

REVIEW THESIS

**EFFICACY AND SAFETY OF POMEGRANATE SEED OIL AS PART OF
THE COMPREHENSIVE TREATMENT OF PATIENTS WITH ACUTE
KIDNEY INJURY**

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Abstract. Pomegranate seed oil (PSO) is rich in punicic acid, a conjugated linolenic acid associated with antioxidant and anti-inflammatory activity in experimental models. These properties create a plausible rationale for studying PSO as an adjunct to standard treatment during recovery from acute kidney injury (AKI). This narrative review evaluates the efficacy and safety evidence relevant to that proposal. Animal studies of gentamicin-, cisplatin-, mercury-, and other toxin-associated renal injury have reported lower oxidative stress, improved biochemical markers, and less histological damage with PSO. Human trials of PSO have been conducted in hyperlipidemia, type 2 diabetes, menopausal symptoms, and mild cognitive impairment, but not specifically in patients with AKI. Their heterogeneous formulations, doses, durations, and outcomes do not establish renal efficacy. Available human studies suggest short-term tolerability, yet they are too small and clinically different from AKI populations to define safety in patients with unstable kidney function. PSO should therefore not replace guideline-based care or be recommended routinely for AKI. Its clinical role can be determined only through an ethics-approved trial using a standardized product, predefined eligibility criteria, renal and hepatic monitoring, adverse-event surveillance, and clinically relevant recovery outcomes.

Keywords. acute kidney injury; pomegranate seed oil; punicic acid; traditional medicine; oxidative stress; renal recovery; safety monitoring

Introduction. Standard management of AKI focuses on identification and correction of the cause, restoration of effective perfusion when appropriate, treatment of infection, avoidance or dose adjustment of nephrotoxic medicines, management of fluid and electrolyte disturbances, nutritional support, and renal replacement therapy when indicated [1,2]. No plant oil has an established role in routine AKI treatment. Nevertheless, oxidative stress, mitochondrial dysfunction, inflammatory signaling, and microvascular injury contribute to many AKI phenotypes, creating interest in adjunctive interventions that could support recovery without delaying standard care. PSO is obtained from *Punica granatum* seeds and contains a high proportion of punicic

acid together with other fatty acids and minor bioactive constituents [3-5]. Its use in traditional medicine and experimental nephroprotection requires a careful distinction between biological plausibility and proven clinical benefit.

Aim. To evaluate the current evidence for the efficacy and safety of PSO as an adjunct to comprehensive treatment in patients with AKI and to define requirements for a clinically valid future study.

Materials and methods. A focused narrative review was conducted using PubMed-indexed experimental studies, human clinical trials, reviews of pomegranate seed composition, AKI guidance, and trial-registry information available through 15 September 2026. Search concepts combined pomegranate seed oil, puniic acid, renal injury, nephrotoxicity, acute kidney injury, efficacy, safety, and clinical trial. Evidence was grouped as mechanistic, preclinical renal, human non-AKI, and AKI-specific. The principal question was whether the available evidence supports routine clinical use in AKI rather than whether PSO shows activity in any experimental or metabolic setting.

Results and discussion. Puniic acid is a conjugated linolenic acid that can influence lipid metabolism, inflammatory signaling, and oxidative balance. Experimental studies describe reductions in lipid peroxidation and preservation of endogenous thiol or antioxidant systems after PSO exposure [3-6]. In toxin-induced renal injury models, PSO has been associated with lower serum creatinine or urea, reduced urinary protein loss, and milder tubular degeneration compared with untreated injured animals [6-8]. These findings are biologically relevant because tubular oxidative injury is a component of several AKI phenotypes. However, most studies used pretreatment, animal-specific doses, and defined nephrotoxins. They do not reproduce the heterogeneity of human AKI caused by sepsis, shock, surgery, obstruction, or multiple simultaneous exposures.

Human evidence and limits of transferability. Randomized or controlled human studies have evaluated PSO in hyperlipidemia, type 2 diabetes, menopausal symptoms, and mild cognitive impairment [9-12]. These trials demonstrate that oral PSO can be administered to selected ambulatory participants and provide preliminary information on tolerability. Their efficacy results are mixed and relate to lipid, metabolic, hormonal, or neurocognitive outcomes rather than renal recovery. No published controlled trial specifically evaluating PSO in patients with AKI was identified in the reviewed literature. Therefore, improvements observed in animal nephrotoxicity models cannot be translated directly into claims of shorter recovery, reduced dialysis requirement, or protection of liver function in human AKI. The current evidence supports a research hypothesis, not a treatment recommendation.

Safety considerations. AKI patients have rapidly changing glomerular filtration, altered volume of distribution, acid-base and electrolyte abnormalities, reduced appetite, nausea, and frequent polypharmacy. A product tolerated by stable outpatients may behave differently during acute illness. Safety assessment should include allergy history, gastrointestinal intolerance, aspiration risk, bleeding risk when anticoagulants or antiplatelet agents are used, and possible interactions with medicines metabolized by hepatic enzymes or transporters. Product variability is another major concern: botanical identity, extraction method, punicic-acid content, oxidation indices, contaminants, storage conditions, and batch reproducibility should be documented. Animal doses must not be converted directly into clinical prescriptions without pharmacokinetic and dose-escalation data. During a trial, creatinine, urine output, estimated renal function after stabilization, ALT, AST, bilirubin, coagulation status when relevant, and all adverse events should be recorded.

Place within comprehensive treatment. If PSO is studied clinically, it should be added only after diagnostic evaluation and hemodynamic stabilization, when enteral intake is safe. It must not delay antibiotics for sepsis, relief of obstruction, withdrawal of a nephrotoxin, correction of hypovolemia, or renal replacement therapy. A pilot randomized controlled design could compare standard care with standard care plus a standardized PSO preparation. Eligibility should exclude known pomegranate allergy, inability to take enteral products, active major bleeding, uncontrolled hepatic failure, pregnancy unless specifically justified, and use of interacting medicines that cannot be monitored. The PSO dose should be selected through prior safety work rather than animal-dose extrapolation. Randomization, allocation concealment, predefined rescue criteria, and independent adverse-event review are needed to minimize bias and protect participants.

Outcome framework. A future study should define renal recovery before enrollment. Relevant outcomes include time to stable serum creatinine improvement, duration of oliguria, change in AKI stage, renal replacement therapy-free days, length of stay, kidney function at 30 and 90 days, and transition to acute kidney disease or chronic kidney disease. Hepatic outcomes are especially relevant to the proposed comprehensive approach and may include ALT, AST, bilirubin, alkaline phosphatase, albumin, and the international normalized ratio, interpreted within clinical context. Patient-reported gastrointestinal symptoms, adherence, and product acceptability should accompany conventional safety outcomes. Laboratory biomarkers of oxidative stress may explain mechanism but should remain secondary to validated clinical outcomes.

Conclusion. PSO has a plausible antioxidant and anti-inflammatory rationale and has shown nephroprotective signals in experimental toxic-injury models. Human experience in other conditions provides limited preliminary tolerability information but does not establish efficacy or safety in AKI. Routine clinical use as part of AKI treatment is not currently supported. A standardized, ethically approved, prospectively registered pilot trial is required to determine dose, safety, interactions, adherence, and any effect on renal and hepatic recovery. Until such evidence is available, PSO should be regarded as an investigational adjunct and never as a substitute for guideline-based comprehensive care.

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