Journal of Translational Critical Care Medicine **2026** vol. 8(3) | e00004S
DOI: 10.14218/JTCCM.2026.00004S

Review Article

Selected Extracorporeal Treatment Options in Acute Poisoning: A Focused Narrative Review of Hemoadsorption in Clinical Practice

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Received: June 15, 2026 | **Revised:** September 12, 2026 | **Accepted:** September 30, 2026 | **Published online:** September 30, 2026

Abstract

Extracorporeal treatment (ECTR) is used in selected severe poisonings to enhance toxin elimination and, in some cases, provide temporary organ support. Modalities include intermittent hemodialysis, continuous renal replacement therapy, and sorbent-based hemoperfusion or hemoadsorption, each with distinct mechanisms and toxicokinetic implications. This narrative review summarizes modality-specific and toxin-specific evidence, operational treatment characteristics, patient-centered and toxicokinetic outcomes, safety considerations, and scenarios in which ECTR should be withheld, and proposes a practical five-step bedside algorithm. Sources were identified through targeted searches of PubMed/MEDLINE and Google Scholar, supplemented by Extracorporeal Treatments in Poisoning (EXTRIP) consensus documents, reference-list screening, and author expertise. The evidence base varies substantially across toxins. For several pharmaceutical poisonings, EXTRIP provides the most actionable guidance on indications, preferred modality, and stopping criteria, while recommending against ECTR for digoxin and methotrexate. Outside these consensus-guided settings, the largest experience with sorbent therapies concerns paraquat and organophosphorus/carbamate poisoning, although the literature is regionally concentrated and predominantly observational. In paraquat poisoning, hemoadsorption-containing strategies have been associated with improved survival in observational cohorts, while pharmacokinetic studies support early and repeated treatment in selected patients because of ongoing toxin removal and post-treatment rebound. In organophosphorus/carbamate poisoning, comparative studies suggest possible benefit in severe presentations, but certainty remains low. In diquat poisoning, recent reports emphasize concentration-directed extracorporeal strategies. Evidence for other toxins is largely limited to feasibility, toxin removal, and case-based experience. ECTR should therefore be regarded as a toxin-specific therapeutic toolbox rather than a uniform intervention. Where available, EXTRIP recommendations should guide practice. Otherwise, modality selection should integrate toxicokinetic plausibility, clinical severity, feasibility, and safety. Prospective studies using standardized prescriptions and clinically meaningful endpoints are needed.

Introduction

Extracorporeal treatment (ECTR) in poisoning encompasses a heterogeneous set of extracorporeal techniques with distinct mechanisms and clinical objectives, and should not be framed simplistically as "hemodialysis versus all other techniques".[1,2] The choice of modality depends on the toxin and on the clinical context, and it combines toxicokinetic reasoning, such as protein binding, volume of distribution, and endogenous clearance, with feasibility at the bedside, such as hemodynamic stability, the trajectory of severity, and local resources.[1,2] Intermittent hemodialysis (IHD) therefore takes precedence when it is effective and technically achievable for a given toxin, whereas sorbent-based blood purification and

Keywords: Extracorporeal treatment; Poisoning; Hemodialysis; Continuous renal replacement therapy; Hemoperfusion; Hemoadsorption.
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How to cite this article: Klinkmann G, Ronco C; on behalf of the Studies Utilizing Blood Purification in Limiting the Overdose in Treatments (SUBPLOT) Investigators. Selected Extracorporeal Treatment Options in Acute Poisoning: A Focused Narrative Review of Hemoadsorption in Clinical Practice. *J Transl Crit Care Med* 2026;8(3):e00004S. DOI: 10.14218/JTCCM.2026.00004S.

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extracorporeal life support have a place when the mechanism justifies them or when the aim is organ support rather than clearance of toxin.[1-3]

The evidence base is uneven. For several drugs, graded recommendations from the Extracorporeal Treatments in Poisoning (EXTRIP) Workgroup give the most usable bedside guidance by defining indications, the preferred modality, and criteria for stopping, as in metformin and carbamazepine poisoning, and by advising against ECTR for digoxin and methotrexate.[4-7] Much of the published experience with sorbent-based hemoperfusion or hemoadsorption (HP/HA), often with resin hemoadsorption cartridges, is observational and geographically concentrated. The largest cohorts with clinical endpoints concern paraquat poisoning, while comparative evidence in organophosphorus and carbamate poisoning includes one randomized trial in the intensive care unit (ICU) and a pooled analysis of randomized studies.[8-12] Small series and single cases extend ECTR to other toxicants such as 2,4-dichlorophenoxyacetic acid (2,4-D), 2,4-dinitrophenol (2,4-DNP), diquat, chloroform, and colchicine, but they rarely allow universal thresholds for starting treatment to be derived, and they seldom separate the effect of ECTR from that of concomitant interventions.[13-17]

The purpose of this narrative review is to synthesize mechanistic, toxicokinetic, and clinical evidence on ECTR into a framework specific to each toxin that clarifies when treatment is likely to help, which modality and intensity the evidence supports, and when treatment should be withheld.[1,2] We pursue four specific aims. The first is to describe, for each toxin and exposure context, which modality was used, with operational parameters and treatment intensity where these were reported. The second is to summarize reported outcomes, giving precedence to endpoints that matter to patients, such as mortality, length of stay in the ICU, and duration of mechanical ventilation, alongside toxicokinetic data where available. The third is to set out considerations that cut across toxins, including complications of the extracorporeal circuit, unintended adsorption of concomitant medication during sorbent therapy, and the situations in which ECTR should not be started.[1,2,18,19] The fourth is to develop from these elements a practical five-step algorithm for use at the bedside. Where graded consensus exists, in particular the recommendations of the EXTRIP Workgroup, it takes precedence in our synthesis, and the nature of the supporting evidence is labeled throughout the Results. This review is narrative and non-systematic by design, and the algorithm proposed here is an expert synthesis that requires prospective validation.

This is a narrative review informed by expert appraisal, written to bring mechanistic reasoning, consensus recommendations, and representative clinical experience together into a framework for practice. No review protocol was registered, and we used neither a protocol-driven search algorithm nor a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram nor quantitative synthesis. Literature was retrieved by targeted searches of PubMed/MEDLINE and Google Scholar with combinations of terms such as extracorporeal treatment, hemoperfusion, hemoadsorption, hemodialysis, blood purification, and poisoning or intoxication, together with the names of individual toxins, among them paraquat, diquat, organophosphate, carbamazepine, metformin, 2,4-D, 2,4-DNP, chloroform, and colchicine. We added the toxin-specific EXTRIP consensus documents and consulted the workgroup's online compilation of recommendations (EXTRIP Workgroup. Recommendations. https://www.extrip-workgroup.org/recommendations. Accessed April 07, 2026).[4-7] We hand-searched the reference lists of retrieved articles and drew on our own subject knowledge. No restriction of date, language, or study design was imposed.

We considered consensus recommendations specific to individual toxins, randomized trials, observational cohorts, pharmacokinetic clearance studies, case reports and series, and *in vitro* adsorption experiments. For each source we recorded the toxin or exposure context, the population, the modality and its operational parameters, the strategy for starting treatment including timing and intensity where reported, outcomes covering both toxin kinetics and clinical endpoints, and safety data covering complications of the procedure and unintended adsorption of concomitant medication.

