

1 **Supplementary materials**

2 **Supplementary Table 1**

3 Literature search strategy for garlic and its derived compounds in the treatment of diabetic kidney
4 disease

| Search Strategy (PubMed) | |
|--------------------------|---|
| #1 | Garlic [Mesh] |
| #2 | garlic [Title/Abstract] |
| #3 | Allium sativum L. [Title/Abstract] |
| #4 | Alliin [Title/Abstract] |
| #5 | S-allylcysteine sulfoxide [Title/Abstract] |
| #6 | PCSO [Title/Abstract] |
| #7 | S-(2-propenyl) cysteine sulfoxide [Title/Abstract] |
| #8 | isoalliin [Title/Abstract] |
| #9 | alliin, (L-Ala)-isomer [Title/Abstract] |
| #10 | alliin, (L-Ala)-(R)-isomer [Title/Abstract] |
| #11 | alliin, (L-Ala)-(S)-isomer [Title/Abstract] |
| #12 | Allicin [Title/Abstract] |
| #13 | thio-2-propene-1-sulfinic acid S-allyl ester [Title/Abstract] |
| #14 | allylthiosulphinic acid allyl ester [Title/Abstract] |
| #15 | diallyl disulfide-oxide [Title/Abstract] |
| #16 | allylthiosulfinate [Title/Abstract] |
| #17 | Allimin [Title/Abstract] |
| #18 | S-allyl cysteine [Title/Abstract] |
| #19 | diallyl trisulfide [Title/Abstract] |
| #20 | allyl trisulfide [Title/Abstract] |
| #21 | Allitridin [Title/Abstract] |
| #22 | Allitridum [Title/Abstract] |
| #23 | Allitrida [Title/Abstract] |
| #24 | Dasuansu [Title/Abstract] |
| #25 | Allyl sulfide [Title/Abstract] |
| #26 | Diallylsulfide [Title/Abstract] |
| #27 | diallyl sulfide [Title/Abstract] |
| #28 | garlic oil [Title/Abstract] |
| #29 | Ajoene [Title/Abstract] |
| #30 | 4,5,9-trithiadodeca-1,6,11-triene 9-oxide [Title/Abstract] |
| #31 | allyl mercaptan [Title/Abstract] |
| #32 | S-methyl L-Cysteine [Title/Abstract] |
| #33 | allyl methyl sulfide [Title/Abstract] |
| #34 | methyl propenyl sulfide [Title/Abstract] |
| #35 | Allylmethylsulfide [Title/Abstract] |
| #36 | 3-methylthio-1-propene [Title/Abstract] |
| #37 | Diallyl disulfide [Title/Abstract] |
| #38 | allyl disulfide [Title/Abstract] |
| #39 | diallyl disulphide [Title/Abstract] |
| #40 | allyll disulfide [Title/Abstract] |
| #41 | Allitin [Title/Abstract] |
| #42 | Garlicin [Title/Abstract] |
| #43 | #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR |

#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17
OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR
#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32
OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR
#40 OR #41 OR #42

- #44 Diabetic Nephropathies [Mesh]
- #45 Diabetic Nephropathies [Title/Abstract]
- #46 Nephropathies, Diabetic [Title/Abstract]
- #47 Nephropathy, Diabetic [Title/Abstract]
- #48 Diabetic Nephropathy [Title/Abstract]
- #49 Diabetic Kidney Disease [Title/Abstract]
- #50 Diabetic Kidney Diseases [Title/Abstract]
- #51 Kidney Disease, Diabetic [Title/Abstract]
- #52 Kidney Diseases, Diabetic [Title/Abstract]
- #53 Diabetic Glomerulosclerosis [Title/Abstract]
- #54 Glomerulosclerosis, Diabetic [Title/Abstract]
- #55 Intracapillary Glomerulosclerosis [Title/Abstract]
- #56 Nodular Glomerulosclerosis [Title/Abstract]
- #57 Glomerulosclerosis, Nodular [Title/Abstract]
- #58 Kimmelstiel-Wilson Syndrome [Title/Abstract]
- #59 Kimmelstiel Wilson Syndrome [Title/Abstract]
- #60 Syndrome, Kimmelstiel-Wilson [Title/Abstract]
- #61 Kimmelstiel-Wilson Disease [Title/Abstract]
- #62 Kimmelstiel Wilson Disease [Title/Abstract]
- #63 #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51
OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR
#59 OR #60 OR #61 OR #62
- #64 #43 AND #63

