

Table 1. Clinical data of male rats treated with APAP

| APAP mg/kg | N | | Body g | Liver | | Kidney (left) | | Kidney (right) | | Urine mL |
|---------------|---|------|-----------|---------|----------|---------------|-------|----------------|-------|-------------|
| | | | | g | g% | g | g% | g | g% | |
| 0 | 5 | Mean | 209.2 | 6.739 | 3.219 | 0.777 | 0.371 | 0.767 | 0.367 | 10.984 |
| | | S.D. | 6.8 | 0.434 | 0.142 | 0.049 | 0.018 | 0.035 | 0.017 | 0.491 |
| 100 | 5 | Mean | 220.7 * | 7.399 * | 3.352 | 0.817 | 0.370 | 0.811 | 0.368 | 11.558 |
| | | S.D. | 4.3 | 0.300 | 0.089 | 0.034 | 0.012 | 0.039 | 0.014 | 0.763 |
| 500 | 5 | Mean | 199.8 | 6.291 | 3.149 | 0.780 | 0.391 | 0.755 | 0.378 | 13.214 * |
| | | S.D. | 6.1 | 0.235 | 0.041 | 0.045 | 0.019 | 0.026 | 0.009 | 1.851 |
| 800 | 5 | Mean | 194.9 ** | 6.803 | 3.492 ** | 0.770 | 0.395 | 0.598 | 0.310 | 13.998 ** |
| | | S.D. | 8.6 | 0.290 | 0.119 | 0.059 | 0.015 | 0.291 | 0.152 | 1.686 |

Significantly different from control (APAP 0 mg/kg) group * $P < 0.05$, ** $P < 0.01$ (Dunnett's test)

Table 2. Serum chemistry profile of male rats treated with APAP

| APAP mg/kg | N | | AST U/L | ALT U/L | ALP U/L | T.BIL mg/dL | T.CHO mg/dL | TG mg/dL |
|---------------|---|------|------------|------------|------------|----------------|----------------|-------------|
| 0 | 5 | Mean | 106.2 | 37.4 | 1186.6 | 0.000 | 49.6 | 51.6 |
| | | S.D. | 9.86 | 8.38 | 83.83 | 0.0000 | 2.97 | 23.22 |
| 100 | 5 | Mean | 95.6 | 38.0 | 1271.0 | 0.000 | 52.0 | 60.2 |
| | | S.D. | 12.26 | 6.28 | 32.00 | 0.0000 | 2.12 | 13.14 |
| 500 | 5 | Mean | 193.4 | 103.6 | 1119.2 | 0.018 | 52.0 | 46.8 |
| | | S.D. | 101.95 | 65.01 | 61.71 | 0.0130 | 1.87 | 21.04 |
| 800 | 5 | Mean | 4406.4 * | 2297.4 * | 1337.8 ** | 0.064 ** | 55.2 | 41.2 |
| | | S.D. | 4638.77 | 2264.44 | 79.85 | 0.0261 | 9.63 | 31.89 |

| APAP mg/kg | N | | GLU mg/dL | T.PRO g/dL | ALB g/dL | GLB g/dL | AVG | UN mg/dL |
|---------------|---|------|--------------|---------------|-------------|-------------|----------|-------------|
| 0 | 5 | Mean | 159.8 | 5.84 | 2.66 | 3.200 | 0.828 | 16.44 |
| | | S.D. | 5.54 | 0.167 | 0.089 | 0.1225 | 0.0192 | 1.412 |
| 100 | 5 | Mean | 151.0 | 5.68 | 2.60 | 3.120 | 0.834 | 16.20 |
| | | S.D. | 9.43 | 0.084 | 0.000 | 0.0447 | 0.0261 | 1.049 |
| 500 | 5 | Mean | 144.0 | 5.86 | 2.68 | 3.180 | 0.844 | 18.14 |
| | | S.D. | 9.11 | 0.167 | 0.110 | 0.1304 | 0.0055 | 1.176 |
| 800 | 5 | Mean | 145.2 | 5.94 | 2.74 | 3.140 | 0.878 ** | 19.18 ** |
| | | S.D. | 11.34 | 0.219 | 0.114 | 0.1517 | 0.0192 | 1.099 |

| APAP mg/kg | N | | CRE mg/dL | Ca mg/dL | IP mg/dL | Na mEq/L | K mEq/L | Cl mEq/L |
|---------------|---|------|--------------|-------------|-------------|-------------|------------|-------------|
| 0 | 5 | Mean | 0.310 | 10.68 | 7.076 | 144.0 | 4.64 | 104.0 |
| | | S.D. | 0.0158 | 0.130 | 0.1029 | 1.00 | 0.336 | 0.00 |
| 100 | 5 | Mean | 0.302 | 10.86 | 7.080 | 143.2 | 4.56 | 103.6 |
| | | S.D. | 0.0148 | 0.114 | 0.4411 | 1.30 | 0.055 | 0.55 |
| 500 | 5 | Mean | 0.302 | 10.58 | 8.562 ** | 145.6 | 4.38 | 103.4 |
| | | S.D. | 0.0130 | 0.148 | 0.5003 | 1.14 | 0.179 | 2.19 |
| 800 | 5 | Mean | 0.322 | 10.32 ** | 8.466 ** | 143.8 | 4.34 | 101.4 |
| | | S.D. | 0.0148 | 0.239 | 0.7537 | 1.30 | 0.498 | 2.70 |

Significantly deferent from control (APAP 0 mg/kg) group * $P < 0.05$, ** $P < 0.01$ (Dunnett's test)

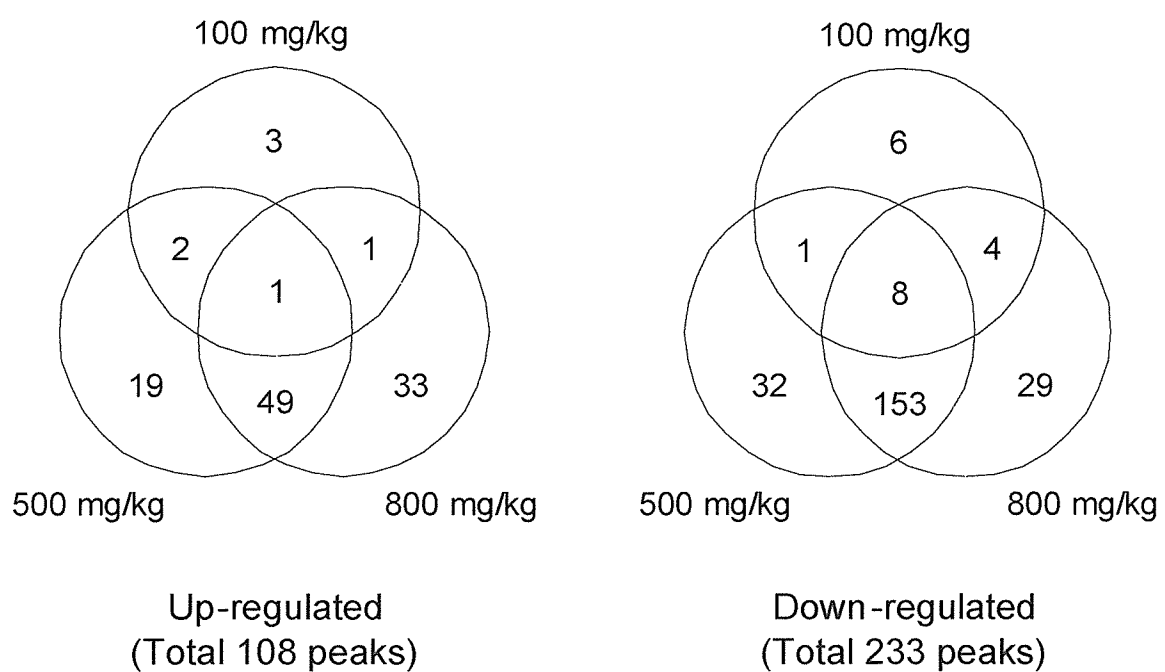


Figure 1. The number of metabolite peaks changed in the urine of the male rat treated with APAP