Given the narrative design, no formal instrument for scoring risk of bias or for grading certainty was applied, and studies were appraised qualitatively according to design and reporting. Two toxin classes dominate the sorbent literature and call for particular caution. Evidence on paraquat and on organophosphorus or carbamate poisoning rests largely on cohorts from single countries, is overwhelmingly observational, and is open to selection bias arising from systematic differences between patients who present early and those who present late, to confounding by severity of illness and by concomitant treatment, to allocation influenced by access and cost, and to bias in publication and language. To limit our own interpretive bias, we gave precedence to graded EXTRIP recommendations where they exist, labeled nonrandomized and single case evidence as such throughout the Results, and avoided presenting kinetic endpoints as evidence of clinical benefit. Associations reported in observational studies should therefore be read as generating hypotheses rather than as demonstrating benefit. A consolidated appraisal of the limitations of the evidence and of this review appears in a dedicated section before the Conclusions.

Herbicides and industrial toxicants

Paraquat

Paraquat is a quaternary bipyridyl herbicide of molecular weight 186.25 Da. It is highly water-soluble, strongly hydrophilic, minimally bound to protein, and eliminated largely unchanged by the kidney. On toxicokinetic grounds these properties favor removal by an extracorporeal circuit soon after ingestion, but rapid distribution into tissue works against this, above all active uptake into the lung, where paraquat accumulates and drives redox cycling with generation of reactive oxygen species. The resulting syndrome comprises acute lung injury, renal dysfunction, hepatic injury and, in survivors, progressive pulmonary fibrosis. In our interpretation, HA and membrane-based techniques are therefore most likely to matter biologically when started very early, before extensive sequestration in tissue, and a later rise in concentration after treatment more plausibly reflects redistribution from peripheral compartments than failure of the extracorporeal circuit.[20]

Paraquat is the most extensively represented toxin in this review. The evidence spans observational cohorts from single and multiple centers, analyses of pharmacokinetic clearance, and case

reports.[8-10,21-24] ECTR is delivered predominantly as HA, for example with a resin hemoadsorption cartridge, combined with continuous renal replacement therapy (CRRT), usually continuous venovenous hemofiltration (CVVH), or with IHD.[8-10,21-24] Prescriptions range from short standardized sessions, such as HA for 2 hours at a blood flow of 200 mL/min in one pharmacokinetic study, to repeated sessions across the first 48 to 72 hours, and to combinations such as HA followed by 72 hours of CVVH.[8-10] All of these studies stress early initiation and intensity of treatment, yet they differ in how often paraquat concentrations were measured, the extent to which dosing was standardized, and in whether kinetic change was linked to clinical outcome.[8-10,21-24]

In cohorts with clinical endpoints, strategies based on HA were associated with better survival than conservative care, although every available comparison is observational and open to confounding. A multicenter retrospective study enrolled patients older than 14 years who were admitted within 24 hours and had measurable paraquat in urine at 5 to 200 μg/mL. Survival at 60 days was 21.3% with conservative treatment, 43.1% with HA, and 46.5% with HA followed by 72 hours of CVVH, and strategies containing HA were protective in multivariable analysis.[8] A cohort from one center likewise emphasized an early window. Among patients who presented within 4 hours of ingestion and were considered eligible, survival was higher in those who received HA than in those who did not, the latter largely because they arrived late, while overall mortality remained high.[21] In a separate ICU cohort, addition of Xuebijing or ulinastatin to a strategy based on HA was associated with lower mortality than HA alone, but allocation was not randomized and the duration of HA was individualized.[22]

Case reports extend this experience to particular settings without offering comparison. One case report described HA combined with continuous venovenous hemodiafiltration in paraquat poisoning during pregnancy, a population absent from the cohort studies.[23] An earlier series of three patients reported survival after multimodal management that included an extracorporeal technique alongside immunosuppressive and antioxidant treatment.[24]

Pharmacokinetic work supports substantial removal of paraquat during HA and also shows patterns consistent with a rise in concentration afterwards when the burden is high. In one cohort treated with HA (resin hemoadsorption cartridge) at a blood flow of 200 mL/min, the mean clearance rate reported after treatment was 73 ± 15%, and in the subgroup with a baseline concentration of 1.0 to 10 μg/mL, the concentration stayed above 0.05 μg/mL after the first session and rose before a second session was started within 24 hours in some patients.[10] In a further study of 85 patients given a standardized session of 2 hours (resin hemoadsorption cartridge at 200 mL/min), mean clearance rose between 1 hour and 2 hours, from roughly 37% to 46%, and higher baseline plasma concentrations were associated with higher clearance.[9] These observations make repeated or intensified early HA biologically plausible in selected patients, but kinetic endpoints alone do not establish a survival benefit.[9,10]

2,4-Dichlorophenoxyacetic acid

2,4-Dichlorophenoxyacetic acid (2,4-D) is a chlorophenoxy herbicide and a weak organic acid of molecular weight 221.03 Da that is excreted largely unchanged in urine. Its kinetics depend on urinary pH, and binding to plasma protein is concentration-dependent and may saturate in severe poisoning. This matters for extracorporeal removal because a larger free fraction increases what a membrane can clear, and the aromatic structure gives a theoretical basis for interaction with sorbents. Severe intoxication depresses the central nervous system and causes skeletal muscle injury, metabolic acidosis, renal dysfunction, and hepatic injury.[25]

In 2,4-D poisoning with injury to the central nervous system, a comparative clinical study of 60 patients compared HA plus routine treatment with routine treatment alone. Sessions lasted 2 hours and were given every 12 hours for 3 consecutive days. The authors reported greater improvement in physiological and neurological indices in the treated group, with lower Acute Physiology and Chronic Health Evaluation II (APACHE II) scores and higher Glasgow Coma Scale scores after treatment and a more favorable distribution of Mini-Mental State Examination categories. They also reported a higher composite clinical response rate, 86.67% versus 26.67%, using their own definitions of response.[13]

Earlier series support the feasibility of IHD, with or without HA, in severe 2,4-D poisoning with coma and high measured serum concentrations.[26,27] In a series of four patients who had ingested concentrated formulations at 40% and became comatose within hours, treatment consisted of IHD alone or IHD with HA, and the authors described clinical recovery. Where monitoring was reported, serum concentrations before treatment were markedly raised and extracorporeal clearance during treatment was substantial, in the region of 56 to 73 mL/min, with higher figures in the earlier of the two accounts. Small and uncontrolled though they are, these reports give direct evidence at the level of the toxin that 2,4-D is removed in severe neurological presentations.[26,27]

Neither diffusion-based nor sorbent-based treatment has been tested against validated concentration thresholds for starting or stopping in 2,4-D poisoning, so decisions at the bedside still rest on clinical severity, on which technique is practicable, and on whether toxin monitoring is available locally.[13,26,27]

2,4-Dinitrophenol

2,4-Dinitrophenol (2,4-DNP) is an aromatic weak acid of molecular weight 184.1 Da and a potent uncoupler of mitochondrial respiration that dissipates the proton gradient across the inner membrane. Toxicity therefore arises not from receptor binding or channel blockade but from failure of oxidative phosphorylation, which produces hyperthermia, tachycardia, tachypnea, lactic acidosis, rhabdomyolysis, and rapidly progressive multiorgan failure. Because 2,4-DNP is not purely hydrophilic and has properties compatible with adsorption, HA is, in our assessment, mechanistically more attractive than dialysis alone. Even so, we consider that removal is likely to help only in the earliest phase, before the hypermetabolic state becomes self-sustaining.[28]