5

Search Strategy (Web of science)

(TS=(garlic) OR AB=(garlic OR Allium sativum L. OR Alliin OR S-allylcysteine sulfoxide OR PCSO OR S-(2-propenyl)cysteine sulfoxide OR Isoalliin OR alliin, (L-Ala)-isomer OR alliin, (L-Ala)-(R)-isomer OR alliin, (L-Ala)-(S)-isomer OR Allicin OR thio-2-propene-1-sulfinic acid S-allyl ester OR allylthiosulphinic acid allyl ester OR diallyl disulfide-oxide OR allylthiosulfinate OR allimin OR S-allyl cysteine OR diallyl trisulfide OR allyl trisulfide OR allitridin OR allitridum OR allitrida OR Dasuansu OR Allyl sulfide OR Diallylsulfide OR diallyl sulfide OR garlic oil OR ajoene OR 4,5,9-trithiadodeca-1,6,11-triene 9-oxide OR allyl mercaptan OR S-methyl L-Cysteine OR allyl methyl sulfide OR methyl propenyl sulfide OR allylmethylsulfide OR 3-methylthio-1-propene OR Diallyl disulfide OR allyl disulfide OR diallyl disulphide OR allyll disulfide OR allitin OR Garlicin))
AND (TS=(Diabetic Nephropathies) OR AB=(Diabetic Nephropathies OR Nephropathies, Diabetic OR Nephropathy, Diabetic OR Diabetic Nephropathy OR Diabetic Kidney Disease OR Diabetic Kidney Diseases OR Kidney Disease, Diabetic OR Kidney Diseases, Diabetic OR Diabetic Glomerulosclerosis OR Glomerulosclerosis, Diabetic OR Intracapillary Glomerulosclerosis OR Nodular Glomerulosclerosis OR Glomerulosclerosis, Nodular OR Kimmelstiel-Wilson

Syndrome OR Kimmelstiel Wilson Syndrome OR Syndrome, Kimmelstiel-Wilson OR Kimmelstiel-Wilson Disease OR Kimmelstiel Wilson Disease))

6

Search Strategy (Cochrane)

#1 MeSH descriptor: [Diabetic Nephropathies] explode all trees

#2 MeSH descriptor: [Garlic] explode all trees

#3 (Diabetic Nephropathies OR Nephropathies, Diabetic OR Nephropathy, Diabetic OR Diabetic Nephropathy OR Diabetic Kidney Disease OR Diabetic Kidney Diseases OR Kidney Disease, Diabetic OR Kidney Diseases, Diabetic OR Diabetic Glomerulosclerosis OR Glomerulosclerosis, Diabetic OR Intracapillary Glomerulosclerosis OR Nodular Glomerulosclerosis OR Glomerulosclerosis, Nodular OR Kimmelstiel-Wilson Syndrome OR Kimmelstiel Wilson Syndrome OR Syndrome, Kimmelstiel-Wilson OR Kimmelstiel-Wilson Disease OR Kimmelstiel Wilson Disease):ti,ab,kw

#4 (Allium sativum OR garlic OR Alliin OR S allylcysteine sulfoxide OR PCSO OR isoalliin OR Allicin OR allylthiosulphinic acid allyl ester OR diallyl disulfide oxide OR allylthiosulfinate OR allimin OR S allyl cysteine OR diallyl trisulfide OR allyl trisulfide OR allitridin OR allitridum OR allitridi OR Dasuansu OR Allyl sulfide OR diallylsulfide OR diallyl sulfide OR garlic oil OR ajoene OR allyl mercaptan OR S methyl L Cysteine OR allyl methyl sulfide OR methyl propenyl sulfide OR allylmethylsulfide OR Diallyl disulfide OR allyl disulfide OR diallyl disulphide OR allyl disulfide OR allitin OR Garlicin):ti,ab,kw

#1 or #3

#2 or #4

#5 and #6

Search Strategy (Embase)