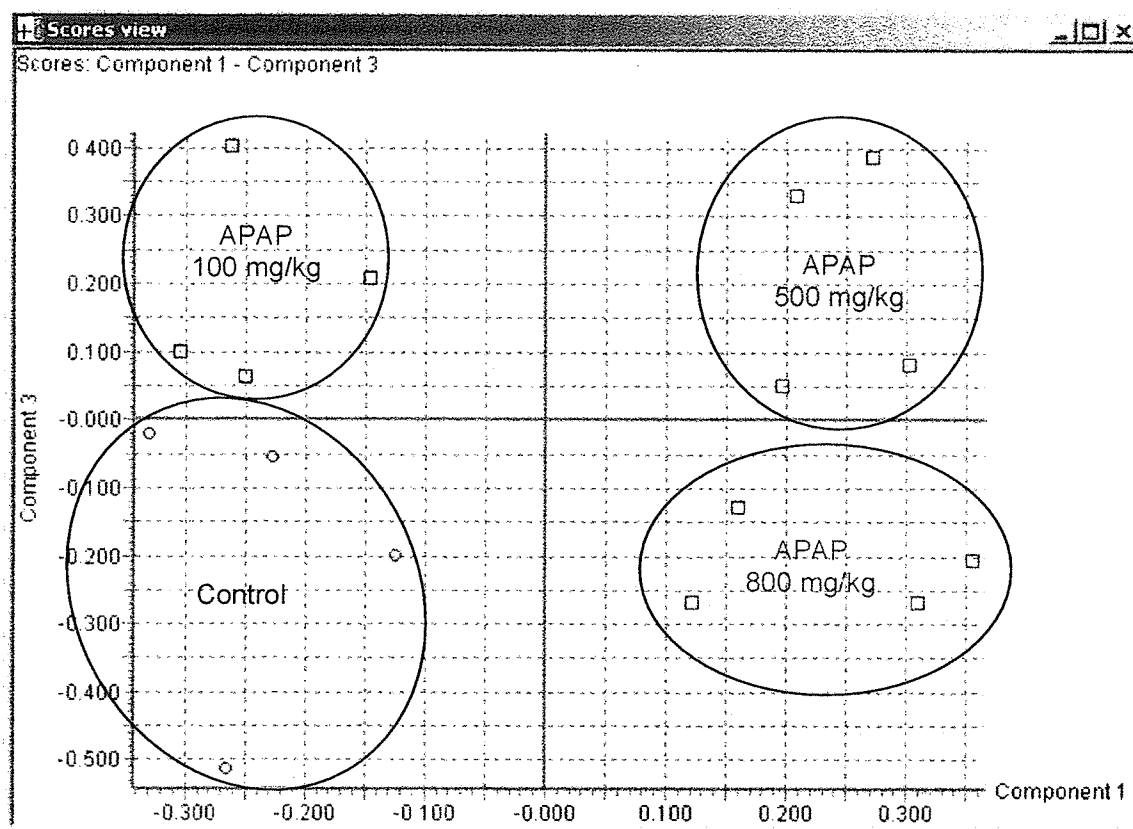


Figure 2. Resulting PCA scores plot from the urine of the male rat treated APAP

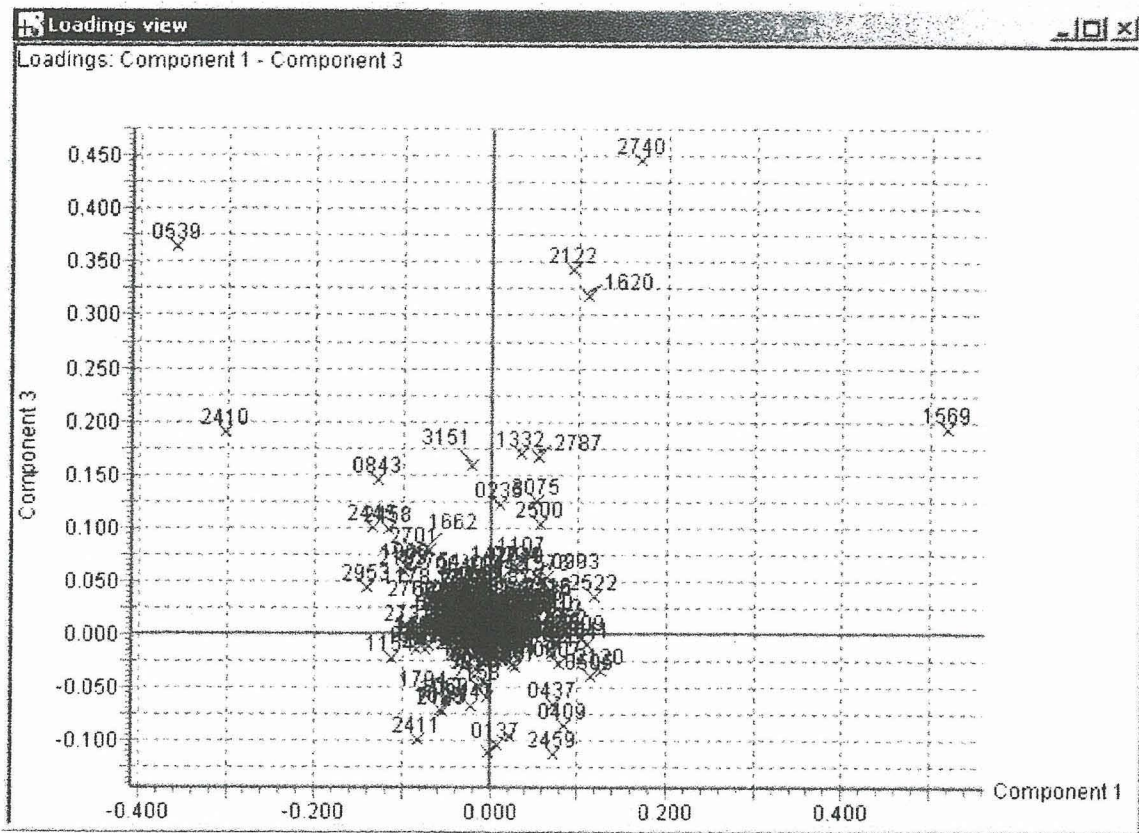
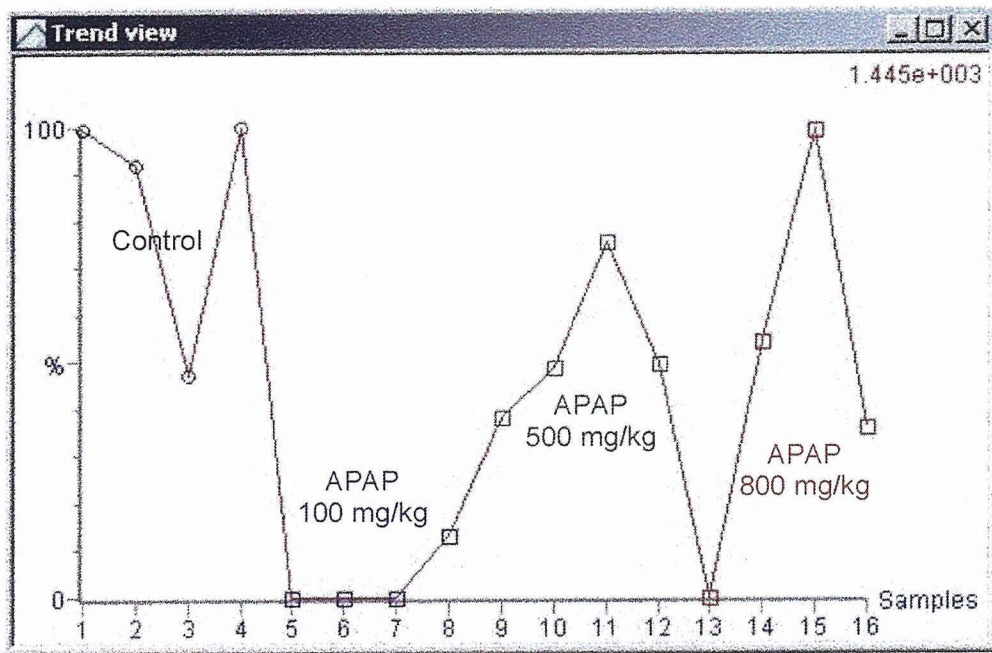
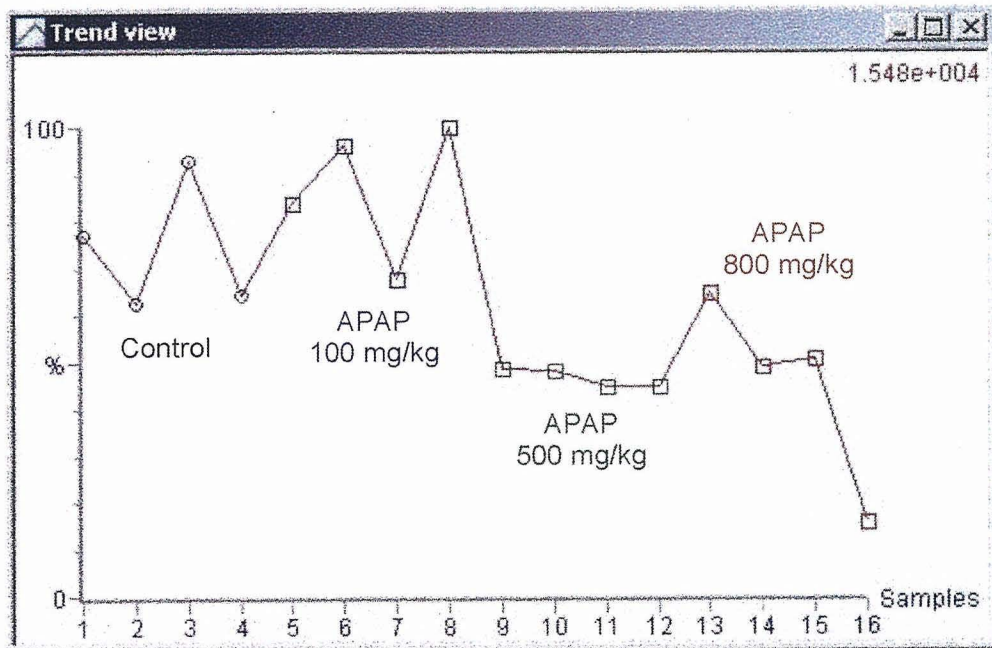


Figure 3. Resulting PCA loadings plot from the urine of the male rat treated APAP

