**Supplementary**



Fig.1. supplementary: Scheme showing experimental protocols employed. Diabetes mellitus induction by streptozotocin (STZ) was injected intraperitoneal as a single dose (50 mg/kg) on day (0). Valsartan was given orally daily at dose of 50 mg. Pharmacological regimen was administered from the 9th week and continued for 4 weeks.

**Table 1 supplementary. Reno-therapeutic effect of valsartan on UAE, SBP and DBP in STZ- induced diabetic nephropathy**

UAE, urine albumin excretion, SBP, systolic blood pressure, DBP, diastolic blood pressure, Valsartan treatment started from 8 week. values are means ± SD (n=6-8) and analyzed using one-way ANOVA followed by Tukey’s *post-hoc* test at P<0.05. ¶ compared with vehicle group, \* compared with diabetic control group at the same time point.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Vehicle | Valsartancontrol | Diabeticcontrol | Valsartantreated |
| valsartan *(**Reno-therapeutic)*treatment from: -9 to 12 weeksUAE (mg /day),SBP (mgHg),DBP (mgHg), | 1.04 ± 0.16130.6 ± 5.2678.13 ± 9.64 | 0.96 ± 0.18\*122.6 ± 7.76\*67.50 ± 6.72\* | 33.70 ± 5.90¶161.8 ± 17.45¶#95.25 ± 5.65¶# | 12.66 ± 2.92¶\*146.1 ± 8.24¶\*#89.25 ± 9.22¶ |



Fig.2. Supplementary: Renoprotective and renotherapeutic effect of valsartan on urinary (a: nephrin “ng/ml”, b: KIM-1“pg/ml”) in STZ- induced diabetic nephropathy. Values are mean ± S.D. (n= 6-8), analyzed by one-way ANOVA followed by Tukey's multiple comparisons test. ¶,\*,@ P< 0.05; ¶ compared with vehicle group, \* compared with diabetic control group at the same time point, @ compared with valsartan treated group “renotherapeutic”.



Fig.3. Supplementary: Renoprotective and renotherapeutic effect of valsartan on renal gene expression of (RT-PCR; a: NF-κB, b: ANGPTL2, c: TLR 4, d: integrin) in STZ- induced diabetic nephropathy. Values are mean ± S.D. (n= 6-8), analyzed by one-way ANOVA followed by Tukey's multiple comparisons test. ¶,\* @ P< 0.05; ¶ compared with vehicle group, \* compared with diabetic control group at the same time point,# compared with diabetic control group at week 4, @ compared with valsartan treated group “renotherapeutic”. Angiopoietin-like protein 2 (ANGPTL2), and toll-like receptor 4 (TLR 4).



Fig.4. Supplementary: Renoprotective and renotherapeutic effect of valsartan on renal protein expression (ELISA; a: angiotensin II ”pg/ml protein“, b: TGF-β “ng/ml protein”, c: collagen IV “ng/ml protein”) in STZ- induced diabetic nephropathy. Values are mean ± S.D. (n= 6-8), analyzed by one-way ANOVA followed by Tukey's multiple comparisons test. ¶,\*, @ P< 0.05; ¶ compared with vehicle group,\* compared with diabetic control group at the same time point, @ compared with valsartan treated group “renotherapeutic”.

**Table 4 supplementary. Renotherapeutic effect of valsartan on renal IL-1β, IL-6, TNFα, MCP-1 inflammatory levels**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Vehicle | Valsartan control | Diabetic control | Valsartan treated |
| IL-1β (pg/mg protein) |
| *Reno-therapeutic* | 380.0±23.51 | 351.8±58.72 | 1495±138.10¶ | 816±104.20¶\*# |
| IL-6 (pg/mg protein) |
| *Reno-therapeutic* | 134.3 ± 10.62 | 140.7 ± 33.43 | 591.5 ± 74.53¶  | 307.7± 61.19¶\*# |
| TNFα (pg/mg protein) |
| *Reno-therapeutic* | 85.63± 6.42 | 75.68± 14.31 | 541.5± 60.48¶  | 387.9± 107.10\*# |
| MCP-1 (pg/mg protein) |
| *Reno-therapeutic* | 39.50± 3.02 | 40.13± 7.16 | 152.8± 22.51¶  | 77.37± 15.36¶\*# |

Interleukin (IL), Tumour Necrosis Factor alpha (TNFα), monocyte chemoattractant protein-1 (MPC-1). values are means ± SD (n=6-8) and analyzed using one-way ANOVA followed by Tukey’s *post-hoc* test at P<0.05. Comparison within the same group, ¶ compared with vehicle group, \* compared with diabetic control group,# compared with valsartan group.