#1'allium sativum':ab,ti OR garlic:ab,ti OR alliin:ab,ti OR 's allylcysteine sulfoxide':ab,ti OR pcco:ab,ti OR isoalliin:ab,ti OR allicin:ab,ti OR 'allylthiosulphinic acid allyl ester':ab,ti OR 'diallyl disulfide oxide':ab,ti OR allylthiosulfinate:ab,ti OR allimin:ab,ti OR 's allyl cysteine':ab,ti OR 'diallyl trisulfide':ab,ti OR 'allyl trisulfide':ab,ti OR allitridin:ab,ti OR allitridum:ab,ti OR allitridi:ab,ti OR dasuansu:ab,ti OR 'allyl sulfide':ab,ti OR diallylsulfide:ab,ti OR 'diallyl sulfide':ab,ti OR 'garlic oil':ab,ti OR ajoene:ab,ti OR 'allyl mercaptan':ab,ti OR 's methyl l cysteine':ab,ti OR 'allyl methyl sulfide':ab,ti OR 'methyl propenyl sulfide':ab,ti OR allylmethylsulfide:ab,ti OR 'diallyl disulfide':ab,ti OR 'allyl disulfide':ab,ti OR 'diallyl disulphide':ab,ti OR 'allyl disulfide':ab,ti OR allitin:ab,ti OR garlicin:ab,ti

#2'diabetic nephropathies':ab,ti OR 'nephropathies, diabetic':ab,ti OR 'nephropathy, diabetic':ab,ti OR 'diabetic nephropathy':ab,ti OR 'diabetic kidney disease':ab,ti OR 'diabetic kidney diseases':ab,ti OR 'kidney disease, diabetic':ab,ti OR 'kidney diseases, diabetic':ab,ti OR 'diabetic glomerulosclerosis':ab,ti OR 'glomerulosclerosis, diabetic':ab,ti OR 'intracapillary glomerulosclerosis':ab,ti OR 'nodular glomerulosclerosis':ab,ti OR 'glomerulosclerosis, nodular':ab,ti OR 'kimmelstiel-wilson syndrome':ab,ti OR 'kimmelstiel wilson syndrome':ab,ti OR

'syndrome, kimmelstiel-wilson':ab,ti OR 'kimmelstiel-wilson disease':ab,ti OR
'kimmelstiel wilson disease':ab,ti
#1 AND #2

Search Strategy (CNKI)

(主题:大蒜(精确))OR(篇文摘:大蒜+蒜+蒜氨酸+S-烯丙基半胱氨酸亚砷+S-(2-丙烯基)半胱氨酸亚砷+异蒜氨酸+大蒜素+硫代-2-丙烯-1-亚磺酸 S-烯丙基酯+烯丙基硫代磺酸烯丙基酯+烯丙基二硫代氧化物+烯丙基硫代磺酸+S-烯丙基半胱氨酸+二烯丙基三硫化物+烯丙基三硫化物(精确))AND((主题:糖尿病肾病))OR(篇文摘:糖尿病肾病+毛细血管间性肾小球硬化症+糖尿病性肾小球硬化症+结节性肾小球硬化症+糖尿病肾疾病+糖尿病性肾小球硬化症(精确)))

Search Strategy (CBM)

((“糖尿病肾病” OR “毛细血管间性肾小球硬化症” OR “糖尿病性肾小球硬化症” OR “结节性肾小球硬化症” OR “糖尿病肾疾病” OR “糖尿病性肾小球硬化症”) OR (“糖尿病肾病”[不加权:扩展])) AND ((“大蒜” OR “蒜氨酸” OR “S-烯丙基半胱氨酸亚砷” OR “S-(2-丙烯基)半胱氨酸亚砷” OR “异蒜氨酸” OR “蒜氨酸” OR “大蒜素” OR “硫代-2-丙烯-1-亚磺酸 S-烯丙基酯” OR “烯丙基硫代磺酸烯丙基酯” OR “烯丙基二硫代氧化物” OR “烯丙基硫代磺酸” OR “蒜氨酸” OR “S-烯丙基半胱氨酸” OR “二烯丙基三硫化物” OR “烯丙基三硫化物”) OR (“大蒜辣素”[不加权:扩展]) OR “大蒜油制剂”[不加权:扩展]) OR (“大蒜氨酸”[不加权:扩展]) OR (“大蒜”[不加权:扩展]))

