**Supplement**

**Table S1** Hematological blood parameters and the leukocyte formula of rats (n=210). Mean±SE.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Day** | **Group** | **Ery**  **mln/mL** | | **Leu**  **103 abs/mL** | | **Hgb**  **g/L** | | **Lymph**  **%** | | **Neu**  **%** | | **Eo**  **%** | | **Mono**  **%** | |
|  |  | M | F | M | F | M | F | M | F | M | F | M | F | M | F |
| 11th | Placebo | 4,38±  1,16 | 4,57±  1,20 | 6,12±  0,95 | 5,93±  0,96 | 121,83±  17,68 | 117,50±  12,08 | 76,67±  5,75 | 81,50±  4,85 | 22,50±  5,86 | 15,83±  3,60 | 0,17±  0,41 | 0,50±  0,84 | 0,67±  0,52 | 2,17±  1,94 |
|  | Adjuvant | 4,55±  1,00 | 4,32±  1,19 | 5,70±  0,86 | 6,70±  1,22 | 113,00±  17,11 | 119,33±  15,22 | 74,33±  3,88 | 80,50±  6,19 | 20,67±  4,59 | 16,50±  6,41 | 0,83±  1,17 | 0,50±  0,55 | 4,17±  2,48 | 2,50±  0,84 |
|  | TetraFluBet, | 4,03±  0,82 | 3,55±  0,83 | 5,57±  1,02 | 6,37±  0,56 | 93,50±  10,11 | 116,50±  15,24 | 72,33±  5,61 | 74,50±  7,50 | 22,00±  6,48 | 18,83±  6,55 | 0,83±  1,17 | 1,50±  1,52 | 4,83±  2,79 | 5,17±  1,47\* |
| 17th | Placebo | 5,75±  1,99 | 6,64±  2,38 | 9,86±  4,89 | 11,30±  3,17 | 160,17±  38,66 | 158,83±  21,15 | 82,67±  7,58 | 82,33±  3,93 | 15,83±  7,03 | 15,83±  3,43 | 1,00±  0,89 | 1,33±  0,82 | 0,50±  0,84 | 0,50±  0,84 |
|  | Adjuvant | 4,38±  1,49 | 4,56±  1,22 | 11,64±  3,96 | 12,73±  4,50 | 144,20±  17,57 | *142,00±*  *20,84\** | 80,83±  9,47 | 79,33±  5,65 | 16,67±  9,22 | 18,17±  6,05 | 1,00±  1,26 | 0,67±  0,52 | 1,50±  1,22 | 1,83±  0,98 |
|  | TetraFluBet, | 3,54±  1,05 | 4,63±  1,28 | 10,42±  3,21 | 12,83±  4,29 | 164,00±  29,48 | *132,67±*  *11,36\** | 77,83±  3,66 | 80,50±  3,89 | 19,67±  3,98 | 17,67±  4,27 | 0,33±  0,52 | 0,67±  0,82 | 1,83±  1,83 | 1,17±  0,98 |
| 24th | Placebo | 7,46±  0,99 | 7,21±  1,12 | 11,07±  3,01 | 14,38±  5,90 | 162,67±  38,13 | 168,00±  33,48 | 77,33±  6,22 | 74,50±  5,89 | 20,00±  5,66 | 21,83±  4,62 | 1,17±  1,33 | 1,67±  1,21 | 1,50±  1,05 | 2,00±  1,41 |
|  | Adjuvant | 6,91±  0,82 | 7,18±  0,97 | 13,09±  4,73 | 13,59±  7,00 | 170,83±  20,72 | 160,83±  19,41 | 77,67±  3,20 | 77,33±  6,06 | 20,50±  3,62 | 21,50±  6,44 | 1,00±  0,89 | 0,67±  0,82 | 0,83±  0,75 | 0,50±  0,55 |
|  | TetraFluBet, | 6,63±  0,94 | 6,04±  1,04 | 13,77±  7,21 | 10,63±  3,10 | 137,67±  24,05 | 138,00±  29,78 | 81,50±  2,17 | 81,00±  7,52 | 16,67±  2,66 | 14,17±  9,41 | 0,17±  0,41 | 0,80±  0,84 | 1,67±  1,03 | 1,20±  0,84 |

\* - р<0.05, Ery – erythrocytes, Leu – leukocytes; Hgb – hemoglobin, Lymph – lymphocytes, Neu – neutrophils, Eo- eosinophils, Mono – monocytes.

