018) Intensity Of Neutrophil Aggregation In Patients With Abdominal Obesity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5):1778-1783.
- [23] Medvedev IN. (2018) Aggregational Properties Of Erythrocytes In Patients With Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 1803-1808.
- [24] Medvedev IN. (2018) Aggregational Capacity Of Platelets In Patients With Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5):1830-1835.
- [25] Medvedev IN. (2018) The Ability To Aggregate Neutrophils In Patients With Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 1861-1866.
- [26] Medvedev IN. (2018) Intensity Of Spontaneous Aggregation Of Erythrocytes In Patients With Abdominal Obesity And Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5):1919-1924.
- [27] Medvedev IN. (2018) Expression Of Aggregation Capacity Of Platelets In Abdominal Obesity And Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5):1941-1946.
- [28] Medvedev IN. (2018) The State Of Aggregation Properties Of Neutrophils In Patients With Abdominal Obesity And Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 1985-1989.
- [29] Medvedev IN. (2018) Severity Of Erythrocyte Aggregation In Patients With Hyperuricemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 2025-2030.
- [30] Medvedev IN. (2018) Activity Of Aggregation Properties Of Neutrophils In Patients With Arterial Hypertension With Type 2 Diabetes Mellitus. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 2043-2047.
- [31] Medvedev IN. (2018) Increased Aggregation Properties Of Platelets In Patients With Hyperuricemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5):2048-2053.
- [32] Medvedev IN. (2018) Severity Of Aggregation Properties Of Neutrophils In Patients With Hyperuricemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 2088-2093.
- [33] Medvedev IN. (2018) The Level Of Erythrocyte Aggregation In Patients With Type 2 Diabetes Mellitus. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 2115-2120.
- [34] Medvedev IN. (2018) Aggregational Activity Of Thrombocytes In Patients With Type 2 Diabetes Mellitus. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5):2137-2142.

2018



- [35] Medvedev IN. (2018) Severity Of Aggregation Neutrophils In Patients With Type 2 Diabetes Mellitus. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5):2162-2167.
- [36] Medvedev IN. (2018) Intensity Of Spontaneous Aggregation Of Erythrocytes In Patients With Impaired Glucose Tolerance And Abdominal Obesity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 2173-2178.
- [37] Medvedev IN. (2018) Activity Of Platelet Aggregation In Patients With Impaired Glucose Tolerance And Abdominal Obesity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 2183-2188.
- [38] Medvedev IN. (2018) Severity Of Aggregation By Neutrophils In Patients With Impaired Glucose Tolerance And Abdominal Obesity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 2194-2199.
- [39] Medvedev IN. (2018) Features Of Erythrocyte Aggregation In Patients With Impaired Glucose Tolerance. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5):2210-2215.
- [40] Medvedev IN. (2018) Aggregation Of Platelets In Patients With Impaired Glucose Tolerance. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5):2226-2231.
- [41] Medvedev IN. (2018) Aggregational Capabilities Of Neutrophils In Patients With Impaired Glucose Tolerance. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 2248-2253.
- [42] Oshurkova Jul, Medvedev IN, Tkacheva ES. (2018) Functional Features Of Platelet Aggregation In Heifers Of The Ayrshire Breed, Which Are Being Prepared For Insemination. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(3): 1155-1160.
- [43] Glagoleva TI, Medvedev IN. (2018) Physiological Features Of Anti-aggregational Control Of Blood Vessels Over The Shaped Elements Of Blood In Calves At The Onset Of Ontogenesis. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 440-447.
- [44] Vorobyeva NV, Mal GS, Skripleva EV, Skriplev AV, Skoblikova TV. (2018) The Combined Impact Of Amlodipin And Regular Physical Exercises On Platelet And Inflammatory Markers In Patients With Arterial Hypertension. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(4): 1186-1192.
- [45] Oshurkova Jul, Medvedev IN, Fomina LL. (2018) Physiological features of platelet aggregation in calves of Ayrshire breed during the phase of plant nutrition. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(2): 1008-1013.
- [46] Bikbulatova AA, Pochinok NB, Matraeva LV, Erokhin SG, Makeeva DR, Karplyuk AV. (2018) The Russian Historical Aspect Of The Development Of The International Federation Of Abilimpix. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 329-335.
- [47] Bikbulatova AA, Pochinok NB, Soldatov AA, Matraeva LV, Erokhin SG. (2018) Organization Of International Competitions Of Professional Skill Among People With Disabilities. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 379-387.
- [48] Bikbulatova AA. (2018) Technology Implementation Of Competitions Of Professional Skill. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 407-419.
- [49] Bikbulatova AA, Kartoshkin SA, Pochinok NB. (2018) Schemes Of Competitions Of Professional Skills Among People With Disabilities In Russia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 357-362.
- [50] Bikbulatova AA, Matraeva LV, Erokhin SG, Makeeva DR, Karplyuk AV. (2018) Methodical Foundations Of Carrying Out Competitions Of Professional Skill Among People With Disabilities. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5): 243-247.
- [51] Bikbulatova AA, Karplyuk AA, Parshin GN, Dzhafar-Zade DA, Serebryakov AG. (2018) Technique for Measuring Vocational Interests and Inclinations in High-School Students with Disabilities. Psikhologicheskaya nauka i obrazovanie-psychological science and education. 23(2): 50-58.doi: 10.17759/pse.2018230206
- [52] Bikbulatova AA, Karplyuk AV, Medvedev IN. (2018) Methodical Bases Of The Help To Young Invalids In A Choice Of Sphere Of Their Future Professional Activity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(4): 571-577.
- [53] Bikbulatova AA, Karplyuk AV, Medvedev IN. (2018) The Problem Of Vocational Guidance Work With Young People, Who Have Limited Health Opportunities In Modern Russia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(4): 586-590.

2018