

**Supplementary Material S2.** Average concentrations ( $\mu\text{g/g}$  or  $\mu\text{g/mL}$ ) of polymer (Table 1) and apocarotenoids (Table 2) in tissues and fluids of mice dosed orally with a single dose of OxBC (300 mg/kg body weight) daily for 2 days and 5 days vs. control mice dosed with vehicle alone. The results were obtained from calibrated Multi-Reaction Monitoring (MRM) of data for the two transitions at  $181 \rightarrow 107$  and  $181 \rightarrow 135$  of DHA released from isolated OxBC polymer after NaOH treatment (Table 1) or present in OxBC apoC hexane extract (Table 2).

**Table 1.** OxBC polymer concentrations ( $\mu\text{g/g}$  or  $\mu\text{g/mL}$ ) in tissues and body fluids.<sup>1</sup>

|                         | Control  |       |                       |                       |             | OxBC dose |       |                       |                       |             |
|-------------------------|----------|-------|-----------------------|-----------------------|-------------|-----------|-------|-----------------------|-----------------------|-------------|
|                         | Day      | Mouse | $181 \rightarrow 107$ | $181 \rightarrow 135$ | Average     | Day       | Mouse | $181 \rightarrow 107$ | $181 \rightarrow 135$ | Average     |
| <b>Kidney</b>           | 2        | 1     | 0.96                  | 1.3                   | <b>1.1</b>  | 2         | 7     | 2.2                   | 2.8                   | <b>2.5</b>  |
|                         | 2        | 2     | 1.4                   | 1.6                   | <b>1.5</b>  | 2         | 8     | 14                    | 15                    | <b>14</b>   |
|                         | 5        | 4     | 1.8                   | 2.2                   | <b>2.0</b>  | 5         | 10    | 4.0                   | 5.0                   | <b>4.5</b>  |
|                         | 5        | 5     | 4.0                   | 4.6                   | <b>4.3</b>  | 5         | 11    | 2.0                   | 2.5                   | <b>2.2</b>  |
|                         | Average: |       |                       |                       | <b>2.2</b>  | Average:  |       |                       |                       | <b>5.9</b>  |
| <b>Abdominal Muscle</b> | 2        | 1     | 3.1                   | 3.3                   | <b>3.2</b>  | 2         | 7     | 2.2                   | 2.8                   | <b>2.5</b>  |
|                         | 5        | 4     | 4.6                   | 5.0                   | <b>4.8</b>  | 5         | 10    | 3.7                   | 4.0                   | <b>2.5</b>  |
|                         | Average: |       |                       |                       | <b>4.0</b>  | Average:  |       |                       |                       | <b>3.2</b>  |
| <b>Lung</b>             | 2        | 3     | 13                    | 20                    | <b>16</b>   | 2         | 8     | 19                    | 22                    | <b>21</b>   |
|                         | 5        | 5     | 25                    | 26                    | <b>26</b>   | 5         | 11    | 17                    | 18                    | <b>18</b>   |
|                         | Average: |       |                       |                       | <b>21</b>   | Average:  |       |                       |                       | <b>19</b>   |
| <b>Plasma</b>           | 1 h      | 5     | 0.20                  | 0.24                  | <b>0.22</b> | 1 h       | 11    | 0.76                  | 0.84                  | <b>0.80</b> |
|                         | 1 h      | 5     | 0.28                  | 0.32                  | <b>0.30</b> | 1 h       | 11    | 1.4                   | 1.5                   | <b>1.42</b> |
|                         | 1 h      | 6     | 0.55                  | 0.76                  | <b>0.65</b> | 1 h       | 12    | 2.5                   | 2.7                   | <b>2.60</b> |
|                         | 2        | 2     | 0.09                  | 0.05                  | <b>0.07</b> | 2         | 8     | 0.90                  | 0.95                  | <b>0.93</b> |
|                         | 2        | 2     | 0.13                  | 0.14                  | <b>0.13</b> | 2         | 9     | 0.89                  | 0.94                  | <b>0.91</b> |
|                         | 2        | 3     | 0.17                  | 0.29                  | <b>0.23</b> | 5         | 11    | 0.76                  | 0.77                  | <b>0.76</b> |
|                         | 5        | 8     | 0.15                  | 0.20                  | <b>0.17</b> | 5         | 12    | 0.73                  | 0.79                  | <b>0.76</b> |
|                         | 5        | 5     | 0.22                  | 0.25                  | <b>0.23</b> | Average:  |       |                       |                       | <b>1.2</b>  |
|                         | 5        | 10    | 0.27                  | 0.43                  | <b>0.35</b> | Average:  |       |                       |                       | <b>0.26</b> |

