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

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Supporting information:

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| **Table S5:** Effect of resveratrol on inflammatory markers | | | | | |
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| **Animal** | **Inducer** | **Resveratrol dose** | **Duration** | **Effect** | **References** |
| Male Wistar rats | Colonic anastomosis | 0.5 mg Resv/ kg, po | 7 d before operation | Plasma IL-6: 3 d after anastomosis: ↑  0 , 5 or 7 d after: →  Tissue NF-κB: 3 and 5 d: ↓ 0, 7 d → | [1] |
| Male Wistar rats | Chronic colonic injury was induced by intra colonic instillation of TNBS | 10 mg Resv/ kg bw/ day, po, staring 24 h after TNBS treatment | 2 weeks | Microscopic damage: Resv↓  TNFα: TNBS↑, TNBS+Resv↓  NF-κBp65: TNBS↑, TNBS+Resv↓  Cox-2: TNBS↑, TNBS+Resv↓  PGE2: TNBS↑, TNBS+Resv↑↑  PGD2: TNBS↑, TNBS+Resv→ | [2] |
| Male Fischer F344 rats | Colitis induced by 5% DSS | 1 mg Resv/ kg bw/ day | 25 days | DSS-induced inﬁltration of inﬂammatory cells ↓  DSS induced PGE2 level ↓ | [3] |
| Male Wistar rats | 20 mg DMH /kg bw, once a week for 15 weeks | 8 mg Resv/ kg bw/ day, simultaneously with DMH, after DMH treatment or in the entire period | 15 / 30 weeks | Colon COX-2 expression:  DMH↑, DMH+Resv ↓ | [4] |
| Male Sprague-Dawley rats | ip injections of 40 mg DMN/ kg bw causing liver fibrosis | 10 mg Resv/ kg bw/ day | 7 d after DMN treatment | IL-1β: DMN↑, DMN+Resv↓  TNFα: DMN↑, DMN+Resv↓  iNOS: DMN↑, DMN+Resv↓ | [5] |
| Male Sprague–Dawley rats | Diabetes induced by 55 mg STZ/ kg bw, ip | resveratrol 10 and 20 mg/ kg bw/ day, 6 weeks  after diabetes induction | 2 weeks | TNFα: STZ↑, STZ+Resv↓  IL-6: STZ↑, STZ+Resv↓  NF-κBp65: STZ↑, STZ+Resv↓ | [6] |
| Male Wistar rats | Diabetes was induced 50 mg STZ/ kg bw | 5 mg Resv/ kg bw/ day | 30 days | In plasma and liver:  TNFα: STZ↑, STZ+Resv↓  IL-1β: STZ ↑, STZ+Resv↓  IL-6: STZ↑, STZ+Resv↓ | [7] |
| Wistar rats | 20 mg MCT/ kg bw, ip | 10 mg Resv/ kg bw/day, po | 5 days | Plasma TNFα: MCT↑, MCT+Resv↓ | [8] |
| Sprague-Dawley rats | MCT induced hypertension | 25 mg Resv/ kg bw/ day, po, from day 1 post MCT |  | mRNA expression of  IL-6: MCT↑, MCT+Resv↓  IL-1: MCT↑, MCT+Resv↓  TNFα: MCT↑, MCT+Resv↓  PDGFα: MCT↑, MCT+Resv↓  PDGFβ: MCT↑, MCT+Resv↓  TGFβ: MCT↑, MCT+Resv→  MCP-1: MCT↑,MCT+Resv↓ | [9] |
| Lean / Obese Zucker rats |  | 10 mg Resv/ kg bw/ day, po | 8 weeks | TNFα: OBS↑, OBS+Resv↓ | [10] |