Search Strategy (VIP)

题名或关键词=糖尿病肾病 or 毛细血管间性肾小球硬化症 or 糖尿病性肾小球硬化症 or 结节性肾小球硬化症 or 糖尿病肾疾病 or 糖尿病性肾小球硬化症 AND
题名或关键词=大蒜 or 蒜 or 蒜氨酸 or S-烯丙基半胱氨酸亚砷 or 异蒜氨酸 or 蒜氨酸 or 大蒜素 or 硫代-2-丙烯-1-亚磺酸 S-烯丙基酯 or 烯丙基硫代磺酸烯丙基酯 or 烯丙基二硫代氧化物 or 烯丙基硫代磺酸 or 蒜氨酸 or S-烯丙基半胱氨酸 or 二烯丙基三硫化物 or 烯丙基三硫化物

Search Strategy (Wanfang)

(主题:(大蒜) or 题名或关键词:(大蒜 or 蒜 or 蒜氨酸 or S-烯丙基半胱氨酸亚砷 or 异蒜氨酸 or 蒜氨酸 or 大蒜素 or 硫代-2-丙烯-1-亚磺酸 S-烯丙基酯 or 烯丙基硫代磺酸烯丙基酯 or 烯丙基二硫代氧化物 or 烯丙基硫代磺酸 or 蒜氨酸 or S-烯丙基半胱氨酸 or 二烯丙基三硫化物 or 烯丙基三硫化物)) and (主题:(糖尿病肾病) or 题名或关键词:(糖尿病肾病 or 毛细血管间性肾小球硬化症 or 糖尿病性肾小球硬化症 or 结节性肾小球硬化症 or 糖尿病肾疾病 or 糖尿病性肾小球硬化症))

9 **Supplementary Table 2 Risk of bias summary**

| Study | A | B | C | D | E | F | G | H | I | J | Total |
|-----------------------|---|---|---|---|---|---|---|---|---|---|-------|
| Al-Qattan 2008 | ? | ? | ? | + | ? | - | ? | + | + | + | 4 |
| Arellano-Buendía 2018 | ? | ? | ? | + | ? | - | ? | + | + | + | 4 |
| Arellano-Buendía 2020 | ? | ? | ? | + | ? | ? | ? | - | + | + | 3 |
| Hfaiedh 2013 | ? | ? | ? | + | ? | - | ? | + | + | + | 4 |
| Huang 2016 | + | + | ? | + | ? | - | ? | + | + | + | 6 |
| Huang 2017 | ? | + | ? | ? | ? | - | ? | + | + | + | 4 |
| Jiang 2019 | ? | ? | ? | ? | ? | - | ? | - | + | + | 2 |
| Kemmak 2011 | ? | ? | ? | + | ? | - | ? | + | + | + | 4 |
| Luan 2017(A) | ? | ? | ? | ? | ? | - | ? | + | + | + | 3 |
| Luan 2017(B) | ? | ? | ? | ? | ? | - | ? | + | + | + | 3 |
| Mariee 2009 | ? | ? | ? | + | ? | - | ? | + | + | + | 4 |
| Mong 2012 | ? | + | ? | + | ? | - | ? | + | + | + | 5 |
| Nasiri 2017 | ? | ? | ? | + | ? | - | ? | + | + | + | 4 |
| Shen 2022 | - | ? | ? | + | ? | - | ? | + | + | + | 4 |
| Shiju(A) | ? | ? | ? | + | ? | - | ? | + | + | + | 4 |
| Shiju(B) | ? | ? | ? | + | ? | - | ? | + | + | + | 4 |
| Thomson 2013 | ? | - | ? | + | ? | ? | ? | ? | + | + | 3 |
| Venkataiah 2016 | ? | ? | ? | + | ? | - | ? | + | + | + | 4 |
| Yin 2007 | ? | + | ? | + | ? | - | ? | + | + | + | 5 |
| Yu 2008 | ? | + | ? | ? | ? | - | ? | + | + | + | 4 |
| Yu 2010 | ? | ? | ? | ? | ? | - | ? | + | + | + | 3 |
| Yuvashree 2020 | ? | ? | ? | + | ? | - | ? | + | + | + | 4 |
| Zhou 2021 | ? | ? | ? | + | ? | - | ? | + | + | + | 4 |
| Ziamajidi 2017 | ? | + | ? | + | ? | - | ? | + | + | + | 5 |

Note: Selection bias: A, Sequence generation; B, Baseline characteristics; C, Allocation concealment. Performance bias: D, Random housing; E, Blinding. Detection bias: F, Random outcome assessment; G, Blinding. Attrition bias: H, Incomplete outcome data. Reporting bias: I, Selective outcome reporting. Other: J, Other sources of bias. ?, unclear; +, low risk; -, high risk.