Evidence in acute 2,4-DNP poisoning includes a series in which plasma concentrations were monitored dynamically, HA was started early, and intensity was adjusted to clinical severity and measured concentration.[14] Of 16 patients, 2 died of cardiac arrest within 3 hours of admission, and the 14 survivors began HA within 6 hours of admission. Dose was individualized. Milder presentations received a routine regimen of 4 hours once daily for 3 days, whereas more severe presentations received an intensive regimen of two devices delivering 6 to 8 hours daily for the first 3 days followed by the routine regimen on days 4 to 6, guided by symptoms and serial plasma concentrations. The intensive

regimen was associated with higher reported clearance and a shorter elimination half-life, 54.58 ± 12.92 hours versus 88.78 ± 14.66 hours.[14]

The same series reported favorable recovery among survivors, who were described as well and without evident sequelae over 3 years of observation, although residual toxin remained detectable in plasma for up to 25 days in some of them.[14] An occupational report of 9 patients described recovery in all of them under a combined strategy of high-dose glucocorticoids and repeated HA, and recommended this approach while acknowledging that the optimal program is unsettled.[29] Early and repeated HA, intensified in severe cases and informed by serial concentrations where these can be measured, is therefore feasible, but the samples are small, allocation followed severity rather than chance, and glucocorticoids and other concomitant treatments confound interpretation.[14,29]

Diquat

Diquat is a bipyridyl herbicide of molecular weight 184.24 Da that shares the marked hydrophilicity and the propensity to oxidative injury of paraquat, but its clinical picture differs in that renal, neurological, hepatic, and cardiovascular injury usually dominate over the delayed pulmonary fibrosis characteristic of paraquat. The parent compound is chemically accessible to an extracorporeal circuit while it remains intravascular, yet the course is shaped by rapid oxidative damage to several organs and by subsequent redistribution. Extracorporeal therapy is thus most plausible soon after exposure, whereas delayed treatment is limited by injury already established rather than by any inability to remove circulating toxin.[30]

Clinical evidence in diquat poisoning is more recent and considerably smaller than in paraquat poisoning, and what exists is built on strategies guided by measured concentrations rather than fixed protocols.[15,31,32] A multicenter retrospective cohort used measured plasma diquat concentrations to guide and optimize extracorporeal treatment, which supports the idea that a quantified burden of toxin, rather than the reported dose ingested or clinical impression alone, should inform both the decision to treat and the intensity delivered.[15] A further study of blood purification directed by concentration proposed that treatment strategy be stratified according to measured plasma concentration.[31] Both therefore frame ECTR in diquat poisoning as an intervention guided by concentration, which fits the narrow early window implied by rapid oxidative injury and redistribution.[30] The clinical picture may nonetheless depart from the classic bipyridyl phenotype. One case report described acute diquat poisoning that presented predominantly as rhabdomyolysis, a reminder that diagnosis may be delayed when muscular and renal rather than pulmonary features dominate.[32] This literature is retrospective or based on single cases; it offers no prospectively validated concentration thresholds for starting, intensifying, or stopping treatment, and it cannot separate the contribution of ECTR from that of concurrent supportive and antioxidant measures. Where a quantitative assay is accessible, serial plasma concentrations are the most rational reported basis for individualizing treatment.[15,31,32]

Organophosphorus and carbamate poisoning

Organophosphorus pesticides are chemically heterogeneous, but many of the clinically important compounds are relatively lipophilic, distribute extensively into tissue, and redistribute from fat and other peripheral compartments. Their defining action is irreversible inhibition of acetylcholinesterase, which leaves excess acetylcholine at muscarinic, nicotinic, and central synapses and produces bronchorrhea, bronchospasm, bradyarrhythmias, neuromuscular weakness, seizures, and respiratory failure. Conventional membrane-based clearance is therefore often limited, whereas HA holds more theoretical appeal for selected agents, particularly early, before wide distribution into tissue and aging of the enzyme.[33-35] In our view, the class remains too heterogeneous for a uniform extracorporeal strategy to be derived from physicochemical assumptions alone.

Evidence here comprises one randomized trial in the ICU, a systematic review with pooled analysis of randomized studies of HA combined with hemofiltration, and several comparative observational cohorts, with HA as the dominant technique.[11,12,36-39] In the randomized trial, HA was given as two cycles of 6 hours begun within 24 hours of admission to the ICU and added to standard care for clinically suspected poisoning.[11] The observational studies describe HA alone or with hemodialysis, usually with resin hemoadsorption cartridges and sessions of roughly 2 to 2.5 hours, and in some designs an escalating dose achieved by repeating sessions within the first 48 hours.[36-39] Indications rest on syndrome and severity rather than on a confirmed concentration, and one comparative study defined severe poisoning by cholinesterase activity below 30% at presentation.[37]

In that trial of 40 patients, the primary endpoint of length of stay in the ICU did not differ between groups in the cohort as a whole, at a median of 6.5 versus 8 days.[11] Among patients classified as having an excess length of stay of 7 days or more, HA was associated with a shorter stay, 10 versus 17 days, fewer days of mechanical ventilation, 6 versus 15, and a lower cumulative requirement for atropine, 316 versus 887 mg.[11] A composite of mortality at 28 days plus severe complications occurred less often with HA, in 10% versus 42%, whereas mortality at 28 days alone did not differ, 1 of 20 versus 2 of 20.[11] Reported safety signals included venous thrombosis and suspected heparin-induced thrombocytopenia without confirmatory testing, which argues for close attention to anticoagulation and for caution in interpretation given the small, open-label, single-center design.[11]

Observational comparisons generally report shorter recovery or better rescue with strategies containing HA, although endpoints and concomitant treatments vary and confounding is probable. In a retrospective cohort of 68 patients with critical poisoning, those given HA plus hemodialysis had lower mortality, 1 of 34 versus 6 of 34, a lower rate of rebound, 1 of 34 versus 4 of 34, and a higher rescue rate, 33 of 34 versus 28 of 34, than those given conventional treatment. Hypotension, bleeding, and infection were tabulated but were not attributed specifically to the extracorporeal circuit as opposed to the management of critical illness.[36] In the study that defined severe poisoning by cholinesterase activity below 30%, penehyclidine hydrochloride plus HA was associated with shorter time to recovery from coma, shorter duration of ventilation, and shorter overall recovery time, but mortality did not differ, 6 of 31 versus 5 of 30.[37] A study of treatment frequency reported better clinical outcomes, including a lower incidence of intermediate syndrome and higher survival rates, with 3 to 4 sessions within 48 hours than with a single session.[38] Further compar-

ative data suggest improved clinical outcomes when HA is combined with protocolized atropine administration, although study-specific outcome definitions and limited reporting constrain generalizability.[39]

The systematic review of randomized trials of HA combined with hemofiltration in acute severe organophosphorus poisoning reported better outcomes than conventional therapy, with lower mortality and shorter endpoints related to recovery such as the requirement for atropine, the duration of mechanical ventilation, and length of stay. The same authors noted methodological weakness across the included trials, among them limited concealment of allocation and rare blinding, and cautioned that heterogeneity of prescriptions and of concomitant treatment limits what the pooled estimates mean.[12] The class as a whole thus justifies considering sorbent-based and combined strategies as adjuncts in selected severe presentations, particularly when respiratory failure and a protracted course are anticipated, while standardized dosing, case definitions confirmed by concentration where feasible, and multicenter randomized evaluation are still needed.[11,12]

