Short communication

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THE DETECTION OF ENDOTOXIN IN PARENTERAL PRODUCTS BY LAL TEST

WYKRYWANIE ENDOTOKSYNY ZA POMOCĄ TESTU LAL W PREPARATACH PODAWANYCH PARENTERALNIE

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The presence of various amounts of bacterial endotoxin was detected by LAL-test in human immunoglobulins, human albumins, virus vaccines, bacterial toxoids and antibiotics.

In the last years, the LAL test has become a significant alternative to the rabbit pyrogen test used in pharmaceutical quality control [1-9]. There are many variants of the LAL test but all of them are based on the reaction between Limulus amoebocyte lysate (LAL) and bacterial endotoxin. In our work we used the semiquantitative gel-clot method and also for some number of samples quantitative chromogenic assays.

We tested the presence of endotoxin in 54 samples of 5 groups of parenteral products: human immunoglobulins (IVIG), human albumins (HSA), virus vaccines, bacterial toxoids and antibiotics. All of them were tested by gel-clot method and 22 samples by chromogenic end point method. The contain of endotoxin was expressed in Endotoxin Units per millilitre (EU/ml).

The concentration of endotoxin in 10 samples of IVIG (fig. 1) was in range from 0,457 EU/ml to 19,46 EU/ml. Only the four of them did not exceed the limit recommended by FDA [4] for human globulins (5 EU/ml).

All of HSA preparations tested by gel-clot method were positive (as a minimum valid concentration 0,5 EU/ml recommended by FDA was used [4]), in spite of the fact that they passed a test for pyrogens on rabbits.

In 9 samples among the 10 samples of virus vaccines (fig. 2) the presence of endotoxin was in range from 0,06 to 0,15 EU/ml. Because of the lack of the official limit for endotoxin concentration for toxoids we applied as a minimum valid concen-

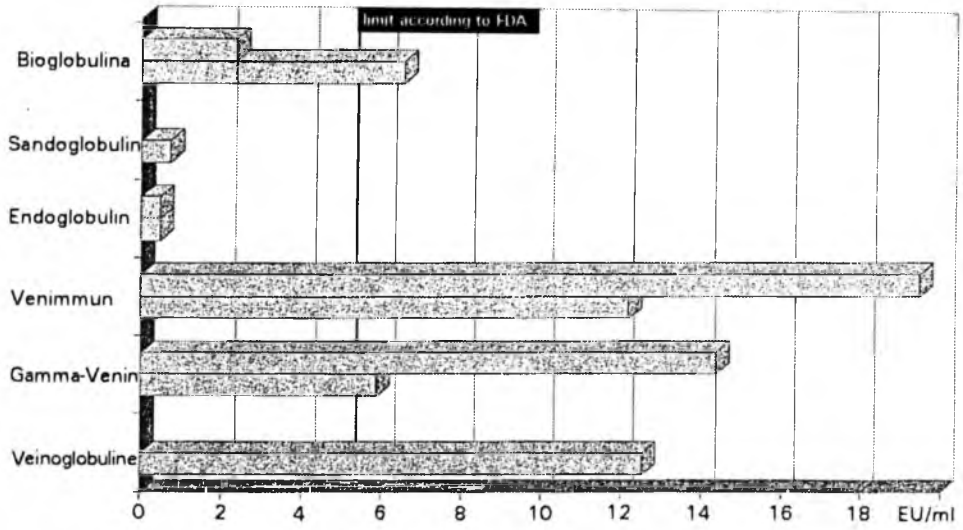

Fig. 1. Endotoxin concentration in 10 samples of IVIG preparations (quantitative chromogenic LAL assay with S-2423 substrate).
Zawartość endotoksyny w 10 próbkach IVIG (ilościowe oznaczenie testem LAL z chromogenicznym substratem S-2423).

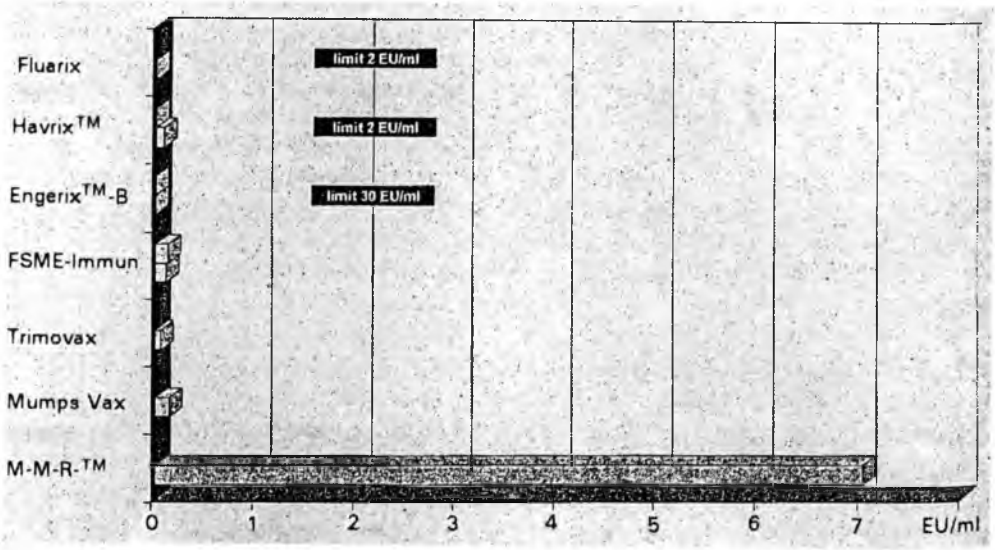

Fig. 2. Endotoxin concentration in 10 samples of virus vaccines (quantitative chromogenic LAL assay with S-2423 substrate).
Zawartość endotoksyny w 10 próbkach szczepionek wirusowych (ilościowe oznaczenie testem LAL z chromogenicznym substratem S-2423).

tration 2 EU/ml for gel-clot method. The results of test were positive in 8 samples of 10 samples of toxoids. In comparison, all samples of antibiotics for which the LAL

test is a routine method of endotoxin estimation according to USP [6] were free of endotoxin.

The presented data show the necessity to introduce the LAL test as an end-product release test for parenteral products.

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Streszczenie

W wybranych grupach biopreparatów przeprowadzono badanie na obecność endotoksyny bakteryjnej. Do oznaczania zawartości endotoksyny zastosowano test LAL (żelowy i chromogeniczny).

W większości szczepionek wirusowych (9/10) stwierdzono bardzo niską zawartość endotoksyny w granicach 0.06-0,15 EU/ml. Dwa preparaty IVIG (2/10) spełniały dopuszczony przez FDA limit zawartości endotoksyny.

Antybiotyki spełniały wymogi podane przez USP. W preparatach szczepionek bakteryjnych i 5% albuminy wykryto testem żelowym obecność endotoksyny (odpowiednio: przy maks. czułości testu 2 EU/ml i 0,5 EU/ml).

Stwierdzono przydatność testu LAL w kontroli biopreparatów.

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