**Table S1. The formulation of the experimental diets**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Ingredient（g/kg） | 28%protein | | | 38%protein | |
| 7%lipid | 7%lipid +fenofibrate | 7%lipid | | 7%lipid +fenofibrate |
| Fish meal | 100 | 100 | 240 | | 240 |
| Fermented soybean meal | 20 | 20 | 20 | | 20 |
| Casein | 200 | 200 | 200 | | 200 |
| Gelatin | 40 | 40 | 40 | | 40 |
| Fish oi | 20 | 20 | 5.3 | | 5.3 |
| Soybean oil | 30 | 30 | 30 | | 30 |
| Corn starch | 289.75 | 289.75 | 289.75 | | 289.75 |
| Soybean lecithin | 10 | 10 | 10 | | 10 |
| Fenofibrate | 0 | 5 | 0 | | 5 |
| Vitamin premix1 | 10 | 10 | 10 | | 10 |
| Mineral premix2 | 20 | 20 | 20 | | 20 |
| Calcium biphosphate | 10 | 10 | 10 | | 10 |
| CMC | 30 | 30 | 30 | | 30 |
| Choline chloride | 5 | 5 | 5 | | 5 |
| Cellulose | 215 | 210 | 89.7 | | 84.7 |
| BHT | 0.25 | 0.25 | 0.25 | | 0.25 |
| Total | 1000 | 1000 | 1000 | | 1000 |
| Composition |  |  |  | |  |
| Crude protein | 29.12% | 28.62% | 37.74% | | 37.10% |
| Crude lipid | 6.00% | 5.90% | 5.65% | | 5.85% |
| Ash | 7.14% | 7.10% | 8.71% | | 8.67% |
| Gross energy(MJ/kg) | 14.5 | | 16.8 | | |

1 Mineral premix, (g/kg): 105.0 g CaCO3; 100.0g KH2PO4; 100.0 g MgSO4·7H2O; 49.8 g NaCl; 12.0 g Fe(II) gluconate; 1.07 g MnSO4·H2O; 4.76 g ZnSO4·7H2O; 0.24 g CuCl2·2H2O; 0.23 g KI; 1.4 g CoCl2·6H2O.

2 Vitamin premix, (mg or IU/100g): 420,000 I.U. (international units) Vitamin A, 120,000 I.U. Vitamin D3, 2000 mg Vitamin E, 1000 mg Vitamin K3, 1000 mg Vitamin B1, 1000 mg Vitamin B2, 1600 mg Vitamin B6, 2mg Vitamin B12, 6,000 mg Inositol, 3,500 mg Pantothenic acid, 5,000 mg Niacin, 400 mg Folic acid, 10 mg Biotin, 60,000 mg Vitamin C.

**Table S2. Primers used in quantitative PCR**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Usage | Item | Primer name | Sequence (5'–3') | Size (bp) | Notes |
| RT-PCR | PPARα | q1f | AACCGAAACAAGTGCCAGTA | 121 | KF871430 |
| cDNA |  | q1r | TTGCTTTCCTCCTTGAGCTT |  |  |
|  | PPARβ | q1f | AACCGAAACAAGTGCCAGTA | 121 | KF871430 |
|  |  | q1r | TTGCTTTCCTCCTTGAGCTT |  |  |
|  | PPARγ | Gq1F | TGGACTACACAAACATGCACAGC | 101 | KF918712 |
|  |  | Gq1R | CACGGGACTATCTGAGTACTGTGGA |  |  |
|  | SREBP1c | S1F | ATTCAGACTCAGCTCCAAGGG |  |  |
|  |  | S1R | TCAGGCTTCAAAGTGGTCAG |  |  |
|  | CPT1a | Ca2F | GTCCCATGGAAAAATGAGTACATCA | 100 | XM\_005470876 |
|  |  | Ca2R | GGTAAGGAGGCCTGGAAACTGTA |  |  |
|  | ACO | Acq1F | AGTCCCACTGTGAGCTCCATCAA | 108 | KF918710 |
|  |  | Acq1R | CAGACCATGGCAGTTTCCAAGA |  |  |
|  | FAS | FS2F | TCATCCAGCAGTTCACTGGCATT | 102 | GU433188 |
|  |  | FS2R | TGATTAGGTCCACGGCCACA |  |  |
|  | DGAT2 | DG2F | GCTTGAATTCTGTCACCCTGAAGA | 106 | blatted |
|  |  | DG2R | ACCTGCTTGTAGGCGTCGTTCT |  |  |
|  | CD36 | CD2F | TCACCTGAAAGGACACATCACCA | 104 | XM\_003451528 |
|  |  | CD2F | CGCTGCATCAAGATGTTCACCT |  |  |
|  | FATP5 | A26F | TACACATCTGGGACCACAGGTTTG | 110 | XM\_003443859.2 |
|  |  | A26R | AAGATGTCCTCTGCTGTGACTCCA |  |  |
|  | MTP | M1F | ACCATTGCCCTCACTGCC |  |  |
|  |  | M1R | CGATTCTGGTGATAAACCCTGT |  |  |
|  | ApoB | Ab1F | TCCCCAGCTACACTGCACAGTT | 98 | NM\_001279533 |
|  |  | Ab1R | CATCGCCTCTTCCTGACATCATC |  |  |
|  | β-actin | Ba1F | CAGGATGCAGAAGGAGATCACA | 92 | KJ126772 |
|  |  | Ba1R | CGATCCAGACGGAGTATTTACG |  |  |
|  | EF1α | E1F | CTACGTGACCATCATTGATGCC | 106 | KJ123689 |
|  |  | E1R | AACACCAGCAGCAACGATCA |  |  |