Pharmaceuticals

In poisoning with pharmaceuticals, the choice of modality is best anchored in evidence and consensus for the individual drug, since the techniques differ substantially in mechanism, whether diffusion and convection, adsorption to a sorbent, or exchange of plasma, and in clinical purpose.[1,2] For several drugs, graded EXTRIP recommendations state when to start ECTR, which modality to prefer, and when to stop, notably for metformin and carbamazepine, and advise against ECTR for others such as digoxin and methotrexate.[4-7] Alongside this sit case reports and small studies of HP/HA alone or with CRRT or IHD in particular situations, such as hemodynamic instability that precludes IHD or persistence of severe manifestations, but these accounts cannot isolate what sorbent therapy adds beyond concomitant treatment.[18,19,40-44]

Carbamazepine

Carbamazepine, of molecular weight 236.27 Da, is a lipophilic anticonvulsant with substantial binding to plasma protein and a moderate volume of distribution. Severe overdose depresses the central nervous system, causes respiratory failure and seizures, and disturbs cardiac conduction through blockade of sodium channels. These properties once made HA particularly attractive, yet modern high-flux IHD achieves clinically meaningful clearance despite the degree of protein binding. Carbamazepine therefore occupies an intermediate position in which both membrane-based and sorbent-based techniques are pharmacologically plausible, and the choice often turns on local expertise and on the stability of the patient rather than on chemistry.[5]

EXTRIP recommends ECTR when multiple seizures are refractory or when dysrhythmias are life-threatening, and suggests it when severe or prolonged coma or respiratory depression requiring mechanical ventilation is present or expected, or when clinically significant toxicity persists despite supportive measures and multiple-dose activated charcoal.[5] Treatment should stop once the patient improves clinically or the concentration falls below 10 mg/L, equivalent to 42 μmol/L. IHD is the preferred modality, with intermittent HA and CRRT as alternatives where IHD is unavailable.[5] Clinical reports match these principles and illustrate the constraints of feasibility. One hemodynamically unstable patient was treated with HA in series with CVVH, with a documented fall in carbamazepine during combined therapy and subsequent stabilization.[40] A retrospective cohort comparing early with delayed HA reported better outcomes in the treated groups than in a small group who received none, although the design was not randomized and causal inference is limited.[41]

Metformin

Metformin, of molecular weight 129.16 Da, is a highly hydrophilic cation with negligible binding to protein and favorable transport across membranes, which makes it among the clearest examples of a poison intrinsically amenable to removal by dialysis. Its toxicity in overdose follows disruption of mitochondrial respiration, above all inhibition of oxidative metabolism dependent on complex I, which impairs handling of lactate and produces severe lactic acidosis. Metformin does distribute beyond plasma, but its physicochemical profile strongly favors IHD over sorbent techniques, which are at best adjunctive. The dominant clinical phenotype is severe acidemia with shock and impaired utilization of oxygen in tissue rather than direct structural injury to organs.

For severe metformin poisoning, including metformin-associated lactic acidosis, EXTRIP recommends ECTR and states explicit criteria for starting and stopping.[4] Treatment is indicated when lactate exceeds 20 mmol/L, a recommendation, or exceeds 15 mmol/L, a suggestion, when pH is 7.0 or below, a recommendation, or 7.1 or below, a suggestion, when standard supportive measures fail, or when comorbidity lowers the threshold, namely shock and impaired kidney function as recommendations and liver failure or reduced consciousness as suggestions. Treatment should stop once lactate falls below 3 mmol/L and pH rises above 7.35. IHD with bicarbonate buffer is the preferred initial modality, and CRRT is considered where hemodialysis is unavailable.[4] One case of severe metformin-associated toxicity was managed with high-volume CVVH alongside HA (resin hemoadsorption cartridge), with serial concentrations falling during therapy and clinical recovery, although what HA added beyond CRRT could not be determined.[42]

Methotrexate

Methotrexate is a comparatively small molecule of molecular weight 454.4 Da with moderate binding to protein and a relatively low volume of distribution, properties that suggest at least partial accessibility to membrane-based removal. Its toxicity, however, arises from intracellular inhibition of folate-dependent metabolism and of DNA synthesis, particularly in rapidly proliferating tissue, so clearance from plasma does not necessarily reverse cellular injury already established. The distinction is important. Methotrexate looks dialyzable on pharmacokinetic grounds, yet the clinical syndrome is driven by events within tissue, namely suppression of the marrow, mucosal injury, nephrotoxicity, and delayed intracellular consequences. Removal by an extracorporeal circuit therefore has conceptual limits, especially when set against a specific rescue strategy such as glucarpidase.[7]

EXTRIP recommends against ECTR in severe methotrexate poisoning, whether or not glucarpidase is given, and specifically

against using ECTR in place of glucarpidase when glucarpidase is indicated.[7] These recommendations rest on evidence of very low quality and reflect the scarcity of clinical outcome data showing meaningful removal relative to the toxicodynamics of the drug and to established antidotal treatment.[7] Concentrations can nonetheless fall during coupled extracorporeal therapy. In a child with delayed elimination after high-dose methotrexate and acute kidney injury, HA coupled to continuous venovenous hemodiafiltration was associated with a substantial reduction in concentration over a short interval.[43] A single kinetic observation of this kind does not establish better outcomes for patients and should be read against the recommendation not to treat.[7,43]

Digoxin

Digoxin is a cardiac glycoside of molecular weight 780.9 Da with relatively low binding to plasma protein but a very large volume of distribution, the consequence of extensive binding to tissue, particularly to sodium and potassium ATPase in myocardium and skeletal muscle. Its toxicity follows directly from inhibition of that pump, which raises intracellular sodium, secondarily raises intracellular calcium, and predisposes to bradyarrhythmias, conduction block, ventricular ectopy and, in acute poisoning, hyperkalemia. Despite the small size of the molecule, removal by an extracorporeal circuit is ineffective, because only a very small proportion of the total body burden remains intravascular. This is the pharmacokinetic reason why neither HA nor hemodialysis is regarded as a definitive means of removal, and why digoxin-specific antibody fragments remain the definitive treatment of significant toxicity.[45,46]

EXTRIP recommends against ECTR in any form for suspected or proven digoxin toxicity and does not recommend it for removal of digoxin Fab immune complexes.[6] A single report describes sorbent therapy performed when definitive antidotal treatment was unavailable: in severe ingestion with suicidal intent and no access to digoxin-specific Fab fragments, HA was performed for 4 hours, and the authors reported a fall in measured concentration across the cartridge and clinical recovery without complications of the procedure.[44] The case shows feasibility under constraint. It establishes no comparative effectiveness and should be read against the recommendation not to treat.[6,44]

Other drug toxicities

Colchicine, of molecular weight 399.4 Da, is an intracellular poison of microtubules that binds tubulin and prevents polymerization. Severe poisoning moves from early gastrointestinal toxicity to shock, suppression of the marrow, rhabdomyolysis, and multiorgan failure. What limits removal is less the size of the molecule than its large volume of distribution and marked sequestration within cells, which leave only a small circulating fraction once distribution is complete. Both membrane-based and sorbent-based techniques are therefore likely to be relevant only very early, and then only to a limited extent.[47]