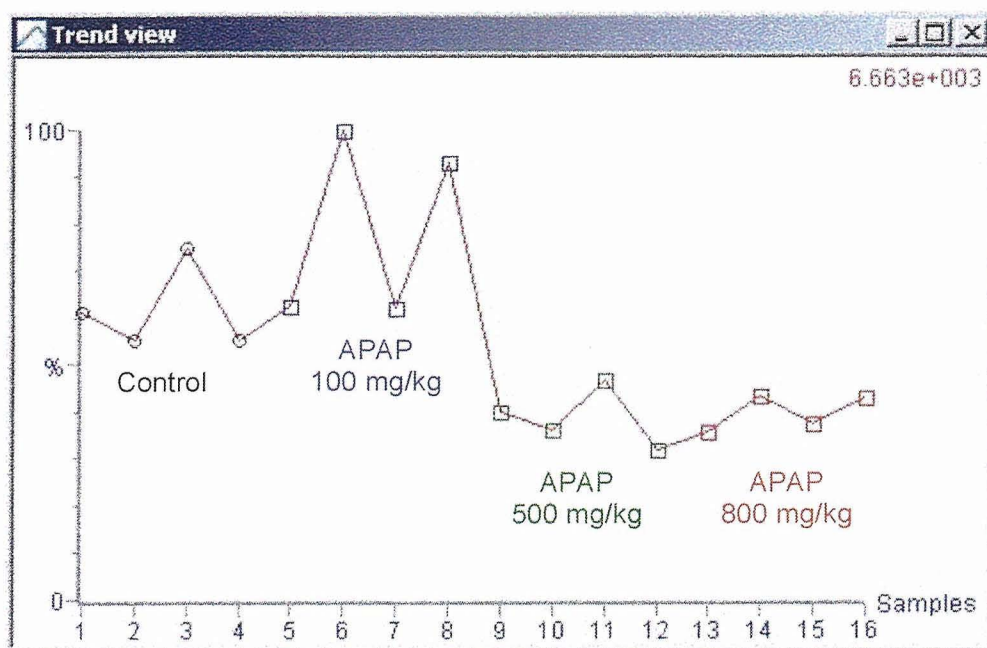


Peak No. 0137, m/z 114.0711, RT 4.8870

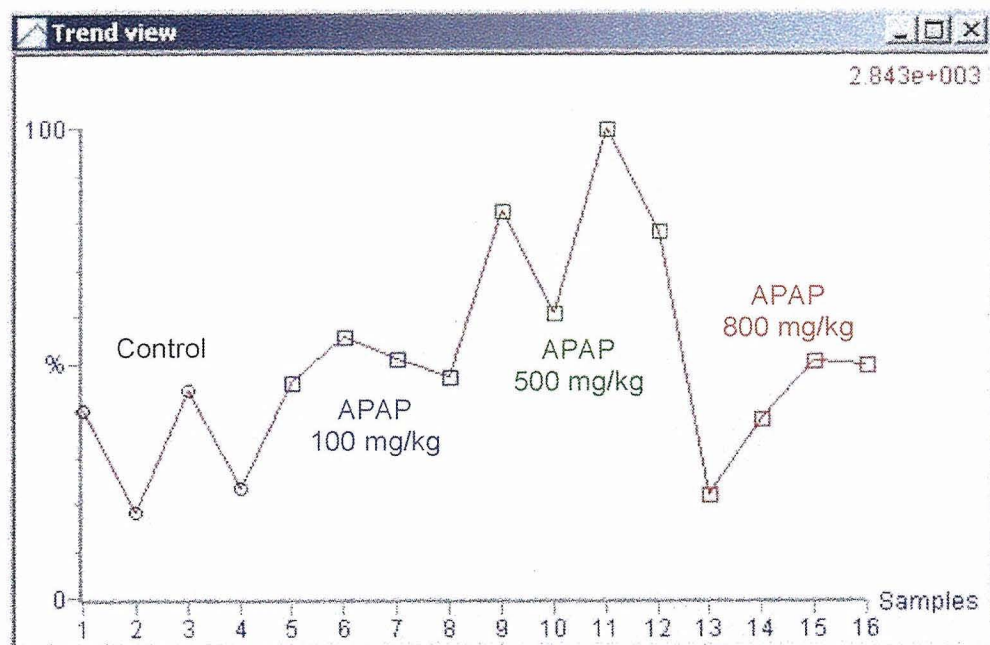


Peak No. 0539, m/z 410.1832, RT 3.6183

Figure 4. Trend plot for the urine of the male rat treated with APAP

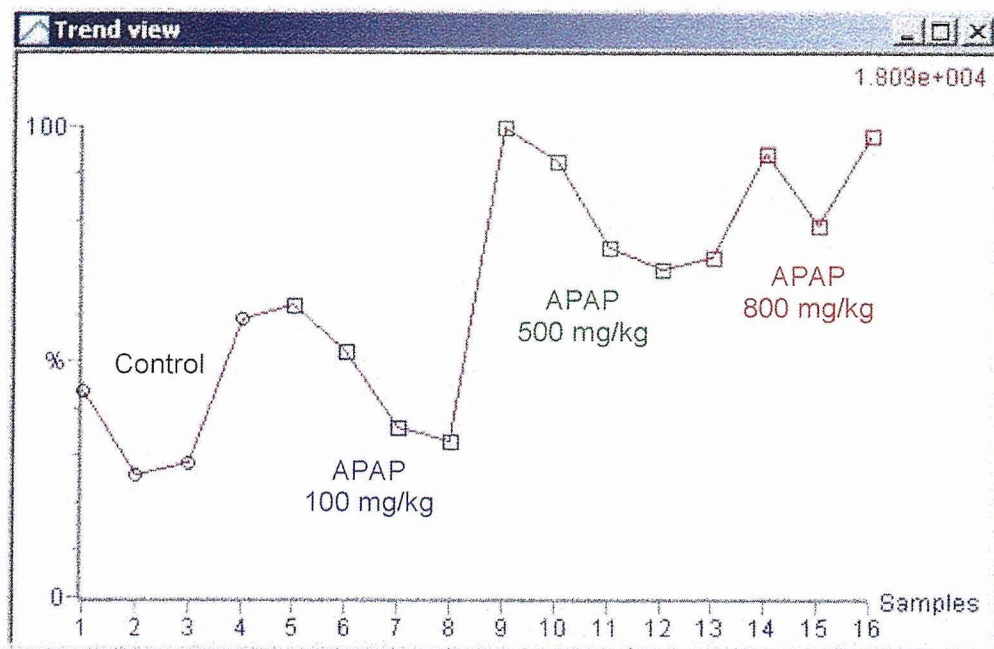


Peak No. 0843, m/z 176.0729, RT 3.1167

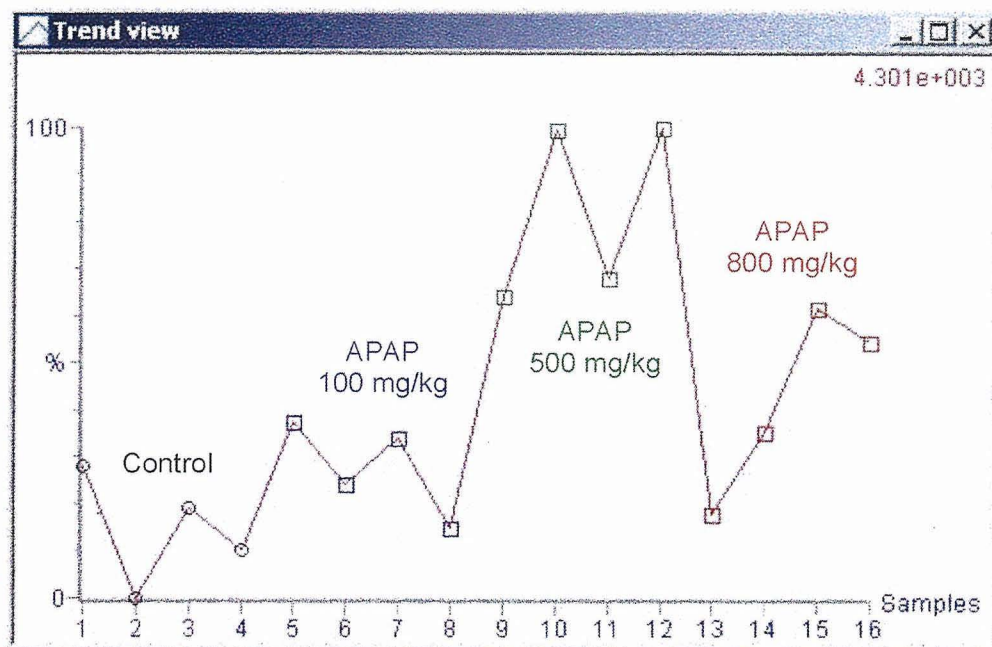


Peak No. 1332, m/z 517.1843, RT 2.1792

Figure 4. Continued

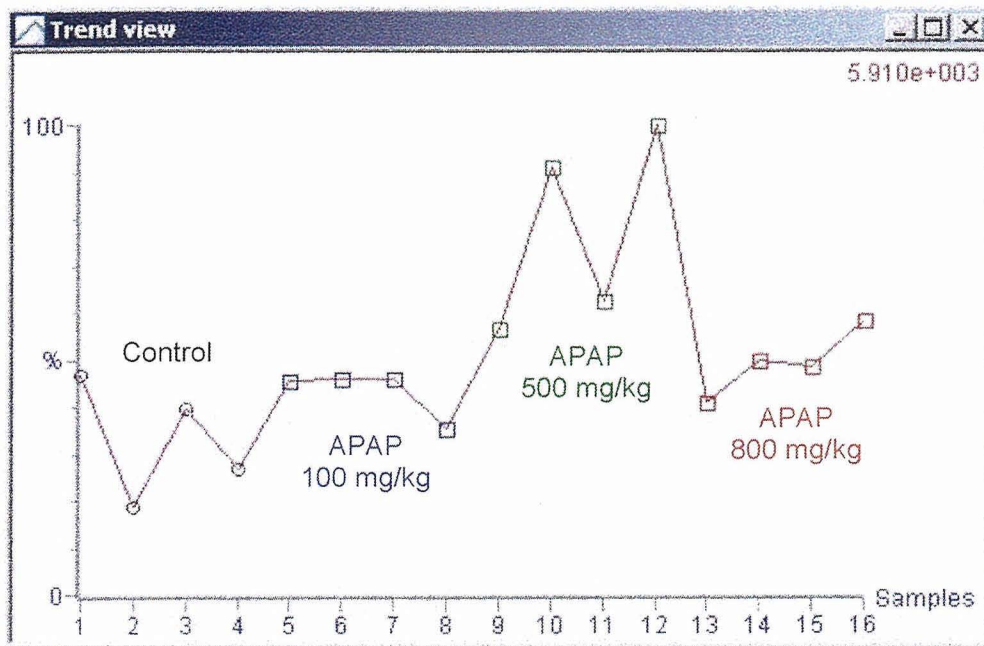