Supplementary Table 3 The subgroup analysis of BUN, SCR, 24-hour urine volume, 24h UAER, and BG.

Subgroup 1: Animal species

| Outcomes | Group | No. of animals | SMD (95% CI) | P value | I ² |
|----------------------|-------|----------------|------------------------|----------|----------------|
| BUN | Rats | 11 | -2.54 [-3.59, -1.48] | <0.00001 | 83% |
| | Mice | 5 | -7.11[-10.27, -3.94] | <0.0001 | 85% |
| | Total | 16 | -3.86 [-5.04, -2.69] | <0.00001 | 88% |
| Scr | Rats | 14 | -1.93 [-2.96, -0.89] | =0.0003 | 88% |
| | Mice | 1 | -11.90 [-18.71, -5.09] | =0.0006 | / |
| | Total | 15 | -2.13 [-3.19, -1.07] | <0.0001 | 88% |
| 24-hour urine volume | Rats | 8 | -2.53 [-4.13, -0.93] | =0.002 | 86% |
| | Mice | 4 | -2.92 [-3.55, -2.28] | <0.00001 | 0% |
| | Total | 12 | -2.58 [-3.68, -1.48] | <0.00001 | 84% |
| 24h UAER | Rats | 10 | -2.91 [-4.36, -1.46] | <0.0001 | 91% |
| | Mice | 1 | -4.52 [-7.34, -1.69] | =0.002 | / |
| | Total | 11 | -3.03 [-4.43, -1.64] | <0.0001 | 91% |
| BG | Rats | 19 | -2.79 [-3.67, -1.90] | <0.00001 | 86% |
| | Mice | 4 | -7.31 [-10.52, -4.10] | <0.00001 | 85% |
| | Total | 23 | -3.60 [-4.58, -2.62] | <0.00001 | 89% |

Subgroup 2: Model category

| Outcomes | Group | No. of animals | SMD (95% CI) | P value | I ² |
|----------------------|-------|----------------|-------------------------|----------|----------------|
| BUN | T1DM | 14 | -1.75 [-2.09, -1.40] | <0.00001 | 90% |
| | T2DM | 5 | -2.52 [-3.54, -1.51] | <0.0001 | 80% |
| | Total | 16 | -3.86 [-5.04, -2.69] | <0.00001 | 88% |
| Scr | T1DM | 10 | -1.96 [-3.10, -0.82] | =0.0008 | 85% |
| | T2DM | 5 | -2.18 [-4.64, 0.29] | =0.08 | 92% |
| | Total | 15 | -2.13 [-3.19, -1.07] | <0.0001 | 88% |
| 24-hour urine volume | T1DM | 10 | -2.26 [-3.21, -1.31] | <0.00001 | 82% |
| | T2DM | 2 | -24.05 [-33.71, -14.38] | <0.00001 | 0% |
| | Total | 12 | -2.58 [-3.68, -1.48] | <0.00001 | 84% |
| 24h UAER | T1DM | 7 | -2.67 [-3.83, -1.51] | <0.00001 | 81% |
| | T2DM | 3 | -5.21 [-7.10, -3.32] | <0.00001 | 54% |
| | Total | 10 | -3.42 [-4.60, -2.24] | <0.00001 | 84% |
| BG | T1DM | 16 | -3.45 [-4.60, -2.31] | <0.00001 | 90% |
| | T2DM | 7 | -4.02 [-6.04, -2.01] | <0.0001 | 86% |
| | Total | 23 | -3.60 [-4.58, -2.62] | <0.00001 | 89% |