Experience in several further drug intoxications rests on single cases in which sorbent therapy was used alone or alongside dialysis without validated thresholds based on concentration. In colchicine poisoning, one report described continuous hemodialysis for 8 hours in parallel with HA for 8 hours using a resin hemoadsorption cartridge in a symptomatic adult who could not tolerate activated charcoal, followed by clinical improvement and discharge. Serum concentrations were not reported, which precludes any assessment of the relation between clearance and outcome.[17] In a mixed overdose of cannabis and methadone complicated by coma and refractory seizures, HA with hemodialysis using a resin hemoadsorption cartridge was performed twice, after which the seizures stopped and neurological recovery followed. Monitoring relied on screening of urine rather than on serial serum concentrations.[48] Consistent with these limits, the graded recommendations developed by the EXTRIP Workgroup cover a defined set of pharmaceuticals, and at the time of writing no consensus statement had been published for colchicine, methadone, or cannabinoids.[49,50]

Solvents - Chloroform

Chloroform, or trichloromethane, is a small lipophilic halogenated solvent of molecular weight 119.4 Da that is absorbed rapidly and distributes widely into lipid-rich tissue. It depresses the central nervous system, depresses cardiorespiratory function and may sensitize the myocardium to catecholamines, and injures the liver and kidney, organ injury being driven largely by oxidative metabolism through cytochrome P450, principally CYP2E1, with formation of reactive intermediates. Because distribution into tissue is rapid and metabolism is predominantly hepatic, removal by an extracorporeal circuit is mechanistically plausible mainly during the early intravascular phase, and its value beyond supportive care remains uncertain.[51-54]

Chloroform poisoning is represented by an incident report with serial blood concentrations measured before and after HA.[16] An adult woman was treated twice on day 1 and once daily on days 2 and 3, at a blood flow of 150 to 180 mL/min with heparin anticoagulation.[16] Concentrations fell during sessions, from 58 to 37 μg/mL across the first treatment, continued to fall over subsequent sessions, and became undetectable by the end of the planned course, and the patient recovered and was discharged. A single case without comparison shows how monitoring of concentration can document removal and support repeated sessions in solvent poisoning wherever a quantifiable assay exists.[16]

Considerations that cut across toxins

Choosing a modality

ECTR in poisoning is a choice among techniques whose mechanisms differ, whether diffusion and convection, adsorption to a sorbent, removal with plasma, or extracorporeal life support, and not a choice between hemodialysis and everything else.[1] Alignment of mechanism rests on toxicokinetic reasoning, such as protein binding, volume of distribution, and endogenous clearance, together with feasibility and urgency at the bedside, such as hemodynamic stability, the anticipated trajectory, and local resources.[1,2] Where graded consensus exists, EXTRIP is the most usable framework, since it states when treatment is indicated, which modality to prefer, usually IHD where feasible, and when to stop, as in metformin and carbamazepine poisoning, and since it advises against treatment for selected toxins such as digoxin and methotrexate.[4-7]

Timing and intensity

Across toxins, the timing and the delivered dose of ECTR, meaning session duration, repetition, and combination with CRRT or IHD, recur as the variables clinicians can modify. In paraquat poisoning, several cohorts began HA within hours of ingestion or presentation and repeated it across the first 48 to 72 hours. Multicenter observational data linked strategies containing HA to better survival at 60 days than conservative care, and pharmacokinetic studies showed substantial removal during treatment with a rise afterwards in patients carrying a high burden, which is consistent with repeating sessions in selected patients.[8-10,21] In organophosphorus and carbamate poisoning, an early protocolized regimen of two cycles of 6 hours within 24 hours of admission produced benefit signals mainly in patients whose ICU course was protracted, and pooled randomized evidence suggests better outcomes with HA combined with hemofiltration, tempered by the quality of the trials.[11,12] Stratification by intensity also appears in 2,4-DNP poisoning, where an intensive regimen shortened the elimination half-life compared with a routine one, so dose may be individualized by severity and by kinetics where these can be measured.[14] In diquat poisoning the same principle has been made explicit through prescriptions directed by measured plasma concentration rather than by the dose reported as ingested.[15,31]

Safety, complications, and unintended removal of drugs

Safety reporting is heterogeneous, but several themes recur. In organophosphorus and carbamate poisoning, the randomized trial reported venous thrombosis and suspected heparin-induced thrombocytopenia without confirmatory testing, which highlights the importance of the anticoagulation strategy and of vigilance for thrombotic complications when sorbents are used.[11] A retrospective cohort of severe organophosphorus poisoning treated with HA plus hemodialysis tabulated hypotension, bleeding, and infection without establishing whether these arose from the extracorporeal circuit or from the underlying critical illness.[36] Beyond complications of the procedure, sorbents raise the practical risk of adsorbing medication given at the same time. *In vitro* models show substantial adsorption of vancomycin, which supports review of the medication list and therapeutic drug monitoring where feasible during treatment.[18,19] These considerations belong in the treatment plan alongside expected benefit, feasibility, and local expertise.[1,2]

When not to start treatment, and the gray zone of consensus

A balanced framework must say when to withhold treatment as well as when to give it. Three situations differ.

First there are toxins for which consensus advises against ECTR on pharmacokinetic grounds. In digoxin toxicity, the very large volume of distribution and extensive binding to tissue leave a negligible intravascular fraction accessible to any technique, and EXTRIP advises against treatment in any form, including for removal of digoxin Fab immune complexes.[6] In methotrexate toxicity, EXTRIP advises against treatment whether or not glucarpidase is given, because clearance from plasma does not reverse the intracellular events that drive the syndrome and because ECTR must not stand in for glucarpidase when the latter is indicated.[7] In neither case is ECTR an appropriate default, even in severe presentations.

Second there is the genuine gray zone of toxins for which no consensus statement had been published at the time of writing and for which only single cases are available, among them colchicine, methadone, and cannabinoids.[17,47-50] Here the absence of a recommendation reflects insufficient evidence rather than endorsement. For colchicine, a large volume of distribution and marked sequestration within cells predict limited removability once distribution is complete, so meaningful benefit should not be expected. We advise treating the decision as an individual one, taken jointly with clinical toxicology and with the nephrology or ECTR team and, where one exists, with a poison control center, on the basis of toxicokinetic plausibility and clinical severity rather than technical feasibility, and using toxin monitoring wherever an assay exists.

Third there is the setting in which a preferred antidote cannot be obtained, as with digoxin-specific Fab fragments.[44] Isolated reports of sorbent therapy under such constraint describe apparent feasibility. They are not comparative evidence; they do not justify overriding consensus, and they do not replace a specific antidote that can still be procured, so efforts to obtain it should continue in parallel.

That ECTR is feasible across many exposures does not mean that it helps. Restraint belongs to competent practice.