Peak No. 1569, m/z 220.1397, RT 3.5075

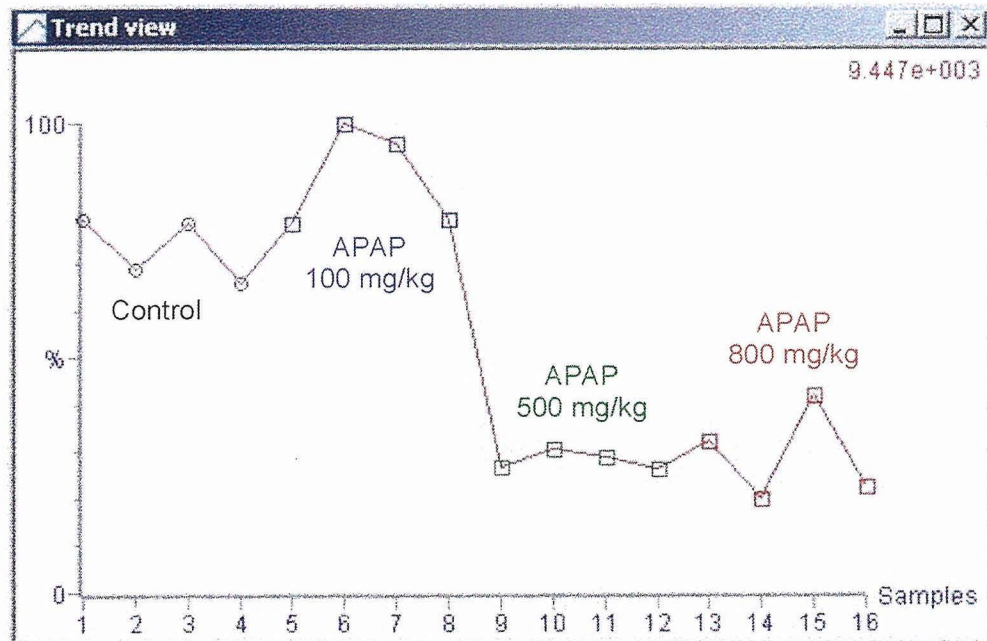


Peak No. 1620, m/z 586.2206, RT 2.1865

Figure 4. Continued

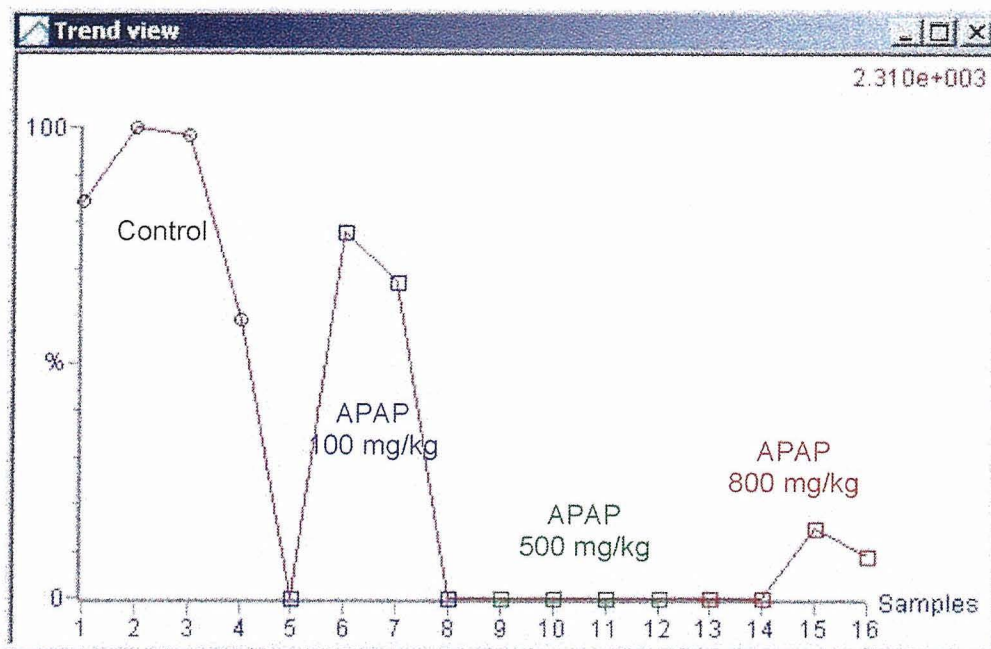


Peak No. 2122, m/z 249.0795, RT 2.1773

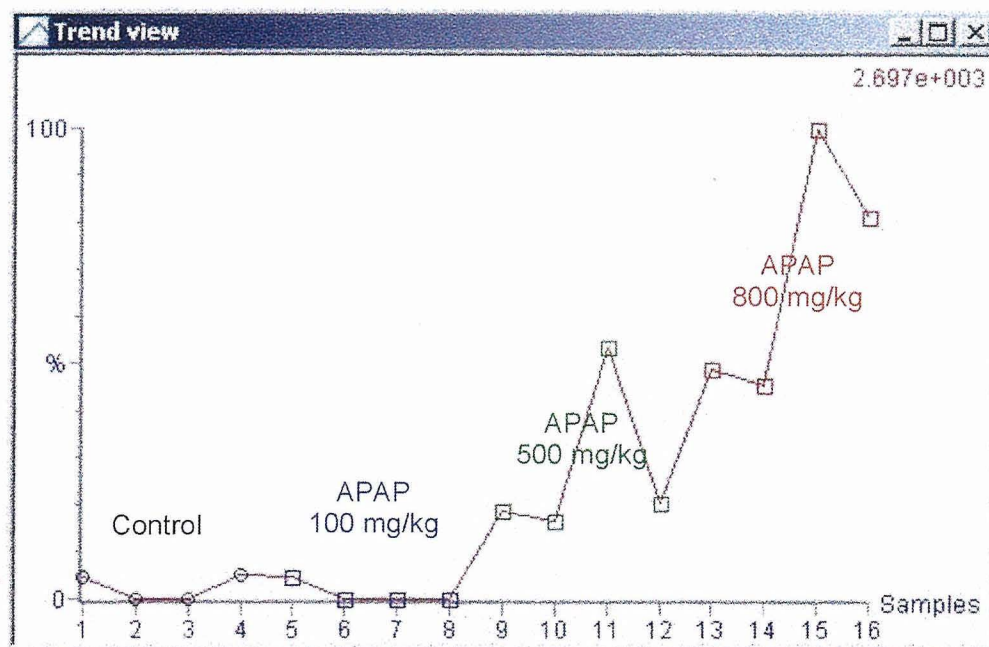


Peak No. 2410, m/z 267.1368, RT 2.7983

Figure 4. Continued

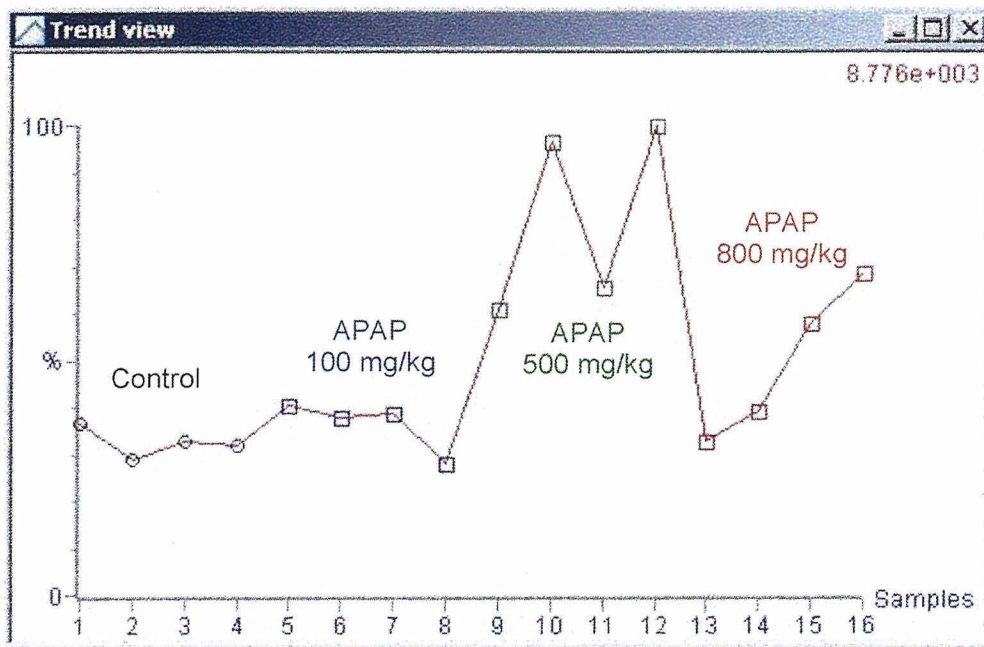


Peak No. 2411, m/z 267.1716, RT 3.6902

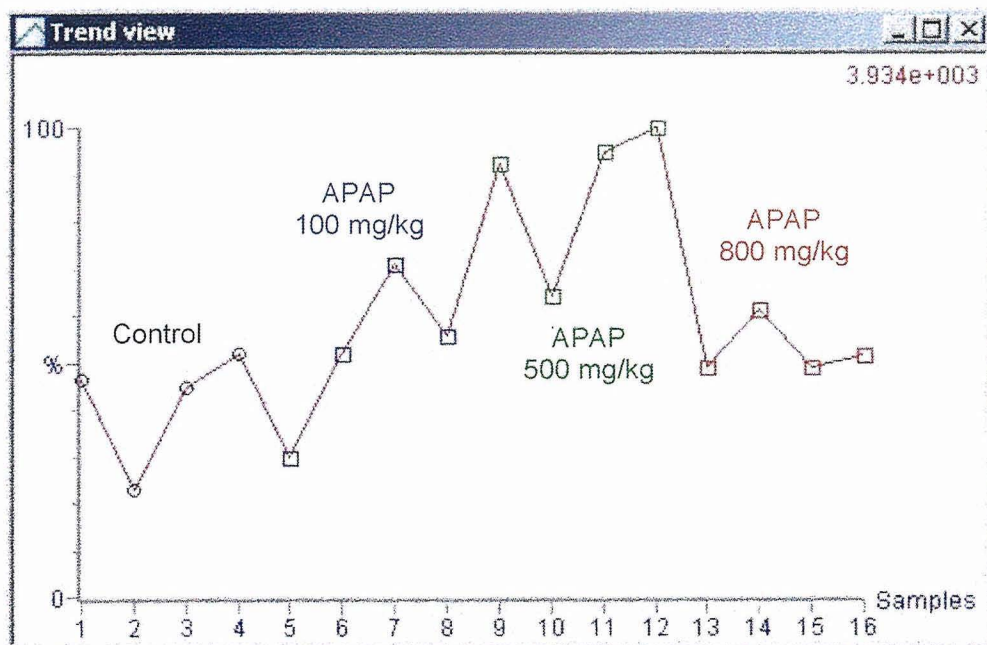