| Male Wistar rats | Exposed to cigarette smoke (CS) for 1 week | 25 mg Resv/ kg bw/ day in drinking water | 2 days pre-treatment | IL-1: CS↑, CS+Resv↓  IL-6: CS↑, CS+Resv↓  ICAM1: CS↑, CS+Resv↓  iNOS: CS↑, CS+Resv↓  TNFα: CS↑, CS+Resv→ | [11] |
| Sprague–Dawley rats | 6-OHDA injected into the right striatum | 10, 20 and 40 mg Resv/ kg was given orally | 10 weeks | Cox-2 expression in the substantia: nigra: 6-OHDA↑, 6-OHDA+Resv↓ | [12] |
| Male Wistar CRL: Wi (Han) rats | Steatosis (ST) by a high carbohydrate-fat free modified diet 4 days per week, and fasted for the remaining 3 days (4 weeks) | 10 mg Resv, po (~ 44 mg/ kg bw/ day) | 4 weeks | TNFα: ST↑, ST+Resv↓ | [13] |
| Male Wistar rats | Idiopathic pulmonary ﬁbrosis induced a single dose of 5mg BLE/ kg | 10 mg Resv/ kg bw/ day | 2 weeks | TNFα: BLE↑, BLE+Resv↓  IL-1β: BLE ↑, BLE +Resv↓  IL-6: BLE ↑, BLE+Resv↓  TGFβ: BLE ↑, BLE+Resv↓ | [14] |
| Male Swiss rats | Bile duct ligation (BDL) | 10 mg Resv/ kg, ip, once a day | 28 days | IL-1β: BDL↑, BDL+Resv↓  IL-6: BDL↑, BDL+Resv↓  TNFα: BDL↑, BDL+Resv↓ | [15] |
| Male and female C57BL/6 mice | Water containing 1% DSS | Resv in diet at 75 to 300 ppm (~ 12 to 48 mg/ kg bw/ day) | 62 days | T cells expressing  TNFα: DSS↑, DSS+Resv↓  IFNγ: DSS↑, DSS+Resv↓ | [16] |
| Female Swiss mice | Ehrlich ascites carcinoma cells from a spontaneous mammary cancer (EAC) | 20 or 40 mg Resv/ kg bw/ day, ip | 20 days | CRP: EAC↑, EAC+Resv↓ (20 & 40 mg)  TNFα: EAC ↑, EAC +Resv↓ (20 & 40 mg) | [17] |
| C57BL/6J mice | Colitis was induced for the last 8 days by 1% DSS in drinking water | 2.1 mg Resv/ kg bw/ day | 29 days | TNFα: DSS→, DSS+Resv→  IL-1β: DSS→, DSS+Resv→  IL-6: DSS ↑, DSS +Resv↓  IL-10: DSS ↑, DSS+Resv↓  IL-3: DSS ↑, DSS+Resv↑  sTNF RI, p55 subunit: DSS ↑, DSS +Resv↓ | [18] |
| Female C57BL/6 mice | 3% DSS in the drinking water for 5 days | Resveratrol in diet at 20 mg/kg (~ 3 mg/ kg bw/ day) | 26 days | TNFα: DSS↑, DSS+Resv↓  IL-1β: DSS↑, DSS+Resv↓  IL-10: DSS↓, DSS+Resv↑  PGES-1: DSS↑, DSS+Resv↓  COX2: DSS↑, DSS+Resv↓  iNOS: DSS↑, DSS+Resv↓ | [19] |
| Female C57BL/6 mice | Drinking water containing 3% DSS | 10, 50, or 100 mg Resv/ kg bw/ day, po | 14 days | TNFα: DSS↑, DSS+ Resv ↓  IL-1β: DSS↑, DSS+ Resv ↓  IL-6: DSS↓, DSS+ Resv ↑  IFNγ: DSS↑, DSS+ Resv ↓  COX2: DSS↑, DSS+ Resv ↓  iNOS: DSS↑, DSS+ Resv ↓ | [20] |
| Male BALB/c mice | Ulcerative colitis induced by 5% DSS in drinking water for 7 days | 30 or 60 mg Resv/ kg bw/ day | 14 days | TNF-α: DSS↑, DSS+ Resv ↓  IL-8: DSS↑, DSS+ Resv ↓  IFN-γ: DSS↑, DSS+ Resv ↓  p22phox: DSS↑, DSS+Resv↓  gp91phox DSS↑, DSS+Resv↓ | [21] |