Discussion

The evidence supports an approach to ECTR that is specific to the toxin, that recognizes how much the techniques differ, and that gives precedence to mechanistic fit and feasibility over any default.[1,2] Where graded recommendations exist, EXTRIP remains the most usable framework at the bedside, defining indications, the preferred modality, usually IHD where feasible, and criteria for stopping, as in metformin and carbamazepine poisoning, and advising against treatment in digoxin and methotrexate toxicity.[4-7] Much of the clinical experience with HA remains tied to particular toxins and particular regions, with the strongest observational signal in paraquat poisoning and mixed comparative evidence in organophosphorus and carbamate poisoning that includes one randomized trial in the ICU and a pooled analysis of randomized studies.[8-12] For toxicants represented largely by series and single cases, among them 2,4-D, 2,4-DNP, diquat, chloroform, colchicine, and mixed drug overdose, the literature documents feasibility and change in kinetics rather than causal benefit, which places a premium on multidisciplinary judgment and on careful reading of concomitant treatment (Table 1).[4-8,11-17,20-27,29-33,35-41,43-54]

One practical theme recurs: the difference between prescribing informed by concentration and prescribing informed by severity. In 2,4-DNP and diquat poisoning, intensity has been titrated against serial plasma concentrations, whereas in organophosphorus and carbamate poisoning the indication remains a matter of syndrome and severity.[14,15,31,37,38] The difference matters, because a strategy guided by concentration at least allows one to ask whether the intended target is being engaged, whereas a strategy guided by severity risks mistaking spontaneous improvement for an effect of treatment. None of the reported thresholds has been tested prospectively, and no study shows that guidance by concentration improves outcomes for patients relative to guidance by clinical state.

The framework offered here, including the algorithm below, is a synthesis proposed by the authors, informed by consensus. It has not been validated prospectively, and it is meant to structure reasoning at the bedside rather than to serve as a decision instrument.

Table 1. Evidence summary for extracorporeal treatment (ECTR) modalities in selected poisonings

Toxin or exposure	Modality reported	Operational parameters and intensity	Evidence base	Key reported outcomes	EXTRIP status	Refs
Paraquat	HA (resin hemoadsorption cartridge) with CVVH or IHD	Sessions of 2 h at 200 mL/min, repeated across 48–72 h, HA followed by 72 h of CVVH	Multicenter and single-center retrospective cohorts, pharmacokinetic studies, case reports	Survival at 60 days 21.3% conservative, 43.1% HA, 46.5% HA plus CVVH. Mean clearance 73 ± 15%. Rise in concentration after treatment when burden high	None	[8-10,20-24]
2,4-D	IHD with or without HA, HA alone	HA 2 h every 12 h for 3 days. IHD alone or with HA	One comparative study of 60 patients, two early case series	Lower APACHE II, higher Glasgow Coma Scale, clinical response rate 86.67% versus 26.67%, extracorporeal clearance 56–73 mL/min	None	[13,25-27]
2,4-DNP	Resin HA	Routine 4 h daily for 3 days. Intensive two devices 6–8 h daily for 3 days, then routine on days 4–6	Case series of 16 with dynamic plasma monitoring, occupational report of 9	Elimination half-life: 54.58 ± 12.92 h in the intensive group versus 88.78 ± 14.66 h in the routine group. 14 of 16 survived without evident sequelae over 3 years	None	[14,28,29]
Diquat	Blood purification directed by concentration (HP or HA with or without CRRT)	Starting and intensity stratified by measured plasma concentration, no fixed protocol	Multicenter retrospective cohort, single-center study directed by concentration, case report	Prescription guided by measured concentration proposed as the basis for starting and for intensity. Presentation as rhabdomyolysis described	None	[15,30-32]
Organophosphorus and carbamate	HA alone or with hemodialysis or hemofiltration	Two cycles of 6 h within 24 h of ICU admission in the trial. Sessions of 2–2.5 h and 3–4 sessions within 48 h in cohorts	One randomized trial of 40 patients, systematic review with pooled analysis, several comparative cohorts	Primary endpoint not met. In the subgroup staying 7 days or more, shorter ICU stay, fewer ventilator days, less atropine. Pooled analysis reported lower mortality with low trial	None	[11,12,33-39]

Table 1. Evidence summary for extracorporeal treatment (ECTR) modalities in selected poisonings (*continued*)

Toxin or exposure	Modality reported	Operational parameters and intensity	Evidence base	Key reported outcomes	EXTRIP status	Refs
				quality		
Carbamazepine	IHD preferred, intermittent HA or CRRT as alternatives	HA in series with CVVH when IHD not tolerated	EXTRIP consensus, case report, retrospective cohort	Stop on clinical improvement or concentration below 10 mg/L	Yes. Recommended for refractory seizures and life-threatening dysrhythmias, suggested for severe or prolonged coma	[5,40,41]
Metformin	IHD with bicarbonate buffer preferred, CRRT if IHD unavailable	High-volume CVVH with a resin hemoadsorption cartridge in one case	EXTRIP consensus, case report	Start at lactate above 20 or above 15 mmol/L, or pH 7.0 or below or 7.1 or below. Stop at lactate below 3 mmol/L and pH above 7.35	Yes. Recommended with explicit thresholds	[4,42]
Methotrexate	None recommended	HA coupled to CVVHDF in one child	EXTRIP consensus, one case report	Concentration fell, no benefit to the patient established	Yes, against treatment with or without glucarpidase and never in its place	[7,43]
Digoxin	None recommended	HA for 4 h in one case when Fab fragments unavailable	EXTRIP consensus, one case report	Concentration fell across the cartridge, recovery reported	Yes, against treatment in any form, including removal of Fab complexes	[6,44-46]
Colchicine	HA (resin hemoadsorption cartridge) with continuous hemodialysis	HA 8 h in parallel with hemodialysis for 8 h	One case report, one toxicological review	Improvement and discharge, no serum concentrations reported	None, gray zone	[17,47]
Methadone with cannabis	HA (resin hemoadsorption cartridge) with hemodialysis	Two combined sessions	One case report	Refractory seizures resolved, neurological recovery, urine screening only	None, gray zone	[48-50]
Chloroform	HA	Twice on day 1, then once daily on days 2 and 3, blood flow 150–180 mL/min, heparin	One incident report with serial blood concentrations	Fell from 58–37 µg/mL across the first session, undetectable at the end of the course, recovery	None	[16,51-54]

"None" and "gray zone" in the EXTRIP status column indicate that no toxin-specific consensus statement had been published at the time of writing.[49,50] 2,4-D, 2,4-dichlorophenoxyacetic acid; 2,4-DNP, 2,4-dinitrophenol;

APACHE II, Acute Physiology and Chronic Health Evaluation II; CRRT, continuous kidney replacement therapy; CVVH, continuous venovenous hemofiltration; CVVHDF, continuous venovenous hemodiafiltration; EXTRIP, Extracorporeal Treatments in Poisoning; HA, hemoadsorption; HP, hemoperfusion; ICU, intensive care unit; IHD, intermittent hemodialysis.

Evaluation in prospective registries and in implementation studies, for instance within collaborative networks such as SUBPLOT, would be needed before it could be recommended for routine use.[1]

Practical decision algorithm

The algorithm below turns the preceding material into a sequence of five steps (Fig. 1). It draws on principles of modality selection that emphasize how much the techniques differ and how well each fits the toxicokinetic profile, on graded consensus where EXTRIP provides it, and on patterns that recur in the clinical literature, such as early repeated HA in paraquat and organophosphorus poisoning and prescription directed by concentration in diquat and 2,4-DNP poisoning. It is a proposal by the authors that has not been validated prospectively, and it is intended to structure rather than to replace clinical judgment and specialist advice. It is written for intensivists, nephrologists, and toxicologists who need to confirm whether ECTR is recommended for the suspected toxin, to select a modality when it is, to define dose and monitoring, and to apply criteria for stopping together with safety checks, including unintended adsorption of concomitant medication during sorbent treatment.