Peak No. 2459, m/z 270.0817, RT 2.4354

Figure 4. Continued

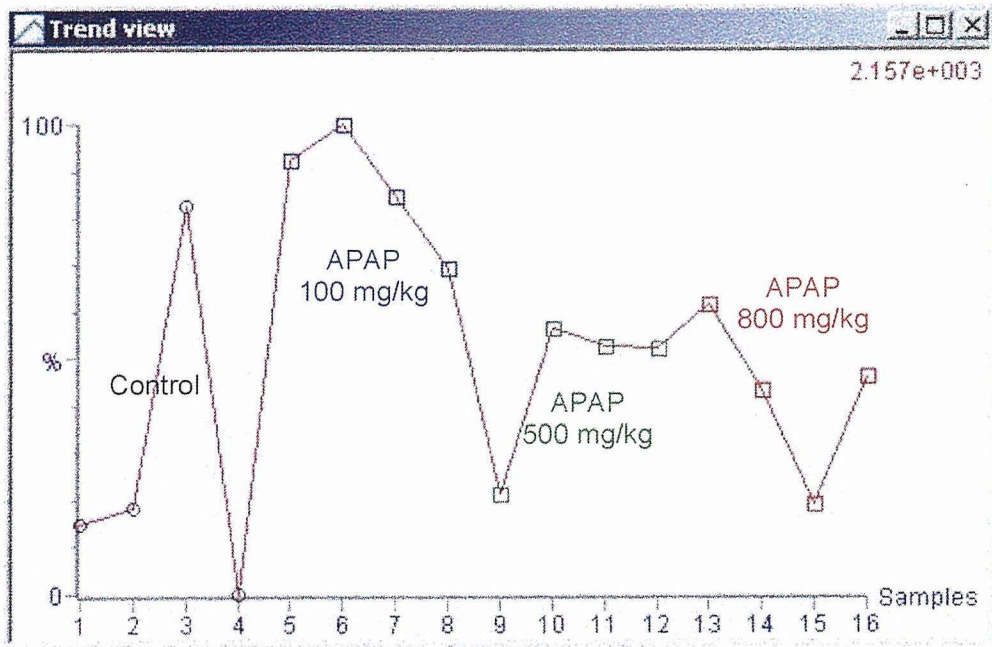


Peak No. 2740, m/z 302.1310, RT 2.1802



Peak No. 2787, m/z 307.2000, RT 3.6884

Figure 4. Continued



Peak No. 3151, m/z 356.2459, RT 3.6261

Figure 4. Continued

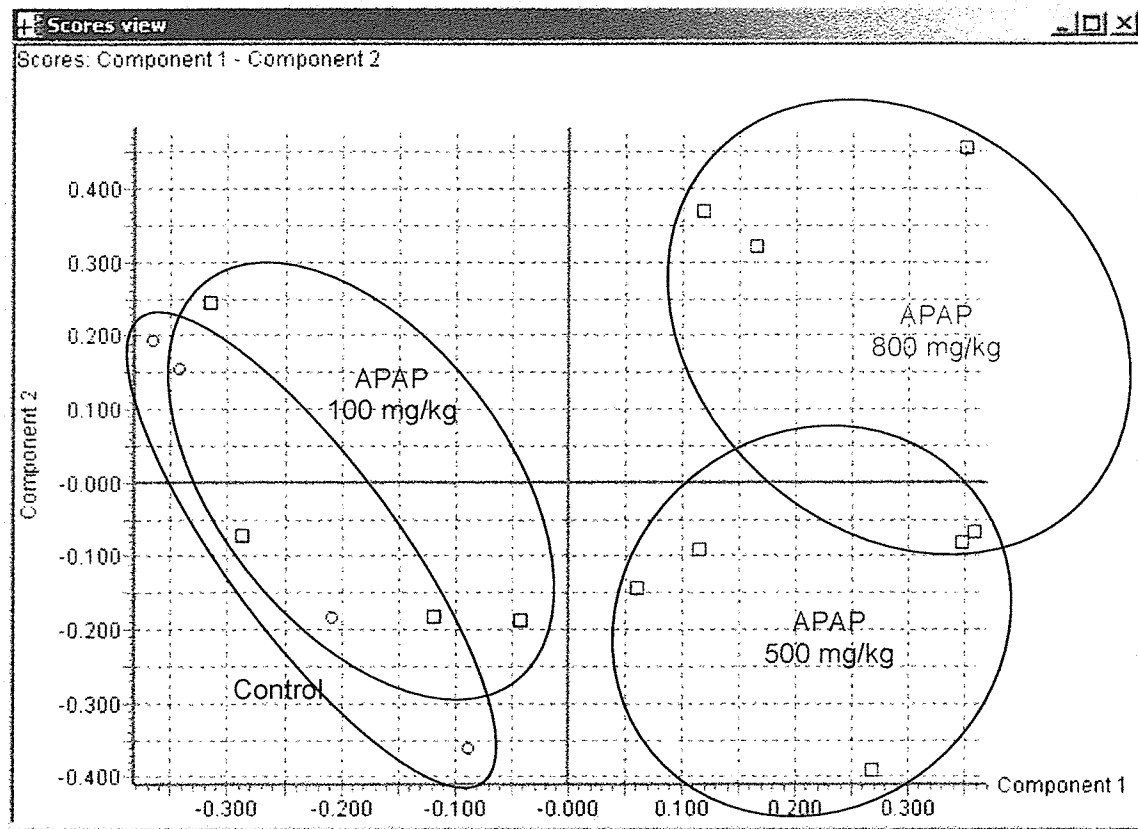


Figure 5. Resulting PCA scores plot for metabolite peaks correlated with Log ALT in the urine of the male rat treated with APAP

