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A nephrological perspective of herbal remedies on the progression of chronic kidney disease: A systematic review

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SUPPLEMENTARY MATERIAL

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			htyui
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	1. Identify the report as a systematic review. 2. Provide an explicit statement of the main objective(s) or question(s) the review addresses. 3. Specify the inclusion and exclusion criteria for the review. 4. Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched. 5. Specify the methods used to assess risk of bias in the included studies. 6. Specify the methods used to present and synthesise results. 7. Give the total number of included studies and participants and summarise relevant characteristics of studies. 8. Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured). 9. Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision). 10. Provide a general interpretation of the results and important implications. 11. Specify the primary source of funding for the review. 12. Provide the register name and registration number.	1. Reported 2. Reported 3. Haven't been mentioned due to the word limitations of the abstract set by the journal 4. Haven't been mentioned due to the word limitations of the abstract set by the journal 5. Reported 6. Reported 7. Reported 8. Reported but without mentioning the number of participants of each study 9. Haven't been mentioned due to the word limitations of the abstract set by the journal 10. Reported 11. Reported: "Therefore, this unfunded review was conducted to provide a more detailed picture on this issue.." 12. Not applicable
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pages 3-4; lines 51-81
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 4; lines 78-81
METHODS			

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pages 4-5; lines 90-94
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 4; lines 84-85
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Pages 4-5; lines 85-100
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5; lines 94-98
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 4-5; lines 94-98
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 5; lines 101-106
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Pages 4-5; lines 90-94
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5-6; lines 107-117 Risk of bias assessment was conducted using ROB-2 tool for included studies.
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Not applicable to this systematic review
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Not applicable to this systematic review
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Not applicable to this systematic review
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Not applicable to this systematic review

Section and Topic	Item #	Checklist item	Location where item is reported
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Not applicable to this systematic review
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Not applicable to this systematic review
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not applicable to this systematic review
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Not applicable to this systematic review
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Not applicable to this systematic review
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 28
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Not applicable for a systematic review paper though the followings 28 articles were included at first but then excluded as the review article aimed at including studies conducted solely on human subjects: Abd El Motteleb DM, Abd El Aleem DI. Renoprotective effect of Hypericum perforatum against diabetic nephropathy in rats: Insights in the underlying mechanisms. Clin Exp Pharmacol Physiol 2017;44(4):509-521. doi: https://doi.org/10.1111/1440-1681.12729. Ahn YM, Kim SK, Lee SH, Ahn SY, Kang SW, Chung JH, et al. Renoprotective effect of Tanshinone IIA, an active component of Salvia miltiorrhiza, on rats with chronic kidney disease. Phytother Res 2010;24(12):1886-1892. doi: https://doi.org/10.1002/ptr.3347 Akinyemi AJ, Onyebueke N, Faboya OA, Onikanni SA, Fadaka A, Olayide I. Curcumin inhibits adenosine deaminase and arginase activities in cadmium-induced renal toxicity in rat kidney. J Food Drug Anal 2017;25(2):438-446. https://doi.org/10.1016/j.jfda.2016.06.004 Chen G, Tan ML, Li KK, Leung PC, Ko CH. Green tea polyphenols decreases uric acid level through xanthine oxidase and renal urate transporters in hyperuricemic mice. J Ethnopharmacol 2015;175:14-20. doi: https://doi.org/10.1016/j.jep.2015.08.043. Chen H, Wang MC, Chen YY, Chen L, Wang YN, Vaziri ND, et al. Alisol B 23-acetate attenuates CKD progression by regulating the renin–angiotensin system and gut–kidney axis. Therapeutic advances in chronic disease 2020;11:2040622320920025. doi: https://doi.org/10.1177/2040622320920025 Chen H, Yang T, Wang MC, Chen DQ, Yang Y, Zhao YY. Novel RAS inhibitor 25-O-methylalisol F attenuates epithelial-to-mesenchymal transition and tubulo-interstitial fibrosis by selectively inhibiting TGF-β-mediated Smad3