Subgroup 3: Garlic category

| Outcomes | Group | NO. of Animals | SMD (95% CI) | P value | I ² |
|----------------------|-------------------|----------------|-----------------------|----------|----------------|
| BUN | Garlic products | 5 | -3.95 [-6.20, -1.69] | =0.0006 | 78% |
| | Garlic components | 11 | -3.89 [-5.32, -2.45] | <0.00001 | 91% |
| | Total | 16 | -3.86 [-5.04, -2.69] | <0.00001 | 88% |
| Scr | Garlic products | 6 | -1.79 [-3.83, 0.26] | =0.09 | 89% |
| | Garlic components | 9 | -2.36 [-3.69, -1.04] | =0.0005 | 89% |
| | Total | 15 | -2.13 [-3.19, -1.07] | <0.0001 | 88% |
| 24-hour urine volume | Garlic products | 5 | -6.43 [-10.34, -2.52] | =0.001 | 88% |
| | Garlic components | 7 | -1.84 [-2.86, -0.83] | =0.0004 | 81% |
| | Total | 12 | -2.58 [-3.68, -1.48] | <0.00001 | 84% |
| 24h UAER | Garlic products | 5 | -1.81 [-3.81, 0.19] | 0.08 | 91% |
| | Garlic components | 6 | -3.94 [-5.42, -2.46] | <0.00001 | 80% |

| | | | | | |
|----|------------|----|----------------------|----------|-----|
| | components | | | | |
| | Total | 11 | -3.03 [-4.43, -1.64] | <0.0001 | 91% |
| BG | Garlic | 11 | -3.56 [-4.96, -2.17] | <0.00001 | 85% |
| | products | | | | |
| | Garlic | 12 | -3.67 [-5.09, -2.24] | <0.00001 | 92% |
| | components | | | | |
| | Total | 23 | -3.60 [-4.58, -2.62] | <0.00001 | 89% |

Subgroup 4: Garlic dose (mg/kg/day)

| Outcomes | Group | No. of animals | SMD (95% CI) | P value | I ² |
|----------------------|---------|----------------|----------------------|----------|----------------|
| BUN | < 100 | 5 | -2.01 [-3.49, -0.54] | =0.007 | 89% |
| | 100-400 | 5 | -6.02 [-9.25, -2.80] | =0.0003 | 85% |
| | >400 | 6 | -4.53 [-6.74, -2.33] | <0.0001 | 87% |
| | Total | 16 | -3.86 [-5.04, -2.69] | <0.00001 | 88% |
| Scr | < 100 | 6 | -1.75 [-3.11, -0.39] | =0.01 | 89% |
| | 100-400 | 4 | -5.34 [-9.57, -1.11] | =0.01 | 90% |
| | >400 | 5 | -1.29 [-3.42, 0.84] | =0.23 | 89% |
| | Total | 15 | -2.13 [-3.19, -1.07] | <0.0001 | 88% |
| 24-hour urine volume | < 100 | 3 | -0.50 [-1.07, 0.07] | =0.09 | 0% |
| | 100-400 | 3 | -3.28 [-4.69, -1.87] | <0.00001 | 39% |
| | >400 | 5 | -4.56 [-6.80, -2.32] | <0.0001 | 81% |
| | Total | 11 | -2.78 [-4.02, -1.54] | <0.0001 | 86% |
| 24h UAER | < 100 | 4 | -4.43 [-6.45, -2.42] | <0.0001 | 85% |
| | 100-400 | 2 | -2.91 [-5.34, -0.47] | =0.02 | 62% |
| | >400 | 4 | -1.69 [-4.06, 0.69] | =0.16 | 92% |
| | Total | 10 | -3.12 [-4.66, -1.59] | <0.0001 | 91% |
| BG | < 100 | 8 | -2.51 [-3.80, -1.23] | =0.0001 | 86% |
| | 100-400 | 5 | -3.83 [-6.42, -1.24] | =0.004 | 91% |
| | >400 | 9 | -5.11 [-7.29, -2.92] | <0.00001 | 92% |
| | Total | 22 | -3.69 [-4.72, -2.66] | <0.00001 | 90% |