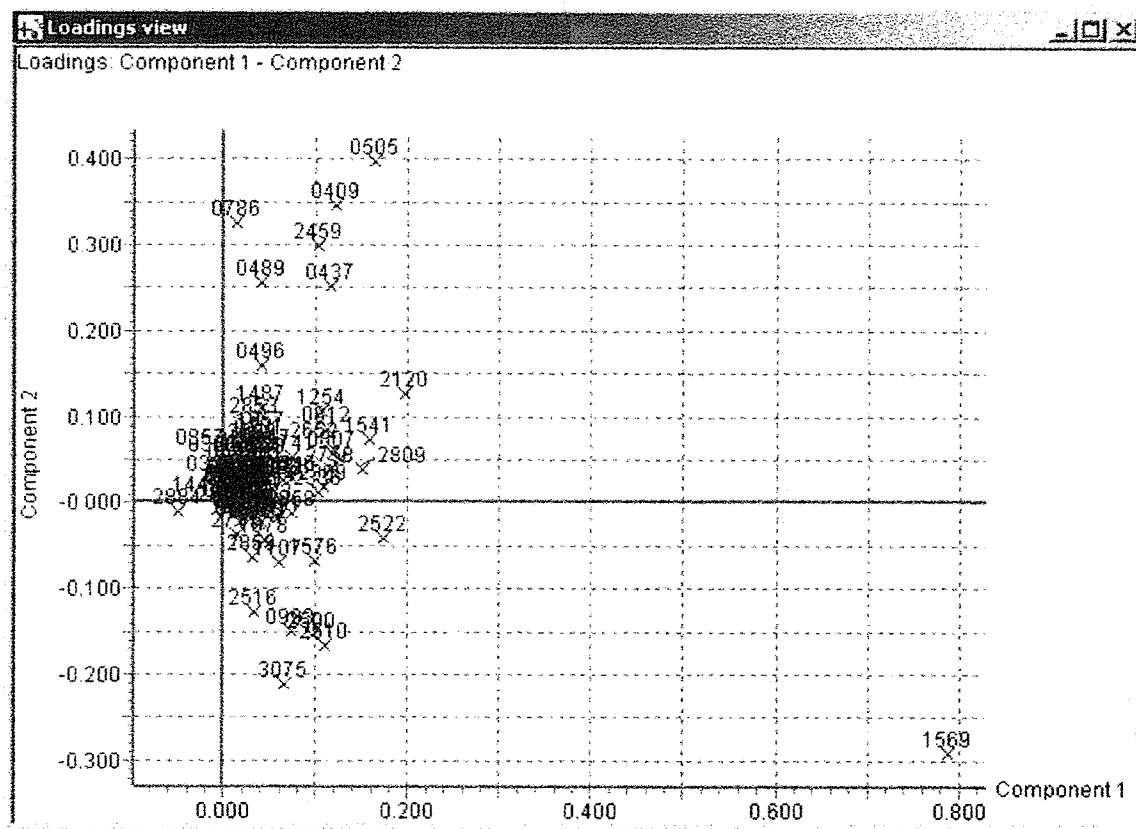
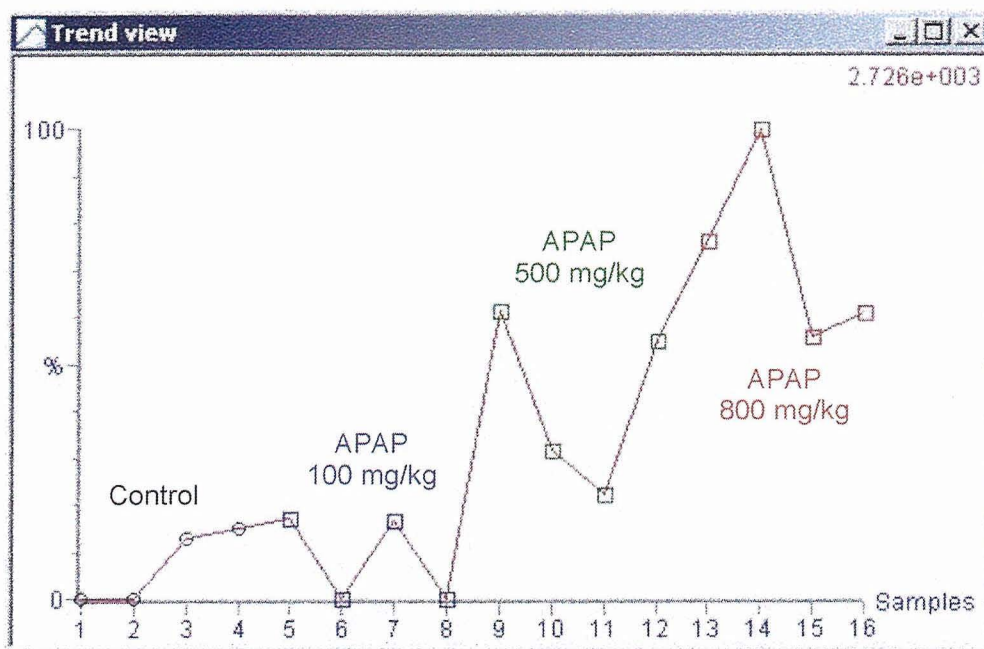
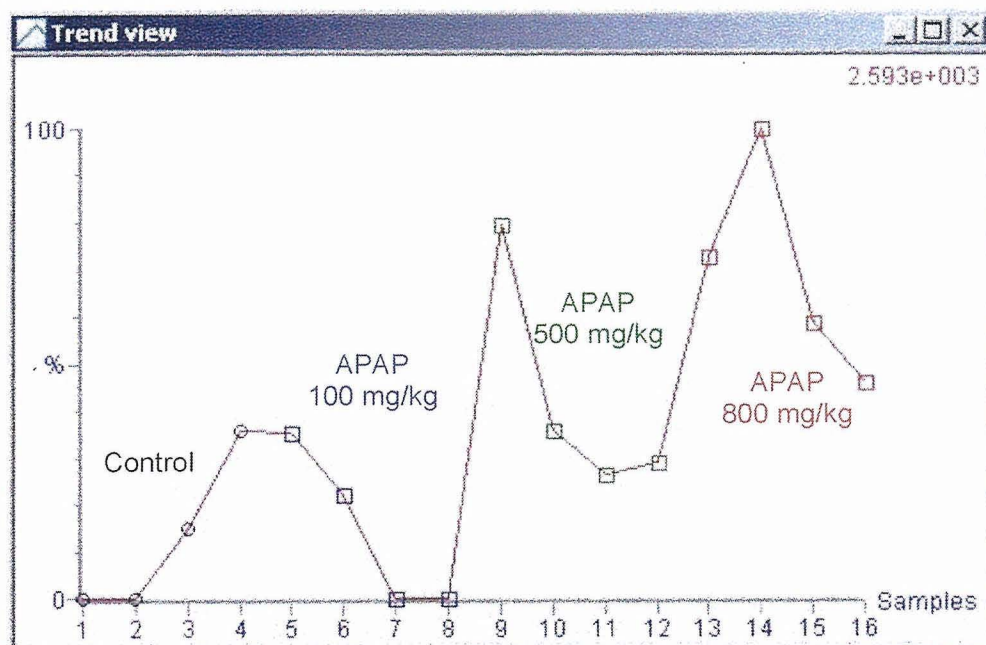


Figure 6. Resulting PCA loadings plot for metabolite peaks correlated with Log ALT in the urine of the male rat treated with APAP

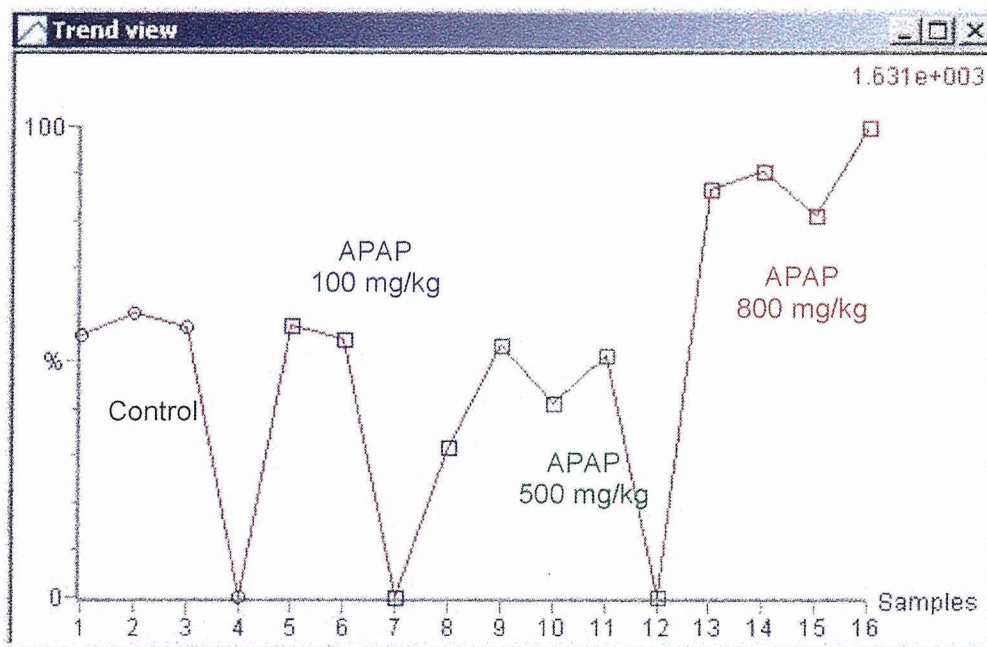


Peak No. 0409, m/z 402.2285, RT 3.6839

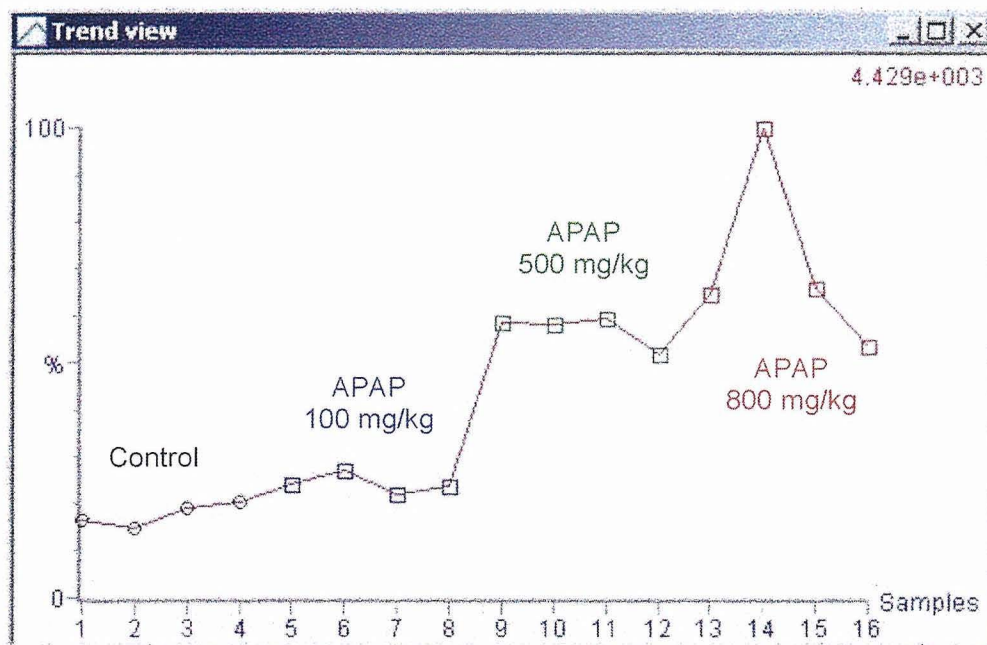


Peak No. 0437, m/z 404.2356, RT 3.4134

Figure 7. Trend plot for metabolite peaks correlated with Log ALT in the urine of the male rat treated with APAP