**Table S3. Growth performance, feed utilization and biological status of Nile tilapia fed diets with different protein levels for 8 weeks**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Parameters | fish | 28%protein | | 38%protein | |
| 7%lipid | 7%lipid  +fenofibrate | 7%lipid | 7%lipid +fenofibrate |
| Average initial body weight (g) | Whole tank | 8.02±0.02 | 8.05±0.02 | 8.03±0.00 | 8.03±0.01 |
| Average final body weight (g) | Whole tank | 53.45±2.07 | 49.10±1.00 | 74.62±4.51 | 78.62±1.08 |
| WGR (%) | Whole tank | 566.14±24.52 | 509.68±12.25# | 862.98±27.24 | 879.50±12.81 |
| Individual final hepatic weight(g) | No.1 | 1.17  1.57  1.39  0.79  0.89  1.15 | 0.95  1.27  1.53  1.04  0.97  1.4 | 1.3  1.2  0.83  1.19  1.76  1.26 | 0.75  1.35  1.23  1.94  1.4  1.38 |
| 2 |
| 3 |
| 4 |
| 5 |
| 6 |
| Individual final body weight(g) | No.1 | 65.84  75.01  64.19  51.89  50.95  66.94 | 45.34  53.23  68.69  45.00  46.52  57.41 | 84.62  83.04  62.38  81.3  96.96  71.31 | 92.63  67.81  78.33  93.87  84  78.02 |
| 2 |
| 3 |
| 4 |
| 5 |
| 6 |
| Individual final body length(cm) | No.1 | 12.9  13.2  12.7  11.9  11.8  12.8 | 11.4  12  12.9  11.8  11.2  12.2 | 13.5  13.3  12.7  13.5  14.4  12.8 | 13.8  12.3  14.2  14.2  13.5  13.5 |
| 2 |
| 3 |
| 4 |
| 5 |
| 6 |
| Individual final condition factor | No.1 | 3.07  3.26  3.13  3.08  3.10  3.19 | 3.06  3.08  3.20  2.74  3.31  3.16 | 3.44  3.53  3.05  3.30  3.25  3.40 | 3.52  3.64  2.74  3.28  3.41  3.17 |
| 2 |
| 3 |
| 4 |
| 5 |
| 6 |

# Mean values between control and fenofibrate treatments of each protein group with unlike superscript were significantly different (p<0.05).

