

PHARMACOKINETICS OF CEFTRIAXONE ENCAPSULATED IN AUTOLOGOUS ERYTHROCYTES

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Background: The rise of antibiotic-resistant microorganisms contributes to postoperative infections and reduced efficacy of therapy. Conventional intramuscular or intravenous delivery distributes drugs systemically, leaving only low concentrations at the infection site—often insufficient to suppress purulent microflora. Targeted delivery can modify antibiotic pharmacokinetics, maintaining high plasma or tissue levels for longer periods, which is crucial for treating surgical infections.

Materials and methods: Experiments were conducted on adult male Wistar rats (250–300 g). Scanning and transmission electron microscopy revealed morphological changes in erythrocytes during drug encapsulation by hypo-osmotic hemolysis. These red blood cells containing ceftriaxone (carrier cells -pharmacocytes) were administered intravenously. Pharmacokinetics were compared with free ceftriaxone given intravenously. Blood samples ($\approx 500 \mu\text{l}$) were collected under inhalation anesthesia at 10 min, 1, 3, 6, 9, and 24 h, and plasma ceftriaxone concentrations were quantified by HPLC.

Results: The pharmacokinetics of ceftriaxone changed markedly with RBC-Ctx compared to the free drug. The elimination half-life increased 2.5-

fold to 4.44 h, the mean residence time doubled, and $\text{AUC}_{0-\text{inf}}$ rose by over 30%. In contrast, clearance decreased by nearly 30% and the elimination constant fell 2.4-fold. Volumes of distribution (V_{ss} and V_{d}) increased by 58–84%. A comparison of these constants showed that k_{12} (blood \rightarrow tissues) exceeded k_{21} (tissues \rightarrow blood), indicating that RBC-Ctx favors ceftriaxone retention in peripheral tissues.

Conclusion: The use of RBC-Ctx for ceftriaxone delivery in rats produces marked pharmacokinetic changes, including prolonged circulation in the blood and increased accumulation in RES tissues. Erythrocyte carriers loaded with ceftriaxone may therefore be useful for extending antibiotic activity and enhancing delivery to phagocytic cells within the RES.

Acknowledgement: This research was funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan Grant №AP19676272,

№AP26102345 and by Nazarbayev University under Collaborative Research Program Grant № 211123CRP1614, A.G.