Subgroup 5: Duration (weeks)

| Outcomes | Group | No. of animals | SMD (95% CI) | P value | I ² |
|----------------------|-------|----------------|----------------------|----------|----------------|
| BUN | < 10 | 8 | -3.22 [-4.63, -1.81] | <0.00001 | 84% |
| | ≥10 | 8 | -4.84 [-6.89, -2.79] | <0.00001 | 91% |
| | Total | 16 | -3.86 [-5.04, -2.69] | <0.00001 | 88% |
| Scr | < 10 | 9 | -2.08 [-3.69, -0.46] | =0.01 | 89% |
| | ≥10 | 6 | -2.36 [-3.73, -0.98] | =0.0008 | 86% |
| | Total | 15 | -2.13 [-3.19, -1.07] | <0.0001 | 88% |
| 24-hour urine volume | < 10 | 7 | -2.46 [-3.59, -1.33] | <0.0001 | 81% |
| | ≥10 | 5 | -3.64 [-6.55, -0.74] | =0.01 | 89% |
| | Total | 12 | -2.58 [-3.68, -1.48] | <0.00001 | 84% |
| 24h UAER | < 10 | 6 | -1.53 [-3.02, -0.03] | =0.05 | 88% |
| | ≥10 | 5 | -4.99 [-7.03, -2.94] | <0.00001 | 84% |
| | Total | 11 | -3.03 [-4.43, -1.64] | <0.0001 | 91% |
| BG | < 10 | 13 | -3.61 [-4.98, -2.24] | =0.01 | 89% |
| | ≥10 | 10 | -3.68 [-5.19, -2.17] | =0.0008 | 86% |
| | Total | 23 | -3.60 [-4.58, -2.62] | <0.00001 | 89% |

Subgroup 6: Route of administration

| Outcomes | Group | No. of animals | SMD (95% CI) | P value | I ² |
|----------------------|------------------------------|----------------|-----------------------|----------|----------------|
| BUN | By intragastric | 9 | -1.84 [-2.81, -0.88] | =0.0002 | 74% |
| | By intraperitoneal injection | 3 | -4.52 [-6.27, -2.77] | <0.00001 | 58% |
| | By free access with meals | 4 | -7.42 [-11.32, -3.53] | =0.0002 | 89% |
| | Total | 16 | -3.86 [-5.04, -2.69] | <0.00001 | 88% |
| Scr | By intragastric | 11 | -1.01 [-1.92, -0.09] | =0.03 | 81% |
| | By intraperitoneal injection | 4 | -4.63 [-5.54, -3.73] | <0.00001 | 0% |
| | By free access with meals | 0 | / | / | / |
| | Total | 15 | -2.13 [-3.19, -1.07] | <0.0001 | 88% |
| 24-hour urine volume | By intragastric | 6 | -1.25 [-2.68, 0.18] | =0.09 | 80% |
| | By intraperitoneal injection | 2 | -5.01 [-6.60, -3.43] | <0.00001 | 0% |
| | By free access with meals | 4 | -2.92 [-3.55, -2.28] | <0.00001 | 0% |
| | Total | 12 | -2.58 [-3.68, -1.48] | <0.00001 | 84% |
| 24h UAER | By intragastric | 8 | -3.00 [-4.75, -1.25] | =0.0008 | 91% |
| | By intraperitoneal injection | 3 | -3.24 [-6.18, -0.30] | =0.03 | 93% |
| | By free access with meals | 0 | / | / | / |
| | Total | 11 | -3.03 [-4.43, -1.64] | <0.0001 | 91% |
| BG | By intragastric | 15 | -1.82 [-2.53, -1.11] | <0.00001 | 74% |
| | By intraperitoneal injection | 4 | -6.47 [-9.83, -3.12] | =0.0002 | 91% |
| | By free access with meals | 4 | -7.31 [-10.52, -4.10] | <0.00001 | 85% |
| | Total | 23 | -3.60 [-4.58, -2.62] | <0.00001 | 89% |

Supplementary Table 4 Meta-regression analysis of BUN, Scr, 24 h urine volume, 24h UAER, and BG.

