

Serum determination of ^{99m}Tc radiolabeled Tirofiban using high performance liquid chromatography in the animal rat model of introduced acute deep venous thrombosis

Marija Darkovska Serafimovska,¹ Emilija Janevik-Ivanovska,¹ Icko Djorgoski,²
Zorica Arsova-Sarafinovska,^{3,1} Trajan Balkanov⁵, Nenad Ugresic³

¹ Goce Delcev University, Faculty of Medical Sciences, Stip, Republic of Macedonia,

² University St. Cyril and Methodius, Faculty of Natural Science and Mathematics, Skopje, Republic of Macedonia,

³ Institute for Public Health of the Republic of Macedonia, Skopje, Republic of Macedonia,

⁴ University of Belgrade, Faculty of Pharmacy, Belgrade, Serbia

⁵ University St. Cyril and Methodius, Faculty of Medicine, Skopje, Republic of Macedonia

The development of radiolabeled small peptide or peptidomimetic ligands can bind platelets and their specific expressed receptor have been suggested as a new approach to detect the clot location and, more essentially, to determine the age and morphology of the evolving thrombus. This new approach is focused on the use of a series of radiolabeled platelet GPIIb/IIIa receptor antagonists.

Tirofiban N-(butylsulfonyl)- 4-O-(4-(4-piperidyl)-L-tyrosine is a non-peptide tyrosine derivate.

The aim of the study was to introduce radioactive-labeled tirofiban as a specific imaging agent for acute DVT and to determine the serum concentrations in normotensive male Wister rats with and without deep acute venous thrombosis in order to confirm the animal model of acute venous thrombosis.

Material and Methods:

Venous thrombosis was induced by ligation of the femoral vein in rats whose blood was made hypercoagulable by intravenous administration of tissue thrombin. The determination of Tirofiban in serum was performed using validated HPL method with UV detection.

Results:

The labeling was performed with technetium-99 in the presence of a stannous reducing agent and biodistribution and visualization of the labeled molecule was carried out using the same experimental model of DVT.

The serum concentrations of Tirofiban measured after 5, 15, 30, 45 and 60 min in the group of rats with DVT were lower as compared to the serum concentrations of Tirofiban in the control group of rats. During the determination of the serum concentration planar imaging was performed at 30 and 60 min after application.

Sensitivity and specificity were determined using the ratio of 'left leg positive for DVT' to 'right leg negative for DVT'. The obtained ratio was 1.54 after 30 min and 5.04 after 60 min.

These values were considered positive in the detection of acute DVT and corresponding to values of serum application obtained from the normal rat and experimental model.

Conclusion: The high DVT uptake and lower serum concentrations of Tirofiban measured in the group of rats with DVT shows that radiolabeled tirofiban in the introduced rat model can be a promising agent for imaging the deep venous thrombosis.