|                        |   |   |                             |       |             |   |    |                            |        |              |
|------------------------|---|---|-----------------------------|-------|-------------|---|----|----------------------------|--------|--------------|
| <b>Stomach tissue</b>  | 2 | 2 | 0.87                        | 1.4   | <b>1.2</b>  | 2 | 8  | 87                         | 89     | <b>88</b>    |
|                        | 2 | 3 | 22                          | 23    | <b>23</b>   | 2 | 7  | 265                        | 267    | <b>266</b>   |
|                        | 5 | 5 | 0.44                        | 0.49  | <b>0.47</b> | 5 | 11 | 211                        | 210    | <b>210</b>   |
|                        | 5 | 4 | 12                          | 11    | <b>11</b>   | 5 | 10 | 844                        | 826    | <b>835</b>   |
|                        |   |   | <i>Average:</i> <b>8.9</b>  |       |             |   |    | <i>Average:</i> <b>350</b> |        |              |
| <b>Feces</b>           | 2 | 1 | 13.38                       | 14.07 | <b>14</b>   | 2 | 7  | 48.96                      | 49.72  | <b>49.3</b>  |
|                        | 2 | 3 | 7.94                        | 8.17  | <b>8.1</b>  | 2 | 9  | 123.28                     | 125.68 | <b>124.5</b> |
|                        | 5 | 4 | 9.42                        | 10.10 | <b>9.8</b>  | 5 | 10 | 19.04                      | 19.38  | <b>19.2</b>  |
|                        | 5 | 6 | 11.94                       | 14.39 | <b>13</b>   | 5 | 12 | 48.49                      | 52.93  | <b>50.7</b>  |
|                        |   |   | <i>Average:</i> <b>11</b>   |       |             |   |    | <i>Average:</i> <b>61</b>  |        |              |
| <b>Intestinal wash</b> | 2 | 1 | 0.16                        | 0.18  | <b>0.17</b> | 2 | 7  | 29.38                      | 29.07  | <b>29</b>    |
|                        | 5 | 4 | 0.23                        | 0.24  | <b>0.24</b> | 5 | 10 | 3.31                       | 3.31   | <b>3.3</b>   |
|                        |   |   | <i>Average:</i> <b>0.20</b> |       |             |   |    | <i>Average:</i> <b>16</b>  |        |              |
| <b>Urine</b>           | 2 | 1 | 0.45                        | 0.43  | <b>0.44</b> | 2 | 7  | 36.30                      | 35.93  | <b>36</b>    |
|                        | 2 | 3 | 0.98                        | 0.72  | <b>0.85</b> | 2 | 9  | 61.56                      | 62.46  | <b>62</b>    |
|                        | 5 | 4 | 0.83                        | 0.82  | <b>0.82</b> | 5 | 10 | 0.88                       | 0.67   | <b>0.77</b>  |
|                        | 5 | 6 | 1.35                        | 1.60  | <b>1.48</b> | 5 | 12 | 29.25                      | 30.30  | <b>30</b>    |
|                        |   |   | <i>Average:</i> <b>0.90</b> |       |             |   |    | <i>Average:</i> <b>32</b>  |        |              |
| <b>Cecum</b>           | 2 | 1 | 6.96                        | 8.73  | <b>7.8</b>  | 2 | 7  | 30.36                      | 39.49  | <b>35</b>    |
|                        | 5 | 4 | 4.28                        | 3.78  | <b>4.0</b>  | 5 | 10 | 7.92                       | 6.05   | <b>7.0</b>   |
|                        |   |   | <i>Average:</i> <b>5.9</b>  |       |             |   |    | <i>Average:</i> <b>21</b>  |        |              |
| <b>Spleen</b>          | 2 | 1 | 2.65                        | 3.98  | <b>3.3</b>  | 2 | 7  | 16.44                      | 14.33  | <b>15</b>    |
|                        | 5 | 4 | 3.92                        | 4.84  | <b>4.4</b>  | 5 | 10 | 12.70                      | 12.01  | <b>12</b>    |
|                        |   |   | <i>Average:</i> <b>3.8</b>  |       |             |   |    | <i>Average:</i> <b>14</b>  |        |              |
| <b>Hamstring</b>       | 2 | 1 | 2.5                         | 3.2   | <b>2.8</b>  | 2 | 7  | 2.0                        | 1.9    | <b>2.0</b>   |
|                        | 5 | 4 | 1.5                         | 2.6   | <b>2.1</b>  | 5 | 10 | 2.8                        | 4.2    | <b>3.5</b>   |
|                        |   |   | <i>Average:</i> <b>2.5</b>  |       |             |   |    | <i>Average:</i> <b>2.7</b> |        |              |
| <b>Liver</b>           | 2 | 3 | 113                         | 113   | <b>113</b>  | 2 | 9  | 81                         | 80     | <b>80</b>    |
|                        | 2 | 2 | 82                          | 96    | <b>89</b>   | 2 | 7  | 37                         | 42     | <b>39</b>    |