Table 4.1 Characteristics for BUN

| Outcomes | Characteristics (covariates) (n=4) | coefficient t | 95% CI | P value | |
|----------|------------------------------------|------------------|-------------|-------------|------|
| BUN | Study quality score | -0.58 | -2.26, 1.11 | 0.50 | |
| | No. sample size | 0.08 | -0.16, 0.32 | 0.68 | |
| | Region ^a | China | -1.69 | -7.18, 3.80 | 0.55 |
| | | Others | -1.59 | -7.83, 4.65 | 0.62 |
| | Year of Pub. ^b | 3.84 | 0.88, 6.79 | 0.01 | |

P value showed that the Year of Publication of the Characteristics had an impact on result of BUN. (Region^a: The region divided into Western, China, and others. When performing meta-regression analysis, the Western was used as a reference object. Year of Pub.^b: Year of publication divided into 2007 to 2016, 2017 to 2022)

Table 4.2 Characteristics for Scr

| Outcomes | Characteristics (covariates) (n=4) | coefficient t | 95% CI | P value | |
|----------|------------------------------------|------------------|-------------|--------------|------|
| Scr | Study quality score | 1.65 | 0.25, 3.06 | 0.02 | |
| | No. sample size | -0.07 | -0.32, 0.18 | 0.58 | |
| | Region ^a | China | -1.79 | -5.34, -1.76 | 0.32 |
| | | Others | 2.04 | -1.55, 5.63 | 0.27 |
| | Year of Pub. ^b | 0.24 | -3.00, 3.47 | 0.89 | |

P value showed that the Study quality score of the Characteristics had an impact on result of Scr. (Region^a: The region divided into Western, China, and others. When performing meta-regression analysis, the Western was used as a reference object. Year of Pub.^b: Year of publication divided into 2007 to 2016, 2017 to 2022)

Table 4.3 Characteristics for 24h urine volume

| Outcomes | Characteristics (covariates) (n=4) | coefficient t | 95% CI | P value | |
|----------------------------|------------------------------------|------------------|-------------|---------------|------|
| 24-hour urine volume | Study quality score | -0.10 | -1.95, 1.75 | 0.92 | |
| | No. sample size | 0.11 | -0.13, 0.36 | 0.36 | |
| | Region ^a | China | 0.93 | -5.83, 7.69 | 0.79 |
| | | Others | -8.63 | -16.95, -0.30 | 0.04 |
| | Year of Pub. ^b | 2.71 | 1.39, 4.03 | 0.00 | |

P value showed that the (1) Region (2) Year of Publication of the Characteristics had an impact on result of 24h urine volume. ((Region^a: The region divided into Western, China, and others. When performing meta-regression analysis, the Western was used as a reference object. Year of Pub.^b: Year of publication divided into 2007 to 2016, 2017 to 2022)

Table 4.4 Characteristics for 24h UAER

| Outcomes | Characteristics (covariates) (n=4) | coefficient t | 95% CI | P value | |
|-------------|------------------------------------|------------------|-------------|--------------|------|
| 24h UAER | Study quality score | -1.46 | -3.03, 0.11 | 0.07 | |
| | No. sample size | 0.07 | -0.27, 0.42 | 0.68 | |
| | Region ^a | China | -2.60 | -8.63, 3.42 | 0.40 |
| | | Others | -4.81 | -12.03, 2.42 | 0.19 |
| | Year of Pub. ^b | -0.68 | -4.24, 2.88 | 0.71 | |

P value showed that no item had any impact on result of 24h UAER. (Region^a: The region divided into Western,

China, and others. When performing meta-regression analysis, the Western was used as a reference object. Year of Pub.^b: Year of publication divided into 2007 to 2016, 2017 to 2022)

Table 4.5 Characteristics for BG

| Outcomes | Characteristics (covariates) (<i>n</i> =4) | coefficient t | 95% CI | <i>P</i> value |
|-----------|---|------------------|--------------|----------------|
| BG | Study quality score | -0.59 | -2.39, 1.20 | 0.52 |
| | No. sample size | -0.27 | -0.49, -0.06 | 0.01 |
| | Region ^a China | 0.14 | -4.04, 4.32 | 0.95 |
| | Others | 0.70 | -3.40, 4.81 | 0.74 |
| | Year of Pub. ^b | 2.92 | -.002, 5.84 | 0.05 |

P value showed that the Sample size had an impact on result of BG. (Region^a: The region divided into Western, China, and others. When performing meta-regression analysis, the Western was used as a reference object. Year of Pub.^b: Year of publication divided into 2007 to 2016, 2017 to 2022)

BUN: Blood urea nitrogen; SCR: serum creatinine; UAER: urinary albumin excretion rates, BG: blood glucose