**Table S2** Hematological blood parameters and the leukocyte formula of guinea pigs (n=100). Mean±SE.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Day** | **Group** | **Ery**  **mln/mL** | | **Leu**  **103 total/mL** | | **Hgb**  **g/L** | | **Lymph**  **%** | | **Neu**  **%** | | **Eo**  **%** | | **Mono**  **%** | |
|  |  | M | F | M | F | M | F | M | F | M | F | M | F | M | F |
| 11th | Placebo | 2,56±  1,07 | 2,22±  1,05 | 7,92±  0,49 | 7,04±  2,12 | 108,67±  20,03 | 103,00±  7,87 | 60,50±  19,89 | 80,67±  4,50 | 36,00±  19,43 | 15,67±  6,92 | 0,50±  0,84 | 0,14±  0,41 | 2,67±  2,16 | 3,33±  2,80 |
|  | Adjuvant | 4,56±  2,54 | 2,94±  0,95 | 7,70±  1,18 | 6,24±  1,95 | 111,67±  7,42 | 92,67±  24,45 | 62,67±  19,80 | 73,00±  7,82 | 34,83±  19,42 | 25,00±  6,78 | 1,33±  0,82 | 0,50±  0,84 | 0,83±  1,60 | 1,00±  0,89 |
|  | TetraFluBet, | 4,89±  0,90 | *4,37±*  *0,63\** | 6,64±  2,82 | 7,10±  1,64 | 110,67±  10,56 | 96,67±  9,61 | 71,67±  7,12 | 72,60±  6,80 | 26,00±  7,04 | 16,83±  10,57 | 1,50±  1,05 | 1,00±  0,63 | 0,67±  0,52 | 3,67±  2,80 |
| 17th | Placebo | 5,67±  1,81 | 6,62±  2,41 | 4,08±  0,54 | 4,30±  3,13 | 119,67±  15,54 | 130,00±  7,45 | 68,33±  11,54 | 81,24±  6,12 | 29,41±  8,30 | 16,58±  8,46 | 0,85±  0,55 | 1,00±  0,51 | 1,83±  0,33 | 1,00±  0,89 |
|  | Adjuvant | 4,38±  1,51 | 4,53±  1,24 | 5,04±  2,45 | 7,38±  4,60 | 105,67±  46,95 | 127,00±  18,51 | 70,12±  10,43 | 82,91±  7,33 | 28,11±  10,68 | 18,65±  5,84 | 0,80±  0,54 | 0,88±  0,51 | 1,67±  0,83 | 1,00±  0,51 |
|  | TetraFluBet, | 4,77±  0,48 | 6,50±  1,49 | 4,27±  2,74 | 4,71±  1,19 | 91,17±  15,84 | 115,00±  20,89 | 69,51±  11,32 | 80,61±  6,10 | 22,19±  9,06 | 16,50±  6,41 | 0,93±  0,50 | 0,94±  0,63 | 0,50±  0,33 | 0,83±  0,33 |
| 24th | Placebo | 5,35±  0,48 | 5,38±  0,59 | 5,58±  1,65 | 6,01±  0,57 | 122,67±  9,73 | 118,40±  14,74 | 75,17±  7,25 | 78,33±  5,61 | 20,50±  6,53 | 18,00±  5,51 | 0,67±  0,52 | 1,00±  0,63 | 3,17±  2,32 | 1,67±  1,03 |
|  | Adjuvant | 5,32±  0,45 | 4,30±  0,90 | 8,06±  1,69 | 6,98±  3,39 | 115,40±  11,61 | 109,60±  14,94 | 75,83±  13,85 | 85,33±  3,72 | 23,17±  13,79 | 12,83±  4,67 | 0,67±  0,52 | 1,33±  1,86 | 0,33±  0,82 | 0,50±  0,84 |
|  | TetraFluBet, | 5,42±  1,26 | 5,18±  0,93 | 7,66±  3,46 | 9,16±  2,91 | 119,17±  11,86 | 116,75±  9,74 | 78,83±  6,11 | 84,17±  3,66 | 20,00±  6,60 | 15,17±  3,87 | 0,67±  0,82 | 0,33±  0,52 | 0,50±  0,55 | 0,17±  0,41 |

\* - р<0.05 Ery – erythrocytes, Leu – leukocytes; Hgb – hemoglobin, Lymph – lymphocytes, Neu – neutrophils, Eo- eosinophils, Mono – monocytes.

**Table S3** Physiological range of values of hematological and biochemical blood parameters and the leukocyte formula of rats and guinea pigs. [Mean-2SD; Mean+2SD].

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Group** | **Ery**  **mn/mL** | **Leu**  **103 abs/mL** | **Hgb**  **g/L** | **Lymph**  **%** | **Neu**  **%** | **Eo**  **%** | **Mono**  **%** | **Glu**  **uM/L** | **Total**  **Protein**  **g/L** | **Cr**  **uM/L** | **Urea**  **uM/L** | **BR**  **uM/L** | **AST**  **U/L** | **ALT**  **U/L** | **Chol**  **uM/L** |
|  | Rats | 2,6-  8,45 | 3,15-  14,91 | 95,81-  168,18 | 65,56-  90,09 | 5,22-  28,66 | 0-  3,03 | 0-  4,33 | 2,23-  6,27 | 53,92-  87,06 | 46,47-  85,98 | 3,37-  12,25 | 1,81-  4,66 | 153,28-  264,12 | 22,27-  88,33 | 1,57-  3,68 |
|  | Guinea Pigs | 1,28-  7,50 | 2,15-  13,06 | 72,16-  133,24 | 38,67-  90,34 | 14,37-  37,06 | 0-  3,95 | 0-  6,70 | 2,42-  8,02 | 31,33-  63,89 | 28,39-  69,00 | 2,51-  8,01 | 2,00-  5,58 | 31,53-  117,79 | 21,06-  77,16 | 0,73-  2,47 |

Ery – erythrocytes, Leu – leukocytes; Hgb – hemoglobin, Lymph – lymphocytes, Neu – neutrophils, Eo- eosinophils, Mono – monocytes, Cr – creatinine, BR – bilirubin, Chol - cholesterol.

**Figure S2** Biochemical blood parameters (Glucose, total protein, ALT, bilirubin, cholesterol) of rats (A, B, C, D, E) and guinea pigs (F, G, H, I, J) on days 11, 17 and 24. Data are depicted as Mean±2SD.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Rats** |  | **Guinea pigs** |
| A |  | F |  |
| B |  | G |  |
| C |  | H |  |
| D |  | I |  |
| E |  | J |  |