Section and Topic	Item #	Checklist item	Location where item is reported
			phosphorylation. Phytomedicine 2018;42:207-218. doi: https://doi.org/10.1016/j.phymed.2018.03.034 Ghalehkandi JG, Ebrahimnezhad Y, Nobar RS. Effect of garlic (Allium sativum) aqueous extract on serum values of urea, uric-acid and creatinine compared with chromium chloride in male rats. Annals of Biological Research 2012;3(9):4485-4490. Gondwe M, Kamadyaapa DR, Tufts M, Chuturgoon AA, Musabayane CT. Sclerocarya birrea [(A. Rich.) Hochst.][Anacardiaceae] stem-bark ethanolic extract (SBE) modulates blood glucose, glomerular filtration rate (GFR) and mean arterial blood pressure (MAP) of STZ-induced diabetic rats. Phytomedicine 2008;15(9):699-709. doi: https://doi.org/10.1016/j.phymed.2008.02.004 Guo H, Kuang Z, Zhang J, Zhao X, Pu P, Yan J. The preventive effect of Apocynum venetum polyphenols on D-galactose-induced oxidative stress in mice. Exp Ther Med 2020;19(1):557-568. doi: https://doi.org/10.3892/etm.2019.8261 Han L, Ma Y, Qin JG, Li LN, Gao YS, Zhang XY, et al. The renal protective effect of jiangya tongluo formula, through regulation of adrenomedullin and angiotensin II, in rats with hypertensive nephrosclerosis. Evid Based Complement Alternat Med 2015; 2015. doi: https://doi.org/10.1155/2015/428106 Hou CW, Lee YC, Hung HF, Fu HW, Jeng KC. Longan seed extract reduces hyperuricemia via modulating urate transporters and suppressing xanthine oxidase activity. Am J Chin Med 2012;40(05):979-991. doi: https://doi.org/10.1142/S0192415X12500723 Hou PY, Mi C, He Y, Zhang J, Wang SQ, Yu F, et al. Pallidifloside D from Smilax riparia enhanced allopurinol effects in hyperuricemia mice. Fitoterapia 2015;105:43-48. doi: https://doi.org/10.1016/j.fitote.2015.06.002. Hu QH, Zhu JX, Ning LI, Miao MX. Effect of jasminoidin on potassium oxonate-induced hyperuricemia in mice and its mechanism. Central South Pharmacy 2013;11(10):721-725. Hua J, Huang P, Zhu CM, Yuan X, Yu CH. Anti-hyperuricemic and nephroprotective effects of Modified Simiao Decoction in hyperuricemic mice. J of Ethnopharmacol 2012;142(1):248-252. doi: https://doi.org/10.1016/j.jep.2012.04.052 Li W, Jiang YH, Wang Y, Zhao M, Hou GJ, Hu HZ, et al. Protective effects of combination of radix astragali and radix salviae miltiorrhizae on kidney of spontaneously hypertensive rats and renal intrinsic cells. Chin J Integr Med 2020;26(1):46-53. doi: https://doi.org/10.1007/s11655-019-3071-1 Liu W, Lin S, Cai Q, Zhang L, Shen A, Chen Y, et al. Qingxuan jiangya decoction mitigates renal interstitial fibrosis in spontaneously hypertensive rats by regulating transforming growth factor-β1/smad signaling pathway. Evid Based Complement Alternat Med 2017;2017. doi: https://doi.org/10.1155/2017/1576328 Luo WM, Kong J, Gong Y, Liu XQ, Yang RX, Zhao YX. Tongxinluo protects against hypertensive kidney injury in spontaneously-hypertensive rats by inhibiting oxidative stress and activating forkhead box O1 signaling. PloS One 2015;10(12):e0145130. doi: https://doi.org/10.1371/journal.pone.0145130 Ojewole JA. Antinociceptive, anti-inflammatory and antidiabetic properties of Hypoxis hemerocallidea Fisch. & CA Mey.(Hypoxidaceae) corm ['African Potato'] aqueous