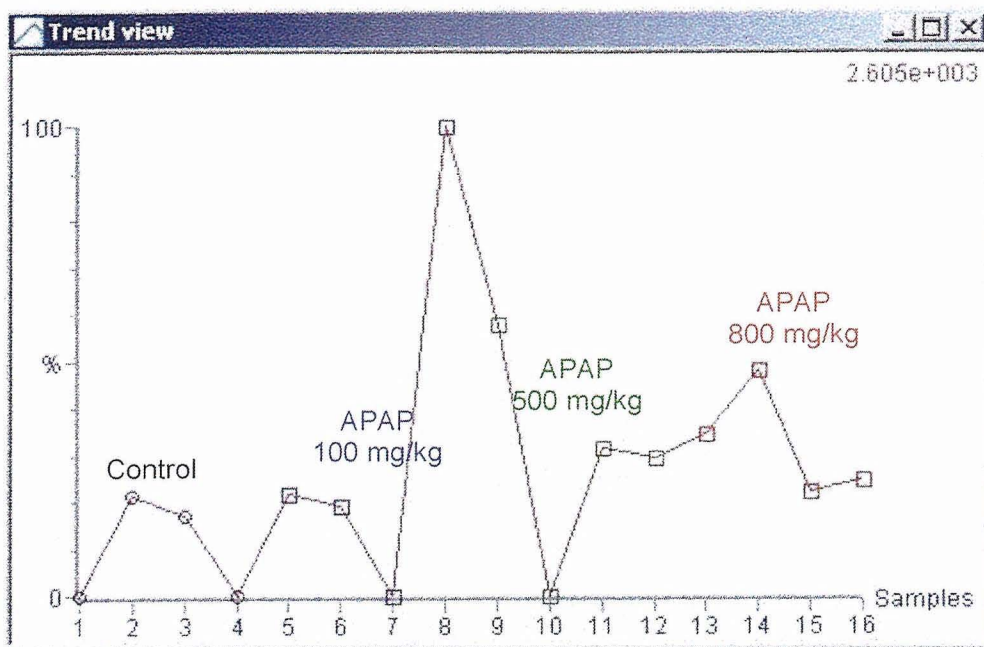


Peak No. 0489, m/z 144.9827, RT 4.4255

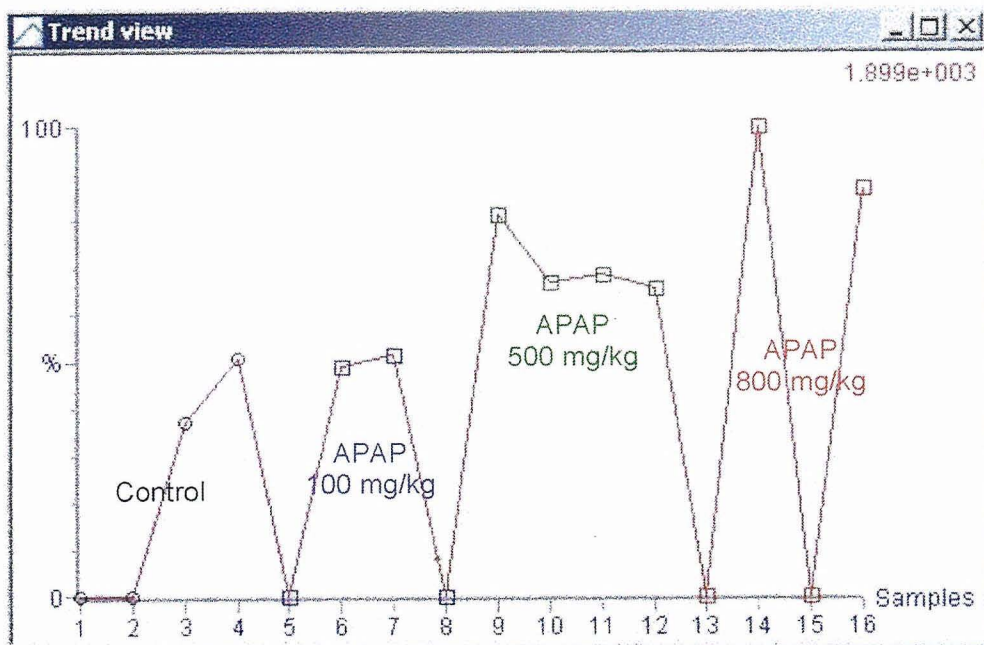


Peak No. 0505, m/z 408.2766, RT 3.5745

Figure 7. Continued

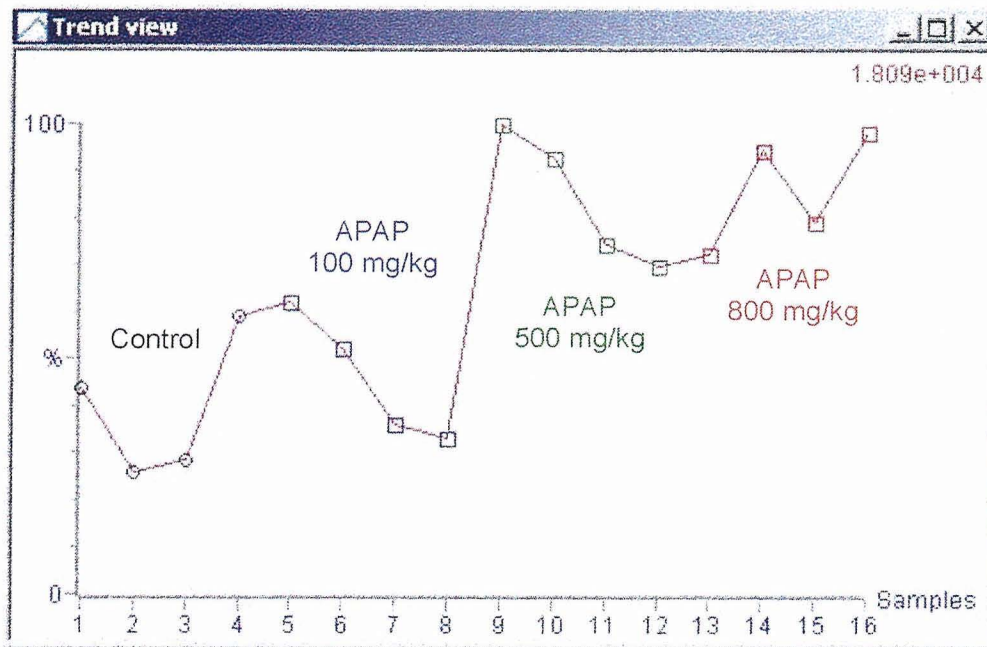


Peak No. 0786, m/z 435.1328, RT 3.5738

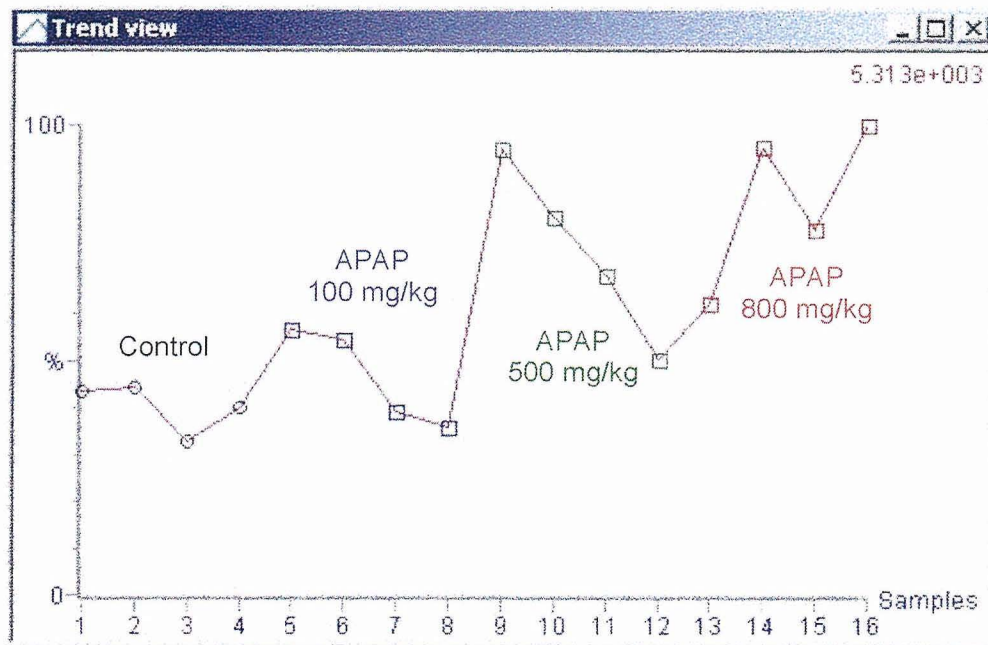


Peak No. 0993, m/z 186.1151, RT 2.5149

Figure 7. Continued

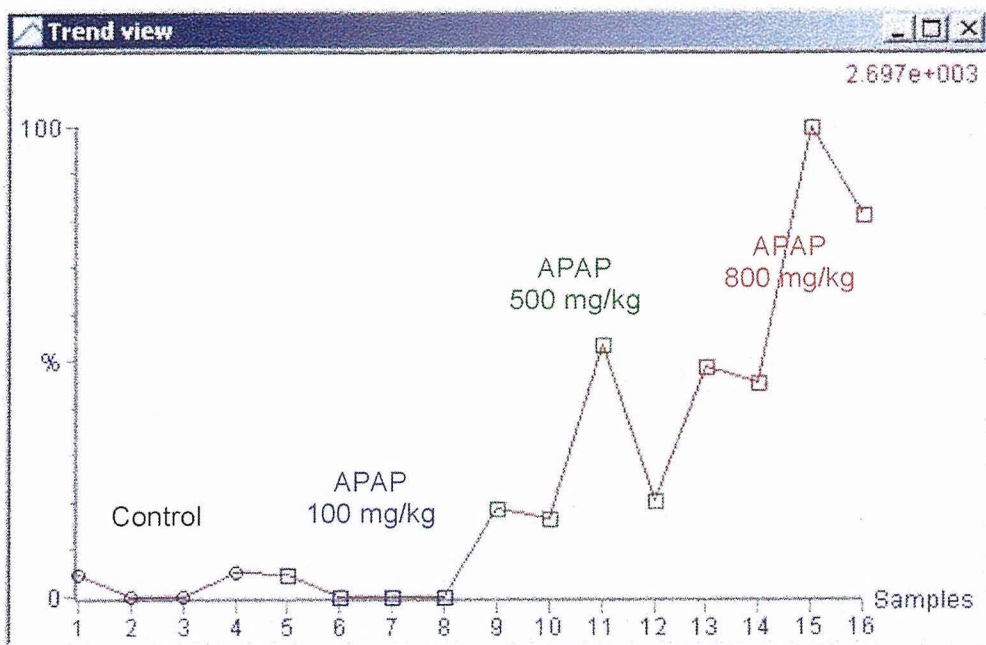