|                        |   |   |     |          |                   |   |    |          |             |                   |
|------------------------|---|---|-----|----------|-------------------|---|----|----------|-------------|-------------------|
|                        | 5 | 4 | 54  | 54       | <b>54</b>         | 5 | 12 | 76       | 76          | <b>76</b>         |
|                        | 5 | 4 | 30  | 33       | <b>31</b>         | 5 | 10 | 86       | 87          | <b>86</b>         |
|                        | 5 | 5 | 29  | 33       | <u><b>31</b></u>  |   |    |          | Average:    | <b>70.6</b>       |
|                        |   |   |     | Average: | <b>64</b>         |   |    |          |             |                   |
| <b>Small intestine</b> | 2 | 1 | 6.2 | 7.1      | <b>6.6</b>        | 2 | 7  | 4.1      | 4.0         | <b>4.1</b>        |
| <b>tissue</b>          | 2 | 2 | 3.5 | 3.7      | <b>3.6</b>        | 2 | 8  | 17       | 19          | <b>18</b>         |
|                        | 5 | 4 | 1.1 | 1.6      | <b>1.4</b>        | 2 | 9  | 24       | 26          | <b>25</b>         |
|                        | 5 | 5 | 1.7 | 2.3      | <u><b>2.0</b></u> | 5 | 10 | 1.6      | 1.4         | <b>1.5</b>        |
|                        |   |   |     | Average: | <b>3.4</b>        | 5 | 11 | 14       | 15          | <b>14</b>         |
|                        |   |   |     |          |                   | 5 | 12 | 2.5      | 3.7         | <u><b>3.1</b></u> |
|                        |   |   |     |          |                   |   |    | Average: | <b>11.0</b> |                   |
| <b>Large intestine</b> | 2 | 1 | 4.7 | 5.3      | <b>5.0</b>        | 2 | 8  | 9.7      | 12          | <b>11</b>         |
| <b>tissue</b>          | 2 | 2 | 4.1 | 6.0      | <b>5.0</b>        | 2 | 9  | 6.1      | 6.6         | <b>6.4</b>        |
|                        | 5 | 4 | 3.8 | 3.9      | <b>3.8</b>        | 2 | 7  | 6.2      | 7.1         | <b>6.6</b>        |
|                        | 5 | 5 | 1.6 | 2.6      | <u><b>2.1</b></u> | 5 | 11 | 3.9      | 4.2         | <b>4.1</b>        |
|                        |   |   |     | Average: | <b>4.0</b>        | 5 | 12 | 3.9      | 4.2         | <b>4.0</b>        |
|                        |   |   |     |          |                   | 5 | 10 | 3.5      | 3.7         | <u><b>3.6</b></u> |
|                        |   |   |     |          |                   |   |    | Average: | <b>5.9</b>  |                   |