Section and Topic	Item #	Checklist item	Location where item is reported
			extract in mice and rats. J of ethnopharmacol 2006;103(1):126-134. doi: https://doi.org/10.1016/j.jep.2005.07.012. Qin T, Wu L, Hua Q, Song Z, Pan Y, Liu T. Prediction of the mechanisms of action of Shenkang in chronic kidney disease: a network pharmacology study and experimental validation. J Ethnopharmacol 2020; 246:112128. doi: https://doi.org/10.1016/j.jep.2019.112128 Shi S, Zhang RT, Shang XY, Wang N, Sen LI, Zhang ZS. Effect of puerarin on serum uric acid in hyperuricemic rats. Food Science & Technology 2014;39(2):216-219. Tian JY, Tao RY, Zhang XL, Liu Q, He YB, Su YL, et al. Effect of Hypericum perforatum L. Extract on Insulin Resistance and Lipid Metabolic Disorder in High-Fat-Diet Induced Obese Mice. Phytother Res 2015;29(1):86-92. doi: https://doi.org/10.1002/ptr.5230. Wang X, Wang H, Zhang Y. Research of polygonim sibircum laxm alcohol extract in reducing formation and excretion of uric acid in hyperuricemia mice. Traditional Chinese Drug Research & Clinical Pharmacology 2015;5**:**626–631. Yan D, Yue B, Qian M, Zhao L, Zhang Z, Qian H, et al. JYYS granule mitigates renal injury in clinic and in spontaneously hypertensive rats by inhibiting NF-κB signaling-mediated microinflammation. Evid Based Complement Alternat Med: eCAM 2018;2018. doi: https://doi.org/10.1155/2018/8472963 Zeng JX, Bi Y, Wei J, Zhu YY, Zhu JX, Wang XY. The research of Plantago asiatica L. Herbs extracts reduce the level of uric acid in hyperuricemia mice and it's mechanism. Lishizhen Medicine and Materia Medica Research 2013;24:2064-2066. Zeng JX, Bing-Bing XU, Min LI. Effect of Lagotis brevituba Maxim. Extract in reducing uric acid level in hyperuricemia mice and it's mechanism. Chinese Journal of New Drugs 2015;24(21):2489-2493. Zhou H, Chen Y. Activity and mechanism research of bergenin on hyperuricemic. Acta Universitatis Medicinalis Anhui 2014; 49, pp. 63–67. Zhou Q, Zhang C, Dong-Hua YU, Liu SM. Study on uric acid reducing effect of total saponins from Rhizoma Dioscoreae Nipponicae in treating hyperuricemia and in vitro study of its anti-inflammatory effect. China Journal of Traditional Chinese Medicine Pharmacy 2013;28(5):1444-1448. Zhu J, Zhang Y, Yang C. Protective effect of 3-n-butylphthalide against hypertensive nephropathy in spontaneously hypertensive rats. Mol Med Rep 2015;11(2):1448-1454.doi: https://doi.org/10.3892/mmr.2014.2791
Study characteristics	17	Cite each included study and present its characteristics.	Pages 6-15; lines 119-325
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Risk of bias assessment was conducted using ROB-2 tool for included studies. A summary of the assessment is presented in table I (Pages 29-32) and Figure 2 (Page 28).
Results of	19	For all outcomes, present, for each study: (a) summary statistics	Not applicable to this systematic review

Section and Topic	Item #	Checklist item	Location where item is reported
individual studies		for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Not applicable to this systematic review
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Not applicable to this systematic review
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Not applicable to this systematic review
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable to this systematic review
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not applicable to this systematic review
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Not applicable to this systematic review
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pages 6-15; lines 119-325
	23b	Discuss any limitations of the evidence included in the review.	Page 15; lines 326-335
	23c	Discuss any limitations of the review processes used.	Page 15; lines 326-335
	23d	Discuss implications of the results for practice, policy, and future research.	Page 16; lines 347-362
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	The review was not registered.
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	A protocol was not prepared
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable for this systematic review
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 17; lines 373-374
Competing interests	26	Declare any competing interests of review authors.	Page 17; lines 371-372
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code;	Available upon request.

Section and Topic	Item #	Checklist item	Location where item is reported
		any other materials used in the review.	

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71