Step 1. Identify the toxin and check consensus

Confirm the toxin or exposure context and look first for guidance specific to that agent. Where the ingested agent is known or strongly suspected, establish whether a graded recommendation exists, as it does for metformin, carbamazepine, digoxin, and methotrexate, and apply its indication, its preference of modality, and its criteria for stopping, including any advice against treatment, as the default. EXTRIP states thresholds of lactate and pH for starting and stopping in metformin-associated toxicity and names IHD as the preferred initial modality, whereas it advises against treatment in digoxin toxicity and in severe methotrexate toxicity, and against using ECTR in place of glucarpidase where glucarpidase is indicated. Where no graded recommendation exists, which is the case for many uncommon exposures represented only by single cases, ECTR is not a default. Proceed instead on principles of modality selection and on the best evidence for that agent, and involve a medical toxicologist, the nephrology or ECTR team and, where one exists, a poison control center early. In this branch, base the decision on toxicokinetic plausibility and clinical severity rather than on technical feasibility, and monitor the toxin wherever an assay exists.

Step 2. Choose a modality and define the dose

Select the modality and prescribe intensity according to consensus where it exists and to feasibility in the individual patient. When EXTRIP indicates treatment, IHD is generally preferred, as in metformin and carbamazepine poisoning, with CRRT or HA as alternatives where IHD is unavailable or impractical, for instance in hemodynamic instability. In carbamazepine intoxication this matches the published case in which HA in series with CVVH was chosen because the patient was too unstable for IHD, with a documented fall in concentration during combined therapy. Where sorbent therapy is the principal modality, as in paraquat, diquat, and organophosphorus poisoning, dose has been delivered through early initiation and repetition, for example repeated HA across the first 48 to 72 hours in paraquat cohorts, repeated sessions within 48 hours in the study of treatment frequency, protocolized cycles of several hours in the randomized trial, and prescriptions stratified by concentration in diquat cohorts. Combining HA with hemofiltration produced benefit signals in pooled randomized data on organophosphorus pesticides.

Step 3. Define triggers and endpoints

State in advance what will trigger treatment and what will end it, giving precedence to thresholds specific to the toxin and, in their absence, to endpoints of clinical severity that mean something. For metformin-associated toxicity, EXTRIP gives biochemical criteria for starting, with clinical modifiers, and targets for stopping, namely lactate below 3 mmol/L and pH above 7.35. For carbamazepine, it recommends treatment for refractory seizures or life-threatening dysrhythmias, suggests it for severe or prolonged coma or persistent toxicity, and ties stopping to clinical improvement or a concentration below 10 mg/L. Where such graded thresholds do not exist or cannot be measured routinely, published studies have used pragmatic triggers based on severity, such as markedly depressed cholinesterase activity in organophosphorus poisoning and escalation of frequency in severe presentations, and, where assays exist, intensification guided by concentration, as in 2,4-DNP regimens adjusted to symptoms and serial plasma concentrations and in prescriptions directed by concentration in diquat poisoning. In paraquat poisoning, cohorts emphasize an early window of eligibility and repeated sessions, supported by kinetic evidence of removal during treatment and of a rise afterwards when the burden is high, so use of concentration and timing at the bedside depends on available assays, on clinical severity, and on whether repeated treatments are practicable. None of these thresholds outside EXTRIP has been tested prospectively.

Step 4. Monitor, reassess, and stop

Follow the response, reassess early, and apply criteria for stopping that suit the toxin, while guarding against a rise in concentration afterwards and against complications. Where validated targets exist they should be used, namely lactate below 3 mmol/L with pH above 7.35 for metformin and clinical improvement or a concentration below 10 mg/L for carbamazepine.

 DOI: 10.14218/JTCCM.2026.00004S | Volume 8 Issue 3, September 2026

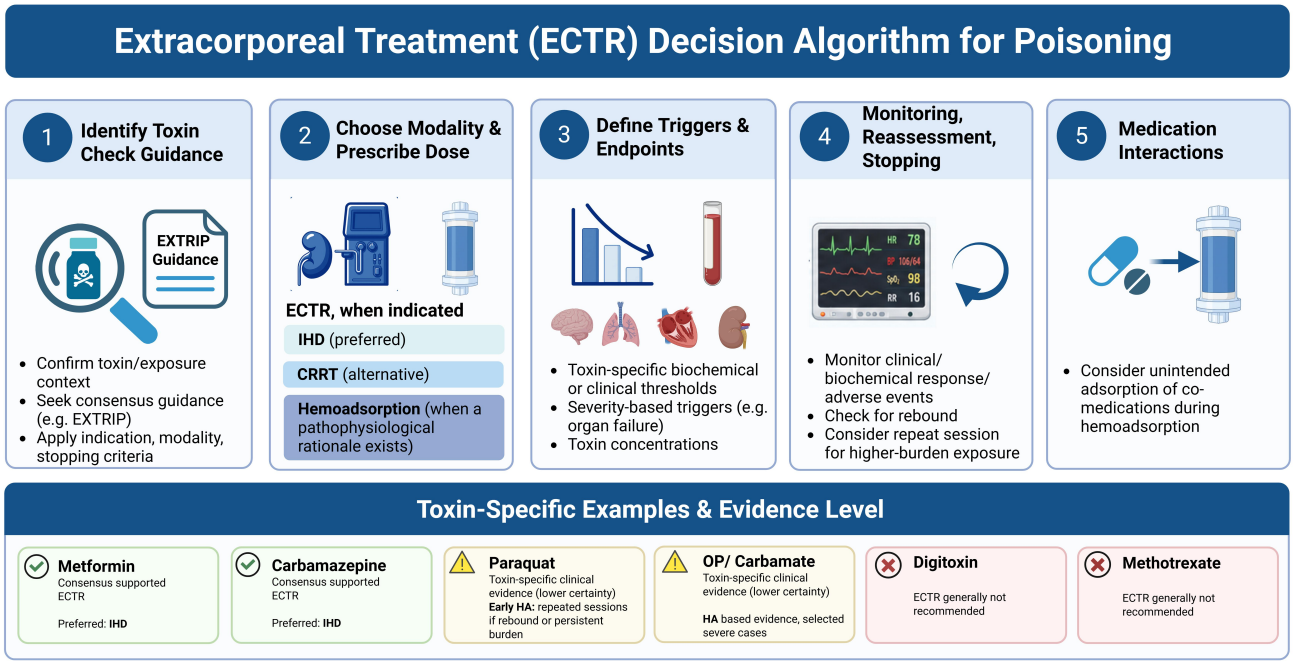


Fig. 1. Clinical algorithm for extracorporeal treatment (ECTR) in poisoning. It illustrates the five-step approach: (1) Confirm the suspected toxin and check for consensus-based recommendations; (2) Select the most appropriate ECTR modality and treatment intensity according to consensus and patient factors; (3) Define specific initiation triggers, monitoring parameters, and therapeutic endpoints; (4) Monitor treatment response, reassess frequently, and apply validated stopping criteria while anticipating complications; (5) Address co-medication removal risks and recognize toxins for which ECTR is not recommended. The diagram integrates practical guidelines, consensus statements, and literature-based patterns to guide multidisciplinary teams in toxin-specific ECTR decision-making. The algorithm is an expert proposal by the authors and has not been validated prospectively. BP, blood pressure; CRRT, continuous renal replacement therapy; ECTR, extracorporeal treatment; EXTRIP, Extracorporeal Treatments in Poisoning; HA, hemoadsorption; HR, heart rate; IHD, intermittent hemodialysis; OP, organophosphorus; RR, respiratory rate; SpO_2, peripheral oxygen saturation.