<sup>1</sup> Calibration was performed against OxBC polymer using DHA released by NaOH treatment

**Table 2.** Total apocarotenoid concentration ( $\mu\text{g/g}$  or  $\mu\text{g/mL}$ ) of OxBC apoC in tissues and body fluids.<sup>1</sup>

|                         | Control    |       |         |         |              | OxBC dose   |       |         |         |              |
|-------------------------|------------|-------|---------|---------|--------------|-------------|-------|---------|---------|--------------|
|                         | Day        | Mouse | 181→107 | 181→135 | Average      | Day         | Mouse | 181→107 | 181→135 | Average      |
| <b>Kidney</b>           | 2          | 1     | 1.6     | 1.8     | <b>1.7</b>   | 2           | 7     | 3.2     | 3.4     | <b>3.3</b>   |
|                         | 2          | 2     | 1.9     | 2.0     | <b>2.0</b>   | 2           | 8     | 3.6     | 3.9     | <b>3.8</b>   |
|                         | 5          | 4     | 3.2     | 3.5     | <b>3.3</b>   | 5           | 10    | -       | -       | -            |
|                         | 5          | 5     | 1.5     | 1.5     | <u>1.5</u>   | 5           | 11    | 2.4     | 2.5     | <u>2.5</u>   |
| Average:                |            |       |         |         | <b>2.1</b>   | Average:    |       |         |         |              |
| <b>Abdominal muscle</b> | 2          | 1     | 2.6     | 2.5     | <b>2.6</b>   | 2           | 7     | 3.0     | 3.0     | <b>3.0</b>   |
|                         | 5          | 4     | 7.1     | 6.8     | <u>7.0</u>   | 5           | 10    | 3.4     | 3.7     | <u>3.5</u>   |
|                         | Average:   |       |         |         |              | Average:    |       |         |         |              |
|                         | <b>4.8</b> |       |         |         |              | <b>3.3</b>  |       |         |         |              |
| <b>Lung</b>             | 2          | 3     | 10      | 10      | <b>10</b>    | 2           | 8     | 21      | 22      | <b>21</b>    |
|                         | 5          | 5     | 24      | 24      | <u>24</u>    | 5           | 11    | 6       | 4       | <u>5</u>     |
|                         | Average:   |       |         |         |              | Average:    |       |         |         |              |
|                         | <b>17</b>  |       |         |         |              | <b>13</b>   |       |         |         |              |
| <b>Plasma</b>           | 1 h        | 5     | 0.004   | 0.004   | <b>0.004</b> | 1 h         | 11    | 0.002   | 0.002   | <b>0.002</b> |
|                         | 1 h        | 6     | 0.109   | 0.112   | <b>0.11</b>  | 1 h         | 12    | 0.28    | 0.28    | <b>0.28</b>  |
|                         | 2          | 2     | 0.001   | 0.001   | <b>0.001</b> | 2           | 8     | 0.11    | 0.08    | <b>0.10</b>  |
|                         | 2          | 3     | 0.073   | 0.064   | <b>0.069</b> | 2           | 9     | 0.12    | 0.14    | <b>0.13</b>  |
|                         | 5          | 8     | 0.001   | 0.001   | <b>0.001</b> | 5           | 12    | 0.09    | 0.08    | <u>0.08</u>  |
|                         | 5          | 5     | 0.024   | 0.036   | <b>0.030</b> | Average:    |       |         |         |              |
|                         | 5          | 10    | 0.048   | 0.055   | <u>0.051</u> | <b>0.12</b> |       |         |         |              |
| Average:                |            |       |         |         | <b>0.038</b> |             |       |         |         |              |
| <b>Stomach</b>          | 2          | 2     | 1.3     | 1.3     | <b>1.3</b>   | 2           | 8     | 38      | 38      | <b>38</b>    |
|                         | 2          | 3     | 2.1     | 2.1     | <b>2.1</b>   | 2           | 7     | 37      | 37      | <b>37</b>    |
|                         | 5          | 5     | 1.0     | 1.0     | <b>1.0</b>   | 5           | 11    | 80      | 80      | <b>80</b>    |
|                         | 5          | 4     | 2.6     | 2.6     | <u>3</u>     | 5           | 10    | 138     | 138     | <u>138</u>   |