| Control: heterozygote m-  Leprdb mice | type 2 diabetes: homozygous Leprdb mice | 20 mg Resv/ kg bw/ day po | 4 weeks | TNF-α: Leprdb-/-↑, Leprdb-/-+Resv ↓ | [22] |
| C57/B6 mice | Angiotensin II (Ang II) | Resv in drinking water at 0.1 mg/ml (~10 mg Resv/ kg bw/ day | 4 weeks | IL-6: Ang II↑, Ang II+Resv↓ | [23] |
| Female BALB/c mice | Asthma sensitization plus challenge with ovalbumin (OVA) | 30 mg Resv/ kg bw, po | 32 days | Recruitment of leukocytes in lung tissue: OVA↑, OVA+Resv↓  IL-4: OVA↑, OVA+Resv↓  IL-5: OVA↑, OVA+Resv↓ | [24] |
| BALB-c mice of either sex | 100 mg Naphthalene (NAP)/ kg bw/ day, ip for 30 days | 10 mg Resv/ kg bw/ day, po | 30 days | TNFα: NAP↑, NAP+Resv↓  IL-1β: NAP↑, NAP+Resv↓  IL-6: NAP↓, NAP+Resv↑ | [25] |
| BALB/c mice | Injected L1210 cells, ip | 12.5, 25, 50 mg Resv/ kg /day, ig | 3 weeks | IL-6: L1210↑, L1210+Resv↓ | [26] |
| Apolipoprotein E KO mice |  | P183/1-mixture: 27% Resv, 1.37 % caffeic acid and 8.35% cathechin | 8 weeks | In vascular wall:  MCP-1↓; MIPα↓, MIPβ↓, IL6↓; IL10→ | [27] |
| Male Laka mice | Diabetes induced by 200 mg STZ/ kg | 20 mg Resv/ kg bw/ day,  po | 4 weeks | TNFα: STZ↑, STZ+Resv↓, Insulin+ STZ+Resv↓↓ | [28] |
| C57BL/6 mice | EAE: sc immunization with 100 µl of 20 or 150 mg myelin oligoden-drocyte glycoprotein | 100 mg Resv/ kg bw/ day, po | 32 days | EAE+Resv relative to EAE: IL12p40↓, IL13↓, IL17↑, G-CSF↑, MIP1a↓, MCP-1↓, RANTES↓ | [29] |
| Female SKH-1 hairless mice | UVB irradiation | 25 mol Resv in 200 µl ace-  tone per mouse |  | ODC: UVB↑, UVB+Resv↓  COX: UVB↑, UVB+Resv↓ | [30] |
| Balb/C mice | Injected mouse hepatocellular carcinoma  cells H22  On day 11, 0.1 mg LPS/ kg, ip; the mice were killed 90 min later | ip injection with Resv: 500, 1000 or 1500 mg/ kg bw/ day | 10 days | TNFα: LPS↑, LPS+Resv→ | [31] |
| 6-OHDA: 6-hydroxydopamine; ANG II: Angiotensin II; BDL: Bile duct ligation; BLE: bleomycin; COX: Cyclooxygenase; CS: the cigarette smoke; DMN: Dimethylnitrosamine; DSS: dextran sulfate sodium; EAC: Ehrlich ascites carcinoma; EAE: Experimental autoimmune encephalomyelitis; iNOS: inducible Nitrogenoxide Synthase; LPS: Lipopolysacharide; MCT: Monocrotaline; MTX: Methotrexate; NAP: Naphthalene; OBS: Obesity; ODC: Ornithine decarboxylase; OVA: ovalbumin; ST: Steatosis; STZ: Streptozotocin; TNBS: trinitrobenzenesulphonic acid; UVB: Ultraviolet radiation B  ig: intra gastrically; iv: intravenous; ip: intraperitoneally; po: per oral;  Effect are indicated by ↓: reduction; ↑: enhancement; →: no effect. | | | | | |

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