**Table S4. The results of two-way ANOVA analysis of Figure 1-6.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  | Two-way ANOVA | | |
| **Figure 1** | Growth |  | Protein  level  (P) | Fenofibrate treatment  (F) | P×F |
| Fig. 1A | WGR | *F* | 619.911 | 2.250 | 7.474 |
| *P* | 0.000 | 0.172 | 0.026 |
| Fig. 1B | FI | *F* | 46.512 | 1.860 | 0.670 |
| *P* | 0.000 | 0.210 | 0.437 |
| Fig. 1C | PER | *F* | 2.376 | 2.709 | 2.376 |
| *P* | 0.162 | 0.138 | 0.162 |
| Fig. 1D | VSI | *F* | 25.488 | 14.468 | 0.120 |
| *P* | 0.001 | 0.005 | 0.738 |
| Fig. 1E | MFI | *F* | 25.489 | 0.229 | 1.765 |
| *P* | 0.001 | 0.645 | 0.221 |
| Fig. 1F | HSI | *F* | 368.182 | 113.636 | 72.727 |
| *P* | 0.000 | 0.000 | 0.000 |
| **Figure 2** | Body parameters |  | Protein  level  (P) | Fenofibrate treatment  (F) | P×F |
| Fig. 2A | Protein | *F* | 56.044 | 1.745 | 1.745 |
| *P* | 0.000 | 0.223 | 0.223 |
| Fig. 2B | Lipid | *F* | 95.870 | 0.011 | 0.174 |
| *P* | 0.000 | 0.920 | 0.688 |
| Fig. 2C | MP | *F* | 0.684 | 0.400 | 0.152 |
| *P* | 0.432 | 0.545 | 0.707 |
| Fig. 2D | ML | *F* | 0.898 | 1.728 | 1.893 |
| *P* | 0.371 | 0.225 | 0.206 |
| Fig. 2E | HL | *F* | 0.689 | 12.404 | 3.636 |
| *P* | 0.431 | 0.008 | 0.093 |
| **Figure 3** | Plasma parameters |  | Lipid  level  (L) | Fenofibrate treatment  (F) | P×F |
| Fig. 3A | TG | *F* | 32.573 | 5.316 | 11.830 |
| *P* | 0.000 | 0.050 | 0.009 |
| Fig. 3B | FFA | *F* | 1.848 | 12.785 | 1.882 |
| *P* | 0.211 | 0.007 | 0.207 |
| Fig. 3C | HDL | *F* | 1.138 | 4.750 | 0.260 |
| *P* | 0.317 | 0.061 | 0.624 |
| Fig. 3D | LDL | *F* | 76.827 | 99.482 | 11.054 |
| *P* | 0.000 | 0.000 | 0.010 |
| Fig. 3E | TP | *F* | 0.018 | 5.246 | 0.454 |
| *P* | 0.896 | 0.051 | 0.520 |
| Fig. 3F | TAA | *F* | 1.510 | 19.258 | 6.933 |
| *P* | 0.254 | 0.002 | 0.030 |
| Fig. 3G | NH4 | *F* | 6.916 | 21.182 | 10.807 |
| *P* | 0.030 | 0.002 | 0.011 |
| Fig. 3H | MDA | *F* | 51.635 | 8.262 | 33.046 |
| *P* | 0.000 | 0.021 | 0.000 |
| **Figure 4-6** | Liver QPCR |  | Protein  level  (P) | Fenofibrate treatment  (F) | P×F |
| Fig. 4A | PPARα | *F* | 0.364 | 9.091 | 0.000 |
| *P* | 0.563 | 0.017 | 1.000 |
| Fig. 4B | PPARβ | *F* | 0.76 | 9.316 | 0.190 |
| *P* | 0.409 | 0.016 | 0.674 |
| Fig. 4C | CPT1α | *F* | 21.684 | 21.776 | 21.500 |
| *P* | 0.002 | 0.002 | 0.002 |
| Fig. 4D | ACO | *F* | 19.289 | 6.465 | 15.442 |
| *P* | 0.002 | 0.035 | 0.004 |
| Fig. 5A | FAS | *F* | 108.671 | 113.083 | 129.219 |
| *P* | 0.000 | 0.000 | 0.000 |
| Fig. 5B | SREBP1c | *F* | 71.276 | 63.363 | 69.656 |
| *P* | 0.000 | 0.000 | 0.000 |
| Fig. 5C | DGAT2 | *F* | 13.547 | 0.422 | 3.797 |
| *P* | 0.006 | 0.543 | 0.087 |
| Fig. 5D | PPARγ | *F* | 1.092 | 14.472 | 13.843 |
| *P* | 0.327 | 0.005 | 0.006 |
| Fig. 6A | CD36 | *F* | 40.383 | 41.139 | 41.139 |
| *P* | 0.000 | 0.000 | 0.000 |
| Fig. 6B | FATP5 | *F* | 17.925 | 22.010 | 18.907 |
| *P* | 0.003 | 0.002 | 0.002 |
| Fig. 6C | MTP | *F* | 6.205 | 83.427 | 0.689 |
| *P* | 0.037 | 0.000 | 0.430 |
| Fig. 6D | ApoB | *F* | 4.116 | 59.440 | 0.000 |
| *P* | 0.077 | 0.000 | 1.000 |

Table S5. Concentrations of fenofibrate and fenofibric acid in water samples

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Lipid regulators | CAS number | Analytical method | Median(ng/L) | Samples/filter system | LOD(ng/L) |
| fenofibrate | 49562-28-9 | GC-MS | n.d. | 3/1 | 20 |
| fenofibric acid | 42017-89-0 | GC-MS | 63 | 3/1 | 20 |

LOD, limit of detection; n.d., not detectable