CONTAINING PHARMACOCYTES

D. Ibrasheva, D. Idrissova*, B. Umbayev, A. Masoud, S. Askarova

Center for Life Sciences, Nazarbayev University, Astana, Kazakhstan; damira.idrissova@nu.edu.kz

Introduction. Viral hepatitis B and C- is a widespread infectious disease of the liver and is a potential threat to human life. Treatment of HCV and HBV requires prolonged (parenteral or oral) administration of antiviral and immune-stimulating agents, which often have serious side effects that lead to abrupt termination of the therapy and the development of viral resistance. Targeted delivery of drugs directly to the affected organ is one of the most promising areas that seek to improve the outcome of treatment of patients with chronic diseases. Among the various drug delivery systems, erythrocytic pharmacocytes are of special interest. They are a shade of red blood cells, that could be loaded with antiviral drugs and drugs that boost the immune system. Owing to the fact that erythrocytes are destroyed by mononuclear phagocytes in the liver, it is assumable that the EP serve as a promising and direct means of delivering antiviral drugs and immune-modulators into the liver parenchyma to treat viral hepatitis.

Since the destruction of erythrocytic pharmacocytes loaded with drugs can differ from that of intact erythrocytes in the body, this study aims to estimate the bio-distribution of erythrocytic pharmacocytes loaded with an antiviral interferon gamma drug in vivo and ex vivo compared to intact erythrocytes.

Materials and methods. White laboratory mice were divided into 3 groups with 6 animals per group: 1. Animals in the control group received with PBS intravenously. 2. Animals in this group received erythrocytes colored with Dir fluorescent dye through intravenous injection. Group 3 animals received an intravenous injection of EP-stained with a Dir fluorescent dye containing IFN- y. Drug encapsulation in erythrocytic pharmacocytes was performed using the dialysis method. Whole venous blood was extracted, poured in a test tube with heparin or EDTA and centrifugated for 10 minutes at 1900g, + 4C°.

Plasma and white blood cells were aspirated and the precipitated erythrocytes were washed twice. 900ul of erythrocytes and 100ul of sample were added to the dialysis bag. Upon completion of dialysis, the constituents were incubated and washed according to the recommended protocol.

Bio-distribution of erythrocytic pharmacocytes was determined using an optical scanner IVIS spectrum CT(Caliper) under in vivo conditions at 3, 6 and 48 hours after being introduced into the body. For a more precise signal location, ex vivo bio-distribution analysis was performed. The animals were euthanized and their internal organs harvested (liver, spleen, gastrointestinal tract, lung, heart, kidney) and analyzed using an optical scanner.

Results. The obtained results show that the fluorescent signal was detected in proximity to the liver after 3 hours in group 2 and 3 animals and it intensified after 6 and 48 hours, whereas in group 1 animals no such signal was detected. Ex vivo analysis showed that in group 2 and 3 animals the signal was detected only in the liver.

Conclusions. Based on the data obtained, it can be concluded that, the destruction of erythrocytic pharmacocytes containing pharmacological agents as well as intact erythrocytes occurs in the liver. Hence erythrocytic pharmacocytes could be an efficient mode of transport for the targeted delivery of antiviral drugs used in the treatment of acute and chronic hepatitis