|                        |   |   |                 |              |              |   |    |                 |                 |             |
|------------------------|---|---|-----------------|--------------|--------------|---|----|-----------------|-----------------|-------------|
|                        |   |   | <i>Average:</i> | <b>1.7</b>   |              |   |    | <i>Average:</i> | <b>73</b>       |             |
| <b>Feces</b>           | 2 | 1 | 0.50            | 0.54         | <b>0.52</b>  | 2 | 7  | 1.6             | 2.4             | <b>2.0</b>  |
|                        | 2 | 3 | 0.38            | 0.33         | <b>0.36</b>  | 2 | 9  | 2.4             | 2.1             | <b>2.2</b>  |
|                        | 5 | 4 | 0.50            | 0.50         | <b>0.50</b>  | 5 | 10 | 1.1             | 1.2             | <b>1.2</b>  |
|                        | 5 | 6 | 0.52            | 0.61         | <b>0.57</b>  | 5 | 12 | 2.1             | 2.3             | <b>2.2</b>  |
|                        |   |   | <i>Average:</i> | <b>0.49</b>  |              |   |    | <i>Average:</i> | <b>1.9</b>      |             |
| <b>Intestinal wash</b> | 2 | 1 | 0.009           | 0.015        | <b>0.012</b> | 2 | 7  | 0.31            | 0.36            | <b>0.34</b> |
|                        | 5 | 4 | 0.010           | 0.014        | <b>0.012</b> | 5 | 10 | 0.11            | 0.10            | <b>0.10</b> |
|                        |   |   | <i>Average:</i> | <b>0.012</b> |              |   |    | <i>Average:</i> | <b>0.22</b>     |             |
| <b>Urine</b>           | 2 | 1 | 0.12            | 0.10         | <b>0.11</b>  | 2 | 7  | 0.76            | 0.94            | <b>0.85</b> |
|                        | 2 | 3 | 0.25            | 0.36         | <b>0.31</b>  | 2 | 9  | 0.61            | 0.64            | <b>0.62</b> |
|                        | 5 | 4 | 0.52            | 0.78         | <b>0.65</b>  | 5 | 10 | 0.45            | 1.21            | <b>0.83</b> |
|                        | 5 | 6 | 0.15            | 0.19         | <b>0.17</b>  | 5 | 12 | 0.21            | 0.25            | <b>0.23</b> |
|                        |   |   | <i>Average:</i> | <b>0.31</b>  |              |   |    | <i>Average:</i> | <b>0.63</b>     |             |
| <b>Cecum</b>           | 2 | 1 | 0.44            | 0.49         | <b>0.46</b>  | 2 | 7  | 0.72            | 0.84            | <b>0.78</b> |
|                        | 5 | 4 | 0.37            | 0.42         | <b>0.40</b>  | 5 | 10 | 1.3             | 1.5             | <b>1.4</b>  |
|                        |   |   | <i>Average:</i> | <b>0.43</b>  |              |   |    | <i>Average:</i> | <b>1.1</b>      |             |
| <b>Spleen</b>          | 2 | 1 | 0.10            | 0.14         | <b>0.12</b>  | 2 | 7  | 0.10            | 0.14            | <b>0.12</b> |
|                        | 5 | 4 | 0.11            | 0.13         | <b>0.12</b>  | 5 | 10 | 0.32            |                 | <b>0.32</b> |
|                        |   |   | <i>Average:</i> | <b>0.12</b>  |              |   |    | <i>Average:</i> | <b>0.22</b>     |             |
| <b>Hamstring</b>       | 2 | 1 | 23              | 23           | <b>23</b>    | 2 | 7  | 16              | 16              | <b>16</b>   |
|                        | 5 | 4 | 11              | 11           | <b>11</b>    | 5 | 10 | 15              | 15              | <b>15</b>   |
|                        |   |   | <i>Average:</i> | <b>17</b>    |              |   |    | <i>Average:</i> | <b>16</b>       |             |
| <b>Liver</b>           | 2 | 3 | 3.6             | 3.6          | <b>3.6</b>   | 2 | 9  | 2.6             | 2.5             | <b>2.6</b>  |
|                        | 2 | 2 | 3.6             | 3.6          | <b>3.6</b>   | 2 | 7  | 3.5             | 3.5             | <b>3.5</b>  |
|                        | 5 | 4 | 2.5             | 2.5          | <b>2.5</b>   | 5 | 12 | 3.5             | 3.5             | <b>3.5</b>  |
|                        | 5 | 4 | 2.6             | 2.5          | <b>2.6</b>   | 5 | 10 | 4.8             | 4.8             | <b>4.8</b>  |
|                        | 5 | 5 | 2.5             | 2.5          | <b>2.5</b>   |   |    |                 | <i>Average:</i> | <b>3.6</b>  |

