What is new for an old Molecule? Systematic Review and Recommendations on the use of Resveratrol

Ole Vang, Nihal Ahmad, Clifton A. Baile, Joseph A. Baur, Karen Brown et al.

Supporting information:

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| **Table S3:** Effect of resveratrol on obesity and models for diabetes in experimental animals |
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| **Species / Strain** | **Treatment** | **Resveratrol dose** | **Duration** | **Effect** | **References** |
| Insulin sensitivity |
| Male Sprague-Dawley rats  | High cholesterol–fructose (HCF) diet for 15weeks  | 1 mg Resv/ kg bw/ day, po  | 15 days / 15 weeks | Metabolic characteristics of rats on an HCF diet shifted toward a standard diet.Insulin-stimulated whole-body glucose uptake ↑Steady-state glucose uptake of soleus muscle and liver in HCF-fed rats ↑ | [1] |
| Male Wistar rats | High-fat diet (59% from fat) for 6 weeks | 100 mg Resv/kg bw/ day po | 10 weeks (16 weeks in total) | lipid accumulation in the liver ↓Abdominal obesity ↓Insulin resistance ↓Fasting serum insulin ↓ | [2] |
| Male Wistar rats | Single ip injection of 50 mg STZ/ kg | 5 mg Resv/ kg bw/ day po | 30 days | Serum insulin↓ | [3] |
| Lean / Obese Zucker rats |  | 10 mg Resv/ kg /day po | 4 weeks/ 8 weeks | fasting plasma insulin concentration ↓ ( 4 weeks) | [4] |
| Male C57Bl/6J mice |  | 200 or 400 mg Resv/ kg bw/ day | 9 weeks | Insulin sensitivity ↑ | [5] |
| male C57BL/6NIA mice | high-calorie diet | 22.4 mg Resv/ kg bw/ day | 6 months | Fasting serum insulin ↓ | [6] |
| IRS2-/- mice |  | 25mg Resv/ml in drinking water (~ 2.5 mg Resv/ kg bw/ day) | 8 weeks | systemic insulin sensitivity ↑glucose tolerance → | [7] |
| AMPKα1-/- and wild-type C57BL/6J mice | Fed a high-fat diet (40% from fat) | 400 mg Resv/ kg bw/ day  | 12 weeks | Metabolic rate ↑Insulin sensitivity → | [8] |
| C57BL/6 male mice | High-calorie diet (58% from fat) - 14 weeks | 79.2 ng Resv/ day, infused intra cerebro ventricularly. | 5 weeks | Serum insulin ↓ | [9] |
| Male New Zealand rabbits | Diabetes induced with alloxan (100 mg/kg) andmaintained for 8 weeks | 5 or 50 mg Resv/ L drinking water(~1.5 or 17 mg/ kg/ day) | 10 weeks, starting 14 days prior alloxan | Serum insulin ↓ | [10] |
| Blood glucose levels |
| Male Wistar rats | High-fat diet for 30 days | 1 mg Resv/ kg bw/ day via drinking water | 15 days | Serum glucose ↓ | [11] |
| Male Wistar rats | Single ip injection of 50 mg STZ/ kg | 5 mg Resv/ kg po | 30 days | Serum glucose ↓ | [3] |
| Sprague–Dawley rats | A single iv injection of 65 mg STZ/kg for 2 weeks | 0.1 or 1 mg Resv/ kg bw/ day +/- 1 mg insulin/ kg bw/ day | 5 days | Plasma glucose ↓ | [12] |
| Sprague Dawley rats | 65 mg STZ/ kg – 15 days | 2.5 mg Resv/ kg bw/ day | 15 days | Blood glucose ↓ | [13] |
| Lean / Obese Zucker rats |  | 10 mg Resv/ kg bw/ day po | 4 weeks/ 8 weeks | Fasting levels of glucose ↓  | [4] |
| Genetically obese mice (Lepob/ob) |  | SRT501 (1,000 mg/ kg) | 3 weeks | Fasting blood glucose ↓ | [14] |
| Diet-induced obesity (DIO) mice |  | SRT501 (500 mg/ kg) | 4 weeks | Fasting blood glucose ↓Hyperinsulinaemia in DIO mice ↓ | [14] |
| Male C57BL/6NIA mice | High-calorie diet | 22.4 mg/ kg / day | 6 months | Fasting glucose ↓ | [6] |
| Male C57BL/6 mice | High-calorie diet (58% kcal from fat) - 14 weeks | 79.2 ng / day, infused intra cerebro ventricularly | 5 weeks | Blood glucose ↓ | [9] |
| C57BL/6 mice | Five consecutive ip injections of 55 mg STZ/ kg bw | 20 mg Resv/ kg bw/ day, po | 1 month | Blood glucose ↓ | [15] |
| Male New Zealand rabbits | Diabetes induced with alloxan (100 mg/ kg bw) and maintained for 8 weeks | 5 or 50 mg Resv/ L drinking water(~1.5 or 17 mg/ kg bw/ day) | 10 weeks, starting 14 days prior alloxan | Blood glucose → | [10] |
| Diet-induced obesity |
| Male C57BL/6NIA mice | High-calorie diet | 22.4 mg Resv/ kg bw/ day | 6 months | Weight gain→ | [6] |
| Male Sprague-Dawley rats | High-caloric diet  | 6, 30 or 60 mg Resv/ kg bw/ day | 6 weeks | Food intake →Final body weight→The size of white adipose tissue ↓ | [16] |
| Female Sprague-Dawley rats | High-fat diet (42% from fat) | 20 mg Resv/ kg bw/ day | 8 weeks | Weight gain →Food intake of standard diet →Food intake of high-fat diet ↓ | [17] |
| Lean / Obese Zucker rats |  | 10 mg Resv/ kg bw/ day po | 8 weeks | Food intake →Body weight → | [4] |
| Male C57Bl/6J mice |  | 200 or 400 mg/kg bw/day | 9 weeks | Weight gain ↓Food intake → | [5] |
| C57BL/6 male mice | high-calorie diet (58% kcal from fat) - 14 weeks | 79.2 ng / day, infused intra cerebro ventricularly | 5 weeks | Body weight →Food intake → | [9] |
| AMPKα1-/- and wild-type C57BL/6J mice | Fed a high-fat diet (40% from fat) | 400 mg Resv/ kg bw/ day  | 12 weeks | Food intake →Body weight of wild-type ↓AMPKα2-/- mice ↓AMPKα1-/- mice →The fat index ↓ in all strains | [8] |
| Grey mouse lemurs |  | 200 mg Resv/ kg bw/ day | 4 weeks | Weight gain ↓Food intake ↓ | [18] |
| Visceral fat index and liver mass index |
| Male Wistar rats | high-fat (59% from Fat) – 6 weeks | 100 mg·Resv/ kg bw/ day | 10 week | Reduced lipid accumulation in liverReduced abdominal obesity  | [2] |
| Lean / Obese Zucker rats |  | 10 mg Resv/ kg bw/ day, po | 8 weeks | In obese rats, abdominal fat ↓plasma triglycerides ↓Free fatty acids ↓Total cholesterol ↓ | [4] |
| Male Wistar CRL: Wi (Han) | High carbohydrate - fat free modified diet + induction of steatosis | 10 mg Resv daily po (~ 44 mg/ kg bw/ day) | 4 weeks | Grade of steatosis ↓ | [19] |
| DIO: Diet-induced obesity; HCF: high cholesterol–fructose; STZ: streptozotocin bw: body weight; iv: intravenous; ip: intraperitoneally; po: per oralEffect are indicated by ↓: reduction; ↑: enhancement; →: no effect. |

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