Where a rise after treatment has been documented kinetically, as in paraquat poisoning, serial concentrations help to identify it and to decide on repeated sessions in patients carrying a high burden. Clinical reassessment should consider the trajectory of organ dysfunction, for example, measures based on the Sequential Organ Failure Assessment score used in paraquat cohorts, and the continuing need for ventilatory or vasopressor support, bearing in mind that benefit in the organophosphorus and carbamate trial was most apparent in patients whose ICU course was protracted. Throughout, watch for thrombosis, bleeding, and clotting of the circuit, and revisit the anticoagulation strategy, given the thrombotic signals in that trial and the complications tabulated in the organophosphorus cohort.

Step 5. Loss of concomitant medication, and when not to treat

Sorbent therapy can remove therapeutics given at the same time. *In vitro* models show substantial adsorption of vancomycin, which supports reconciliation of the medication list and therapeutic drug monitoring where feasible during HP or HA. Conversely, recognize the three situations that call for restraint. The first covers toxins for which consensus advises against treatment on pharmacokinetic grounds, namely digoxin, including removal of Fab complexes, and methotrexate, whether or not glucarpidase is given and never in its place. The second is the gray zone of consensus, as with colchicine, methadone, and cannabinoids, for which no consensus statement had been published at the time of writing and where a large volume of distribution and sequestration within cells often predict little benefit, so each case should be decided with specialist input. The third is the setting in which a preferred antidote cannot be obtained, where published reports of ECTR describe feasibility only and must not override consensus or displace a specific antidote that can still be procured.

Limitations of the evidence and of this review

Narrative design: This is a narrative review informed by expert appraisal rather than a systematic one. No protocol was registered, no formal search algorithm or PRISMA flow was used, and no instrument for scoring risk of bias or for grading certainty was applied. Selection of sources may therefore be incomplete and open to bias on our part.

Quality and design of the studies: Outside the graded EXTRIP recommendations, most of the evidence consists of retrospective cohorts, small comparative studies with limited methodological safeguards, and reports of single cases or small series, so causal inference is correspondingly weak.

Randomized and pooled evidence: Even where randomization was used, the single trial in organophosphorus and carbamate poisoning was small, open-label, and confined to one center, and its favorable signals came largely from a subgroup analysis. The accompanying pooled analysis combined trials with limited

concealment of allocation and rare blinding.[11,12]

Regional concentration and bias in publication and language: The sorbent literature, particularly on paraquat, diquat, and organophosphorus or carbamate poisoning, is geographically concentrated and predominantly observational, which raises the possibility of bias in publication and language and of allocation influenced by local access and cost.

Confounding and effects of timing: Allocation was frequently driven by severity, by time to presentation, or by affordability. In paraquat cohorts in particular, patients who did not receive treatment often arrived late, so an apparent benefit may partly reflect selection by time of presentation rather than any effect of treatment.

Heterogeneity of interventions and outcomes: Prescriptions vary in modality, type of cartridge, duration and repetition of sessions, and combination with CRRT or IHD. Comparators, concomitant treatments such as glucocorticoids, antioxidants, penehyclidine, Xuebijing, and ulinastatin, and definitions of outcome vary as well. Several studies used composite endpoints of their own devising, such as clinical response rate, rescue success, and rate of rebound, which precludes quantitative synthesis.

Kinetic against clinical endpoints: Even where kinetics were reported, as in paraquat, 2,4-D, 2,4-DNP, diquat, chloroform, metformin, carbamazepine, and methotrexate poisoning, better clearance or a shorter half-life does not necessarily translate into survival or function, and a rise after treatment may reflect redistribution rather than failure of treatment.

Absence of validated thresholds: Apart from the EXTRIP criteria for selected pharmaceuticals, no validated thresholds based on concentration exist for starting, intensifying, or stopping ECTR. The strategies directed by concentration reported in 2,4-DNP and diquat poisoning are promising but unvalidated, and quantitative assays are often unavailable in real time.

Incomplete reporting of safety: Reporting of adverse events is heterogeneous and often cannot be attributed to the extracorporeal circuit as distinct from the underlying critical illness. Sorbents may additionally adsorb concomitant medication, as shown for vancomycin *in vitro*, a phenomenon that is probably not widely recognized.[11,18,19,36]

Generalizability of the algorithm: The algorithm proposed here has not been validated prospectively. It presumes access to specialist advice, to the modalities themselves and, in some branches, to assays that many settings do not have. Its effectiveness and safety in practice remain to be established.

These constraints together call for cautious multidisciplinary interpretation and for standardized prospective evaluation.

Conclusions

ECTR in acute poisoning should be approached as a heterogeneous "toolbox" of modalities selected according to toxin characteristics, clinical context, and feasibility rather than as a binary choice between hemodialysis and "other" techniques. Where graded recommendations exist, EXTRIP provides the most actionable bedside framework for indications, preferred modality (often intermittent hemodialysis when feasible), and stopping criteria (eg, metformin and carbamazepine), and equally for when ECTR should be withheld (eg, digoxin and methotrexate). Outside these consensus-guided settings, the strongest clinical experience with sorbent-based HP/HA is concentrated in paraquat and organophosphorus poisoning, but much of the evidence remains observational, regionally concentrated, and susceptible to confounding, underscoring the need for cautious interpretation and multidisciplinary decision-making.

Key evidence gaps persist across toxins and modalities. Outside of EXTRIP guidance, much of the literature remains observational or case-based, with heterogeneous co-interventions, ECTR prescriptions (session duration, repetition, and combination strategies), and outcome definitions that limit causal inference and generalizability. Even in toxin areas with comparative data, such as organophosphorus/carbamate poisoning, benefit signals are tempered by small trial size, open-label design, and methodological limitations across pooled randomized studies. Paraquat cohorts similarly highlight strong timing and selection effects, reinforcing the need for future prospective studies that standardize ECTR timing/intensity and report toxin kinetics and patient-centered outcomes in parallel. The practical algorithm presented here is an expert proposal that requires prospective validation. Until higher-quality evidence is available, bedside decisions should prioritize toxin-specific consensus recommendations where available, including recommendations against ECTR, and transparently balance expected benefit, feasibility, and extracorporeal risks for the individual patient.

Acknowledgments

None.

Funding

None.

Conflict of interest

Gerd Klinkmann has received funding for lectures for Artcline GmbH and CytoSorbents Europe GmbH and has received research grants from the German Society of Anaesthesiology and Intensive Care. Claudio Ronco has served on advisory boards or as a speaker for AstraZeneca, Aferetica, Asahi, B. Braun, Baxter, bioMérieux, CytoSorbents, GE, Medica, Medtronic, and Jafron. Claudio Ronco is the Editor-in-Chief of *Journal of Translational Critical Care Medicine*.

Author contributions

Concept, editing, and manuscript drafting (GK, CR).

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