|                                   |   |   |       | <i>Average:</i> | <b><u>3.0</u></b> |                 |    |       |       |  |
|-----------------------------------|---|---|-------|-----------------|-------------------|-----------------|----|-------|-------|--|
| <b>Small intestine<br/>tissue</b> | 2 | 1 | 0.29  | 0.30            | <b>0.29</b>       | 2               | 8  | 0.72  | 0.67  |  |
|                                   | 2 | 2 | 0.17  | 0.16            | <b>0.17</b>       | 2               | 9  | 1.0   | 1.0   |  |
|                                   | 5 | 4 | 0.15  | 0.15            | <b>0.15</b>       | 5               | 11 | 1.2   | 1.3   |  |
|                                   | 5 | 5 | 0.24  | 0.24            | <b>0.24</b>       | 5               | 12 | 0.22  | 0.23  |  |
| <i>Average:</i>                   |   |   |       |                 | <b>0.21</b>       | <i>Average:</i> |    |       |       |  |
| <b>Large intestine<br/>tissue</b> | 2 | 1 | 0.81  | 0.05            | <b>0.43</b>       | 2               | 8  | 0.46  | 0.54  |  |
|                                   | 2 | 2 | 0.12  | 0.14            | <b>0.13</b>       | 2               | 9  | trace | trace |  |
|                                   | 5 | 4 | trace | trace           | <b>trace</b>      | 5               | 11 | 0.18  | 0.19  |  |
|                                   | 5 | 5 | trace | trace           | <b>trace</b>      | 5               | 12 | 0.22  | 0.24  |  |
| <i>Average:</i>                   |   |   |       |                 | <b>0.28</b>       | <i>Average:</i> |    |       |       |  |

<sup>1</sup>Calibration was performed against OxBC using DHA present in hexane extract of OxBC