Peak No. 1569, m/z 220.1397, RT 3.5075

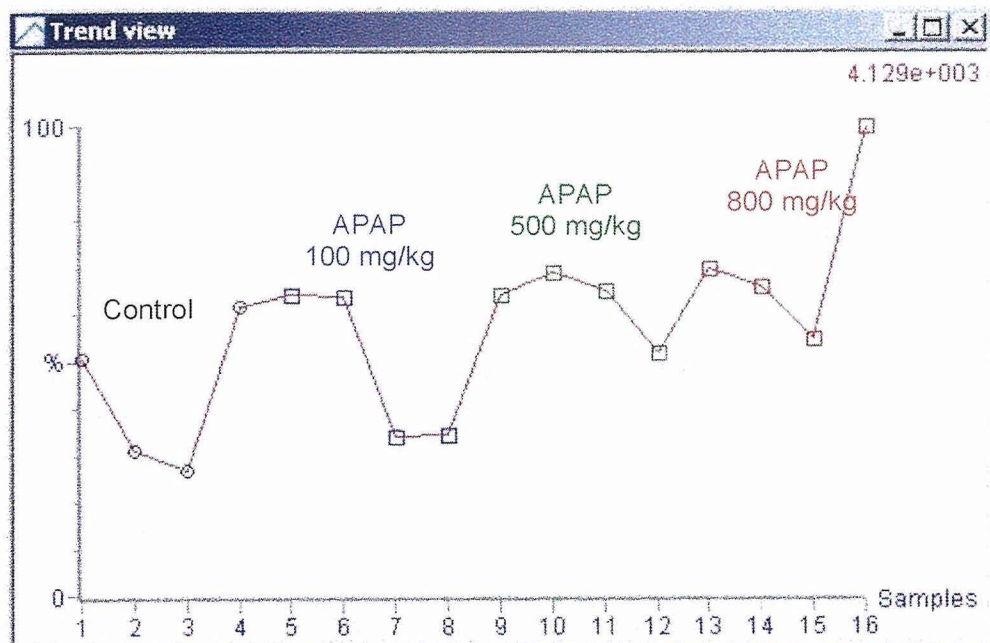


Peak No. 2120, m/z 248.1612, RT 3.7008

Figure 7. Continued

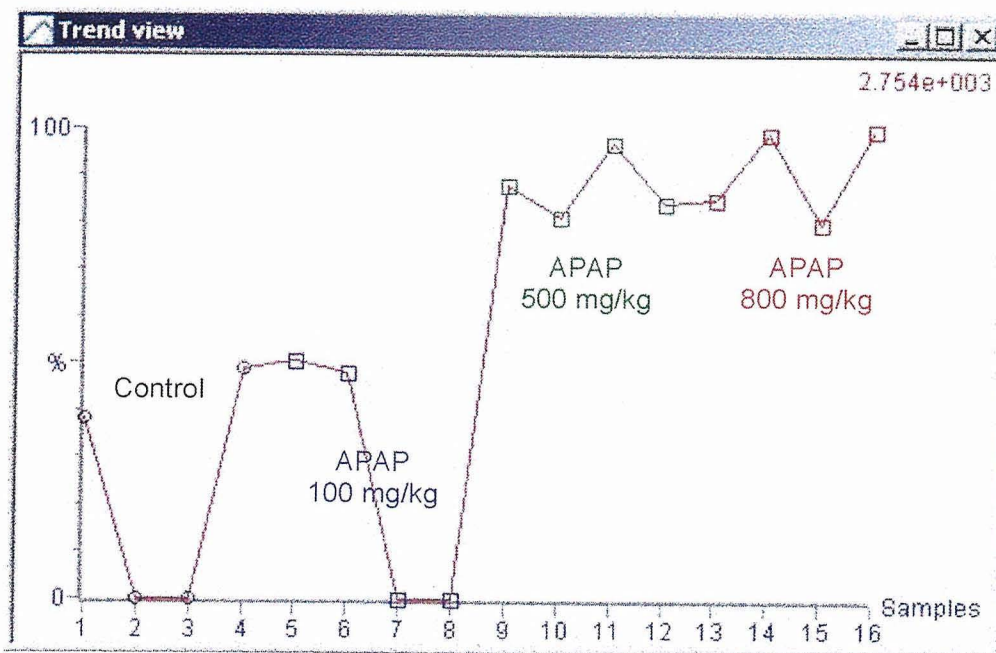


Peak No. 2459, m/z 270.0817, RT 2.4354

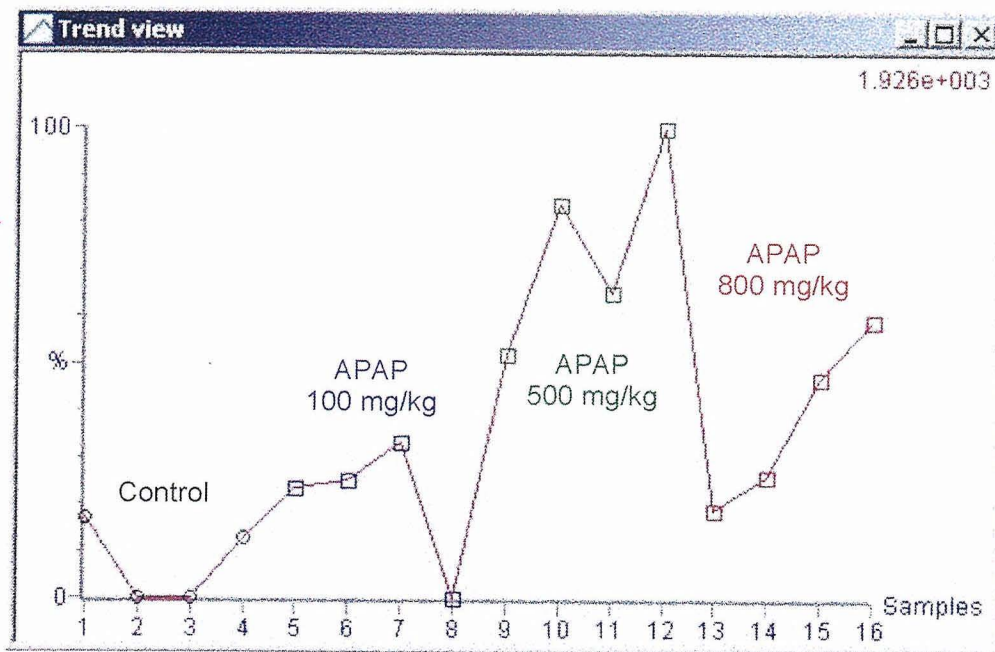


Peak No. 2510, m/z 276.1302, RT 2.0692

Figure 7. Continued



Peak No. 2522, m/z 278.1428, RT 2.4419



Peak No. 3075, m/z 345.1308, RT 2.1874

Figure 7. Continued